

8.1 HEADACHE

the proportion of patients who experience early recurrence (so-called rebound headache). A meta-analysis of published papers reports a 26% reduction in the relative risk of headache recurrence within 72 hours. Doses used were 10–24 mg IV or 8 mg orally.⁸

Trigeminal neuralgia

Trigeminal neuralgia is a debilitating condition in which patients describe pain that is like 'lightning' or a 'hot poker' that is severe and follows the distribution of the trigeminal nerve. Individual episodes of pain last only seconds, but may recur repeatedly within a short period and can be triggered by minor stimuli, such as light touch, eating or drinking, shaving or a passing gust of wind. It is most common in patients who are middle-aged or older.

Aetiology and pathophysiology

Evidence suggests that the pathological basis of trigeminal neuralgia is the demyelination of sensory fibres of the trigeminal nerve in the proximal (central nervous system) portion of the nerve root or, rarely, in the brain stem, most commonly due to compression of the nerve root by an overlying artery or vein. A minority of cases are symptomatic of multiple sclerosis or nerve compression by tumour.

Trigeminal neuralgia is classified as classic trigeminal neuralgia (no cause identified) and symptomatic trigeminal neuralgia (secondary to another condition). Characteristics associated with symptomatic trigeminal neuralgia are trigeminal sensory deficits and bilateral involvement.

Clinical investigations

In approximately 15% of cases, there is a structural cause for trigeminal neuralgia. For this reason there is some support for routine neuroimaging (CT, MRI) in these patients. Electrophysiological assessment of trigeminal reflexes can also be helpful in distinguishing classic from symptomatic trigeminal neuralgia. The choice between the two approaches will depend on

availability, expertise, cost and patient and the treating clinician's preference.

Treatment

Trigeminal neuralgia is most commonly treated with carbamazepine, the mainstay of therapy. The usual starting dose is 200 to 400 mg/day in divided doses, increased by 200 mg/day until relief up to a maximum of 1200 mg/day. The average dose required is 800 mg/day. If the patient responds well, a controlled-release preparation can be substituted and the dose can gradually be reduced. For patients who fail first-line therapy a range of options have been proposed including baclofen, gabapentin, lamotrigine, oxcarbazepine, phenytoin and pimozide. There is little evidence to guide choice among these agents. Referral for consideration of surgery is appropriate in patients who are refractory to medical therapy.^{9,10}

Temporal (giant cell) arteritis

Giant cell arteritis is the most common form of vasculitis in patients aged over 50 years. It affects large and middle-sized blood vessels with a predisposition for the cranial arteries arising from the carotid arteries. Clinical features include headache, painless vision loss, jaw claudication, fatigue, fever, anorexia and temporal artery tenderness. Loss of vision is the most common severe complication. Involvement of extracranial arteries including the aorta is more frequent than previously assumed. Inflammation markers in blood are usually elevated, but specific laboratory tests for the diagnosis of giant cell arteritis are not available. Imaging using ultrasonography, MRI and positron emission tomography can be useful to confirm, localize and assess the extent of vascular involvement. Temporal artery biopsy is the gold standard for diagnosis. Glucocorticoids are the standard therapy (50 to 100 mg/day). Patients with acute visual changes secondary to giant cell arteritis should receive parenteral corticosteroid therapy and be admitted until their condition stabilizes.

CONTROVERSIES

- Choice of drug therapy for migraine.
- Role and timing of investigations in atypical migraine. CT or MRI may be indicated acutely to rule out other intracranial pathology.
- The role of corticosteroids in prevention of recurrent/rebound migraine.
- Role and timing of investigations, in particular neuroimaging, for persistent or atypical headache.
- Second-line treatment for trigeminal neuralgia.

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8.2 STROKE AND TRANSIENT ISCHAEMIC ATTACKS

8.2 Stroke and transient ischaemic attacks

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ESSENTIALS

- 1** Ischaemic strokes and transient ischaemic attacks (TIAs) are most commonly due to atherosclerotic thromboembolism of the cerebral vasculature or emboli from the heart. Other causes should be considered in younger patients, those presenting with atypical features or when evaluation is negative for the more common aetiologies.
- 2** Haemorrhagic and ischaemic strokes cannot be reliably differentiated on clinical grounds alone; therefore further imaging, most commonly computed tomography (CT) scanning, is required prior to the commencement of antiplatelet, thrombolytic or interventional therapies.
- 3** The risk of a completed stroke following a TIA can be high—up to 15% in the first week. Clinical scoring systems, such as the ABCD² score, along with the results of brain and carotid vessel imaging, provide assessment tools for estimating stroke risk following TIA. Patients with TIA identified as at low risk for progression to stroke (e.g. ABCD² <4, minimal large vessel disease on imaging) can be safely managed through integrated rapid-access TIA assessment clinics in an outpatient setting, with admission reserved for those at higher risk.
- 4** Differentiating strokes from other acute neurological presentations may be difficult in the emergency department. This issue has implications for the use of high-risk therapies such as thrombolysis.
- 5** The early phase of stroke management concentrates on airway and breathing, rapid neurological assessment of consciousness level, pupillary size, lateralizing signs and blood sugar measurements. Hyperglycaemia may worsen neurological outcome in stroke; therefore glucose should not be given in likely stroke patients unless a low blood sugar level is objectively demonstrated.
- 6** Outcomes in stroke patients are improved when they are admitted to a dedicated stroke unit. This involves a multidisciplinary approach to all aspects of stroke management.
- 7** Treating doctors should be fully aware of the risks/benefits and indications/contraindications of thrombolytic therapy in treating acute strokes. Currently, thrombolytic therapy should be considered for use in selected acute ischaemic strokes when administered within 4.5 hours of symptom onset, but controversies remain.
- 8** More complex imaging modalities, such as CT perfusion and diffusion/perfusion magnetic resonance imaging, continue to be evaluated in acute stroke workup in an attempt to better define the patient group that will benefit from aggressive vessel-opening strategies.
- 9** In the setting of acute large cerebral vessel occlusion, intra-arterial therapies such as clot retrieval devices continue to be evaluated and improved. The place of these interventions in acute stroke therapy is the subject of ongoing research. Recent trials suggest that clot retrieval may be safe in selected patients up to 24 hours after the onset of stroke symptoms.

Introduction

Cerebrovascular disease is the third most frequent cause of death in developed countries, after heart disease and cancer. A stroke is an acute

neurological injury secondary to cerebrovascular disease, either by infarction (80%) or by haemorrhage (20%). The incidence of stroke is steady and, although mortality is decreasing, it is still a leading cause of long-term disability. Transient

ischaemic attacks (TIAs) are defined as transient episodes of neurological dysfunction caused by focal brain, spinal cord or retinal ischaemia without acute infarction. Causes are similar to those of ischaemic stroke, particularly atherosclerotic thromboembolism related to the cerebral circulation and cardioembolism. Diagnosis of the cause of TIAs with appropriate management is important in order to prevent a potentially devastating stroke.

Pathophysiology

Brain tissue is very sensitive to the effects of oxygen deprivation. Following cerebral vascular occlusion, a series of metabolic consequences may ensue, depending on the extent, duration and vessels involved, which can lead to cell death. Reperfusion of occluded vessels may also occur, either spontaneously or via therapeutic intervention, with the potential for reperfusion injury. An area of threatened but possibly salvageable brain may surround an area of infarction. The identification of this so-called ischaemic penumbra and therapeutic efforts to ameliorate the extent of irreversible neuronal damage have been the subject of ongoing research efforts.

Large anterior circulation ischaemic strokes can be associated with increasing mass effect and intracranial pressure (ICP) in the hours to days following onset. Secondary haemorrhage into an infarct may also occur, either spontaneously or related to therapy. Clinical deterioration often follows.

Ischaemic strokes

These are the results of several pathological processes (Box 8.2.1):

- Ischaemic strokes are most commonly due to thromboembolism originating from the cerebral vasculature, the heart or, occasionally, the aorta. Thrombosis usually occurs at the site of an atherosclerotic plaque secondary to a combination of shear-induced injury of the vessel wall, turbulence and flow obstruction. Vessel wall lesions may also be the site of emboli that dislodge and subsequently occlude more distal parts of the cerebral circulation. Atherosclerotic plaque develops at the sites of vessel bifurcation. Lesions affecting the origin of the internal carotid artery (ICA) are the most important source of thromboembolic events. The more distal intracerebral branches of the ICA, the aorta and the vertebrobasilar system are also significant sites. Acute plaque change is likely to be the precipitant of symptomatic cerebrovascular

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Box 8.2.1 Causes of stroke

Ischaemic stroke

Arterial thromboembolism

Carotid and vertebral artery atheroma

Intracranial vessel atheroma

Small vessel disease—lacunar infarction

Haematological disorders—hypercoagulable states

Cardioembolism

Aortic and mitral valve disease

Atrial fibrillation

Mural thrombus

Atrial myxoma

Paradoxical emboli

Hypoperfusion

Severe vascular stenosis or a combination of these factors

Hypotension

Vasoconstriction—drug-induced, post-SAH, pre-eclampsia

Other vascular disorders

Arterial dissection

Gas embolism syndromes

Moyamoya disease

Arteritis

Intracerebral haemorrhage

Hypertensive vascular disease

Lipohyalinosis and microaneurysms

Aneurysms

Saccular

Mycotic

Arteriovenous malformations

Amyloid angiopathy

Bleeding diathesis

Anti-coagulation

Thrombolytics

Thrombocytopenia/disseminated intravascular coagulation

Haemophilia

Secondary haemorrhage into a lesion—tumour or infarction

SAH, Subarachnoid haemorrhage.

disease, particularly in patients with carotid stenosis. Hence the most effective therapies will probably not only target the consequences of acute plaque change, such as thrombosis and embolism, but also aim for plaque stabilization using such agents as antiplatelet drugs, statins and antihypertensive drugs along the lines used in the management of acute coronary syndromes.

- Approximately 20% of cerebrovascular events are due to emboli originating from the heart. Rarely, emboli may arise from the peripheral venous circulation, the embolus being carried to the cerebral circulation via a patent foramen ovale.
- Lipohyalinosis of small arteries is a degenerative process associated with diabetes and hypertension, which mainly

affects the penetrating vessels that supply areas such as the subcortical white matter and is the postulated cause of lacunar infarcts.

- Dissection of the carotid or vertebral arteries may cause TIAs and stroke. This may occur spontaneously or following trauma to the head and neck region, particularly in young people not thought to be at risk of stroke. Distal embolization from the area of vascular injury is the main pathological process involved.
- Haemodynamic reduction in cerebral flow may occur as a result of systemic hypotension or severe carotid stenosis. In these cases, cerebral infarction typically occurs in a vascular watershed area.
- Cerebral vasoconstriction may occur in association with subarachnoid haemorrhage (SAH), migraine and pre-eclampsia and with drugs such as sympathomimetics and cocaine, which may precipitate stroke.
- Less common vascular disorders—such as arteritis, venous sinus thrombosis, sickle cell disease and moyamoya disease—may be causes of stroke.
- Venous sinus thrombosis may occur spontaneously or in relation to an underlying risk factor, such as an acquired or congenital prothrombotic disorder, dehydration or meningitis. The consequences depend on the extent and localization of the thrombosis. Stroke secondary to venous thrombosis is due to venous stasis, increased hydrostatic pressures and associated haemorrhage.

Haemorrhagic stroke

Haemorrhagic stroke is the result of vessel rupture into the surrounding intracerebral tissue or subarachnoid space. SAH is the subject of a separate chapter in this book (see Chapter 8.3).

The neurological defect associated with an intracerebral haemorrhage (ICH) is the consequence of direct brain injury, secondary occlusion of nearby vessels, reduced cerebral perfusion caused by associated raised ICP and cerebral herniation. The causes of ICH include the following:

- Aneurysmal vessel dilatation. Vascular dilatation occurs at a site of weakness in the arterial wall, resulting in an aneurysm that expands until it ruptures into the subarachnoid space and in some cases the brain tissue as well.
- Arteriovenous malformation (AVM). A collection of weakened vessels exists as a result of abnormal development of the arteriovenous connections. AVMs may rupture to cause haemorrhagic stroke or, more rarely, cerebral ischaemia from a 'steal' phenomenon.

- Hypertensive vascular disease. Lipohyalinosis, mentioned earlier as a cause of micro-atheromatous infarcts, is also responsible for rupture of small penetrating vessels causing haemorrhage in characteristic locations, typically the putamen, thalamus, upper brain stem and cerebellum.
- Amyloid angiopathy. Post-mortem pathological examination has found these changes, particularly in elderly patients with lobar haemorrhages.
- Haemorrhage into an underlying lesion (e.g. tumour or infarction).
- Drug toxicity from sympathomimetics and cocaine.
- Anticoagulation and bleeding diatheses.

Risk factors for transient ischaemic attack/stroke and prevention

This particularly applies to cerebral ischaemic events, both TIAs and strokes. Non-modifiable risk factors for ischaemic stroke include the following:

- Increasing age: the stroke rate more than doubles for each 10 years above age 55 years.
- Gender: stroke is slightly more common in males than in females.
- Family history.

In terms of primary prevention, hypertension is the most important modifiable risk factor. The benefit of antihypertensive treatment in stroke prevention has been well shown. The other major risk factors for atherosclerosis and its complications—diabetes, smoking and hypercholesterolaemia—often contribute to increased stroke risk. These should be managed according to standard guidelines.

The most important cardiac risk factor for TIA and stroke is atrial fibrillation (AF), both chronic and paroxysmal. Anticoagulation is recommended to prevent cardioembolism where the risk:benefit ratio of anticoagulation (target international normalized ratio [INR] 2.0 to 3.0) favours this. Prediction tools, such as the CHADS₂ (Congestive heart failure, Hypertension, Age >74, Diabetes and previous stroke /TIA) and CHA₂DS₂-VASc (Congestive heart failure, age, hypertension, sex, stroke / TIA history, vascular disease, diabetes) scores, have been developed to standardize the approach to primary stroke prevention in patients with non-valvular AF. The choice of appropriate anticoagulation should be tailored to each patient in consultation with his or her usual treating doctor and follow counselling and assessment of the risk:benefit ratio. The non-vitamin K antagonist oral anticoagulants - or NOACs (apixaban, rivaroxaban or dabigatran) have been shown to be non-inferior to warfarin for the prevention of stroke in patients with non-valvular AF. Patients with valvular disease and AF should be commenced on warfarin unless there

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are contraindications to this therapy. Patients with contraindications to warfarin or very low stroke risk should initially receive aspirin.

A carotid bruit or carotid stenosis found in an otherwise asymptomatic patient is associated with an increased stroke risk. However, the role of carotid endarterectomy in these patients is controversial. Although early trials suggested some minor benefit, more recent studies have refuted this, and it is increasingly clear that intensive medical therapy in patients with asymptomatic carotid stenosis reduces stroke risk well below the reduction achieved with either endarterectomy or carotid stenting.

Other major cardiac conditions associated with increased TIA/stroke risk include endocarditis, mitral stenosis, prosthetic heart valves, recent myocardial infarction and left ventricular aneurysm. Less common ones include atrial myxoma, a patent foramen ovale and cardiomyopathies.

Secondary prevention involves detection and modification, if possible, of conditions that may have caused a TIA or stroke in order to prevent further events that could result in worse clinical outcomes. As well as the risk factors already mentioned, many other uncommon conditions, such as arterial dissection and prothrombotic states, may cause TIA and stroke. These are discussed later in the chapter.

Ischaemic stroke syndromes

The symptoms and signs of stroke or TIA correspond to the area of the brain affected by ischaemia or haemorrhage (Table 8.2.1).

In ischaemic brain injury, the history and pattern of physical signs may correspond to a characteristic clinical syndrome according to the underlying cause and the vessel occluded. This has a bearing on the direction of further investigation and treatment decisions. Differentiating between anterior and posterior circulation ischaemia/infarction is important in this respect but is not always possible on clinical grounds alone.

Determining the cause of the event is the next step. Once again, clues such as a carotid bruit or AF may be present on clinical evaluation. For accurate delineation of the site of the brain lesion, exclusion of haemorrhage and assessment of the underlying cause, it is usually necessary to undertake imaging studies.

Anterior circulation ischaemia

The anterior circulation supplies blood to 80% of the brain and consists of the ICA and its branches, principally the ophthalmic, middle cerebral and anterior cerebral arteries. This system supplies the optic nerve, retina, frontoparietal lobes and most of the temporal lobes. Ischaemic injury involving the anterior cerebral circulation commonly has its origins in atherothrombotic disease

Table 8.2.1 Location of transient ischaemic attack

Symptom	Arterial territory		
	Carotid	Either	Verte-basilar
Dysphasia	+		
Monocular visual loss	+		
Unilateral weakness ^a		+	
Unilateral sensory disturbance ^a		+	
Dysarthria ^b		+	
Homonymous hemianopia		+	
Dysphagia ^b		+	
Diplopia ^b		+	
Vertigo ^b		+	
Bilateral simultaneous visual loss		+	
Bilateral simultaneous weakness		+	
Bilateral simultaneous sensory disturbance		+	
Crossed sensory/motor loss		+	

^aUsually regarded as carotid distribution.

^bNot necessarily a transient ischaemic attack if an isolated symptom.

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of the ICA. Atherosclerosis of this artery usually affects the proximal 2 cm, just distal to the division of the common carotid artery. Advanced lesions may be the source of embolism to other parts of the anterior circulation or cause severe stenosis with resultant hypoperfusion distally if there is inadequate collateral supply via the circle of Willis. This is usually manifest by signs and symptoms in the middle cerebral artery (MCA) territory (Box 8.2.2). Less commonly, lesions of the intracranial ICA and MCA may cause similar clinical features.

Embolism to the ophthalmic artery or its branches causes monocular visual symptoms of blurring, loss of vision and field defects. When transient, this is referred to as amaurosis fugax or transient monocular blindness.

The territory of the anterior cerebral artery is the least commonly affected by ischaemia because of the collateral supply via the anterior communicating artery. If occlusion occurs distally

Box 8.2.2 Signs of middle cerebral artery occlusion

Homonymous hemianopia
Contralateral hemiplegia affecting face and arm more than leg
Contralateral hemisensory loss
Dysphasias with dominant hemispheric involvement (usually left)
Spatial neglect and dressing apraxia with non-dominant hemispheric involvement

or the collateral supply is inadequate, then ischaemia may occur. This manifests as sensorimotor changes in the leg more than in the arm. More subtle changes of personality may occur with frontal lobe lesions, as may disturbances of micturition and conjugate gaze.

Major alterations of consciousness, with Glasgow Coma Scale scores below 8, imply bilateral hemispheric or brain stem dysfunction. The brain stem may be primarily involved by a brain stem stroke or secondarily affected by an ischaemic or haemorrhagic lesion elsewhere in the brain owing to a mass effect and/or increased ICP.

Posterior circulation ischaemia

Ischaemic injury in the posterior circulation involves the vertebra-basilar arteries and their major branches, which supply the cerebellum, brain stem, thalamus, medial temporal and occipital lobes. Posterior cerebral artery occlusion is manifested by visual changes of homonymous hemianopia (typically with macular sparing if the MCA supplies this part of the occipital cortex). Cortical blindness, of which the patient may be unaware, occurs with bilateral posterior cerebral artery infarction.

Depending on the area and extent of involvement, brain stem and cerebellar stroke manifest as a combination of motor and sensory abnormalities that may be uni- or bilateral; cerebellar features of vertigo, nystagmus and ataxia; and cranial nerve signs, such as diplopia/ophthalmoplegia, facial weakness and dysarthria. Consciousness may also be affected.

Examples of cerebellar and brain stem stroke patterns include the following (this list is by no means exhaustive):

- Ipsilateral cranial nerve with crossed corticospinal motor signs.
- Lateral medullary syndrome: clinical features include sudden onset of vertigo, nystagmus, ataxia, ipsilateral loss of facial pain and temperature sensation (V) with contralateral loss of pain and temperature sensation of the limbs (anterior spinothalamic), ipsilateral Horner syndrome and dysarthria and dysphagia (IX and X).
- Internuclear ophthalmoplegia manifesting as diplopia and a horizontal gaze palsy due

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- to involvement of the medial longitudinal fasciculus (MLF).
- ‘Locked-in’ syndrome: this is caused by bilateral infarction of a ventral pons with or without medullary involvement. The patient is conscious due to an intact brain stem reticular formation but cannot speak and is paralysed. Patients can move their eyes owing to sparing of the third and fourth cranial nerves in the midbrain.
 - Acute vertigo. Cerebellar and small strokes involving the cerebellum’s connections with the brain stem may present as acute ataxia and vertigo without other neurological signs. Signs that point to a central cause of vertigo include severe ataxia, inco-ordination and features outlined in the HINTS exam: maintained fixation on Head Impulse test, multidirectional Nystagmus and positive Test of Skew.
 - Acute deterioration of conscious state may be the presentation of acute basilar artery occlusion and should be in the differential diagnosis of coma for investigation.

Lacunar infarcts

Lacunar infarcts are associated primarily with hypertension and diabetes. They occur in the small penetrating arteries supplying the internal capsule, thalamus and upper brain stem. Isolated motor or sensory deficits are most commonly seen.

Clinical features

History

This includes the circumstances, time of onset, associated symptoms such as headache, and any resolution/progression of signs and symptoms. It may be necessary to take a history from a relative or friend, particularly in the presence of dysphasia or reduced conscious state. The history of a stroke is usually that of the acute onset of a neurological deficit over minutes; occasionally, however, there may be a more gradual or stuttering presentation over a period of hours. A past history of similar events suggestive of a TIA should be carefully sought. The presence of severe headache with the onset of symptoms may indicate ICH or SAH. However, headache may also occur with ischaemic strokes. Acute neck pain in association with neurological symptoms should raise the concern of arterial dissection or SAH.

A declining level of consciousness may indicate increasing ICP due to an ICH or a large anterior circulation infarct—so-called malignant MCA infarction. It may also be caused by pressure on the brain stem by an infratentorial lesion, such as a cerebellar haemorrhage.

The possibility of trauma or drug abuse should be remembered along with the past medical and

medication history, particularly anticoagulant/antiplatelet therapy. Risk factors for vascular disease, cardiac embolism, venous embolism and increased bleeding should be sought.

In young patients with an acute neurological deficit, the possibility of paradoxical embolization should be considered as well as dissection of the carotid or vertebral artery. Arterial dissection is often associated with neck pain and headaches/facial pain with or without a history of neck trauma. Trauma, if present, may be minor, such as a twisting or hyperextension/flexion injury sustained in a motor vehicle accident, in playing sports or caused by neck manipulation.

Cardioembolism tends to produce ischaemic injury in different parts of the brain, resulting in non-stereotypical recurrent TIAs of longer duration (hours), whereas atherothrombotic disease of the cerebral vessels tends to cause recurrent TIAs of a similar nature with a shorter duration (minutes), particularly in stenosing lesions of the internal carotid or vertebrobasilar arteries.

Examination

Central nervous system This includes assessing the level of consciousness, pupillary size and reactivity, extent of neurological deficit, presence of neck stiffness and fundoscopy for signs of papilloedema and retinal haemorrhage. Quantifying the neurological deficit using a stroke scale, such as the 42-point National Institute of Health Stroke Scale (NIHSS), is useful in the initial assessment and also for monitoring progress in a more objective way than clinical description alone. Strokes with a NIHSS score greater than 22 are classified as severe.

In the case of TIA, all clinical signs may have resolved. The average TIA lasts less than 15 minutes.

Cardiovascular This includes carotid auscultation and is directed toward findings associated with a cardioembolic source. The absence of a carotid bruit does not exclude significant carotid artery disease as the cause of a TIA or stroke. Major risk factors for cardioembolism that can be identified in the emergency department (ED) include AF, mitral stenosis, prosthetic heart valves, infective endocarditis, recent myocardial infarction, left ventricular aneurysm and cardiomyopathies.

Differential diagnosis

The acute onset of stroke and TIA is characteristic; however, misdiagnoses (the so-called stroke mimics) can occur. The most common stroke mimics are seizures (particularly when there is associated Todd paresis), hypoglycaemia, systemic infection, brain tumour and toxic/metabolic disorders. Others include subdural haematoma, hypertensive encephalopathy,

Box 8.2.3 Differential diagnosis of stroke

Intracranial space-occupying lesion
Subdural haematoma
Brain tumour
Brain abscess
Postictal neurological deficit—Todd paresis
Head injury
Encephalitis
Metabolic or drug-induced encephalopathy
Hypoglycaemia, hyponatraemia, etc.
Wernicke-Korsakoff syndrome
Drug toxicity
Hypertensive encephalopathy
Multiple sclerosis
Migraine
Peripheral nerve lesions
Functional

encephalitis, multiple sclerosis, migraine and conversion disorder. (Box 8.2.3) This has implications when more aggressive stroke interventions, such as thrombolysis, are being considered.

Complications

Central Nervous System complications of stroke include the following:

- Cerebral oedema and raised ICP. This is an uncommon problem in the first 24 hours following ischaemic stroke, but it may occur with large anterior circulation infarcts. It is more commonly seen with ICH, where acutely raised ICP may lead to herniation and brain stem compression in the first few hours.
- Haemorrhagic transformation of ischaemic strokes may occur either spontaneously or associated with treatment.
- Seizures can occur and should be treated in the standard way. Seizure prophylaxis is not generally recommended.
- Non-CNS complications include aspiration pneumonia, hypoventilation, deep venous thrombosis and pulmonary embolism, urinary tract infections and pressure ulcers. In the ED, it is particularly important to be aware of the risk of aspiration.

Clinical investigations

The investigations of TIA and stroke often overlap, but the priorities and implications for management may differ significantly.

General investigations

Standard investigations that may identify contributing factors to stroke/TIA or guide therapy include a complete blood picture, blood glucose, coagulation profile, electrolytes, liver function tests, fasting lipids and, in selected cases, C-reactive protein (CRP). An electrocardiogram (ECG) should be performed to identify arrhythmias and signs of pre-existing cardiac disease. A

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prothrombotic screen may be indicated, particularly in younger patients. Further investigations depend on the nature of the neurological deficit and other risk factors for stroke identified on evaluation but that usually involve a combination of brain, vascular and cardiac imaging.

Imaging in transient ischaemic attacks

Prompt diagnosis and management of patients presenting with TIAs and non-disabling strokes has been shown to reduce the risk of subsequent stroke by up to 80%. Risk stratification for patients presenting with TIAs can guide the urgency of investigations required to determine the underlying cause of the TIA; this is discussed more fully later.

Brain imaging A head computed tomography (CT) or magnetic resonance imaging (MRI) scan is indicated in all patients with TIA in order to exclude lesions that occasionally mimic TIA, such as subdural haematomas and brain tumours. CT and, more particularly MRI, may show areas of infarction matching the symptoms of an ischaemic event that, on clinical grounds, has completely resolved. CT is less sensitive than MRI in detecting posterior territory ischaemic lesions, particularly in the brain stem. In TIAs due to AF or another known cardiac source, brain imaging to exclude ICH is necessary prior to commencing anticoagulation. The exception is in cases of emboli from endocarditis, in which anticoagulation is contraindicated owing to the increased risk of secondary ICH.

Imaging vessels *Ultrasound:* Carotid ultrasound has classically been the most commonly used initial study to investigate the presence and degree of a carotid stenosis. More recently, many centres have moved to the use of CT angiography (CTA) for assessment of carotid patency.

CTA: CTA is increasingly being used to image vessels in cases of TIA, commonly in conjunction with contrast studies examining cerebral perfusion. Advantages include ease of access and avoidance of further delay waiting for second-modality imaging. Disadvantages include exposure to contrast dye and ionizing radiation.

MRI and magnetic resonance angiography (MRA): this provides non-invasive imaging of the brain and major cerebral vasculature. MRA can show lesions suggestive of a vascular aetiology for TIAs, such as a stenosis due to atherosomatous disease and dissection. MRA is more prone to artefact than CTA, hence CTA is generally the preferred modality. MRI/MRA is not routine in TIA workup but may be indicated in more prolonged TIAs, in patients in whom an uncommon cause is suspected or in younger patients and in those where CTA is contraindicated.

Angiography: The use of formal angiography has declined in recent years, with greater use of both CT angiography and MRA studies as confirmatory tests where atheroma is found on carotid ultrasound.

Cardiac imaging If the clinical evaluation indicates that a cardioembolic source is a likely cause of a TIA, echocardiography is a priority. However, if there is no evidence of cardiac disease on clinical evaluation and the ECG is normal, then the yield of echocardiography is relatively low. A transthoracic echocardiogram (TTE) is the first-line investigation in cardiac imaging. A transoesophageal echocardiogram (TOE) is more sensitive than TTE in detecting potential cardiac sources of emboli, such as mitral valve vegetations, atrial/mural thrombi and atrial myxoma. TOE should be considered in patients with inconclusive or normal TTE with ongoing clinical concern of a cardioembolic source or patent foramen ovale. This particularly applies to younger patients with unexplained TIAs/non-disabling stroke.

Imaging in stroke

Brain imaging *Computed tomography:* in the setting of completed stroke, the usual first-line investigation is a non-contrast CT scan. The main value of CT is its sensitivity in the detection of ICH and its ready availability. However, CT scans are often normal in the first hours following ischaemic stroke. In only about half of cases will there be changes detected 24 hours after the onset of symptoms.

The early signs of ischaemic stroke include loss of the cortical grey/white matter distinction and hypoattenuation in the affected arterial distribution (e.g. the insular ribbon sign and obscuration of the lenticulostriate territory in MCA infarcts). Occasionally, a hyperdense clot sign will be seen in the region of the MCA. As well as the presence of haemorrhage, the degree of acute ischaemic change—typically change affecting greater than a third of the MCA territory—has been used to exclude patients from some thrombolytic trials due to possible lack of therapeutic benefit and increased haemorrhage risk. The degree of acute ischaemic change involving the anterior circulation on plain CT can be more reliably quantified by using the ASPECTS (Alberta stroke program early CT score), a stroke scoring system based on the extent of brain involvement evident on CT.

A CT scan should be performed as soon as possible following stroke onset. Urgent CT scanning is indicated in patients with a reduced level of consciousness, deteriorating clinical state, symptoms suggestive of ICH, associated seizures prior to thrombolytic therapy, in younger patients, in patients who are on warfarin and in cases of diagnostic doubt. A CT scan should also be performed to exclude haemorrhage prior to the commencement of antiplatelet therapies. It

should, however, be noted that ICH may be subtle and difficult to diagnose, even for radiologists.

CT perfusion/CT angiography: Following plain CT, CT perfusion studies are the primary imaging modality employed in stroke centres and in cases where reperfusion therapies may be planned. Following intravenous contrast injection, an area of the brain is imaged and analysed using computer software with respect to the cerebral blood volume (CBV), cerebral blood flow (CBF) and mean transit time (MTT). Using predetermined cut-offs of these values, the areas of likely irreversibly infarcted brain (infarct core) and at-risk ischaemic brain (ischaemic penumbra) can be demonstrated (*e-Fig. 8.2.1*). A CT angiogram that includes the carotid vessels is also performed to determine if there is a site of large vessel occlusion. This technology is seen as offering an alternative to diffusion/perfusion MRI and MRA, as it is more readily available, generally quicker and less subject to artefact.

CTA: CTA is the imaging modality of choice in the evaluation of primary ICH to identify the underlying cause, such as an aneurysm or AVM. CTA should be performed in cases of stroke due to suspected arterial dissection and basilar artery thrombosis.

Formal angiography may be performed if intra-arterial therapy, such as embolectomy, is being considered in specialized centres.

MRI: there are many magnetic resonance modalities available for imaging the brain in acute stroke. Even standard MRI is superior to CT in showing early signs of infarction, with 90% showing changes at 24 hours on T2-weighted images. Multimodal MRI typically involves additional modes, such as gradient recalled echo (GRE) and fluid-attenuated inversion recovery (FLAIR) sequences for the detection of acute and chronic haemorrhage and diffusion-weighted imaging (DWI) for the detection of early ischaemia or infarction. MR DWI images show areas of reduced water diffusion in the parts of the brain that are ischaemic and likely to be irreversibly injured. This occurs rapidly after vessel occlusion (less than an hour after stroke onset) and manifests as an area of abnormal high signal in the area of core ischaemia. Hence it is much more sensitive in detecting early ischaemia/infarction than standard T2-weighted MRI modalities or CT. Perfusion-weighted MRI scans (PWI) reveal areas of reduced or delayed CBF following MRI contrast injection. This area of the brain is likely to become infarcted if flow is not restored. The DWI and PWI lesions can then be compared. A PWI lesion significantly larger than a DWI lesion is a marker of potentially salvageable brain: the ischaemic penumbra. It is postulated that acute ischaemic stroke patients with this pattern are

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most likely to benefit from vessel opening strategies, such as thrombolysis. Large areas of diffusion abnormality may also be a marker for increased risk of ICH with thrombolysis. An MRA can be performed at the same time to identify a major vessel occlusion. DWI/PWI imaging is generally considered to be easier to interpret and more reliable than CT perfusion studies. However, MRI may not be as available or feasible. A significant number of patients are unsuitable for MRI, and the multimodal imaging takes longer than CT, which increases the risk of motion artefact and potential delay of treatment. Radiation and iodinated contrast exposure are absent in MRI.

The place of advanced imaging modalities, such as CT perfusion and DWI/PWI MRI, in acute stroke workup continues to evolve. For over a decade now it has been hoped that the information provided by these studies will help to better select patients who will benefit from aggressive stroke therapies such as thrombolysis and extend the current time window for such treatment on the basis of the existence of a significant ischaemic penumbra. They are now a common feature of acute stroke imaging workup protocols if thrombolysis is being considered. However, there remains no convincing evidence supporting the use of these modalities in patients undergoing thrombolysis up to 4.5 hours after symptom onset. Some positive studies of the use of clot retrieval after thrombolysis up to 6 hours beyond symptom onset in large-vessel occlusion (LVO) did employ selection criteria based on the results of perfusion studies, but others have not. Recently the DAWN and Defuse 3 studies have been published; they studied the use of clot retrieval devices from 6 to 24 and 6 to 16 hours, respectively, after the onset of symptoms (including wake-up strokes). Both these trials, which revealed benefit, used selection criteria based on the presence of a significant penumbra/small-core infarct pattern on CT perfusion or DWI/PWI MRI as well as the presence of LVO on angiography. Decisions around the use and implications for therapy of using these perfusion-based imaging modalities remain best made by stroke specialists and neuroradiologists.

MRI is indicated in strokes involving the brain stem and posterior fossa, where CT has poor accuracy. MRA/MRV is particularly useful in the evaluation of unusual causes of stroke, such as arterial dissection, venous sinus thrombosis and arteritis. Basilar artery thrombosis causes a brain stem stroke with an associated high mortality. If the diagnosis is suspected, urgent specialist consultation should be obtained. If MRA or CTA confirms the diagnosis, then aggressive therapies such as thrombolysis and clot retrieval may improve outcome.

Other investigations

Other investigations may be indicated, particularly in young people, in whom the cause of stroke/TIA may be obscure. These include tests to detect prothrombotic states and uncommon vascular disorders. The list of tests is potentially long and includes a thrombophilia screen, vasculitic and luetic screens, echocardiography and angiography.

Treatment

The treatment of cerebrovascular events must be individualized. It is determined by the nature and site of the neurological lesion and its underlying cause. The benefits and risks of any treatment strategy can then be considered and informed decisions made by the patient or his or her surrogate. This is particularly the case with the use of more aggressive therapies, such as anticoagulation, thrombolysis, clot retrieval and surgery.

Pre-hospital care

The pre-hospital care of the possible stroke patient involves the usual attention to the ABCs of resuscitation and early blood sugar measurement. It is unusual for interventions to be required.

Of potentially greater significance is the development of stroke systems (along the lines of trauma systems) in which the sudden onset of neurological signs and symptoms, identified in the pre-hospital evaluation as being consistent with acute stroke, is used to direct patients to stroke centres with the facilities and expertise to manage them, particularly with regard to the delivery of thrombolytic agents and/or clot retrieval. Closer hospitals without these capabilities may be bypassed.

Pre-hospital evaluation and early hospital triage tools that have been developed for the rapid identification of stroke include the Cincinnati Prehospital Stroke Scale or FAST (F, facial movements; A, arm movements; S, speech and T, test) and the Rosier score. Using these simple scales, pre-hospital personnel who identify patients with acute onset of neurological deficits consistent with stroke can potentially be directed to stroke centres and in-hospital acute stroke responses can be activated so as to expedite assessment and imaging, particularly if thrombolysis is being considered. The specificity of these scoring systems in identifying stroke is affected by the fact that both involve relatively imprecise elements such as speech disturbance, which may be caused by many non-stroke pathologies.

General measures

The ED management of a TIA and stroke requires reassessment of the ABCDs and repeated blood glucose testing. Airway intervention may be necessary in the setting of a severely depressed

level of consciousness, neurological deterioration or signs of raised ICP and cerebral herniation.

Hypotension is very uncommon in stroke patients except in the terminal phase of brain stem failure. Hypertension is much more likely to be associated with stroke because of the associated pain, vomiting and raised ICP and/or pre-existing hypertension, but it rarely requires treatment and usually settles spontaneously. It may be a physiological response to maintain cerebral perfusion pressure in the face of cerebral hypoxia and raised ICP. The use of anti-hypertensives in this situation may aggravate the neurological deficit. Current guidelines in ischaemic stroke recommend that only systolic BP greater than 220 mm Hg be lowered by no more than 20% in the first 24 hours. Patients otherwise eligible for thrombolytic therapy should have their blood pressure reduced to less than 185/110 mm Hg prior to commencing treatment and be maintained below this level for 24 hours. Local guidelines should be followed.

An elevated temperature can occur in stroke and should be controlled. It should also raise the suspicion of other possible causes for the neurological findings or an associated infective focus. Hyperglycaemia should be treated appropriately; however, intensive euglycaemic therapy is not indicated.

Transient ischaemic attacks

Risk stratification As already stated, the main aim in therapy in TIAs and minor strokes is to prevent a major subsequent cerebrovascular event through initiation of secondary prevention measures. Not all patients presenting after a TIA require admission to hospital for inpatient workup. Risk-stratification tools exist to help identify higher-risk patients for inpatient workup as well as lower-risk patients who may be suitable for early outpatient follow-up in rapid-access 'TIA clinics'.

The classical tool for risk stratification in this population is the ABCD² score. The ABCD² stroke risk score for TIA has been developed and validated to evaluate the very early risk of a stroke following a TIA. The scoring system is shown in Table 8.2.2. In patients with an ABCD² score less than 4, there is minimal short-term risk of stroke. With scores of 4 to 5 and 6 to 7, the 2-day risk is 4.1%, and 8.1%, respectively. The use of the ABCD² score is not universally accepted, however, as ongoing validation studies have had mixed results. More recently, the ABCD² score has been modified to include a history of two or more TIAs within the preceding week as well as the results of DWI MRI and carotid imaging to form the ABCD₃-I score, which has shown superior performance as a risk-stratification tool. These changes underscore a move to imaging based risk stratification and on the observation

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that patients with established areas of infarction on brain imaging, and imaging evidence (ultrasound [US] or CTA) of significant (>50%) carotid stenosis in a distribution consistent with their TIA symptoms are at highest risk for early recurrent cerebrovascular events. Other patient groups are at increased risk of stroke independent of the classical risk stratification systems. These include patients with multiple TIAs within a short period ('crescendo TIAs') and those with a probable or proven cardioembolic source.

Antiplatelet therapy Following CT scanning that excludes ICH, aspirin should be commenced at a dose of 300 mg and maintained at 75 to 150 mg/day in patients with TIAs or minor ischaemic strokes. It has been shown to be effective in preventing further ischaemic events. The ESPRIT trial showed a modest additional benefit from a combination of dipyridamole with aspirin over aspirin alone. There was no increased risk of bleeding complications but a significantly increased rate of withdrawal of patients from the combination arm owing to side effects from dipyridamole, principally headache. Clopidogrel or ticagrelor may be substituted for aspirin if the patient is intolerant of aspirin or aspirin is contraindicated. There is some evidence that ticagrelor may be more effective than aspirin in the prevention of recurrent cerebrovascular events in patients with carotid atherosclerosis; however, further work is needed to confirm this. The combination of aspirin and clopidogrel is not recommended, as it does not appear to provide any greater therapeutic benefits in the longer term and there is increased bleeding risk. Anticoagulation with heparin and warfarin has not been shown to be superior to aspirin except in cases of TIA/minor stroke due to cardioembolism (excluding endocarditis).

Anticoagulant therapy Patients with a cardioembolic source of TIA should be considered for full anticoagulation following neurological consultation and normal brain imaging with the exception of those with endocarditis, in whom the risk of haemorrhagic complications is increased.

Surgery Trials have demonstrated a beneficial outcome of urgent surgery for symptomatic carotid stenosis in patients with anterior circulation TIAs and minor stroke with a demonstrated carotid stenosis of between 70% and 99%. The benefit of surgery may extend to lesser grades of stenosis down to 50% in selected patients. The patient's baseline neurological state, co-morbidities and operative mortality and morbidity rate also need to be assessed when surgery is being considered. The recent CREST trial compared carotid artery stenting (CAS) with endarterectomy (CEA). It revealed slightly superior stroke prevention for CEA in symptomatic patients.

In patients with significant co-morbidities, CAS remains an option.

Other medical therapies Risk factors for stroke and TIAs should be identified and treated. Statins should be considered regardless of cholesterol levels. The benefit of lowering low-density lipoprotein (LDL) cholesterol levels using atorvastatin in preventing further cerebro- and cardiovascular events following an initial episode of cerebral ischaemia was demonstrated in the SPARCL trial.

Ischaemic stroke

A more active approach to the acute management of ischaemic stroke is seen as having the potential to improve neurological outcomes. The ED is the place where these important treatment decisions will largely be made. Most patients with stroke will require hospital admission for further evaluation and treatment as well as for observation and rehabilitation. Studies of stroke units show that patients benefit from being under the care of physicians with expertise in stroke and a multidisciplinary team that can manage all aspects of stroke care.

Antiplatelet therapy In two large trials, aspirin administered within 48 hours of the onset of stroke was found to improve the outcomes of early death or recurrent stroke compared with placebo. A CT or MRI scan should be performed to exclude ICH prior to commencing aspirin. Aspirin should be withheld for at least 24 hours in patients treated with thrombolytics.

Thrombolysis As a critical factor in ischaemic stroke outcome is occluded vessel reopening, thrombolytic agents and more recently clot retrieval devices are seen as having an important place in the management of acute ischaemic stroke. The critical starting points are a significant neurological deficit, a non contrast CT (NCCT) showing no evidence of haemorrhage and ascertaining the time of onset or when the patient was last seen well. Many studies have been performed since the pivotal National Institute of Neurological Disorders and Stroke (NINDS) study of intravenous alteplase in 1996. The current state of these therapies in treating acute ischaemic stroke is summarized here.

IV alteplase (0.9 mg/kg with a maximal dose of 90 mg over 60 minutes and 10% of the total dose given as a bolus) is recommended for eligible patients who can be treated within 3 hours of onset of symptoms. The number needed to treat (NNT) to achieve a good neurological outcome is approximately 10. The number needed to harm (NNH), primarily due to increased spontaneous intracranial haemorrhage rates is approximately 40. An ACEM statement on intravenous thrombolysis for acute ischaemic stroke supported this therapy. Current indications and

contraindications for intravenous alteplase are published in the most recent 2018 American Heart Association (AHA) guidelines for the management of ischaemic stroke. Specific clinical presentations where thrombolysis is contraindicated are ischaemic stroke known or likely to have been caused by infective endocarditis and aortic arch dissection.

Extending the use of alteplase to 4.5 hours is recommended in guidelines published by the Stroke Foundation of Australia and the AHA, although the likelihood of benefit is reduced and significant risk of SICH remains. This recommendation is principally based on the ECASS 3 study and registry data. The ECASS 3 study had additional exclusion criteria of age above 80 years, NIHSS score above 25, acute ischaemia score of greater than one-third of the MCA territory on CT, any anti-coagulation therapy or previous history of diabetes or stroke. The AHA guidelines acknowledge that these factors should be taken into account in deciding on thrombolysis therapy in this time window. Alteplase is not approved by the US Food and Drug Administration for use in this time window.

Every effort should be made to reduce the door-to-needle time with thrombolysis, as current evidence indicates that time to administration strongly influences outcome within the 0- to 4.5-hour time window. Prehospital notification and 'code stroke' teams to streamline this process are now commonplace. Pre-hospital CT scanners are also being introduced in some cities to image patients en route to the ED.

Explanation of the potential risks of thrombolysis, particularly SICH, is an important and sometimes overlooked aspect of the consent process before commencing this treatment.

Clot retrieval A number of similar studies (MR Clean, ESCAPE, SWIFT PRIME, EXTEND 1A and REVASCAT) have shown that in patients with large vessel occlusion typically involving the intracranial internal carotid, proximal MCA and basilar artery, endovascular interventions using the latest clot retrieval devices can improve neurological outcomes up to 6 hours after the onset of symptoms. Inclusion criteria included adults with pre-existing good neurological status, ongoing significant neurological deficit, limited early ischaemic change on NCCT and clot retrieval skin puncture time achieved within 6 hours. In these studies all eligible patients received thrombolysis prior to being randomized into the clot retrieval or standard therapy arms. As stated previously, only some of these studies used advanced imaging criteria showing a significant penumbra/small infarct pattern as part of the selection criteria. Delays to clot retrieval in potentially suitable patients should be minimized, and such patients may have to be transferred

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Table 8.2.2 The ABCD² transient ischaemic attack risk score

ABCD ²	Risk factor	Score
Age	Below 60	0
	Above 60	1
Blood pressure	BP above systolic 140 mm Hg and/or diastolic 90 mm Hg on first assessment after TIA	1
Clinical	Unilateral weakness of face, arm, hand or leg	2
	Speech disturbance without weakness	1
Duration	Symptoms lasted >60 min	2
	Symptoms lasted 10–60 min	1
	Symptoms lasted <10 min	0
Diabetes	Presence of diabetes	1

TIA, Transient ischaemic attack.

(Reproduced with permission from Johnston SC, Rothwell PM, Nguyen-Huynh MN, et al. Validation and refinement of a score to predict very early stroke risk after transient ischaemic attack. *Lancet*. 2007;369:283–292.)

to centres with necessary neuro-interventional expertise with ongoing thrombolysis infusions. Waiting for a possible response to thrombolysis before activating the pathway to potential clot retrieval in suitable patients is not advised.

Clot retrieval within 6 hours of onset can also be considered in patients with ischaemic stroke due to LVO and contraindications to thrombolysis or who present beyond the 4.5-hour thrombolysis window if the skin puncture can be achieved within 6 hours of onset.

Delayed clot retrieval The DAWN and DEFUSE 3 trials have shown that in a small number of highly selected patients, extending the time window for clot retrieval up to 24 hours after symptom onset, including wake-up strokes, can improve outcomes. Other inclusion criteria were internal carotid or M1 MCA occlusion on CTA or MRA and ‘penumbral selection’ (based on advanced imaging modalities) indicating a small infarct core and persisting significant neurological deficit. Patients who had failed thrombolysis were still eligible. A total of approximately 400 patients were enrolled. In the DAWN study (6 to 24 hours), the rate of functional independence (modified Rankin Score, mRS 0 to 2) was a highly significant 49% in the intervention group, compared with 13% in the control group. Similar results were found in the DEFUSE 3 study (6 to 16 hours). There were no significant differences in mortality or complication rates.

The implication of these two studies for stroke care is now a topic of intense

discussion, but it is likely that it will result in more stroke patients with significant ongoing neurological disability being transferred to stroke centres.

Overall, the rise in neuro-intervention as a treatment in selected strokes will mean that the presence and utilization of advanced imaging modalities, tele-radiology and assessment of stroke patients in ‘primary’ stroke centres in order to select appropriate patients for transfer to ‘comprehensive’ neuro-interventional centres is likely to be increasingly incorporated into stroke care systems.

Anticoagulation Therapeutic anticoagulation with heparin or clexane is associated with increased risk of haemorrhagic transformation in acute ischaemic stroke. Stroke due to endocarditis poses a particularly high risk for this complication. Anticoagulation following acute ischaemic stroke should not be commenced in the ED. In cases of stroke due to cardioembolism, the timing and manner of anticoagulation should be determined by stroke physicians.

Neuroprotection A range of neuroprotective agents has been trialled in the setting of acute stroke in the hope that modulation of the ischaemic cascade of metabolic changes that follows vascular occlusion may result in improved neurological outcomes. At this stage, however, none of these therapies is recommended for use in the treatment of acute stroke.

Surgery As for TIAs, patients with non-disabling stroke should be considered for investigation with a vascular imaging modality to detect a significant carotid artery stenosis that may be appropriate for urgent surgery or, in some selected cases, stenting.

Large infarcts of the anterior circulation have a significant risk of developing cerebral oedema and raised ICP with associated clinical deterioration, particularly manifest by a declining conscious state with or without progression of other signs. These are termed *malignant MCA infarcts*. Along with standard measures for managing raised ICP, there may be a place for early decompressive craniotomy in carefully selected cases. Studies in young patients (<61 years) have shown improved survival, but with rates of significant residual disability (mRS >3) approaching 50%.

Intracerebral haemorrhage

Primary ICH is most commonly caused by long-standing hypertension-induced small vessel disease. Hypertensive haemorrhage tends to occur in characteristic locations,

such as the basal ganglia, thalamus and cerebellum. Berry aneurysms most commonly arise around the circle of Willis, hence ICH due to aneurysmal rupture is often located around this area. Secondary ICH may occur into an underlying lesion, such as a tumour or infarct, and clinical deterioration may result—so-called symptomatic ICH—but this is not always the case.

The clinical presentation of primary ICH is typical of sudden onset of a neurological deficit with associated headache, collapse/transient loss of consciousness, hypertension and vomiting. However, clinical features alone cannot serve to differentiate ICH from infarction; hence the requirement for brain imaging to confirm the diagnosis. Both CT and MRI (using gradient echo sequences) are equivalent in the detection of ICH.

Medical Treatment

Primary ICH is a medical emergency with a high mortality (between 35% and 50%), with half of these deaths occurring in the first 2 days. There is also a very high risk of dependency. Haematomas can expand rapidly, and there is a significant risk of early neurological deterioration and increasing ICP. General measures, as for TIAs and ischaemic stroke, should be initiated, in particular with attention to airway and ventilatory support. Treatment of raised ICP in a setting of ICH involves a range of modalities similar to those used in head trauma. These include elevation of the head of the bed, analgesia, sedation, an osmotic diuretic such as mannitol and hypertonic saline, hyperventilation, drainage of cerebrospinal fluid (CSF) via ventricular catheter and neuromuscular paralysis.

The INTERACT 2 trial showed that acute reduction of blood pressure to an end point aim of 140 mm Hg systolic was safe and may improve neurological outcomes. Treatment should be individualized and take place in consultation with stroke/neurosurgery/intensive care specialists. Hypotension should be avoided.

Use of recombinant factor VIIa is not recommended. Steroids are also not indicated in ICH. Anticonvulsant prophylaxis is common practice.

Management of ICH associated with anticoagulation or thrombolysis is a matter of urgency and should be done in consultation with a haematologist and a neurosurgeon. Depending on the clinical situation, agents such as protamine sulphate, vitamin K, prothrombin complex concentrate and fresh frozen plasma (FFP) may be indicated. Patients on direct oral anticoagulants should receive a specific antidote where available. Otherwise consultation with a haematologist is recommended.

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Surgery

Surgical management of ICH depends on the location, cause, neurological deficit and patient's overall clinical state. Early neurosurgical consultation should be obtained. High-level evidence for improved outcomes following drainage of large supratentorial haematomas by craniotomy is lacking. The procedure may be lifesaving in selected patients, but consideration of the likely level of long-term disability is required.

The presence of a large cerebellar haematoma is a particular indication for surgery, with the potential for a good neurological recovery.

External ventricular drainage devices (EVDs) may be indicated if hydrocephalus develops in the setting of ICH.

CONTROVERSIES

- Thrombolysis beyond 3 hours.
- Delayed neuro-interventional therapies up to 6 hours post onset and beyond.
- Advances in neuroimaging, particularly diffusion/perfusion MRI and perfusion CT/CTA, show promise for improved selection of patients likely to benefit from vessel opening strategies.

- The place of interventional therapies in acute ischaemic stroke is the subject of intense research. These approaches have the potential to improve outcome by prolonging the treatment window, increasing recanalization rates in LVOs and reducing haemorrhagic complications. A number of clot retrieval devices are being evaluated, as is intra-arterial thrombolysis.
- The place of DOACs in AF/stroke prevention. Although uptake in the community has been rapid, more time is needed to see whether industry-sponsored trials of efficacy translate into real-world benefits.
- The follow-up investigation and management of patients presenting to EDs with TIA is moving increasingly to an outpatient model of care. The optimum method of risk stratification and patient selection for this approach has yet to be conclusively determined.
- Neuroprotective therapies continue to be evaluated; however, at this stage they cannot be recommended outside of a clinical trial.

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8.3 Subarachnoid haemorrhage

Íomhar O'Sullivan

ESSENTIALS

- 1** The diagnosis of subarachnoid haemorrhage (SAH) requires a high index of suspicion.
- 2** Up to a third of patients with SAH experience a warning leak—the sentinel haemorrhage—in the hours to days prior to the major bleed.
- 3** Risk of re-bleeding is maximal in first 2 to 12 hours and is associated with a poor prognosis and high mortality.
- 4** Severe sudden headache is the primary clinical feature.
- 5** A computed tomography (CT) scan of the brain without contrast is the initial investigation of choice.
- 6** A negative CT scan for SAH should be followed by lumbar puncture and examination of the cerebrospinal fluid.
- 7** Patients with SAH require urgent neurosurgical referral and management.
- 8** Early definitive isolation and occlusion of the aneurysm reduces early complications and improves outcome.
- 9** Endovascular treatment is the treatment of choice in most cases.

Introduction

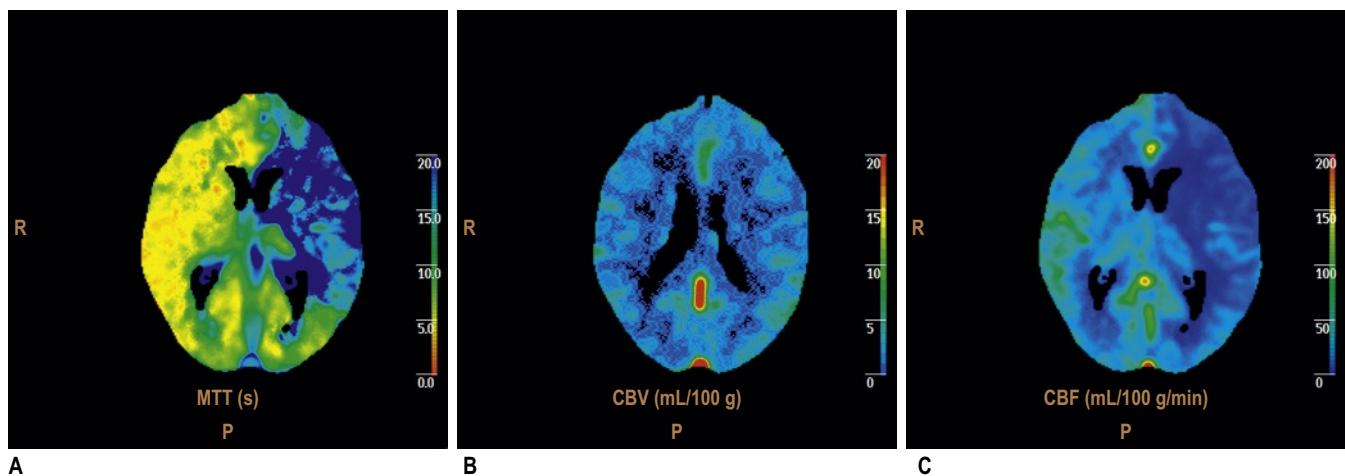
Patients with headache account for approximately 1% of all emergency department (ED) visits; of these, 1% to 5% have a final diagnosis of subarachnoid haemorrhage (SAH). Early accurate diagnosis of aneurysmal SAH is imperative, as early occlusion of the aneurysm has been shown to reduce early complications of re-bleeding and vasospasm and to improve outcome.

Epidemiology and pathology

SAH is the presence of extravasated blood within the subarachnoid space. The incidence in Australia is approximately 10 cases per 100,000 patient-years, but, for reasons that are unclear, it is significantly higher (around 20 per 100,000) in Japan and Finland. Although incidence increases with age, about half of those affected are aged under 55.

The most common cause of SAH is head trauma, which is dealt with elsewhere in this book. Non-traumatic or spontaneous SAH

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E-FIG. 8.2.1 Computed tomography perfusion study of a left middle cerebral artery stroke. (A) mean transit time; (B) cerebral blood volume; (C) cerebral blood flow.

8.3 SUBARACHNOID HAEMORRHAGE

results from rupture of a cerebral aneurysm in approximately 85% of cases, non-aneurysmal perimesencephalic haemorrhage in 10% and the remaining 5% from other rare causes including rupture of mycotic aneurysms, intracranial arterial dissection, arteriovenous malformations, vasculitis, central venous thrombosis, bleeding diatheses, tumours and drugs, such as cocaine, amphetamines and anticoagulants.

Aneurysms

Intracranial aneurysms are not congenital. Rather, they develop during the course of life. An estimate of the frequency for an adult without risk factors is 2.3%, with the proportion increasing with age. Most aneurysms will never rupture, but the risk increases with size. Paradoxically, because the vast majority of aneurysms are small, most aneurysms that rupture are small. An aneurysm of the posterior circulation is more likely to rupture than one of comparable size in the anterior circulation.

Risk factors can be divided into those that are modifiable and those that are not. Modifiable risk factors include cigarette smoking, hypertension, the use of sympathomimetic drugs (e.g. cocaine) and excessive alcohol intake. Non-modifiable factors include history of previous aneurysmal SAH, a family history of first-degree relatives with SAH, inherited connective tissue disorders (particularly polycystic kidney disease, Marfan syndrome, Ehlers-Dahnlos syndrome and neurofibromatosis), coarctation of the aorta, sickle cell disease and α_1 -antitrypsin deficiency.

Non-aneurysmal peri-mesencephalic haemorrhage

This type of SAH is defined by the characteristic distribution of blood in the cisterns around the midbrain in combination with normal angiographic studies. It usually carries a relatively benign prognosis. A small proportion of patients with this distribution of blood may have a ruptured aneurysm of a vertebral or basilar artery.

Clinical features

History

The history is critical to the diagnosis of SAH.

- Headache is the principal presenting symptom, being present in up to 95% of patients with SAH and being the solitary symptom in up to 40% of patients. It is typically occipital, severe ('worst'), of sudden onset, almost instantaneously reaching peak intensity and often being the worst headache ever experienced. Approximately 25% of patients presenting with sudden severe headache will have SAH. The pain differs from any other headache the patient might have had ('first').

Table 8.3.1 Clinical grading schemes for patients with subarachnoid haemorrhage

Grade	Grading scheme of Hunt and Hess	Grading scheme of WFNS	
		GCS	Motor deficit
1	No symptoms or minimal headache, slight nuchal rigidity	15	No
2	Moderate to severe headache, no neurological deficit other than cranial nerve palsy	13–14	No
3	Drowsy, confused, mild focal deficit	13–14	Yes
4	Stupor, moderate to severe hemiparesis, vegetative posturing	7–12	Yes or no
5	Deep coma, decerebration, moribund	3–6	Yes or no

GCS, Glasgow Coma Scale score; SAH, subarachnoid haemorrhage; WFNS, World Federation of Neurosurgeons (Reproduced with permission from Sawin PD, Loftus CM. Diagnosis of spontaneous subarachnoid hemorrhage. *Am Fam Phys*. 1997;55:145–156.)

- One-third of patients experience a warning leak (sentinel haemorrhage) in the hours to weeks before the major bleed. This headache may be mild, generalized or localized and of variable duration; it may resolve spontaneously within minutes to hours or last several days and usually responds to analgesic therapy. It does, however, tend to develop abruptly and to differ in quality from other headaches that the patient may previously have experienced. Hence a patient's worst or first headache is suggestive of SAH.
- Upper neck pain or stiffness (and then meningism) is common.
- About half of patients will develop SAH during strenuous exercise (e.g. bending or lifting).
- Nausea and vomiting are present in 75% of patients.
- Brief or continuing loss of consciousness may occur, the headache typically occurring just prior to loss of consciousness.
- Seizures occur in circa 10%. When associated with headache, they are a strong indicator of SAH, even if the patient is neurologically normal when assessed.
- Prodromal symptoms—particularly involving the third cranial nerve with pupillary dilation and sixth cranial nerve palsies—are uncommon but may suggest the presence and location of a progressively enlarging unruptured aneurysm.
- No clinical feature can reliably identify SAH.

Examination

There is a wide spectrum of clinical presentations, the level of consciousness and clinical signs being dependent on the site and extent of the haemorrhage, as follows:

- On ED presentation, two-thirds of patients have an impaired level of consciousness, 50% with coma. Consciousness may improve or deteriorate. An acute confusional state can occur, which may be mistaken for a psychological problem.

- Signs of meningism, photophobia and neck stiffness are present in 75% of patients but may take several hours to develop and may be absent (particularly with more severe bleeds). Absence of neck stiffness does not exclude SAH. Photophobia is neither sensitive nor specific for SAH. Fever may be present.
- Focal neurological signs are present in up to 25% of patients and are secondary to associated intracranial haemorrhage, cerebral vasospasm, local compression of a cranial nerve by the aneurysm (e.g. oculomotor nerve palsy by posterior communicating aneurysm or bilateral lower limb weakness due to anterior communicating aneurysm) or raised intracranial pressure (sixth-nerve palsy).
- Ophthalmological examination may reveal papilloedema (40%), retinal haemorrhages (25%) or, rarely, subhyaloid haemorrhages (see Entezari et al., 2009).
- Systemic features associated with SAH include hypertension, hypoxia and acute electrocardiographic (ECG) changes that may mimic acute myocardial infarction.
- Neurogenic pulmonary oedema is more common in obtunded SAH patients.
- A small proportion of patients present in cardiac arrest. Resuscitation attempts are vital, as half of the survivors regain independent function.

Patients are categorized into clinical grades from I to V, according to their conscious state and neurological deficit. Two grading schemes, that of Hunt and Hess and that of the World Federation of Neurosurgeons, which is preferred, are depicted in Table 8.3.1. The higher the score, the worse the prognosis.

Differential diagnosis

Important differential diagnoses include benign thunderclap headache (40%), migraine, cluster headache, headache associated with sexual exertion, vascular headaches of stroke, intracranial



FIG. 8.3.1 Non-contrast computed tomography scan of the head demonstrating widespread subarachnoid and intraventricular blood.

haemorrhage, venous thrombosis and arterial dissection, meningitis, encephalitis, acute hydrocephalus, intracranial tumour and intracranial hypotension.

Clinical investigations

Imaging

Computed tomography

Non-contrast CT of the brain is the initial investigation of choice. In the first 24 hours after haemorrhage it can demonstrate the presence of subarachnoid blood in more than 95% of cases (Fig. 8.3.1). Some (Perry, 2011) report a sensitivity of 100% if completed within 6 hours of symptom onset. Others, including patients with atypical presentations and interpretation by non-neuroradiologists, claim a sensitivity closer to 95%. The sensitivity of CT in detecting acute haemorrhage decreases with time owing to the rapid clearance of iron (haemoglobin) with only 80% of scans being positive at 3 days and 50% positive at 1 week. CT will also demonstrate the site and extent of the haemorrhage, indicate the possible location of the aneurysm and demonstrate the presence of hydrocephalus and other pathological changes.

Magnetic resonance imaging

Magnetic resonance imaging (MRI) has little role in the diagnosis of acute SAH. It is less sensitive than CT (with or without lumbar puncture) but may assist in identifying the location of the 'guilty' aneurysm when CT is positive and the patient has multiple aneurysms on angiography. Availability and logistical considerations, including longer procedure time, make MRI impractical for use in the initial diagnostic workup of SAH, but it may be considered in patients who present late.

Computed tomography angiography

CT angiography (CTA) is the preferred angiographic technique once SAH has been identified.

Compared with catheter angiography, it has a sensitivity of 98% for cerebral aneurysms, is readily available and has a lower complication rate. It should be performed as soon as the diagnosis is made. Where diagnosis has been made by CT, CTA should preferably be performed while the patient is still in the scanner. CTA is usually of sufficient quality to allow the planning of endovascular or neurosurgical interventions. It is important to note that small aneurysms (<3 mm in diameter) may not be detected reliably on CTA; therefore further investigations may be warranted in CTA-negative SAH.

A CT/CTA approach has been suggested as an alternate diagnostic strategy to CT/lumbar puncture (LP) in the diagnosis of SAH. However, this approach focuses on identifying an aneurysm rather than on the presence of intracranial haemorrhage. The consequence of this strategy may be that the aneurysm detected is an incidental finding, as aneurysms are known to occur in about 2.5% of the normal population. This would then result in unnecessary investigation and treatment of an asymptomatic aneurysm and is therefore not currently supported.

Cerebral angiography

Cerebral angiography is the gold standard for confirming the presence of an aneurysm, its location and the presence of vasospasm; it was previously the preferred angiographic test. It is not, however, without risk. Neurological complications occur in \approx 1.8% of cases, with re-rupture of an aneurysm reported in 2% to 3%. It is also less available than CTA. These factors have seen it become less favoured, so that it is used in selected cases only.

Magnetic resonance angiography

Magnetic resonance angiography (MRA) is currently useful as a screening tool for the diagnosis of intracranial aneurysms in patients at increased risk.

Further imaging when no cause for subarachnoid haemorrhage is found

In patients where SAH is present and no cause is found, the distribution of extravasated blood on the CT scan should be reviewed. If this conforms to the peri-mesencephalic distribution of non-aneurysmal haemorrhage, then no further investigations may be warranted. If, however, an aneurysmal pattern of haemorrhage is present, then a second CTA is recommended, as occasionally an aneurysm may have gone undetected on the original test.

Lumbar puncture

Lumbar puncture is necessary when there is clinical suspicion of SAH; the CT scan is negative, equivocal or technically inadequate; and no mass

lesion or signs of raised intracranial pressure are found. In about 3% to 5% of patients with SAH, the CT scan will be normal. Although it has been suggested that a negative CT scan performed in the first 6 hours following headache onset is sufficient to exclude a diagnosis of SAH, evidence is inadequate to support this practice; therefore it cannot be recommended to replace a CT/LP strategy.

The diagnosis of SAH, then, is dependent on the finding of red blood cells not due to traumatic tap or red blood cell breakdown products within the CSF. Lumbar puncture should be delayed for at least 6 and preferably 12 hours after symptom onset to allow bilirubin to be formed from cell breakdown in SAH. Detection of bilirubin and xanthochromia is the only reliable method of distinguishing SAH from a traumatic tap. Proceeding to angiographic studies in every patient with bloodstained CSF would be expected to identify an incidental finding of a small unruptured aneurysm in about 2%.

It is important to measure the opening pressure when performing a lumbar puncture, as CSF pressure may be elevated in SAH or in other conditions, such as intracranial venous thrombosis or pseudotumour cerebri, or low in spontaneous intracranial hypotension.

Xanthochromia, the yellow discolouration of CSF caused by the haemoglobin degradation products oxyhaemoglobin and bilirubin due to lysis of red blood cells, is generally agreed to be the primary criterion for diagnosis of SAH and differentiates SAH from traumatic tap. It is usually present within 6 hours of SAH and has been demonstrated in all patients with SAH between 12 hours and 2 weeks following the haemorrhage. Spectrophotometric analysis of CSF for bilirubin is considered to be the most sensitive means of detecting xanthochromia.

Controversy exists as to the optimal timing of lumbar puncture. Early lumbar puncture within 12 hours may have negative or equivocal CSF findings, whereas delayed lumbar puncture may result in an increased risk of early rebleeding as well as having practical implications for the ED. In general at least 6 to 12 hours should have elapsed between the onset of headache and lumbar puncture. Although the detection of xanthochromia is indicative of SAH, it does not entirely rule out traumatic lumbar puncture and can occur in extremely bloody taps (>12,000 red blood cells per millilitre) or where the lumbar puncture has been repeated after an initial traumatic tap.

Other studies of the CSF—such as three tube-cell counts, D-dimer assay and the detection of erythrophages—have been found to be inconsistent in differentiating SAH from traumatic tap.

8.3 SUBARACHNOID HAEMORRHAGE

General investigations

General investigations to be performed include full blood examination, erythrocyte sedimentation rate, urea, electrolytes including magnesium, blood glucose, coagulation screen, chest x-ray and 12-lead ECG. ECG changes are frequently present and include ST- and T-wave changes, which may mimic ischaemia, QRS and QT prolongation and arrhythmias. Cardiac biomarkers, including troponin, may also be elevated.

Complications

Early complications

- Re-bleeding occurring in up to 15% of patients within hours of the initial haemorrhage. Overall, 40% of patients re-bleed within the first 4 weeks if there is no intervention. Re-bleeding is associated with 60% mortality and half of the survivors remain disabled.
- Subdural haematoma or a large intracerebral haematoma can be life threatening and requires immediate drainage. Similarly, a large intracerebral haematoma may be contributing to the patient's poor clinical condition and warrants drainage along with simultaneous treatment of the aneurysm.
- Global cerebral ischaemia. Irreversible brain damage resulting from haemorrhage at the time of aneurysmal rupture is probably secondary to a marked rise in intracranial pressure, resulting in inadequate cerebral perfusion.
- Cerebral vasospasm. Clinically significant vasospasm occurs in approximately 20% of patients with SAH and is a major cause of death and morbidity. It tends to occur between days 3 and 15 after SAH, with a peak incidence at days 6 to 8. Vasospasm causes ischaemia or infarction and should be suspected in any patient who suffers a deterioration in neurological status or develops neurological deficits. The best predictor of vasospasm is the amount of blood seen on the initial CT scan.
- Hydrocephalus occurs in approximately 20% of patients with SAH. It can occur within 24 hours of haemorrhage and should be suspected in any patient who suffers a deterioration in mentation or conscious state, particularly if associated with slowed pupillary responses.
- Seizures.
- Fluid and electrolyte disturbances. Patients with SAH may develop hyponatraemia and hypovolaemia secondary to excessive natriuresis (cerebral salt wasting) or, alternatively, such patients may develop

a syndrome of inappropriate antidiuretic hormone (SIADH).

- Hyperglycaemia and hyperthermia, both being associated with a poor outcome.
- Medical complications include cardiogenic or neurogenic pulmonary oedema (23%), cardiac arrhythmias (35%), sepsis, venous thromboembolism and respiratory failure.

Late complications

- Late re-bleeding, from a new aneurysm or regrowth of the treated aneurysm is estimated at ≈1.3% in 4 years for coiling and ≈2% to 3% in 10 years for surgical clipping.
- Anosmia: up to 30%.
- Epilepsy: 5% to 7%.
- Cognitive deficits and psychosocial dysfunction are common even in those who make a good recovery; 60% of patients report personality change.

Treatment

The management of SAH requires general supportive measures, particularly airway protection and blood pressure control, as well as specific management of the ruptured aneurysm and the complications of aneurysmal haemorrhage.

General measures

- Stabilization of the unconscious patient, with particular attention to the airway. Endotracheal intubation with oxygenation and ventilation will be required in patients with higher-grade (4 to 5) SAH.
- Close observation of the Glasgow Coma Scale (GCS) score and vital signs.
- In all patients, oxygenation and circulation must be maintained to ensure adequate (euvolaemic) blood volume.
- Analgesia, using reversible narcotic analgesic agents, sedation and antiemetics as required. Bed rest with minimal stimulation is to be ensured; aspirin and non-steroidal analgesic agents (NSAIDs) are to be avoided.
- Blood pressure control. Blood pressure levels are often of the order of 150/90 mm Hg immediately following SAH and, in most patients, can be adequately controlled by analgesia. Normotensive levels extending to mild to moderately hypertensive levels, especially in patients with pre-existing hypertension, are acceptable. Antihypertensive therapy should be reserved for patients with severe (mean arterial pressure >130 mm Hg) hypertension or who have evidence of progressive end-organ dysfunction; short-acting antihypertensive agents (e.g. esmolol) and intensive haemodynamic monitoring should be employed.

- Fever should be regulated to maintain normothermia, which is associated with improved functional outcome.
- Seizures should be treated as they occur. The routine use of prophylactic phenytoin is controversial.
- Electrolyte imbalances must be corrected. Hyponatraemia due to excessive natriuresis must be differentiated from that of SIADH. Hypovolaemia is to be avoided.
- There is no convincing evidence for the use of steroids.
- Effective glucose control, importantly avoiding hyper- and hypoglycaemia.
- Venous thromboembolism prophylaxis, initially with compressive devices and later with subcutaneous heparin following treatment of the aneurysm.
- Treatment of hydrocephalus by ventricular drainage may be required.

Specific treatment

Prevention of re-bleeding

Obliteration of the ruptured aneurysm by endovascular coiling or surgical clipping should be performed as early as possible to prevent re-bleeding, remove clot, reduce the incidence of early complications and improve outcomes.

Endovascular occlusion, achieved by placing detachable coils in aneurysms under radiological guidance (coiling), has largely replaced surgical occlusion as the method of choice for the prevention of re-bleeding in suitable cases. The method of treatment, however, depends on anatomical considerations, as aneurysms are not equally amenable to this option. In aneurysms that are suitable to treatment by either modality, the 4-year outcome has been demonstrated to be better with coiling, although there are higher aneurysmal recurrence and re-bleeding rates.

Surgical clipping is now a second-line option for most patients. It is usually done early—within 3 days and preferably within 24 hours.

Antifibrinolytic agents may reduce the incidence of early re-bleeding, but current evidence does not support their routine use in SAH ([Baharoglu et al., 2013](#)).

Prevention of delayed cerebral ischaemia

Cerebral ischaemia is often gradual in onset and involves the territory of more than one cerebral artery. Peak frequency is at 5 to 14 days after SAH. Nimodipine, a calcium channel antagonist, improves clinical outcome in SAH, with a relative risk reduction of 18% and an absolute risk reduction of 5.1%. The current standard regimen is nimodipine 60 mg orally every 4 hours for 3 weeks. It should be commenced within 48 hours of haemorrhage. Nimodipine is indicated irrespective of whether a ruptured aneurysm has been coiled or not.

8.4 ALTERED CONSCIOUS STATE

There is insufficient evidence to support medically induced hypertension, hypervolaemia and haemodilution in the management of vasospasm (Loan et al., 2018).

Other treatments—including magnesium sulphate, the statins and antiplatelet agents—have not been demonstrated to improve clinical outcomes.

There are no definitive treatments for delayed cerebral ischaemia, although improving cerebral perfusion by the maintenance of euvolaemia and induced hypertension is recommended where blood pressure and cardiac status permit. In vasospasm unresponsive to medical management and where focal vessel narrowing is demonstrated, emergency cerebral angiography with intra-arterial vasodilator infusion or transluminal balloon angioplasty may be considered.

Prognosis

SAH has a 40% to 60% mortality rate from the initial haemorrhage, with up to one-third of survivors having a significant neurological deficit. The most important prognostic factor is the patient's clinical condition at the time of presentation, with coma and major neurological deficits generally being associated with a poor prognosis. Survival rates have been reported at 70% for grade I, 60% for grade II, 50% for grade III, 40% for grade IV and 10% for grade V SAH.

It is worth noting, however, that survival without brain damage is possible even after respiratory arrest. Even patients who make a good recovery may suffer cognitive and psychosocial dysfunction.

Aneurysm screening in patients who have survived aneurysmal SAH is advocated, as these patients are at increased risk of new or recurrent aneurysmal bleeds.

Incidental unruptured aneurysms

If an unruptured aneurysm is found incidentally, it raises the dilemma of the risk-benefit rationale between intervention and conservative management. Factors taken into account include the patient's age, aneurysmal size and location, gender, country, co-morbidity and family history. Such patients should be referred to a neurosurgical service for advice and counseling.

Conclusion

Clinical suspicion of the diagnosis of SAH gained from a history of sudden, severe or atypical headache demands a full investigation, including a CT scan of the brain and, if necessary, lumbar puncture. Once SAH has been diagnosed, urgent neurosurgical referral and management are required.

CONTROVERSIES

- The timing of lumbar puncture (LP) following a negative CT scan for SAH.
- Non-contrast CT without LP within first 6 hours of headache and CT/CTA as diagnostic strategies for SAH.
- Vascular imaging for patients with a negative CT scan and negative CSF is indicated in those with ambiguous test results, those at high risk for SAH and patients presenting more than 2 weeks after the event.
- Prophylactic anticonvulsant therapy for patients with SAH.
- Follow-up for patients after coiling.

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Full references are available at <http://expertconsult.inkling.com>

8.4 Altered conscious state

Ruth Hew

ESSENTIALS

- For clinical purposes, the ability of the individual to respond appropriately to environmental stimuli provides a quantifiable definition of consciousness.
- The causes of altered conscious state can be divided pathophysiologically into structural and metabolic insults.
- A thorough history and examination is the key to guiding investigation choice and identifying the cause of the primary insult. Management is directed towards resuscitation, specific correction of the primary pathology and minimization of secondary injury.
- Bedside blood glucose measurement is essential and may be lifesaving.

Introduction

Consciousness is variously termed *lucidity*, *orientation*, *awakeness* and *mentation* in the context of emergency department (ED) patients. None of these terms comprehensively defines consciousness. The Glasgow Coma Scale (GCS) (Box 8.4.1), developed for head-injured patients in a time when computed tomography (CT) scanning was unavailable, is routinely used but not specifically suited to measuring conscious state. Ultimately, consciousness is an amalgam of alertness, orientation and clarity of cognition. Of

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8.4 ALTERED CONSCIOUS STATE

Box 8.4.1 The Glasgow Coma Scale

The GCS scores range between 3 and 15, 3 being the worst and 15 the best. This scale is composed of three parameters: best eye response, best verbal response, best motor response, as given below:

Best eye response (score out of 4)
1—No eye opening
2—Eye opening to pain
3—Eye opening to verbal command
4—Eyes open spontaneously
Best verbal response (score out of 5)
1—No verbal response
2—Incomprehensible sounds
3—Inappropriate words
4—Confused
5—Orientated
Best motor response (score out of 6)
1—No motor response
2—Extension to pain
3—Flexion to pain
4—Withdrawal from pain
5—Localizing pain
6—Obey commands

note, isolated absence or derangement of cognition and mentation (e.g. caused by dementia or psychiatric illness or both, considered elsewhere) does not result in the clinical entity of altered conscious state. In the same way, simple lack of orientation does not constitute a clinical alteration in conscious state.

In the clinical context, an alteration in conscious state requires a drop in alertness and 'awakeness'. This drop may result in a corresponding loss of orientation and/or a clouding of cognition, thereby altering a patient's response to environmental stimuli or provocation. The reverse, an increase in alertness, could also be considered an alteration in conscious state but, in practice, is most often due to pharmacological agents or a mood-elevating psychiatric illness, both of which are beyond the scope of the present discussion.

Pathophysiology

The level of consciousness describes the rousability of the individual, whereas the content of consciousness may be assessed in terms of the appropriateness of the individual's response. Broadly speaking, the first is a brain stem function and the second is an attribute of the forebrain.

The physical portions of the brain involved in consciousness consist of the ascending arousal system, which begins with monoaminergic cell groups in the brain stem and culminates in extensive diffuse cortical projections throughout the cerebrum. En route there is input and modulation from both thalamic and hypothalamic nuclei as well as basal forebrain cell groups.

Box 8.4.2 Causes of alteration in conscious state

Structural Insults

Supratentorial

Haematoma
 epidural
 subdural
Cerebral tumour
Cerebral aneurysm
Haemorrhagic CVA

Infratentorial

Cerebellar AVM
Pontine haemorrhage
Brain stem tumour

Metabolic Insults

Loss of substrate

Hypoxia
Hypoglycaemia
Global ischaemia
Shock
 hypovolaemia
 cardiogenic
Focal ischaemia
TIA/CVA
vasculitis

Derangement of Normal Physiology

Hypo- or hypernatraemia
Hyperglycaemia/hyperosmolarity
Hypercalcaemia

Hypermagnesaemia

Addisonian crisis

Seizures
 status epilepticus
 post-ictal

Post concussive state
Hypo- or hyperthyroidism
Co-factor deficiency
Metastatic malignancy

Toxins

Drugs
 alcohol
 illicit
 prescription
Endotoxins
 subarachnoid blood
 liver failure
 renal failure
Sepsis
 systemic
Focal
 meningitis
 encephalitis
Environmental
 hypothermia/heat exhaustion
 altitude illness/decompression
 envenomations

AVM, Arteriovenous malformation; CVA, cerebrovascular accident; TIA, transient ischaemic attack.

Integration of the brain stem and the forebrain is illustrated by individuals who have an isolated pontine injury. They remain aware, but the intact forebrain is unable to interact with the external world, hence the aptly named 'locked-in syndrome'. At the other end of the spectrum are individuals with unresponsive wakefulness syndrome (persistent vegetative state) who, in spite of extensive forebrain impairment, appear awake but totally lack the content of consciousness. These clinical extremes emphasize the important role of the brain stem in modulating motor and sensory systems through its descending pathways and regulating the wakefulness of the forebrain through its ascending pathways.

Differential diagnosis

Given the pathophysiology, the causes of an altered conscious state are myriad and include any cause of insult or injury either directly or indirectly to the brain (Box 8.4.2). Direct injury resulting in structural insults may be traumatic or non-traumatic (e.g. subdural haemorrhage, stroke). Indirect injury may encompass any change in the metabolic and chemical milieu of the brain, resulting in a depression of neuronal function (e.g. sepsis, hyper- or hypoglycaemia, drug ingestion).

Structural insults, commonly focal intracranial lesions that exert direct or indirect pressure on the brain stem and the more caudal portions of the ascending arousal system, tend to produce lateralizing neurological signs that help to pinpoint the level of the lesion. As there is little space in and around the brain stem, any extrinsic or intrinsic compression will rapidly progress through coma to death unless the pressure on the brain stem is relieved surgically or pharmacologically.

Metabolic insults, commonly due to systemic pathology that affects primarily the forebrain (although direct depression of the brain stem may also occur) seldom result in lateralizing signs. The appropriate treatment is correction of the underlying metabolic impairment. Naturally, as in all clinical practice, there are no absolute distinctions. Uncorrected, any of the metabolic causes can eventually cause cerebral oedema and herniation, leading thence to brain stem compression with lateralizing signs, coma and death.

Clinical assessment

In approaching a patient with an altered conscious state, the initial imperatives are to ensure the safety of the airway, breathing and

8.4 ALTERED CONSCIOUS STATE

circulation and to determine the cause for the alteration with a view to correcting the rapidly reversible causes and offering supportive care while working through the remainder. To this end, assessment and management must proceed concurrently. As in other time-critical situations, the primary and secondary survey approach is useful, seeking to identify and correct the primary insult whilst preventing or minimizing secondary injury, such as hypoxia, acidosis and raised intracranial pressure.

Primary survey and resuscitation

Immediate, easily reversible causes that can be identified and corrected include hypoxia and hypoglycaemia. These should be prioritized.

Thereafter an assessment of the airway, breathing and circulation of the patient is urgently required to ensure that lifesaving measures, such as airway and ventilation support, can be instituted. Initially, supplemental oxygen and non-invasive monitoring should be applied and attention paid to the absolute value and trends in the GCS score and vital signs. Normotension should be the goal of blood pressure monitoring, and this may require inotropic or antihypertensive support.

Early endotracheal intubation may be required if the GCS score is less than 8 or the patient's ventilatory effort is inadequate. Mechanical ventilation to maintain normocapnia, a pCO_2 of 35 to 40 mm Hg may assist in correcting underlying acidosis and reducing intracranial pressure; over-correction may be detrimental. Accurate end-tidal CO_2 monitoring correlated with arterial pCO_2 is required. In the setting of trauma, spinal precautions should be maintained until any possibility of trauma is excluded or clearance of the spine can be obtained.

In certain patient populations, pinpoint pupils and a depressed respiratory response may suggest a diagnosis of opiate toxicity and the administration of naloxone as a diagnostic and therapeutic tool. Often this has already been assayed in the prehospital arena, where intranasal naloxone has significantly reduced the risk of needlestick injuries. Although the adverse reactions to naloxone in initial doses is small, the greater risk is in the unmasking of the proconvulsant or proarrhythmic effects of other co-ingestants. Thus naloxone should not be given unless clinically indicated. There is also the potential of introducing diagnostic bias, as a percentage of non-opioid ingestants also appear to respond clinically to naloxone.

Secondary survey

Following initial assessment and resuscitation, it is important to complete the assessment by obtaining a full history, conducting a full examination and performing adjunctive investigations.

This will help to identify the cause of the condition and to plan further management.

History

This is often difficult with an obtunded or confused patient and may have to rely heavily on ancillary sources, such as first responders, caregivers, primary-care physicians, medical records and patient alert identification.

It is crucial to establish the events leading up to the presentation with specific questioning about prodromal events (e.g. ingestions; intravenous drug usage; trauma; underlying illness, particularly infective prodromes; medications, allergies), associated seizures and abnormal movements. For example, a sudden-onset headache may signal subarachnoid haemorrhage and a history of head injury with loss of consciousness would increase the likelihood of an extra-axial intracranial collection. Patients on anticoagulants also have an increased risk of intracranial haemorrhage with minimal trauma. Patients with a history of hepatic failure may require specific treatment for hepatic encephalopathy. The recent delineation of the complex symptomatology of anti-N-methyl-D-aspartate (NMDA) receptor encephalitis highlights the importance of a detailed history and examination.

In the elderly, dementia, itself a progressive illness, may be exacerbated by delirium caused by an acute illness. Then only a careful corroborated history from caregivers and the passage of time will allow the two to be distinguished. Often the most helpful portion of the history lies in ascertaining the patient's usual pattern of behaviour and the degree and time course of any changes that have occurred. In these patients, it is important to remember that dementia as a cause of altered conscious state is a diagnosis of exclusion.

Examination

A general physical examination, bearing in mind the various differential diagnoses, is very important. In the absence of adequate history, a thorough physical examination may offer the only pointers to initial treatment. Vital signs (e.g. tachycardia, hypotension, temperature) may suggest sepsis or other causes of shock. If infection is suspected, a search for possible sources should be pursued, the common culprits being chest and urine; but more occult infections such as endocarditis, meningitis and encephalitis should not be overlooked. As a rule, in the presence of sepsis, presumptive antibiotic administration should not be delayed for the sake of identifying a specific infective source. A keen sense of smell might detect fetor hepaticus or the sweet breath of ketosis. A bitter-almond scent is pathognomonic of cyanide poisoning. Of note, alteration of consciousness can be attributed to alcoholic

intoxication only by the process of exclusion. Thus the characteristic odour of alcoholic liquor is indicative but cannot be presumed to be diagnostic. A bedside blood glucose determination is mandatory, as deficits are easily correctable.

Neurological examination must be as comprehensive as possible. There are several obstacles to this. Initial resuscitation measures, such as endotracheal intubation, will reduce the ability of the patient to cooperate with the examination, and language difficulties will be accentuated, as the neurological examination is strongly language orientated. Thus patients who do not share a common language with clinicians and those with dysphasia may be disadvantaged. Also, sensory modalities are difficult to assess in patients with impaired mentation, although these deficits are often paralleled by deficits in the motor system.

The aim of the neurological examination is first to differentiate structural and non-structural causes; second, to identify groups of signs that may indicate specific diagnoses, such as meningitis; and finally, to pinpoint the location of any structural lesion. Therefore emphasis must be placed on signs of trauma, tone, reflexes, pupillary responses and eye signs as well as serial calculation of the GCS score. Circumstances permitting, as much as possible of the neurological examination should be performed before the patient receives neuromuscular paralysing agents.

Signs of trauma must be documented and spinal precautions maintained as indicated. Palpation of the soft tissues and bones of the skull may detect deformity or bruising, and a haemotympanum may herald a fracture of the base of the skull.

Hypotonia is common in acute neurological deficits. Specific examination of anal sphincter tone will uncover spinal cord compromise and is crucial in trauma patients who have a depressed level of consciousness. An upgoing Babinski response is indicative of pyramidal pathology, and asymmetry of the peripheral limb reflexes may help to localize a unilateral lesion. Heightened tone in the neck muscles may indicate meningitis or subarachnoid haemorrhage.

Pupillary responses and eye signs may be useful to differentiate metabolic and structural insults and, more importantly, to detect incipient uncal herniation. Intact oculocephalic reflexes and preservation of the 'doll's eyes' response indicates an intact medial longitudinal fasciculus and, by default, an intact brain stem, suggesting a metabolic cause for coma. Four pairs of nuclei spread between the midbrain and the pons govern ocular movements. Patterns of their dysfunction can be used to pinpoint the site of a brain stem lesion (Table 8.4.1). Likewise, specific testing of the oculovestibular reflex and the cranial

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Table 8.4.1 Ocular responses to cold caloric testing of the oculovestibular reflex

Response	Cerebrum	Medial longitudinal fasciculus	Brain stem
Bilateral nystagmus	Intact	Intact	Intact
Bilateral conjugate deviation towards the stimulus	Metabolic dysfunction	Intact	Intact
No response			Structural or metabolic dysfunction
Ipsilateral dysconjugate deviation			Structural dysfunction

Table 8.4.2 Patterns of dysfunction in various parameters determined by the site of the structural or metabolic insult

	Respiratory pattern	Motor response	Pupillary light response	Eye movements
Forebrain	Cheyne-Stokes waxing and waning	Localizing to pain	Symmetrical, small, reactive Prefrontal • symmetrical, large, fixed	
Midbrain	Hyperventilation	Decorticate	Fixed	Upper midbrain CN III palsy Lower midbrain • CN IV deficit • Loss of ipsilateral adduction
Pons	Apnoeas • Halts briefly in full inspiration	Decerebrate	Symmetrical, pinpoint, reactive Uncal—ipsilateral, fixed, dilated	CN VI deficit; loss of ipsilateral abduction
Medulla	Ataxic irregular rate and uneven depth Apnoeic Bilateral ventrolateral medulla lesions			

nerve examination can be used to locate a brain stem lesion precisely, but this is of limited use in the emergency setting except as a predictor of herniation ([Tables 8.4.1 and 8.4.2](#)). However, with increasing access to CT scanning, the most commonly utilized eye sign is the unilateral or bilateral fixed or dilated pupil, potential signs of early or late herniation and incipient brain and metabolic death.

More generally, skin examination may reveal needle tracks suggestive of drug use, envenomation bite marks or a meningococcal rash. Mucosal changes, such as cyanosis or the cherry-red glow of carbon monoxide poisoning, can be diagnostic. Cardiac monitoring and cardiovascular examination should identify rhythm disturbances, the murmurs of endocarditis and valvular disease or evidence of shock from myocardial ischaemia or infarction. Respiratory patterns may aid in identifying the site of the lesion (see [Table 8.4.2](#)). Abdominal examination may detect organomegaly, ascites, bruits or pulsatile masses.

Toxidromes (e.g. anticholinergic or serotonergic) should be sought, as these are not uncommon causes of alterations in conscious state, with or without psychiatric symptoms. Further information on toxidromes can be found in the relevant chapters of this text.

A mental state examination may also serve to differentiate between psychiatric and organic disease, stable dementia and acute delirium.

Clinical investigations

Given the breadth of differential diagnoses, clinical investigations must be guided by the preceding history and examination and their timing dictated by the resuscitation imperatives. The following is an extensive list of possible investigations, but there is no suggestion that they should all be performed in every patient with an altered conscious state without due consideration of the patient's context and condition. A comprehensive history and thorough examination are crucial to direct investigation choices.

Haematology

A full blood examination may reveal anaemia, immunocompromise, thrombocytopaenia, inflammation or infection but is rarely diagnostically specific. In the setting of trauma, a bedside haemoglobin determination can direct immediate blood-product replacement. C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are non-specific acute-phase reactants and single determinants are not initially useful, although they may later be followed to monitor resolution of the illness or response to therapy. Coagulation profiles are particularly useful in haematological and liver disease or if patients are taking anticoagulants such as warfarin, usage of which should lower the threshold for radiological imaging of the brain.

Biochemistry

Serum electrolyte levels aid in the differentiation of the various hypo- and hyper-elemental causes of coma. Electrolyte imbalances may also be secondary to the causative insult and may not need specific correction. In hypotensive patients, a high to normal sodium and low potassium may suggest primary or secondary Addisonian crisis.

Cardiac markers as well as liver, renal and thyroid function tests may confirm focal organ dysfunction. The last may not always be immediately available, but hypothyroidism should be considered in the hypothermic patient and hyperthyroidism in the presence of tremor and tachyarrhythmias.

Serum glucose provides confirmation of bedside testing. Serum lactate determinations may reveal a metabolic acidosis and reflect the degree of tissue hypoxia; this, again, may be primary or secondary. Creatinine kinase and myoglobinuria are useful to determine the presence and extent of rhabdomyolysis and to predict the likelihood that the patient will require dialysis. Serum and urine osmolarity may be useful in toxic ingestions, such as ethylene glycol, and in other hyperosmolar states.

Blood gas analysis may give important information regarding acid-base balance, a useful marker of severity of disease; along with the anion gap and the serum electrolytes, it can help to distinguish between the various types and causes of acidosis and alkalosis. Knowledge of the partial pressures of oxygen and carbon dioxide is vital to resuscitative efforts.

Microbiology

Sepsis is a major metabolic cause of alteration in conscious state and may present with no localizing symptoms or signs, especially in the elderly. In this case, blood cultures—preferably multiple sets obtained before antibiotic therapy—may be the only means of isolating the causative organism. Naturally, system-specific specimens—such

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as sputum, urine and cerebrospinal fluid—should be collected when clinically indicated. A bedside dipstick of the urine sample can provide valuable information to guide initial treatment. Although as a rule specimens should be obtained prior to therapy, the administration of antibiotics or antiviral agents in suspected meningitis or encephalitis should not be delayed while a lumbar puncture (LP)/CT scan is performed.

Specific laboratory testing

Based on information from the history and examination, specific drug assays and urine screens may be indicated. These may include over-the-counter or prescribed medications (e.g. paracetamol, antiepileptics, lithium or theophylline) or drugs of addiction (e.g. amphetamine or opiates). Routine urine drug screens are of very limited overall value and of no help to emergency management.

Venom detection kits can be used in specific clinical situations, and screening for systemic envenomation should include coagulation profiles and creatinine kinase.

Imaging

Intracranial imaging is best achieved with a plain CT of the head, which, if normal and concern regarding intracranial pathology persists, may be followed by a contrast-enhanced scan or magnetic resonance imaging (MRI). The latter has a higher sensitivity for encephalitis and cerebral vasculitis, although it may not always be easily accessible from the ED. Also, the technical constraints of MRI require a 'stable' patient. Emergency CT angiography has a role in the delineation of cerebral aneurysms, and interventional angiography can provide therapeutic options, particularly in a patient who is progressing towards herniation. A normal CT scan does not completely exclude treatable intracranial infection or subarachnoid haemorrhage. Therefore, depending on the patient's conscious state and the level of clinical suspicion, an LP may further assist with diagnosis. However, it must be emphasized that in suspected intracranial infection, an obtunded patient should be treated empirically with appropriate antiviral agents and antibiotics and the LP deferred till the risk of herniation is minimized.

A chest x-ray may reveal primary infection or malignancy. In a patient with an altered conscious state and any suspicion of head trauma, imaging of the cervical spine must be considered and spinal precautions maintained until resuscitation

imperative are satisfied. Imaging of the rest of the spine and other trauma imaging should be guided by clinical assessment.

Other tests

The 12-lead ECG can highlight rate and rhythm disturbances. Specific changes—such as the U wave of hypokalaemia, the J wave of hypothermia and focal infarction and ischaemic patterns—serve to confirm and offer pointers to the cause of the conscious state alteration. It is worth noting that intracranial bleeding, such as subarachnoid haemorrhage, can be associated with an ischaemic-looking ECG. Care is required in cases of depressed level of consciousness with ECG changes, as the use of thrombolysis or anticoagulation based on the ECG in the presence of intracranial bleeding may well be fatal.

Treatment

Management, by necessity, is governed by assessment findings, projected differential diagnoses and the patient's response to initial management. The algorithm in Fig. 8.4.1 is aimed at correcting immediate life-threatening pathology and then identifying and treating reversible structural and metabolic causes. Treatment of specific causes is addressed elsewhere in this text.

In the Australian and New Zealand context, the common causes of alteration in conscious state include infection and sepsis, intracranial pathology, metabolic derangement (e.g. hypo-/hyperglycaemia, hyponatraemia and complications of drugs including prescription medication).

General measures

The priorities of ED management include avoiding of hypoxia, hypotension, hyperthermia and hypoglycaemia; maintaining normovolaemia and cerebral and renal perfusion; and minimizing any increase in intracranial pressure.

To optimize haemodynamics and ventilation, the monitoring of arterial blood pressure and central venous pressure is often required, particularly if the patient is intubated or on inotropic support. The choice of inotropes should be dictated by the underlying pathology. Strict attention to fluid replacement and the need to monitor end-organ perfusion necessitate a urinary catheter. This can also be used to maintain normothermia.

With regard to drugs required to manage the airway and ventilation, propofol is a powerful, fast-acting, short-duration sedative that provides

potentially neuroprotective effects through decreases in peripheral vascular tension. However, reviews of multiple small trials and datasets do not suggest any overall long-term mortality benefits of propofol over the opiate class in the management of sedation and ventilation of the traumatic brain-injured patient. It is important to provide analgesia and sedation, as their absence will result in physiological stimulation and increase intracranial pressure. Optimization of ventilation is useful to reduce hypoxia; neuromuscular paralytic agents may assist to this end.

Management of intracranial pressure

There are no class I studies comparing the efficacy of either mannitol (0.5 g/kg) or hypertonic saline (5 mL/kg of 3% saline) with placebo for intracranial pressure reduction. Osmotic diuretics for the reduction of intracranial pressure should be used only in consultation with the receiving neurosurgical team due to their potential for additional haemodynamic compromise and secondary neurological embarrassment.

Disposition

Patients with continuing altered consciousness should be admitted to a hospital with the range of services and clinical disciplines to manage the primary diagnosis. This may require stabilization prior to transfer and transport, sometimes over long distances. The exigencies of transfer may also dictate some of the initial management choices. The level of care required will depend on the state of the patient on presentation and his or her subsequent response to treatment. Patient wishes, premorbid status and prognosis may also temper treatment choices and pathways.

Prognosis

Discussion of prognosis is difficult, as it depends on the cause and patient-specific factors. Effective cerebral resuscitation with optimal oxygenation and minimization of intracerebral hypercarbia and acidosis as well as the maintenance of other end-organ perfusion and metabolic equilibrium will promote the best recovery potential while addressing the underlying disease process. Prognosis is naturally dependent on the degree of irreversible cellular damage and the ability to correct the primary insult while minimizing secondary brain injury.

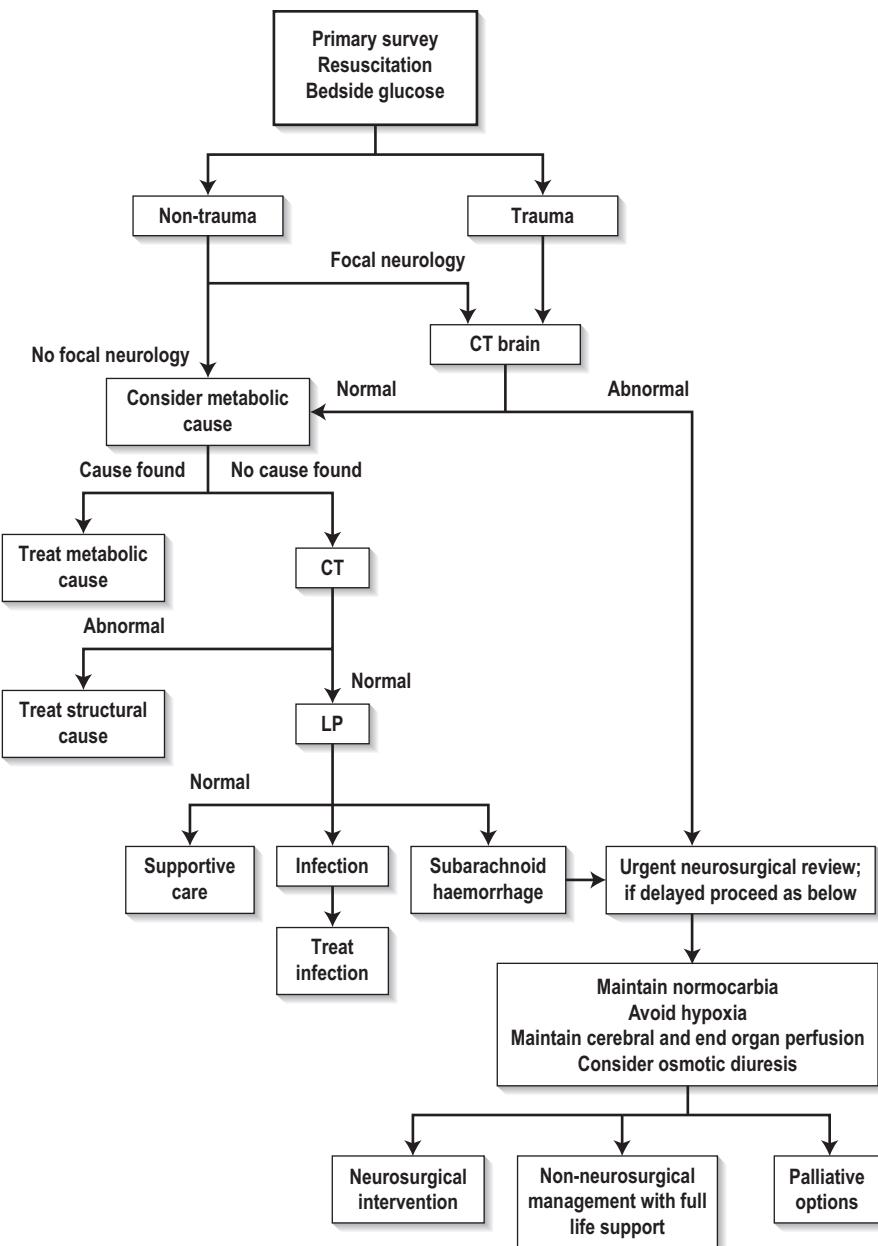


FIG. 8.4.1 Altered conscious state: treatment algorithm.

CONTROVERSIES

- The role and choice of osmotic diuretics in the management of acute elevations in intracranial pressure
- The interplay between patient and family wishes, premorbid status, prognosis and medical futility in the decision-making process determining management pathways and disposition, particularly given the uncertainties of diagnosis and prognosis early on in the ED stay

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8.5 SEIZURES

8.5 Seizures

Garry Wilkes

ESSENTIALS

- 1** Approximately 9% of the population will have at least one seizure in their lifetimes but only 1% to 3% will develop epilepsy.
- 2** The management of an acute episode is directed at rapid control of seizures, identification of precipitating factors and prevention/correction of complications.
- 3** Benzodiazepines and phenytoin are the principal anticonvulsant agents for acute seizures.
- 4** Management of drug-related seizures (including those related to alcohol) includes measures to reduce drug absorption and enhance elimination. Specific therapy is available for only a few agents. Phenytoin is usually ineffective in the management of alcohol and drug-related seizures.
- 5** Persistent confusion should not be assumed to be due to a post-ictal state until other causes have been excluded.
- 6** Investigation of first seizures should be directed by history and clinical findings. Routine laboratory and radiological investigations are not warranted for uncomplicated first seizures with full recovery.
- 7** It is important to distinguish pseudoseizures from neurogenic seizures in order to prevent inadvertent harm to patients and allow appropriate psychotherapeutic treatment.
- 8** Status epilepticus and eclampsia are severe life threats. Management plans for these conditions should be developed in advance.
- 9** Severe head injuries are associated with an increased incidence of post-traumatic epilepsy, half of which instances will be manifest in the first year. Phenytoin is effective as prophylaxis for the first week only.
- 10** Patients with epilepsy should be encouraged to have ongoing care.

Introduction

The terms 'seizure', 'convulsion' and 'fit' are often used both interchangeably and incorrectly. A seizure is an episode of abnormal neurological function caused by an abnormal electrical discharge of brain neurons. The seizure is also referred to as an ictus or ictal period. A convulsion is an episode of excessive and abnormal motor activity. Seizures can occur without convulsions and convulsions can be caused by other conditions. The term 'fit' is best avoided in medical terminology, but it is a useful term for non-medical personnel.

Epidemiology

Seizures are common. It has been estimated that 9% of the population will have at least one seizure in their lifetimes and 1% to 3% of the population will develop epilepsy. A single seizure may be a reaction to an underlying disorder, part of an established epileptic disorder or an isolated event with no associated pathology. The challenge is rapidly to identify and treat life-threatening conditions as well as to identify

benign conditions that require no further investigation or treatment.

The diagnosis of epilepsy requires at least two unprovoked seizures more than 24 hours apart or a single seizure with a known predisposing cause (e.g. central nervous system [CNS] structural abnormality or interictal electroencephalographic [EEG] changes). An episode of status epilepticus is considered a single seizure. Childhood febrile and neonatal seizures are usually excluded from this definition.

Classification (see video Types of seizures <https://www.youtube.com/watch?v=jrYVudPCYog>)

Epileptic seizures can be classified into focal-onset and generalized types. Focal-onset seizures are further classified into simple focal (preserved consciousness) and complex focal seizures. Either may secondarily become generalized.

Generalized seizures can be divided into convulsive and non-convulsive types. Convulsive seizures are generalized tonic-clonic (grand mal) seizures. Non-convulsive generalized seizures include absence seizures (previously termed *petit mal*), myoclonic, tonic and atonic

('drop attack') seizures. Epilepsy and epileptic syndromes are also classified as focal or generalized. Each disorder can be further classified according to its relationship to aetiological or predisposing factors. Seizures can also be classified as provoked (acute symptomatic) or unprovoked ('unknown-onset'). The terms 'idiopathic' and 'cryptogenic' from previous classifications are discouraged.

Different seizure types are associated with differing aetiological and prognostic factors. A number of epileptic seizure classifications are supported by different bodies. The details of the classification systems are not as important in emergency medicine as the concept of recognizing the different seizure types and being aware of the accepted terminology (as outlined earlier) when cases are being discussed and referred.

Management principles

Given the high frequency of this condition in emergency departments (EDs), it is important to have an evidenced-based management strategy formulated in advance. The main management concepts are as follows:

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- Altered mental state should be thoroughly assessed and not assumed to be due to a post-ictal state.
- Patients with known epilepsy who have recovered completely from a typical seizure require little further investigation. If they remain obtunded or have atypical features, they must be fully evaluated (e.g. through biochemical analysis, a computed tomography [CT] scan, etc.).
- Patients with epilepsy should be encouraged to seek continuing care.
- Patients at risk for recurrent seizures should be advised about situations of increased personal risk, such as driving, operating power machinery or swimming alone.

Differential diagnosis

Various conditions may be confused with epileptic seizures. Syncope is accompanied by some myoclonic activity in 90% of cases (see video Myoclonic activity during syncope https://www.youtube.com/watch?v=DOHGxoiS_Dk). Migraine, transient ischaemic attacks, hyperventilation episodes and vertigo are all important conditions to consider in the differential diagnosis. Pseudoseizures are discussed further on.

First seizures

A generalized convulsion is a dramatic event. Patients and those accompanying them will often be frightened, anxious and concerned, not only for the acute event but for what it may signify. A diagnosis of epilepsy may profoundly influence occupation, social activities, ability to drive a car and long-term health. It is therefore vital that the diagnosis be correct and explained fully to the patient and his or her relatives.

Clinical features

The first and most important task is to determine whether a seizure has occurred. As the majority have ceased at the time of presentation, the diagnosis is made primarily on history. Patients will not remember seizures other than simple partial seizures, and the reports of witnesses may be unreliable or inconsistent. With the exception of partial seizures, generalized seizures are not accompanied by an aura. Most seizures last less than 2 minutes, are associated with impaired consciousness, loss of memory for the event, purposeless movements and a period of post-ictal confusion. Although witnesses may grossly overestimate the duration, prolonged seizures, those occurring in association with a strong emotional event and those with full recall of events should be regarded with suspicion. Similarly, motor activity that is co-ordinated and not bilateral (such as side-to-side head movements,

pelvic thrusting, directed violence and movement that changes in response to external cues) are less likely to be true seizures.

ED assessment is aimed at identifying associated conditions and treatable causes of seizures. The aetiology of seizures can be classified into five groups on the following basis:

- Acute symptomatic: occurring in association with a known CNS insult. Causes of this large, important group are listed in **Box 8.5.1**.
- Remote symptomatic: occurring without provocation in a patient with a previous history (>1 week prior) of CNS insult known to be associated with an increased risk of seizures (e.g. encephalopathy, meningitis, head trauma or stroke).
- Progressive encephalopathy: occurring in association with a progressive neurological disease (e.g. neurodegenerative diseases, neurocutaneous syndromes and malignancies not in remission).
- Febrile: patients whose sole provocation is fever. This is almost exclusively confined to children and therefore is beyond the scope of this book.
- Unknown onset (previously 'idiopathic' or 'cryptogenic'): patients without an identified precipitant. This is probably the most common group; however, this classification is by exclusion of the other causes.

A careful history is needed to decide whether this is part of an ongoing process or an isolated event. Patients may not recall previous events, may not recognize their significance or may even avoid reporting previous episodes for fear of being labelled 'epileptic', with the associated consequences. Particular attention should be paid to any history of unexplained injuries, especially when they occur during blackouts or during sleep. A history of childhood seizures, isolated myoclonic jerks and a positive family history increases the likelihood of epilepsy.

A full physical and neurological examination is mandatory. Evidence of alcohol and drug ingestion and head trauma is particularly important. A comprehensive medication history will include agents known to reduce seizure threshold in susceptible individuals (e.g. tramadol and selective serotonin reuptake inhibitors). A careful mental state examination in seemingly alert patients may reveal evidence of a resolving post-ictal state or underlying encephalopathy. Patients not fully alert should never be assumed simply to be in a post-ictal state until other causes are excluded. Evidence of underlying causes includes fever, nuchal rigidity (meningitis), cardiac murmurs (endocarditis), needle tracks, evidence of chronic liver disease, dysmorphic features and marks such as café-au-lait spots (neurofibromatosis). Complications—such as tongue biting, broken

Box 8.5.1 Acute symptomatic causes of seizures

Hypoxia

Hypoglycaemia

Head trauma

Meningitis and encephalitis, including HIV disease

Metabolic, including hyponatraemia, hypocalcaemia, hyperthyroidism, uraemia and eclampsia

Drug overdose, including alcohol, antidepressants, theophylline, cocaine, amphetamine and isoniazid

Drug withdrawal, including alcohol, benzodiazepines, narcotics, cocaine and anticonvulsants

Cerebral tumour or stroke

teeth and peripheral injuries—are not uncommon in generalized seizures. Stress fractures can occur, particularly in the elderly. Posterior dislocation of the shoulder is uncommon but significant and easily overlooked.

Clinical investigations

Although it is common practice to order a variety of tests following an uncomplicated seizure, these are rarely of benefit in the fully recovered patient. Elevated neutrophil counts in blood and cerebrospinal fluid (CSF) may be seen as a result of a generalized seizure in the absence of an infectious disorder. Electrolyte abnormalities may cause seizures but are unlikely to be the cause if the patient has recovered. Serum prolactin level 20 to 60 minutes post-seizure may be helpful if the diagnosis is in doubt. An abnormal neurological examination and features of meningitis, encephalitis or subarachnoid haemorrhage are indications for cranial CT scan and lumbar puncture.

Imaging

There are no clear guidelines to the routine need for or urgency of neuroimaging following a single uncomplicated seizure. Patients with focal neurological signs, those who do not recover to a normal examination and those with a history of head trauma or intracranial pathology should all undergo cranial CT as soon as possible. The dilemma arises in patients with complete recovery and no focal signs. The incidence of abnormalities on CT in this group of patients is less than 1%. The decision as to whether and when to scan patients in this group will be determined largely by local factors. Magnetic resonance imaging (MRI) is more sensitive than CT for infarcts, tumours, inflammatory lesions and vascular lesions, but its availability may be limited.

Electroencephalography

EEG at the time of a seizure will make a definitive diagnosis. It is not usually performed in the acute setting except when non-convulsive activity is suspected. Typically an EEG is obtained electively

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on an outpatient basis, when it may still indicate an underlying focus of activity and may be able to detect specific conditions.

Treatment

Once a diagnosis of first seizure has been made and intercurrent conditions have been excluded or treated, the patient may be discharged home. It must be stressed to the patient that a diagnosis of epilepsy has not been made but is being considered. When the suspicion is reasonable, the patient should be given the same precautionary advice as epileptic patients with regard to driving and other activities that may place them or others at risk.

The planning of investigation and follow-up for patients suspected of having a first seizure is best done in conjunction with a neurology service to make sure that appropriate investigations are completed in a timely fashion. Generally an inter-ictal EEG and contrast CT and/or MRI are completed prior to review.

Status epilepticus

Epidemiology and pathophysiology

Status epilepticus may be defined as 'two or more seizures without full recovery of consciousness between seizures, or recurrent epileptic seizures for more than 30 minutes'.

Status epilepticus accounts for 1% to 8% of all hospital admissions for epilepsy, 3.5% of admissions to neurological intensive care and 0.13% of all visits to a university hospital ED. It is more common at the extremes of age, with over 50% of all cases occurring in children and a disproportionately high incidence in those over 60 years of age. Status epilepticus is also more frequent in those with intellectual disability or with structural cerebral pathology, especially of the frontal lobes. Four to 16% of adults and 10% to 25% of children with known epilepsy will have at least one episode of status epilepticus during their lives; however, status epilepticus occurs most commonly in patients with no previous history of epilepsy.

Many compensatory physiological changes accompany seizures. As duration increases, these mechanisms begin to fail, with an increased risk of permanent damage. Brain damage resulting from prolonged status epilepticus is believed to be caused by excitatory amino acid neurotransmitters, such as glutamate and aspartate, leading to the influx of calcium into neuronal cytoplasm and an osmolytic cell destruction. Continuing seizure activity itself contributes to neuronal damage, which is further exacerbated by hypoxia, hypoglycaemia, lactic acidosis and hyperpyrexia. The longer an episode of status epilepticus continues, the more refractory to treatment it becomes and the more likely it is to result in permanent neuronal damage. Mortality

increases from 2.7% with seizure duration under 1 hour to 32% with duration beyond this. Generalized convulsive status epilepticus is therefore a medical emergency.

Treatment

Treatment of status epilepticus is along the same lines as the resuscitation of all seriously ill patients. Management is in a resuscitation area with attention to the following:

- Rapid stabilization of airway, breathing and circulation
- Termination of seizure activity (clinical and electrical)
- Identification and treatment of precipitating and perpetuating factors
- Identification and treatment of complications

Each stage of resuscitation is made more difficult by the presence of active convulsions. Do not prise clenched teeth apart to insert an oral airway; a soft nasal airway will suffice. Place the patient in the left lateral position to minimize the risk of aspiration and administer oxygen if hypoxia is present or suspected. Intravenous access is important for drug treatment and fluid resuscitation but may be difficult in actively seizing patients. Although status epilepticus cannot be diagnosed until seizures have persisted for 30 minutes, patients still seizing on arrival at the ED should be treated with anticonvulsants immediately.

The principal pharmacological agents used are benzodiazepines and phenytoin. Opinions vary regarding the optimal benzodiazepine, with little clinical evidence to support any particular one. Lorazepam is preferred by most neurologists because of its prolonged CNS action (protective effect for 30 to 120 minutes). It typically takes 5 to 10 minutes to stop seizures and can cause hypotension. Midazolam is popular among emergency physicians for a variety of purposes. Being water-soluble, it is not irritating and can be administered intramuscularly with a fairly rapid onset of action (2 to 5 minutes). It has a short duration of action (another reason for its popularity in emergency medicine) and may require further intravenous doses or ongoing infusion. Diazepam has previously been popular owing to its extreme lipid solubility and rapid brain entry. It typically stops seizures rapidly (1 to 2 minutes). Preparations are, however, irritant, produce complications with intravenous extravasation and are unsuitable for intramuscular use. Diazepam can be administered rectally if necessary, and this technique can be taught to parents with high-risk children. All benzodiazepines share the disadvantages of respiratory depression, hypotension and short duration of clinical effect.

Phenytoin is usually used as a second-line agent in a dose of 15 to 20 mg/kg at a rate of no

more than 50 mg/min. Rapid administration is associated with bradycardia and hypotension. The common practice of administering 1 g is inadequate for most adults. The effect of phenytoin does not commence until 40% of the dose has been administered; for this reason, if it is to be used, it should be commenced at the same time that intravenous benzodiazepines are given. Most people on anticonvulsants who present in status epilepticus have negligible drug levels, and the side effects from a full loading dose on top of a therapeutic level are minimal. The full loading dose should therefore be given even when the patient is known to be on therapy.

The most common causes of failure to control seizures are as follows:

- Inadequate antiepileptic drug therapy
- Failure to initiate maintenance antiepileptic drug therapy
- Hypoxia, hypotension, cardiorespiratory failure, metabolic disturbance (e.g. hypoglycaemia)
- Failure to identify an underlying cause
- Failure to recognize medical complications (e.g. hyperpyrexia, hypoglycaemia)
- Misdiagnosis of pseudoseizures

Causes of failure to regain consciousness following treatment of seizures include the medical consequences of status epilepticus (hypoxia, hypoglycaemia, cerebral oedema, hypotension, hyperpyrexia), sedation from antiepileptic medication, progression of the underlying disease process, non-convulsive status epilepticus and subtle generalized status epilepticus.

When benzodiazepines and phenytoin are ineffective, expert advice should be sought. Drugs that may be used in the control of status epilepticus are summarized in Table 8.5.1. Anaesthetic agents require expert airway control and, in some cases, inotropic support. Management in an intensive care unit is mandatory.

For all patients with status epilepticus, early consultation with intensive care and neurology services is essential in planning definitive management and disposition.

Non-convulsive seizures

Not all seizures are associated with convulsive activity. Convulsive seizures are generally easy to recognize, whereas non-convulsive seizures are more subtle and often require a high index of suspicion. These types of seizure are an important cause of alterations in behaviour and conscious level and may precede or follow convulsive episodes. Seizures can involve any of the sensory modalities, vertiginous episodes, automatism, autonomic dysfunction or psychic disturbances,

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Table 8.5.1 Doses of drugs used in refractory status epilepticus

Drug	Bolus (intravenous unless stated otherwise)	Maintenance infusion
Lorazepam	0.05–0.1 mg/kg over 2–5 minutes; not to exceed 4 mg/dose; may repeat every 10–15 min	N/A
Midazolam	0.02–0.1 mg/kg 0.1–0.2 mg/kg intramuscular	0.05–0.4 mg/kg/h
Phenytoin/fosphenytoin	15–20 mg/kg at up to: Phenytoin max 50 mg/min Fosphenytoin 100–150 mg/min	N/A
Phenobarbitone	10–20 mg/kg at 60–100 mg/min	1–4 mg/kg/day
Thiopentone	5 mg/kg	1–3 mg/kg/h
Pentobarbitone	5 mg/kg at 25 mg/min	0.5–3 mg/kg/h
Propofol	2 mg/kg	5–10 mg/kg/h
Lignocaine	2 mg/kg	0.5–3 mg/kg/h

including *déjà vu* and *jamais vu* experiences. Non-convulsive seizures can easily be confused with migraine, cerebrovascular events or psychiatric conditions. The definitive diagnosis can be made only by EEG during the event.

Non-convulsive seizures may be focal or generalized. Simple and complex focal seizures account for approximately one-third of all seizures, whereas primary generalized non-convulsive seizures (absence seizures) account for 6%.

Non-convulsive status epilepticus accounts for at least 25% of all cases of status epilepticus and is diagnosed more frequently when actively considered. Absence seizures rarely result in complete unresponsiveness and patients may appear relatively normal to unfamiliar observers. Non-convulsive status epilepticus may precede or follow convulsive seizures and may easily create the perception of a cerebro-vascular or psychiatric event. The longest reported episode of absence status is 60 days and that of complex focal status 28 days.

Acute treatment of non-convulsive seizures is the same as for convulsive seizures. An estimated 50% of patients with simple focal seizures have abnormal CT scans. Long-term seizure control uses different agents from those used for convulsive seizures, highlighting the importance of involving a neurological service when follow-up is being planned.

Pseudoseizures

Pseudoseizures or psychogenic seizures are events simulating neurogenic seizures but without the accompanying abnormal neuronal activity. Differentiation from neurogenic seizures may be extremely difficult, even for experienced

neurologists. Neurogenic and psychogenic seizures may coexist, making the diagnostic dilemma even more complex. Differentiation will often require video-EEG monitoring, but this facility is not available in the ED and other methods must be used. It is important to recognize pseudoseizures so as to prevent the possible iatrogenic consequences of unnecessary treatment while at the same time not withholding treatment from patients with neurogenic seizures.

Pseudoseizures are more common in women, less common after 35 years of age and rare in patients aged over 50. They may be associated with a conversion disorder, malingering, Munchausen syndrome or Munchausen syndrome by proxy.

Pseudoseizures typically last more than 5 minutes, compared with 1 to 2 minutes for neurogenic seizures. Multiple patterns of seizures tend to occur in individual patients, and post-ictal periods are either very brief or absent. Recall of events during what appears to be a generalized convulsive seizure suggests a psychogenic seizure. Extremity movement out of phase from one side to the other and head turning from side to side typify pseudoseizures. Forward pelvic thrusting occurs in 44% of patients with pseudoseizures and is highly suggestive of the diagnosis.

Several manoeuvres are useful in identifying pseudoseizures. Characteristic are eye-opening and arm-drop tests accompanied by avoidance, eyes turning away from the moving examiner and termination of the event when the mouth and nostrils are occluded. Simple verbal suggestion and reassurance are also frequently successful.

The most definitive means of identifying pseudoseizures is by ictal EEG or video-EEG monitoring. Unfortunately this is of little value in the ED. A fall in SpO₂ on pulse oximetry and a degree of

acidemia on blood gas analysis occur during neurogenic seizures but not pseudoseizures. Serum prolactin levels rise and peak three- to fourfold 15 to 20 minutes after generalized tonic-clonic seizures and then fall, with a half-life of 22 minutes. The levels do not consistently rise with partial seizures and remain normal with pseudoseizures.

Patients with pseudoseizures usually demonstrate resistance to anticonvulsant medication and many will therefore present with therapeutic or supra-therapeutic levels. Correct diagnosis will prevent unnecessary and potentially harmful treatment. Doubtful cases should be discussed with a neurology service and arrangements made for emergency EEG.

Once the diagnosis has been confirmed, it must be presented in an open and non-threatening manner. Patients often have underlying personal and/or family problems that will have to be addressed. Psychotherapy is effective, but seizures often relapse at times of stress.

Alcohol-related seizures

Alcohol contributes to half of seizures presenting to EDs. Acute toxicity and withdrawal are both associated with an increased incidence of seizures. Alcohol intoxication and chronic alcohol abuse are also associated with increased incidences of intercurrent disease, such as trauma, coagulopathy, falls, assaults and other drug intoxication, all of which further increase the likelihood of seizures. The management of seizures presumed to be alcohol-related must include a search for associated disease and other causes.

Benzodiazepines are the principal anticonvulsant agents for acute seizures. These agents are also valuable in the treatment of withdrawal. Phenytoin is ineffective in the control of acute alcohol-related seizures or as a preventative for them.

Drug-related seizures

Seizure activity in the setting of acute drug overdose is an ominous sign associated with greatly increased mortality and morbidity. The most commonly reported occur in association with cyclic antidepressants, antihistamines, theophylline, isoniazid and illicit drugs such as cocaine and amphetamines. The diagnosis and management of these are discussed in Section 25, Toxicology Emergencies.

Some medications are also associated with lowering seizure threshold in susceptible individuals. Tramadol, in particular, has been associated with new-onset seizures at normal therapeutic doses. A complete medication history is therefore essential.

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Post-traumatic seizures

Post-traumatic epilepsy develops in 10% to 15% of those who have survived serious head injury. More than half will have their first seizure within 1 year. Risk factors are central parietal injury, dural penetration, hemiplegia, missile wounds and intracerebral haematomas. Early treatment with phenytoin for severe head injuries reduces the incidence of seizures in the first week only.

Seizures and pregnancy

Seizures can occur during pregnancy as part of an established epileptic process; they can occur as new seizures or may be induced by pregnancy. The most significant situations are eclampsia and generalized convulsive status epilepticus. At all times the management is directed at both mother and baby, with the realization that the best treatment for the baby will relate to optimal maternal care.

In individuals previously diagnosed with epilepsy, there is a 17% increased risk of seizures during pregnancy. Anticonvulsant levels are influenced by reduced protein binding, increased drug binding and reduced absorption of varying degrees. The final effect on free drug levels is unpredictable and is most variable around the time of delivery.

Isolated simple seizures place both mother and fetus at increased danger of injury but are otherwise generally well tolerated. Generalized seizures during labour cause transient foetal hypoxia and bradycardia of uncertain significance. Generalized convulsive status epilepticus is life threatening to both mother and fetus at any stage of pregnancy.

All anticonvulsants cross the placenta and are potentially teratogenic. The risk of malformation in children is increased from 3.4% in the general population to 3.7% in epileptic mothers. In general the types of malformation associated are not drug specific apart from the increased risk of neural tube defects associated with valproate and carbamazepine. Prenatal screening for such defects is advised in patients who become

pregnant while they are taking these agents. The risk from uncontrolled seizures greatly outweighs the risk from prophylactic medication in patients with good seizure control.

The management of seizures in pregnant patients is along the same lines as that for non-pregnant patients. After 20 weeks' gestation, the patient should have a wedge placed under her right hip to prevent supine hypotension; eclampsia must also be considered. Investigation will include an assessment of foetal well-being by heart rate, ultrasound and/or tocography as indicated. Management and disposition should be decided in consultation with neurology and obstetric services.

Eclampsia is the occurrence of seizures in patients with pregnancy-induced toxæmia occurring after the 20th week of pregnancy. Toxæmia consists of a triad of hypertension, oedema and proteinuria. One in 300 women with pre-eclampsia progresses to eclampsia. Seizures are typically brief and self-terminating; usually preceded by headache and visual disturbances, they tend to occur without warning. Treatment is directed at controlling the seizures and hypertension and expedient delivery of the baby. Magnesium sulphate is effective in seizure control and is associated with a better outcome for both mother and baby than standard anticonvulsant and antihypertensive therapy.

Management of status epilepticus in pregnancy includes consideration of eclampsia, positioning in the left lateral position and assessment and monitoring of foetal well-being. Urgent control of seizures is essential for both mother and baby. Phenobarbital may reduce the incidence of intraventricular haemorrhage in premature infants and should be considered in place of phenytoin in this circumstance. Early involvement of obstetric and neurology services is essential. Pre-eclampsia and eclampsia are addressed specifically in [Chapter 19.6](#).

Future directions

Non-invasive portable modalities allowing definitive, precise diagnosis of seizures in the ED will reduce the need for subsequent investigations in the

majority of patients who do not have true epilepsy and thus permit early focused therapy. Advances in pharmacotherapy and neurosurgical techniques will also improve seizure control with minimal side effects, allowing patients to resume normal activities more effectively. Advances in neurobiology—as well as in the understanding of channels, receptors and the genetic expression of proteins—will enable the correction of underlying defects, thus removing the need for anticonvulsive therapy.

CONTROVERSIES

- Whether investigations are required for patients with uncomplicated first seizures
- The place of lumbar puncture in the investigation of first seizures

Further reading

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8.6 Syncope and vertigo

Rosslyn Hing

ESSENTIALS

- 1 It is important to distinguish between syncope and true vertigo.**
- 2 The most common cause of syncope is neurally mediated syncope.**
- 3 A detailed history and physical examination are more useful than extensive investigations.**
- 4 It is essential to identify high-risk patients for the serious potential cardiac causes of syncope so that appropriate treatment can be given.**
- 5 A key diagnostic step is to determine whether a central or peripheral cause of vertigo is more likely.**
- 6 Dynamic manoeuvres may be both diagnostic and therapeutic.**

Introduction

Syncope and vertigo are relatively common symptoms. They are often described by patients using the term 'dizziness'; however, it is essential to differentiate between the two. Syncope and vertigo both represent a significant diagnostic challenge and it is important to risk stratify patients accurately to distinguish between potentially life-threatening and benign causes.

Syncope

Syncope as a presenting symptom represents about 1% to 1.5% of all emergency department (ED) attendances. It is a symptom, not a diagnosis. It is defined as a loss of consciousness induced by the temporarily insufficient flow of blood to the brain. Patients recover spontaneously, without therapeutic intervention or prolonged confusion.

There is no simple test to distinguish between the benign and potentially life-threatening causes of syncope, but a careful history, examination and bedside investigations can help to determine appropriate disposition.

The causes of syncope are summarized in Box 8.6.1. The most common cause in all age groups is neurally mediated syncope, also known as neuro-cardiogenic or vasovagal syncope. Orthostatic hypotension and cardiac causes are the next most common.

Clinical features

Patients with syncope are often completely asymptomatic by the time they arrive at hospital. A thorough history and physical examination is

the key to finding the correct cause of the syncope. The history should focus on the patient's recollection of the preceding and subsequent events, including environmental conditions, physical activity, prodromal symptoms and any intercurrent medical problems. Accounts from eyewitnesses or first responders are also vital. Medications that may impair autonomic reflexes must be scrutinized and a postural blood pressure measurement performed. Physical examination should concentrate on finding signs of structural heart disease as well as assessing any subsequent injuries.

Neurally mediated syncope causes a typical prodrome: patients complain of feeling light-headed and faint and often describe a blurring or 'tunnelling' of their vision. This may be accompanied by other vagally mediated symptoms, such as nausea or sweating. If patients are unable or unwilling to follow the body's natural instincts to lie flat, they may collapse to the ground as they lose consciousness. This reflex brings the head level with the heart, resulting in an improvement in cerebral perfusion and a return to consciousness. During this time the patient may exhibit brief myoclonic movements, which can be mistaken for seizure activity but, in contrast with true epileptic seizures, there are no prolonged post-ictal symptoms. Fatigue is common following syncope.

Orthostatic hypotension occurs when the patient moves from a lying position to a sitting or standing position. If the required autonomic changes fail to compensate adequately, even healthy individuals will experience light-headedness or a blurring of vision and possibly

loss of consciousness. The most vulnerable people are those with blunted or impaired autonomic reflexes, such as the elderly, those on certain medications (particularly vasodilators, antihypertensive agents and β -blockers) and those who are relatively volume-depleted due to heat, excessive fluid losses or inadequate oral intake.

Cardiac syncope is more likely to present with an absent or brief prodrome. Sudden unexplained loss of consciousness should raise suspicion for a cardiac arrhythmia, particularly in the high-risk patient. Both tachycardia and bradycardia can be responsible. A syncopal event while supine is of particular concern and a predictor of a cardiac cause. Syncopal events that occur during exertion should prompt a search for structural heart disease, in particular aortic stenosis.

Risk stratification

Most of the published literature on the assessment of patients presenting to EDs with syncope has focused on identifying risk factors for mortality or an adverse cardiac outcome. These assessments include a number of scores and clinical decision rules, such as the Osservatorio Epidemiologico sulla Sincope nel Lazio (OESIL) score and the San Francisco Syncope Rule (SFSR). Patients with syncope can be divided into high- and low-risk groups, as shown in Box 8.6.2. Low-risk patients can be safely discharged for outpatient follow-up, but controversy over high-risk patients remains. It is likely that there is a significant proportion of patients in the high-risk group who actually have an intermediate risk and, given further evaluation in the ED or a short-stay unit, could also be safely discharged; however, it is more difficult to identify this subset.

Differential diagnosis

Seizures are commonly listed as a cause of syncope. Although they do cause a transient loss of consciousness, the pathophysiology is very different. Post-ictal confusion often helps to differentiate the two; however, urinary incontinence may also occur in syncope. True tonic-clonic activity must be distinguished from the brief myoclonic jerks occasionally seen in syncope.

Transient ischaemic attacks (TIAs) are often cited as potential causes for syncope, but this is rare. Only TIAs involving the vertebra-basilar territory can affect the reticular activating system of the brain to cause a loss of consciousness; however, a TIA should not be named as a cause of the

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Box 8.6.1 Aetiology of syncope

Neurally mediated Cardiac

Vasovagal/neurocardiogenic
Situational: cough, micturition, defaecation
Carotid sinus syndrome
Structural valvular disease, such as aortic stenosis
Unstable angina
Myocardial infarction
Bradyarrhythmias, such as sinus node disease, atrioventricular block
Tachyarrhythmias, such as ventricular tachycardia, supraventricular tachycardia and torsades de pointes
Pacemaker/defibrillator dysfunction
Pulmonary hypertension
Pulmonary embolus
Aortic dissection

Orthostatic hypotension

Dehydration
Vasodilatation

Medication

Anti-hypertensives
β-blockers
Cardiac glycosides
Diuretics
Antiarrhythmics
Anti-parkinsonian drugs
Nitrates
Alcohol

Neurological

Vertebo-basilar transient ischaemic attack
Subclavian steal

Psychiatric

syncope unless it is associated with other brain stem signs, such as cranial nerve defects or ataxia.

Syncope may also be the presenting symptom of a potentially life-threatening condition, such as pulmonary embolus, subarachnoid haemorrhage, gastrointestinal bleed or aortic aneurysm.

Clinical investigations

The only two mandatory investigations are a 12-lead ECG and blood glucose. These should add enough information to the clinical findings to stratify the patient as at high or low risk for an adverse outcome. Research has found that a serum troponin taken at least 4 hours after a syncopal event is not a sensitive predictor of an adverse cardiac outcome.

If a pulmonary embolus, subarachnoid haemorrhage, gastrointestinal bleed or aortic aneurysm is suspected, appropriate investigations based on clinical suspicion should be initiated.

Treatment

Treatment depends on the presumptive diagnosis. Patients with neurally mediated syncope require explanation and reassurance only. After ensuring that the vital signs have returned to baseline, their blood glucose and ECG are within

Box 8.6.2 Risk stratification for an adverse outcome

High risk

Chest pain consistent with ischaemic heart disease
History of congestive cardiac failure
History of ventricular arrhythmias
Pacemaker/defibrillator dysfunction
Abnormal electrocardiogram (findings such as prolonged QTc interval, conduction abnormalities, acute ischaemia)
Exertional syncope/valvular heart disease
Age >60 years

Low risk

Age <45 years
Otherwise healthy
Normal electrocardiogram
Normal cardiovascular exam
Prodrome (consistent with neurally mediated syncope or orthostatic hypotension)

normal limits and that they have had something to eat and drink, these patients may be discharged without further investigations.

Patients with orthostatic hypotension often require intravenous fluids and an adequate oral intake to reverse their postural blood pressure changes. Any decision regarding potential changes to chronic medications should ideally include the patient's primary care/treating doctor.

Patients who are deemed at high risk for a cardiac cause need continuous cardiac monitoring for at least 24 hours and admission for further evaluation. This may include echocardiography to identify structural heart problems and to quantify an ejection fraction or electrophysiological studies.

Prognosis

Syncope in a patient with underlying heart disease implies a poor prognosis, with data suggesting that one-third will die within a year of the episode. Overall, patients with syncope on a background of congestive cardiac failure are at the highest risk for an adverse outcome. In the absence of underlying heart disease, syncope is not associated with excess mortality.

Vertigo

Vertigo is defined as a disabling sensation whereby the affected individual feels that his or her surroundings are in a state of constant movement. It has a reported 1-year incidence of 1.4%. Like syncope, it is a symptom, not a diagnosis, and has as many causes. The difficulty is that, whereas many of the causes of vertigo are benign, it can also be a symptom of a serious neurological condition, such as vertebrobasilar stroke.

Box 8.6.3 Aetiology of vertigo

Peripheral

Benign paroxysmal positional vertigo (BPPV)
Vestibular neuritis
Acute labyrinthitis
Ménière disease
Ototoxicity
Eighth-nerve lesions, such as acoustic neuromas
Cerebellopontine angle tumours
Post-traumatic vertigo

Central

Cerebellar haemorrhage and infarction
Vertebrobasilar insufficiency
Neoplasms
Multiple sclerosis
Wallenberg syndrome (lateral medullary syndrome)
Migrainous vertigo

Aetiology

The causes of vertigo may be divided into peripheral and central, as shown in Box 8.6.3.

Clinical features

It is vital to establish whether the patient is suffering true vertigo as opposed to pre-syncope, loss of consciousness or mild unsteadiness. It is also necessary to clarify whether the individual has a sense of continuous motion (vertigo) or whether he or she feels 'lightheaded' or 'dizzy'.

As previously described, vertigo may be central or peripheral in origin. Peripheral vertigo tends to be more intense and to be associated with nausea, vomiting, diaphoresis and auditory symptoms, such as tinnitus or hearing loss (although hearing loss can rarely occur with vascular insufficiency in the posterior cerebral circulation, as the auditory apparatus is supplied via the anterior inferior cerebellar artery or the posterior inferior cerebellar artery). There may also be a history of ear trauma, barotrauma, ear infection or generalized illness. The onset of the vertigo tends to be subacute, coming on over minutes to hours. Benign paroxysmal positional vertigo (BPPV) has the classic history of position-induced vertigo, lasting only seconds. Central vertigo tends to be less severe and is associated with neurological symptoms and signs (e.g. headache, weakness of the limbs, ataxia, poor coordination and dysarthria). These symptoms may be the harbinger of more serious causes, such as cerebellar lesions or demyelinating diseases (Table 8.6.1).

Physical examination concentrates on any positional factors plus a detailed search for neurological signs, in particular nystagmus. This is the main objective sign of vertigo. Any spontaneous movement of the eyes must be noted, including its direction and persistence. Peripheral vertigo tends to produce unidirectional nystagmus with

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Table 8.6.1 Clinical features of vertigo

	<i>Peripheral</i>	<i>Central</i>
Onset	Acute	Gradual
Severity	Severe	Less intense
Duration, pattern	Paroxysmal, intermittent; minutes to days	Constant; usually weeks to months
Positional	Yes	No
Associated nausea	Frequent	Infrequent
Nystagmus	Rotatory—vertical, horizontal	Vertical
Fatigue of symptoms, signs	Yes	No
Hearing loss/tinnitus	May occur	Not usually
Central nervous system symptoms, signs	No	Usually

the slow phase towards the affected side. In addition, patients with vestibular nystagmus are often able to suppress it by fixating on a stationary object.

The 'head impulse' or 'head thrust' test is a simple bedside manoeuvre that can be used to identify the affected labyrinth. With the patient fixating on the examiner's nose, the examiner holds the patient's head and performs a few high-acceleration but brief turns to either side. The patient's eyes will automatically move in the opposite direction, in order to maintain visual fixation. The test is positive when this fails to happen and, instead, the patient's eyes are seen to perform a series of catch-up movements, or 'saccades', in order to refixate on the examiner's nose. When the 'head impulse' test is positive, the lesion causing the nystagmus is extremely likely to be peripheral. The affected labyrinth is the one in the direction in which the head was moved.

The 'HINTS' examination includes the Head Impulse test, the evaluation for Nystagmus and a Test of Skew. Skew deviation is a vertical misalignment of the two eyes resulting from a central lesion. A normal head impulse test, direction-changing nystagmus or a skew deviation all suggest a central rather than a peripheral cause (<http://www.6osecondem.com/the-hints-exam/>).

Cardiovascular examination should focus on the risk factors for CNS thromboembolic events such as arrhythmias, murmurs and bruits.

Clinical investigations

Most patients who present with vertigo do not need laboratory tests apart from a blood glucose level. If there is a history of trauma or suspicion of a space-occupying lesion, a computed tomography (CT) or magnetic resonance imaging (MRI) scan of the brain is indicated. If differentiation from syncope is problematic, an ECG should also be performed to help rule out arrhythmias.

Dynamic manoeuvres can be both diagnostic and therapeutic. The Dix-Hallpike test can diagnose BPPV. It should not be performed in patients with carotid bruits and all patients must be warned that the test may provoke severe symptoms.

Initially the patient should be seated upright, close enough to the head of the bed so that when he or she is supine, the head will be able to extend back a further 30 to 45 degrees. To test the right posterior semicircular canal, the head is initially rotated 30 to 45 degrees to the right. Keeping the head in this position, the patient is quickly brought to the horizontal position with the head placed 30 to 45 degrees below the level of the bed. A positive test is indicated by rotatory nystagmus towards the affected ear. The test is then repeated on the left side.

Treatment

Treatment depends on the cause. If BPPV is suspected, the Dix-Hallpike test is performed to identify the affected ear. The Epley manoeuvre or 'canalith repositioning manoeuvre' aims to move any unwanted particles out of the semicircular canals and thus ease the symptoms for which they are responsible. The steps of this manoeuvre are as follows:

- The patient is seated as for the Dix-Hallpike test, with the head turned 45 degrees toward the affected ear.
- The patient is brought to the horizontal position with the head hyperextended 30 to 45 degrees below the bed.
- The head is gently rotated 45 degrees towards the midline.
- The head is then rotated a further 45 degrees towards the unaffected ear.
- The patient rolls onto the shoulder of the unaffected side, at the same time rotating the head a further 45 degrees.
- The patient is returned to the sitting position and the head is returned to the midline.

These movements may induce nystagmus in the same direction as that seen during the Dix-Hallpike test. Be aware that nystagmus in the opposite direction indicates an unsuccessful test. The manoeuvre may have to be repeated a few times.

Vestibular neuritis is unilateral and thought to be caused by a viral infection or inflammation. Episodes are acute in onset and may be severe, lasting for days; they are usually associated with nausea and vomiting. The sense of perpetual movement is present even with the eyes closed and is made worse by movement of the head. Symptomatic treatment—with medications such as antihistamines, antiemetics and benzodiazepines—is often all that is indicated. If nausea and vomiting are severe, intravenous fluid therapy may be needed. There are some reports of trials using steroids for vestibular neuritis, but there are conflicting results regarding both the short- and long-term outcomes.

Acute labyrinthitis may be viral or bacterial in origin. If it is viral, the course and treatment are similar to those of vestibular neuritis. Bacterial labyrinthitis may develop from an otitis media. The key feature here is severe vertigo with hearing loss. Patients are febrile and toxic and require admission for intravenous antibiotics.

Ménière disease comprises the classic triad of vertigo, sensorineural hearing loss and tinnitus. Attacks last from minutes to hours and may recur with increasing frequency as the disease progresses. It is caused by dilation of the endolymphatic system due to the excessive production of endolymph or problems with its reabsorption (endolymphatic hydrops). Medical management traditionally involves salt restriction and diuretics, although evidence is limited.

Vertebral-basilar insufficiency can produce vertigo, often accompanied by unsteadiness and visual changes. Symptoms may be provoked by head position and often include headache.

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Importantly, however, patients with cerebellar infarction occasionally present with vertigo without other symptoms or signs of neurological impairment. Treatment involves addressing cardiovascular risk factors as well administering as antiplatelet therapy.

Migrainous vertigo is an increasingly recognized condition that is incompletely understood. In the acute setting, it poses a diagnostic challenge that will often necessitate exclusion of other central causes for vertigo, such as cerebrovascular disease.

CONTROVERSIES

- Identifying and determining disposition for syncope patients who do not fall into the high- or low-risk groups
- Role of a dedicated syncope evaluation unit
- The use of corticosteroids to treat vestibular neuritis

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8.7 Weakness

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ESSENTIALS

- 1** The differential diagnosis of weakness in the emergency department (ED) is very broad. Careful history taking and examination with targeted investigations will help to identify most of the important causes.
- 2** Causes of weakness must be distinguished as neuromuscular or non-neuromuscular.
- 3** Most patients presenting to the ED with a complaint of weakness have a non-neuromuscular cause for their symptoms.
- 4** Guillain-Barré syndrome is the most common cause of acute-onset symmetrical progressive weakness in the developed world. Patients presenting with acute-onset symmetrical weakness require early assessment of airway and ventilation. Early intubation should be considered in high-risk cases. Admission to an intensive care is required for any patient with impaired ventilatory function.
- 5** Patients presenting with a multiple sclerosis relapse should usually be offered pulse steroid therapy in the form of methylprednisolone 1 g IV daily for 3 days (or equivalent oral dosage).
- 6** Supportive care is the priority in ED management in cases of weakness due to any cause.
- 7** If a neuromuscular cause is suspected, disposition decisions should be made in consultation with a neurologist.
- 8** Some patients with weakness will not be definitively diagnosed in the ED and may require referral for further investigations.

Introduction

Weakness is a subjective term that patients use to describe feelings of malaise, fatigue or frailty experienced as the result of myriad medical and psychological conditions. The *Oxford Dictionary* defines 'weak' as 'lacking the power to perform physically demanding tasks; having little physical strength or energy'.

In this chapter, we mainly consider the assessment and management of patients presenting with acute-onset, generalized, symmetrical or rapidly progressive weakness, primarily in the context of neuromuscular disease. Conditions that cause focal or unilateral weakness are not discussed in any great depth, nor is weakness related to non-neuromuscular causes. It should, however, be remembered that the latter group affects the majority of patients presenting to the emergency department (ED) complaining of weakness.

Aetiology and pathogenesis

Weakness is essentially due to a neuromuscular problem or something else. The primary goal in

ED is to determine if there is actual quantitative loss of muscle strength indicative of a neuromuscular cause or whether the weakness results from a non-neuromuscular cause. The latter cases are often the result of multiple system disorders—for example, endocrine, cardiac and metabolic factors.

Neuromuscular weakness may reflect deficits anywhere along the neural pathway from the cerebral cortex to the myocyte. This pathway includes the pyramidal system as upper motor neurons (UMNs) synapse with lower motor neurons (LMNs) of the anterior spinal cord. LMN axons then descend through the anterior spinal cord to exit and synapse with myocytes. At the neuromuscular junction, LMNs release the presynaptic neurotransmitter acetylcholine (Ach) into the synaptic cleft, and post-synaptic Ach receptors then trigger depolarization of the motor end plate and contraction of the muscle cell. Pathology at any level of this neural pathway will result in weakness. An intact myelin nerve sheath, functioning calcium and sodium channels and the presence of acetylcholinesterase to limit the response are all necessary for normal neuromuscular function.

Specific signs—such as altered deep tendon reflexes (DTRs) and tone, muscle atrophy, fasciculations and distribution of weakness—aid in localizing the site of the neuromuscular pathology ([Table 8.7.1](#)).

Non-neuromuscular causes of weakness are myriad and generally reflect a combination of age, general physical and mental health factors and specific systemic disorders that co-exist to result in a general feeling of weakness or malaise ([Table 8.7.2](#)).

Pathology

Diverse pathological processes may underlie neuromuscular weakness. Of these, genetic, autoimmune and toxic causes predominate in the ED ([Table 8.7.3](#)). Patients with congenital genetic syndromes, such as muscular dystrophies or mitochondrial disorders, are rarely seen in the ED unless they are suffering from acute respiratory decompensation in the context of an acute reversible precipitant, such as pneumonia. Management of these cases will be guided by consideration of the clinical context, the stage of disease and disability and any advance care directives from the patient or their advocates.

In industrialized countries such as Australia, Guillain-Barré syndrome (GBS) is the most common cause of acute-onset neuromuscular weakness. GBS variants, multiple sclerosis (MS) and myasthenia gravis (MG) are other autoimmune disorders that precipitate ED presentations, either as de novo diagnoses or in the context of acute exacerbations. Toxic triggers—such as organophosphates, tetanus, botulism and envenomations—are relatively rare but can be fatal if not recognized and treated aggressively.

Other pathologies, such as paraneoplastic syndromes (Eaton-Lambert syndrome [ELS]) and electrolyte disturbances (e.g. hypokalaemic periodic paralysis), should be considered if the clinical context is suggestive. Poliomyelitis is an example of an infectious disease that was previously a major cause of acute-onset weakness. It has been eradicated in the Western world and is well on the way to eradication in the developing world. Post-polio syndrome is a rare late complication seen in ED.

Differential diagnosis

The differential diagnosis of weakness in the ED is very broad and it may not be possible to arrive at a definitive diagnosis during one

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Table 8.7.1 Clinical signs that point to the origin of neuromuscular weakness

Sign	UMNs	LMNs	NMJ	Myopathy
Atrophy	None	Severe	Mild	Mild
Fasciculation	None	Common	None	None
Deep tendon reflexes	Hyperreflexic	Areflexic/hyporeflexic	Normal/hyporeflexic	Normal/hyporeflexic
Distribution of weakness	Pyramidal/regional	Distal/segmental	Variable/fatigable weakness	Proximal > distal
Tone	Spastic	Decreased/flaccid	Decreased/flaccid	Normal/decreased
Plantar response	Upgoing	Downgoing or absent	Downgoing or absent	Downgoing or absent

LMNs, Lower motor neurons; NMJ, neuro-muscular junction; UMN, upper motor neurons.

Table 8.7.2 Non-neuromuscular conditions associated with weakness

Condition	Manifestations
Anaemia	Breathlessness and fatigue usually worse with acute-onset anaemia
Cardiac failure	Fatigue and weakness are common symptoms of heart failure in elderly patients, especially weakness in females over 50 years
Malignancy	Paraneoplastic syndromes (e.g. generalized wasting)
Psychological disorders	Depression/anxiety, psychosis, medication side effects, malingering
Malnutrition	Institutionalized patients, impoverished elderly, anorexia nervosa
Chronic fatigue syndrome	Possibly post-viral syndrome
Rheumatological disorders	Rheumatoid arthritis, systemic lupus erythematosus, fibromyalgia
Medications	Many medications have been associated with weakness; the commonly encountered ones include glucocorticoids, statins, antiretrovirals, alcohol, colchicine and polypharmacy, especially in the elderly
Acute electrolyte derangement (e.g. hypokalaemia, hypocalcaemia)	Acute onset weakness and/or tetany with hypocalcaemia
Sepsis	Acidosis, deranged metabolic state
Dehydration	Lethargy/fatigue
Hypothyroidism	Lethargy, cold intolerance, weight gain, weakness
Chronic disease	Respiratory, renal, hepatic failure

ED visit. Recognition of neuromuscular disorders that have the potential to deteriorate rapidly and require intensive supportive care with assisted ventilation is the most crucial element of ED diagnosis. In particular, GBS, MS exacerbations, myasthenic crises and intoxications, such as botulism, must be recognized early.

Clinical features

The diagnosis of neuromuscular disease is dependent on history, examination and specific investigation findings. A starting point for diagnosis should include a thorough history, noting in particular the following:

- Known underlying neuromuscular disorders, such as amyotrophic lateral sclerosis (ALS), muscular dystrophy, MS or MG

- Pre-existing medical conditions, such as malignancy suggesting a paraneoplastic syndrome, monoclonal gammopathy associated with chronic inflammatory polyradiculopathy (CIDP) or HIV infection/post-transplant immunosuppressive states associated with CIDP, polyradiculopathy or HIV myopathy
- Recent infections (diarrhoeal, viral) or major surgery associated with GBS.
- Recent exposures/ingestions suggestive of intoxications, for example botulism, organophosphate, ciguatera toxin.

Clinical findings generally reflect the site of the lesion within the motor unit (see Table 8.7.1).

Clinical investigations

Given the broad differential diagnosis possible for weakness, a broad screen of laboratory

parameters—including full blood count (for anaemia or inflammation), electrolytes and renal function, liver function, thyroid function plus muscle creatine kinase (CK), inflammatory markers (erythrocyte sedimentation rate [ESR] and C-reactive protein [CRP]) as indicated—should be performed. An ECG should be obtained urgently if an electrolyte imbalance is possible. A rheumatoid screen may be suggested by clinical signs. Lumbar puncture (LP) may be indicated and can be performed to corroborate the diagnosis of GBS or MS if there are no contraindications. Specific investigations—such as brain stem evoked potentials and magnetic resonance imaging (MRI) scanning for MS—should be arranged by specialist neurology services. Chest x-ray or a computed tomography (CT) scan may be indicated to exclude thymoma in association with MG.

Treatment and prognosis

The mainstay of treatment for weakness caused by neuromuscular disorders is supportive care with a particular focus on ventilatory support commenced early rather than later, as emergency intubations are associated with higher complication rates. General supportive measures will also include maintenance of homeostasis with respect to normothermia, euglycaemia, normotension and control of any other autonomic dysregulation, such as paralytic ileus and urinary retention.

Prophylaxis against peptic ulcers and deep vein thrombosis as well as pressure area care are all crucially important in the mechanically ventilated and sedated patient. This will require admission to an ICU, but treatment is usually commenced in the ED. Early neurological consultation and ICU review are crucial, especially for conditions in which there are effective interventions, such as plasmapheresis or intravenous immunoglobulin (IVIG) administration for GBS. For acute envenomations or intoxications, supportive care is still the priority in combination with anti-venoms or antidotes when indicated.

For non-neuromuscular causes of weakness, the treatment priority is to address the underlying

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Table 8.7.3 Key features of conditions associated with the symptom of weakness

Disease	Pathophysiology	Assessment	ED management
Primary neurological			
Guillain-Barré syndrome, most common cause of acute symmetrical weakness	Immune-mediated polyradiculopathy Post-infective (15%–40%), esp. due to <i>Campylobacter</i> or viral infection; >50% are idiopathic	Suggestive history (e.g. diarrhoea) Symmetrical ascending flaccid weakness; loss of DTRs; early facial palsy common; ± autonomic dysfunction Serial assessment of respiratory function crucial to predict need for intubation/ventilation CSF high protein with normal glucose and cell count	Supportive care; early intubation for respiratory failure Early neurology and ICU consultation Early administration of IVIG ± plasmapheresis beneficial Corticosteroids <i>not</i> indicated
Myasthenia gravis, localized variant more common Myasthenic crises/respiratory decompensation (rare) are main ED issues	Immune-mediated Ach receptor dysfunction; may be precipitated by thymic disorders	Fluctuating, fatigable weakness of voluntary muscles especially ocular muscles or proximal limbs. Cranial nerve involvement with ptosis in >25% cases; ± dysphagia, weakness of masticatory muscles; normal sensation; normal reflexes Improves with rest Serial respiratory assessment if severe Ice-pack test if there is ptosis	Supportive care Avoid potential precipitants including corticosteroids Anticholinesterase treatment as directed by neurologist
Multiple sclerosis, relapsing/remitting course most common	Immune-mediated scattered neuron demyelination; affects motor, sensory, visual and cerebellar function Classically ≥2 separate episodes of neurological dysfunction indicating white matter or spinal cord lesions at distinct locations	Acute exacerbations, acute worsening of clinical signs; variable weakness, hyperreflexia, spasticity, clonus, altered pain/temp/vibration and proprioceptive senses Lhermitte sign Optic neuritis in up to 30% with acute central vision loss, afferent papillary defect, red desaturation lung puncture, MRI, evoked potentials in consultation with neurologist	Pulse methylprednisolone therapy for exacerbations Supportive care for generalized weakness Neurology consultation Long-term disease modification and lifestyle strategies (e.g. vitamin D)
Cord compression	Spinal stenosis ± malignancy or infection	Thorough neurological exam Red flags (e.g. fever, malignancy, IVDU warrant MRI)	Neurosurgical consultation Decompression, antibiotics, targeted radiotherapy as indicated
Myopathies			
Congenital Dystrophin disorders, Duchenne Muscular Dystrophy (DMD); Becker Muscular Dystrophy (BMD) DMD/BMD, mitochondrial disorders	X-linked dystrophin gene dysfunction Males affected more severely by DMD; life expectancy to early 20s; BMD of later onset less severe	Generalized weakness Usual ED presentation is acute deterioration with respiratory compromise Spirometry/respiratory assessment Mitochondrial disorders—variable episodic weakness and fluctuating consciousness	Supportive care Discussion with patient, advocates, neurologists regarding appropriateness of intensive intervention Consider advance care directives Ventilatory support as appropriate
Acquired Metabolic/electrolyte disorders Hypokalaemic periodic paralysis Endocrine Cushing disease Addison disease Thyrotoxicosis Toxic Statins, corticosteroids	Variable weakness; may be acute episodic weakness with hypokalaemia ± thyrotoxicosis Drug-induced or history of endocrine myopathies suggestive	Periodic paralysis; may be preceded by vomiting/diarrhoeal illness; may have family history Check electrolytes, especially K ⁺ ECG if K ⁺ deranged Endocrine—assess for other stigmata of endocrinopathy (e.g. cushingoid, addisonian)	Electrolyte (K ⁺) reconstitution Supportive care Correct endocrine abnormalities Discontinue offending medications
Intoxications			
Botulism due to <i>Clostridium botulinum</i> toxin	Deranged neurotransmission Ingested botulinum toxin prevents Ach release at NMJ	History of ingestion GI symptoms in 50% Descending flaccid paralysis Postural hypotension, diplopia, blurred vision, ptosis, dysphagia, respiratory compromise, progressing to limb weakness Ileus common	Supportive care ICU admission for ventilatory support as needed Specific antiserum in consultation with toxicology/neurology
Tetanus due to <i>Clostridium tetani</i> tetano-spasmin toxin Endemic in developing countries	Impaired inhibitory neurotransmission causing skeletal muscle spasm and rigidity Classically infected deep wounds in non-immunized patients	Suggestive history—recent wound, vulnerable patient (e.g. elderly, non-immune) Trismus/dysphagia common early; progressive to painful skeletal muscle spasms; exacerbated by minor stimuli (e.g. touch) May be a localized form Clinical diagnosis	Supportive care, ICU for ventilatory support and sedation Tetanus antitoxin Tetanus immunization is protective Antibiotics (penicillin) to treat clostridial infection

Continued

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Table 8.7.3 Key features of conditions associated with the symptom of weakness—cont'd

Disease	Pathophysiology	Assessment	ED management
Tick paralysis due to tick toxin, ascending flaccid paralysis mimics Guillain-Barré syndrome	Impaired neurotransmission <i>Ixodes holocyclus</i> (Australian paralysis tick) Death from respiratory paralysis	Mostly children in tick-endemic area ± tick found on patient; ataxia, weakness ± extra-ocular palsy/dysphagia May progress after tick removal to generalized/respiratory paralysis	Tick removal/observation sufficient in most cases If severe, ventilatory support Antiserum administration as directed by toxicology/neurology
Marine intoxications Ciguatera Puffer fish Blue-ringed octopus	Ciguatera toxin (from reef fish) Tetrodotoxin (puffer fish, blue-ringed octopus) block sodium channels and impair neurotransmission Tetrodotoxin also acts on CTZ and impairs ventilation	History of tropical fish ingestion; onset of symptoms within a few hours Ciguatera—paraesthesia, electrical sensations in response to hot/cold Tetrodotoxin—progressive flaccid weakness with respiratory compromise	Supportive treatment esp. ventilatory support

CSF, Cerebrospinal fluid; CTZ, chemoreceptor trigger zone; DTRs, deep tendon reflexes; ED, emergency department; GI, gastrointestinal; ICU, intensive care unit; IVDU, intravenous drug user; IVIG, intravenous immunoglobulin; MRI, magnetic resonance imaging; NMJ, neuro-muscular junction.

disease state. This will variously include electrolyte reconstitution, rehydration, correction of thyroid function, treatment of systemic diseases and infections, optimization of organ function and psychological assessment as indicated by clinical assessment and investigations. Appropriate referral should follow. In cases where no apparent cause can be found for a complaint of weakness, an expectant approach is warranted.

The prognosis for neuromuscular disease depends on the specific condition.

Criteria for diagnosis

Table 8.7.3 summarizes the key pathophysiology, assessment findings to elucidate and management strategies for the conditions likely to present to the ED with weakness as a predominant feature.

Specific conditions

Guillain-Barré syndrome

GBS is an acute, acquired, inflammatory demyelinating polyradiculoneuropathy (AIDP) caused by autoimmune attack on peripheral nerves/nerve roots. It is the most common cause of acute progressive generalized weakness in the ED. GBS variants exist, such as the Miller-Fisher syndrome with particular ocular muscle involvement, but these are much less common. GBS has an annual incidence in the developed world of about 1 to 2 cases per 100,000 and mortality of 3% to 10%. It is more common in older people.

Pathophysiology

The pathophysiology involves an aberrant autoimmune response associated in about two-thirds of cases with an antecedent respiratory or gastrointestinal tract infection 3 weeks or less before the onset of signs. *Campylobacter jejuni* is the most commonly associated pathogen (up to 40% of cases) and a positive *C. jejuni* IgM titre is associated with a worse prognosis. Cytomegalovirus is the second most common infection associated with GBS. Others include

Epstein-Barr virus, *Mycoplasma pneumoniae*, HIV and *Haemophilus influenzae*.

Clinical features

The hallmark of GBS is progressive ascending weakness with loss of DTRs and maximal weakness present within 2 to 4 weeks after onset. Proximal and distal limb muscles as well as truncal and respiratory muscles are affected. Cranial nerve involvement is common, with facial nerve palsy occurring in up to 70% of cases. Ocular muscle involvement is less common. Sensory symptoms are common but variable, with paraesthesia or even severe pain arising in some patients. Autonomic dysregulation occurs in about two-thirds of patients and can be fatal due to severe fluctuations in blood pressure and cardiac arrhythmias.

The diagnosis of GBS is based on suggestive history (e.g. recent diarrhoeal infection or major surgery), clinical features of an ascending weakness with loss of DTRs and exclusion of other pathologies.

Clinical investigations

LP should be performed; classic cerebrospinal fluid (CSF) findings are of high CSF protein and normal glucose and cell count. Mild CSF pleocytosis is common; however, the presence of CSF leucocytosis should prompt careful consideration of alternative diagnoses, such as lymphoma or HIV.

Complications

Respiratory failure may occur in up to 30% of cases and is the most life-threatening short-term complication of GBS. This is attributed to the high incidence of phrenic nerve involvement.

Treatment

Attention to ventilation is a priority of treatment. Assessment of Forced Vital Capacity (FVC) every 2 to 4 hours during the acute phase is recommended, and FVC of 10 to 12 mL/kg (<30% of predicted) is generally considered to be an indication for intubation and assisted ventilation.

Other suggested criteria for elective intubation and ventilation include significant respiratory distress, fatigue, sweating, tachycardia, active aspiration and PaCO₂ greater than 50 mm Hg, but clinical judgement should guide the decision to intubate, particularly if the patient has co-morbidities. Suxamethonium should not be used during intubation. Swallowing difficulty and inability to lift the head or elbow off the bed are features predicting the need for intubation. Elective intubation is associated with less adverse events than a late emergency intubation, so the timing of intervention must be carefully considered. About 25% of patients with GBS who cannot mobilize and 30% to 50% of patients admitted to the ICU need mechanical ventilation. Of note, non-invasive ventilation (NIV) is not recommended for GBS and respiratory failure, especially if there is significant bulbar weakness.

In large studies, IVIG, usually 2 g/kg over 3 to 5 days has been found to be as effective as plasmapheresis in the treatment of GBS, and it is often easier to access in most hospitals.

Prognosis

Most people recover fully, but a significant minority (20%) survive with persistent neurological deficits. The most common causes of death are the complications of dysautonomia and respiratory failure.

Multiple sclerosis

MS is a chronic demyelinating condition. It is the commonest chronic neurological condition, with an estimated prevalence of 40,000 cases in Australia. Its incidence is related to latitude, with Tasmania being among the areas with the highest incidence in the world (1:1000). Sixty percent of cases occur in women. MS is frequently characterized by exacerbations and remissions. It is usually diagnosed in individuals aged 15 to 45 years.

Common relapse patterns include ataxia, proximal weakness (more frequently in the

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lower limbs), urinary symptoms and cranial nerve disorders, such as optic neuritis, diplopia and vertigo. Fatigue is a common symptom in MS and should be distinguished from a focal relapse. Heat sensitivity is a common phenomenon in MS and symptoms are often worse in summer. Exacerbations associated with febrile illness can be minimized with careful antipyretic therapy.

Undiagnosed patients may present to the ED with myriad neurological symptoms, although life-threatening presentations with respiratory compromise are exceedingly rare.

Clinical investigations and diagnosis

The diagnosis is usually made when typical clinical features are supported by the findings of neuroimaging, CSF examination and evoked potentials. Nearly all MS patients show discrete white matter lesions or homogeneous periventricular lesions on T2-weighted MRI scans of the brain and/or spinal cord. Elevated protein and gammaglobulins (oligoclonal bands) and pleocytosis with mild lymphocytosis are the typical CSF findings. Delays in latencies on testing of visual, somatosensory or brain stem evoked potentials is diagnostic of demyelination in the visual pathways, posterior columns or auditory pathways, respectively.

Treatment

Relapses usually respond to brief pulse therapy with corticosteroids (methylprednisolone 1 g IV daily for 3 days or equivalent oral dosage). More severe episodes may require high-dose corticosteroids and plasmapheresis therapy.

Vitamin D has now been confirmed as an important aetiological factor in MS, and a vitamin D level of 150 to 200 nmol/L obtained by sun exposure and/or vitamin D supplementation is recommended. A range of dietary and lifestyle interventions are also associated with better outcomes in MS. Long-term disease modification therapies are increasingly available and are the remit of the neurologists. It is important to be aware of these therapies as patients may present with side effects from these increasingly potent immune-modulating drugs.

Disposition

Neurology consultation for directing investigations and management is indicated for all patients with MS exacerbations, and hospital admission is often required.

Myasthenia gravis

MG is rare but its prevalence is rising in developed countries due to earlier diagnosis and good survival rates. During exacerbations, patients are very likely to attend an ED with localized or, less commonly, generalized weakness. The disease is caused by an idiopathic autoimmune

attack of post-synaptic Ach receptors leading to weakness of the muscle response to stimulus. The weakness tends to be fatigable and is usually relieved by rest. Most patients experience facial and bulbar muscle weakness; therefore dysphagia and dysarthria are common symptoms. More serious exacerbations are associated with respiratory compromise.

Myasthenic crisis, which occurs in 15% to 20% of patients (mostly within the first 2 years of diagnosis, when the disease has an unpredictable course), refers to generalized weakness with respiratory failure, requiring intubation and mechanical ventilation. Respiratory failure rarely presents in isolation. Myasthenic crisis can be precipitated by acute disease progression, intercurrent infections, pregnancy, surgery and treatment with high-dose glucocorticoids and a long list of other medications that may affect neuromuscular transmission.

Diagnosis

The diagnosis is based on clinical features and the demonstration of antibodies to the Ach receptor, which are found in about 85% of cases. Clinical suspicion of MG can be supported by a positive bedside ice-pack test in patients with ptosis, where the eyelids are covered with an ice pack for 2 minutes, bringing immediate improvement in the ptosis. The Tensilon test is now rarely performed. Electromyography (EMG) may be necessary to differentiate MG from GBS, myopathy or motor neuron disease (MND).

Treatment and disposition

Supportive care is the main priority in the ED. Neurological consultation is mandated by suspicion of MG. Treatment for MG should not be commenced until the diagnosis has been confirmed. Many patients take pyridostigmine over the long term, and the dose may be increased in exacerbations. Paradoxically, high-dose pyridostigmine can lead to acute deterioration, so treatment decisions should always be made in consultation with a neurologist.

Respiratory failure is the main life-threatening issue in acute myasthenic crisis; however, the condition tends to fluctuate, so reliable criteria for intubation are difficult to define. Serial measurement of PEF/FVC and PaCO_2 are recommended. Intubation is recommended for marginal or deteriorating patients, as elective intubation is associated with fewer complications. Early use of NIV (bi-phasic positive airway pressure [BiPAP]), which can reduce the need for intubation, has been shown to be of benefit in myasthenic crisis. Plasmapheresis and IVIG (2 g/kg over 3 to 5 days) have also been shown to be effective in myasthenic crisis. Corticosteroids may exacerbate the condition and should therefore be avoided unless the patient is mechanically ventilated. In some

patients, thymectomy or immunosuppressive strategies are indicated.

Prognosis

The mortality of myasthenic crisis is about 4% overall, with age above 50 years and FVC below 25 mL/kg being predictors of poor outcome and a long ICU stay. Most patients with MG have a normal life span.

Cord compression/cauda equina syndrome

Patients may present with weakness from acute or chronic conditions that lead to compression of the spinal cord and nerve roots, usually due to a combination of progressive age-related spinal stenosis, infections or malignancy. Cord compression is over-represented in medico-legal claims resulting from ED presentations and a high index of suspicion is required to achieve an early diagnosis and the best outcomes. Progressive spinal stenosis is a common feature of ageing and can occur in isolation or be associated with acute disc herniations. Acute deterioration or neurological deficits of sudden onset in the presence of other systemic illness, such as fever, should be 'red flags' that prompt urgent consideration and investigation for sinister pathologies. These include malignancy (e.g. lymphoma or metastatic deposits), infection (e.g. epidural abscess or discitis, especially in high-risk groups, such as intravenous drug users [IVDUs] or patients who have had recent epidural or spinal anaesthetics) or trauma (e.g. falls in the elderly). Any patient presenting to the ED with lower limb neurological deficits, in particular with signs of bladder or bowel dysfunction, warrants urgent imaging to assess for spinal cord compression. Therapeutic interventions—including antibiotics, surgical decompression and radiotherapy—will be tailored to the individual patient following specialist consultation.

Amyotrophic lateral sclerosis (motor neuron disease)

MND/ALS is a rapidly progressive muscle atrophy and weakness caused by degeneration of both the UMN and LMNs. It causes a variable picture of spasticity, hyperreflexia and muscle weakness with an inexorable decline to respiratory failure and dependence on mechanical ventilation, usually within 2 to 4 years. UMN or LMN bulbar muscle weakness is invariably present and complicates the condition with aspiration and impaired cough. There is no curative therapy and treatment is therefore supportive. In the ED, ALS patients usually present with acute respiratory compromise as a result of an acute precipitant, such as aspiration pneumonia or a choking episode. Management of these patients will be directed at treating the precipitant and increasing respiratory

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support during the period of acute exacerbation as directed by the patient and any advance care plans that he or she might have in place. NIV should be avoided due to the risks of aspiration and increased work required by already weak respiratory muscles. Medications that reduce respiratory drive, such as opiates, should also be avoided. New diagnoses are rarely made in the ED and, if so, usually present with variable UMN and LMN signs and variable weakness. Neurological consultation is mandated by such presentations.

Eaton-Lambert syndrome

ELS is a rare autoimmune paraneoplastic condition that is usually associated with small cell lung cancer. The major clinical feature is severe limb weakness as a result of autoimmune destruction of voltage-gated calcium channels in the presynaptic membrane at the neuromuscular junction, which, in turn, inhibits the release of presynaptic Ach vesicles. It often improves with exercise, which distinguishes it from MG. Tendon reflexes are variable but usually reduced. EMG is required to confirm the diagnosis. Management is to treat the underlying malignancy; therefore prognosis depends on the prognosis of the malignancy. Symptomatic treatments, such as glucocorticoids, are usually ineffective. Supportive care is the goal of ED management.

Myopathies

Congenital muscular dystrophies

The X-linked disorders Duchenne muscular dystrophy and Becker muscular dystrophy are the most common forms of congenital muscular dystrophy. Boys with Duchenne muscular dystrophy are normal at birth but, by the age of about 5 years, exhibit proximal weakness, which gradually deteriorates until they are wheelchair-dependent by age 10 to 12 years. Thereafter, the weakness progresses inexorably and the average life span is only about 21 years, after which death due to respiratory failure ensues. Becker muscular dystrophy has a later onset and slower progression; therefore immobility and respiratory complications may occur in adult life, and many patients have a normal life span. ED presentations in both of these conditions are almost always related to respiratory compromise due to disease progression or an acute precipitant, such as pneumonia. The management is supportive and aimed at treating any acute precipitants as guided by disease stage, patient preference and any advance care directives.

Mitochondrial myopathies, such as those associated with MELAS syndrome (mitochondrial myopathy, encephalopathy, lactic acidosis and stroke) tend to present to ED similarly, with variable weakness and fluctuating conscious state on a known background

of mitochondrial disorder. Ventilatory support and the attendant supportive care are the key aspects of treatment. In these cases, a brief period of mechanical ventilation can support patients through an acute exacerbation, and they may return to being relatively independent until the next acute deterioration. Management should be guided by the patient and his or her neurologist.

Inflammatory myopathies: polymyositis/ dermatomyositis

Polymyositis and dermatomyositis are idiopathic inflammatory myopathies that mostly affect women over 30 years of age. Dermatomyositis is associated with a heliotrope rash, erythroderma and other skin changes and is more commonly associated with cancer. Patients present with proximal symmetrical weakness associated with muscle pain and tenderness. DTRs are intact unless weakness is severe. There are no sensory or autonomic deficits. Proximal weakness is demonstrated by asking patients to stand from a sitting position while folding their arms or by asking them to lift an object above the head. In severe cases, respiratory function may be affected. Diagnosis is based on clinical findings and elevated ESR and CK. Management is with immunosuppressive agents, primarily corticosteroids. Differential diagnosis includes HIV myopathy, viral myositis or myositis due to substances such as alcohol, statins, corticosteroids and Azidothymidine also known as zidovudine (AZT). Endocrine myopathies occur rarely.

Acute periodic paralyses

Acute periodic paralyses are an interesting group of rare disorders occasionally seen in the ED. They may be associated with normal, low or elevated serum potassium. Patients are usually well between attacks, but some can have residual muscle stiffness. A genetic defect has been linked to these diseases but, in some instances, hypokalaemia may cause acute weakness in healthy individuals.

Acute hypokalaemic periodic paralysis may be primary (i.e. familial) or secondary to excessive renal or gastrointestinal losses or endocrinopathy. Familial periodic paralysis usually occurs in Caucasian males, is autosomal dominant and may last as long as 36 hours. Attacks usually occur at night or in the early morning upon awakening and can be precipitated by a diet high in carbohydrates, rest following exercise or glucose and insulin given intravenously. Supportive care and replenishment of serum potassium are the main management priorities.

Thyroid toxic periodic paralysis associated with hypokalaemia is more common in Asian males. Treatment of the underlying disease and electrolyte disorder are the goals of treatment.

Rhabdomyolysis

Rhabdomyolysis is a disorder with many causes that leads to muscle necrosis and the release of intracellular muscle constituents into the circulation. The characteristic triad in rhabdomyolysis is weakness, muscle pain and dark urine. Causes can be classified as due to trauma or compression, exertional and non-exertional. Non-exertional causes include drugs, toxins, viruses and electrolyte abnormalities. ED management is dependent on the cause and the emphasis is on preservation of renal function.

Intoxications

Botulism

Botulism is an acute paralytic illness caused by a neurotoxin produced by *Clostridium botulinum*. It is characterized by severe descending weakness and gastrointestinal slowing. In adults, the toxin is ingested preformed in foodstuffs; in infants, the disease is usually due to ingestion of foods such as honey that contain bacterial spores. Botulinum toxin inhibits Ach release from the presynaptic membrane of the neuromuscular junction. Early characteristic findings include normal mentation with bulbar weakness manifesting as dysphagia and extra-ocular palsies with absent papillary light reflex (which distinguishes botulism from MG). Limb weakness is more obvious proximally and DTRs are usually intact. Sensation is not affected. Postural hypotension tends to be a feature in adults. Management is supportive with ventilatory support in the ICU if necessary. An antitoxin is available.

Tetanus

Tetanus is an acute painful paralytic illness caused by the tetanospasmin toxin of the soil-dwelling organism *Clostridium tetani*. It is characterized by painful severe and uncontrolled skeletal muscle spasms. Respiratory muscle involvement leads to hypoxia and death. It remains endemic throughout the world, and most of the 1 million cases annually occur in developing countries. In the developed world, tetanus should be considered in the elderly and vulnerable groups such as the homeless and poor in particular, where tetanus-prone wounds and lack of immunization are more common. Typically, tetanus is caused by a deep penetrating wound, but up to 50% of patients have only a trivial wound, if any, evident. The onset is highly variable, from days to months. Generalized tetanus is the most common form and causes generalized skeletal muscle spasms, which can be greatly exacerbated by minor stimuli such as touching or a loud noise. Trismus or 'lockjaw' is the classic initial presenting symptom with spasm of the masseter muscle. Other early symptoms include myalgias, cramps, dysphagia and drooling. Violent muscle spasms can cause vertebral and long bone fractures. Death is due to either respiratory failure or autonomic dysfunction. The

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illness is progressive, with an increase in severity over 3 to 5 days and a gradual reduction after 10 days. The diagnosis is made on clinical grounds alone. The priorities of treatment are supportive care with sedation and ventilation, administration of tetanus anti-toxin and avoidance of complications. Localized tetanus also occurs with spasms near the original wound site and rarely progresses to generalized tetanus. This variant carries a good prognosis with or without treatment.

Envenomations

Several envenomations can present to the ED with weakness as part of the clinical syndrome. These include the *Ixodes holocyclus* paralysis tick, puffer fish, blue-ringed octopus (tetrodotoxin) and reef fish (ciguatera toxin) (see Table 8.7.3). These envenomations are covered in detail elsewhere.

CONTROVERSIES AND FUTURE DEVELOPMENTS

- A number of the causes of weakness discussed in this chapter—including GBS, cord compression and MS—are often misdiagnosed in the ED or diagnosed late. Emergency physicians must maintain a high level of critical thinking to distinguish functional, non-neuromuscular and time-critical neuromuscular emergencies.

- Orthodox neurological opinion stresses the primacy of modern immune-modulating therapies for the management of relapsing-remitting MS. Recent studies suggest an equally important role for other therapeutic approaches, including vitamin D supplementation, avoidance of animal fat, promotion of a whole-food diet rich in fish and omega 3 fatty acids and meditation/stress reduction techniques.
- Plasmapheresis and IVIG are just as effective as definitive therapy for GBS, but combining the two treatments is not beneficial.
- Ventilatory support for patients with GBS should be instituted early when indicated, whereas patients with end-stage muscular dystrophy, MELAS, MND/ALS or MG present difficulties for emergency physicians balancing quality of life, potential reversibility and the patient's expressed advance care directive. Therapeutic decisions must be made with extensive consultation with the treating neurologist, patient and family. NIV may be an effective modality in patients with MG but should be avoided in cases of GBS and MNS/ALS, where intubation and mechanical ventilation is preferred.

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SECTION
9

INFECTIOUS DISEASE EMERGENCIES

Edited by Peter Cameron

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9.1 Approach to undifferentiated fever in adults

Arun Ilancheran

ESSENTIALS

- 1** Over one-third of patients who have fever for more than 2 to 3 days with no localizing symptoms and signs are likely to have a bacterial infection; half of these will be in the respiratory or urinary tracts.
- 2** An unexplained fever in a person over the age of 50 should be regarded as due to a bacterial infection until proved otherwise.
- 3** An undifferentiated fever in an alcoholic patient, an intravenous drug user or an insulin-dependent diabetic is generally an indication for admission to hospital.
- 4** Any fever in a traveller returned from a malaria-endemic area should be regarded as due to malaria until proved otherwise.
- 5** Severe muscle pain, even in the absence of overt fever, may be an early symptom of meningococcaemia, staphylococcal or streptococcal bacteraemia.
- 6** An unexplained rash in a febrile patient should be regarded as meningococcaemia until proved otherwise.
- 7** The diagnosis of meningococcaemia should be considered in every patient with an undifferentiated fever.
- 8** There will always be a small number of febrile patients whose sepsis is not initially recognized because they do not appear toxic and their symptoms are non-specific. It is essential that all such patients be encouraged to seek review if they have any clinical deterioration.
- 9** The omission of fever from the Sepsis 3 definition or Sequential Organ Failure Assessment (SOFA) scoring system should not preclude the clinician from considering sepsis or septic shock when a patient with an undifferentiated fever is being assessed.

Introduction

Fever is a common presenting symptom to the emergency department (ED); about 5% of patients give fever as the reason for their visit. Most patients with fever have symptoms and signs that indicate the site or region of infection. A prospective study of patients aged 16 years or older who presented to an ED with fever $\geq 37.9^{\circ}\text{C}$ found that 85% had localizing symptoms and signs that suggested or identified a source of fever and 15% had unexplained fever after the history and examination.¹

Fever with no localizing symptoms or signs at presentation is often seen in the first day or two of the illness. Patients with such a problem will ultimately prove to have a self-limiting viral infection, but others will have non-viral infections requiring treatment. Among the latter group are illnesses that may be serious and even rapidly fatal.

Over one-third of patients who have fever for more than a few days with no localizing symptoms and signs are likely to have a bacterial infection.^{1,2}

If no cause is found in an adult with fever present for over 3 days, there is a good chance the patient will have a bacterial infection that needs treatment. Over half of these infections are likely to be in the respiratory or urinary tracts.¹

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The most important task in the ED for febrile patients without localizing features is not to miss early bacterial meningitis, bacteraemia (such as meningococcaemia) and early staphylococcal and streptococcal toxic shock syndromes.

Approach

The management of febrile patients varies according to the severity, duration and tempo of the illness, the type of patient and the epidemiological setting. Although steps in the management of a febrile patient in the ED, listed here, may be set out in a sequential manner, in reality the mental processes involved occur simultaneously by the bedside.

- Step 1: Identify the very ill.
- Step 2: Find localizing symptoms and signs.
- Step 3: Look for 'at-risk' patients.

Step 1: identify the seriously ill patient who requires urgent intervention

The first step in managing febrile patients is to identify those in need of immediate resuscitation, urgent investigations and empirical therapy. The presence of any of the following features justifies immediate intervention: shock, coma/stupor, cyanosis, profound dyspnoea, continuous seizures and severe dehydration.

Step 2: identify those with localized infections or easily diagnosable diseases

Having excluded those who need urgent intervention, the doctor has more time to attempt a diagnosis. The history and physical examination are usually sufficient to localize the source of community-acquired fever in most cases, especially if the illness has been present for several days.

History

A precise history remains the key to diagnosis of a febrile illness. An inability to give a history and to think clearly is a sign of potential sepsis.

Illness

An abrupt onset of fever, particularly when accompanied by chills or rigors and generalized aches, is highly suggestive of an infective illness.

Localizing symptoms, their evolution and relative severity, help to identify the site of infection; localized pain is particularly valuable in this way.

The severity and course of the illness can be assessed by the patient's ability to work, to be up and about, to eat and sleep and the amount of analgesics taken.

Previous state of health

Underlying diseases predispose patients to infection at certain sites or those caused by certain specific organisms. Knowledge of any defects in the immune system is similarly helpful. For example, asplenic patients are more prone to overwhelming pneumococcal septicaemia and renal transplant patients to *Listeria* meningitis.

A past history of infectious diseases, particularly if properly documented, may be useful in excluding infections such as measles and hepatitis. Immunocompromised patients are at significantly higher risk compared with the standard population for contracting an infective illness.

Predisposing events

Recent operations, accidents and injuries and medications taken may be the direct cause of the illness (e.g. drug fever or rash from co-trimoxazole, ampicillin) or may affect the resistance of the patient, predisposing to certain infections. Concurrent menstruation raises the possibility of toxic shock syndrome.

Epidemiology

Information on occupation, exposure to animals, hobbies, risk factors for blood-borne viruses and travel overseas or to rural areas may suggest certain specific infections (e.g. leptospirosis, acute HIV infection, hepatitis C, malaria, etc.).

Contact with similar diseases and known infectious diseases

This information is useful in the diagnosis of problems such as meningococcal infection, viral exanthema, respiratory infection, diarrhoea and zoonoses.

Examination

Physical examination in the febrile patient serves two purposes: to assess the severity of the illness and to find a site of infection.

Bedside assessment of severity and 'toxicity' based on intuitive judgement is frequently wrong and many patients with severe bacterial infections do not appear obviously ill or toxic.

Physical examination may yield a diagnosis in a febrile patient who has not complained of any localizing symptoms. The following checklist of special areas to be examined is often useful:

- Eyes: Conjunctival haemorrhages are seen in staphylococcal endocarditis and scleral jaundice may be present before cutaneous jaundice is obvious.
- Skin: Rashes of any sort, especially petechial rash; cellulitis in the lower legs may present with fever and constitutional symptoms before pain in the leg develops. Evidence of intravenous drug use should be sought at the common injection sites. Be sure to

examine the pannus or skin folds in the morbidly obese patients.

- Heart: Murmurs and pericardial rubs may be heard.
- Lungs: Subtle crackles may be heard in pneumonic patients without respiratory symptoms.
- Abdominal organs: Tenderness and enlargement without subjective pain may be the only clue to infections in these organs.
- Assess the groin, particularly in a diabetic patient, for signs of necrotizing infection (example: Fournier gangrene).
- Lymph nodes: Especially the posterior cervical glands. Tenderness of the jugulo-digastric glands is a good sign of bacterial tonsillitis.
- Sore throat may be absent in the first few hours of streptococcal tonsillitis. Examination of the throat may give the diagnosis. Oedema of the uvula is also a useful sign of bacterial infection in that region.
- Marked muscle tenderness is a frequent sign of sepsis.
- Neck stiffness may be a clue to meningitis in a confused patient who cannot give a history.
- Any area that is covered (e.g. under plasters or bandages) must be examined for evidence of sepsis. There are two caveats when local symptoms and signs are being assessed:
 - Localizing features may not be present or obvious early in the course of a focal infection (e.g. the absence of cough in bacterial pneumonia, sore throat in tonsillitis or diarrhoea in gastrointestinal infections in the first 12 to 36 hours of the illness).
 - Localizing features may occasionally be misleading. For example, diarrhoea, which suggests infection of the gastrointestinal tract, may be a manifestation of more generalized infection, such as gram negative septicaemia, and crepitations at the lung base may indicate a sub-diaphragmatic condition rather than a chest infection.

Step 3: look for the 'at-risk' patient

If no diagnosis is forthcoming after the first two steps, the next task is to identify the 'at-risk' patient who may not appear overtly ill but who, nonetheless, requires medical intervention. This applies particularly to those with treatable diseases that can progress rapidly.

Four sets of pointers are helpful in identifying these patients: the type of patient (host characteristics), exposure history, the nature of the non-specific symptoms and how rapidly the illness evolves.

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Clinical pointers: type of patient

Clinical manifestations of infection are often subtle or non-specific in young children, the elderly and the immunocompromised. The threshold for intervention in these patients should be lowered. The issue of fever in children is not addressed in this chapter.

Elderly patients Elderly patients with infections often do not mount much of a febrile response and fever may be absent in 20% to 30% of these patients.³

Infectious diseases in the elderly, as in the very young, often present with non-specific or atypical symptoms and signs and may progress rapidly.⁴

In adult patients with unexplained fever, up to one-third may have bacteraemia or a focal bacterial infection. This proportion is even higher in those over the age of 50 years.¹ In the elderly, a fever above 38°C indicates a possible serious infection⁵ and is associated with an increasing risk of death.⁶

The urinary tract is the most frequent site of infection and source of bacteraemia; symptoms of urinary tract infection are frequently absent in the elderly. The respiratory tract is the next most common site of infection; fever and malaise may be the only clues of pneumonia in the elderly. Urinalysis and chest x-ray will identify about half of occult infections.¹

An unexplained fever in a person over the age of 50 years should be regarded as being caused by a bacterial infection until proved otherwise and is generally an indication for admission to hospital.

Alcoholic patients Alcoholic patients present with multiple problems, many of which cause fever. Most are caused by infections, the commonest of which is pneumonia. Multiple infections may occur at the same time.⁷

Non-infectious causes of fever frequently coexist with infections and conditions such as subarachnoid haemorrhage, alcoholic withdrawal and alcoholic hepatitis and require admission.

The initial history and physical examination in the alcoholic may be unreliable and diagnosis may be difficult.

Alcoholic patients with fever for which no obvious cause is found should be admitted to hospital for investigations and observation.

Injecting drug users The risk of injecting drug users acquiring serious or unusual infections is high through repeated self-injection with non-sterile illicit substances, the use of contaminated needles and syringes and poor attention to skin cleansing prior to injections.⁸

Many intravenous drug users presenting with fever have a serious infection. Some have

obvious focal infections, such as cellulitis and pneumonia. Others present simply with fever and bacteraemia, in which case endocarditis must be suspected.

Clinical assessment cannot differentiate trivial from potentially serious conditions in these patients.⁸ A history of chills, rigors and sweats strongly suggests the presence of a transient or ongoing bacteraemia. Back pain may be a subtle symptom of endocarditis or vertebral osteomyelitis.

It is difficult to distinguish the patient with endocarditis from other drug users with fever due to another cause. Hospitalization of febrile injecting drug users is prudent when 24-hour follow-up is not possible. Intravenous drug use in the previous 5 days is a predictor of occult major infection and is an indication for admission to hospital.⁹

Patients with diabetes mellitus Diabetic patients are more prone to developing certain bacterial infections.¹ A diabetic patient with an unexplained fever is more likely to have an occult bacterial infection than a non-diabetic patient. In general, an insulin-dependent diabetic patient, especially if over 50 years of age, with fever and no obvious source of infection should be investigated and preferably admitted.

Febrile neutropaenic patients Febrile neutropaenic patients (absolute neutrophil count <500/ μ L or <1000/ μ L and falling rapidly) must be hospitalized regardless of their clinical appearance. Infections may become fulminant within hours in these patients and the clinical manifestations of their infective illnesses are frequently modified by the underlying disease, therapy received and coexisting problems.

Splenectomized patients Splenectomized patients with fever must be very carefully assessed because of their increased risk of overwhelming bacterial infection. If the fever cannot be readily explained, admission for intravenous antibiotics is usually indicated.

Other immunocompromised patients Fever in transplant patients (renal, hepatic or cardiac) and those with HIV infection is not an absolute indication for admission, but the threshold of intervention should be considerably lowered and they are best assessed by their usual treating doctors.

Patients recently discharged from hospital may have hospital-acquired infections or infections caused by multi-resistant organisms. Recent operations or procedures may be a clue to the site of infection.

Clinical pointers: exposure history

Overseas travellers or visitors Returned travellers or overseas visitors may have diseases such as malaria and typhoid fever that need early diagnosis and treatment. Any fever in a traveller returned from a malaria-endemic area should be regarded as due to malaria until proved otherwise.

Influenza in febrile returned travellers is a concern to EDs worldwide. Outbreaks of avian influenza occur periodically in bird populations throughout Asia. Although the virus does not typically infect humans, direct bird-to-human transmission of H5N1 influenza has been documented. The virus is highly pathogenic and the mortality of the disease is high. Travellers acquiring influenza overseas may also introduce this infection. Most cases occur within 2 to 4 days after exposure, but incubation is as long as 8 days. Suspected influenza infection requires isolation and respiratory precautions. The peak season is generally during the winter months but can vary, especially in the tropics.¹⁰ The impact of influenza is now wide-reaching, with international travel becoming commonplace and the rise of influenza syndromes like MERS-CoV and SARS. The use of rapid diagnostic tests is increasing to meet the surveillance needs of institutions such as airports and hospitals.¹¹ The World Health Organisation (WHO) recommends rapid diagnosis for influenza when the result will influence a clinical decision. SARS¹² and MERS CoV are particular examples of epidemics that had incredibly high mortality rates and put hospitals and governments under extreme pressure during their outbreaks, prompting international responses and WHO guidance and surveillance.¹³

Although rare, viral haemorrhagic fever in returned travellers represents a true medical emergency and a serious public health threat. Viral haemorrhagic fevers are caused by several distinct families of virus, including Ebola and Marburg, Lassa fever, the New World arenaviruses (Guanarito, Machupo, Junin and Sabia) as well as Rift Valley fever and Crimean Congo haemorrhagic fever viruses. Most exist in Africa, the Middle East or South America. Although some types cause relatively mild illnesses, many can cause severe, life-threatening disease. Viral haemorrhagic fever should be considered in any febrile patient who has returned from an area in which viral haemorrhagic fever was endemic, especially if they have come into contact with blood or other body fluids from a person or animal infected with viral haemorrhagic fever or worked in a laboratory or animal facility handling viral haemorrhagic fever specimens. All these infections have incubation periods of up to 2 to 3 weeks, so it may be possible to exclude viral haemorrhagic fever on epidemiological grounds

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alone. Isolation measures should be instituted immediately in these persons.¹⁴

Staff working in EDs should be aware of regional outbreaks of unusual pathogens. These are reported by state and national departments of health. Returning travellers who are unwell will commonly go directly to an ED, and this may be a critical point to limit further spread.

Contact with animals A contact history with animals, either at work or at home, is frequently the clue to a zoonosis, particularly if the illness is a perplexing fever of several days' duration. The occurrence of multiple cases at work or at home should also make one suspect these infections early.

Contact with meningococcal and *Haemophilus* meningitis Close contacts of patients with these infections have a high risk of acquiring the same infections. Early symptoms may be subtle and a high index of suspicion must be maintained.

Clinical pointers: non-specific clinical features There are several non-specific clinical features whose presence should suggest the possibility of sepsis. These warrant careful scrutiny even when the patient does not appear toxic. They are by no means specific indicators of serious problems and there will be many false positives. However, ignoring them is frequently the cause of missed or delayed diagnosis of sepsis (Box 9.1.1).

Severe pain in muscles, neck or back Severe muscle pain, even in the absence of overt fever, may be an early symptom of meningococcaemia or staphylococcal or streptococcal bacteraemia. It is also a feature of myositis and necrotizing fasciitis.

Impairment of conscious state A change in conscious state may be the sole presenting manifestation of sepsis, especially in the elderly.

Box 9.1.1 Clinical pointers: non-specific clinical features ('alarm bells')

- Severe pain in muscles, neck or back
- Impairment of conscious state
- Vomiting, especially in association with headache or abdominal pain
- Severe headache in the presence of a normal cerebrospinal fluid
- Unexplained rash
- Jaundice
- Severe sore throat or dysphagia with a normal-looking throat
- Repeated rigors

Vomiting Unexplained vomiting, especially in association with headache or abdominal pain, should raise concern. Vomiting without diarrhoea should not be attributed to a gastrointestinal infection. It is a common symptom of central nervous system (CNS) infections and occult sepsis.

Severe headache in the presence of a normal cerebrospinal fluid This is especially important in a person who seldom gets headaches. Severe headache in a febrile patient with normal CSF should not be diagnosed as a viral infection; many focal infections (e.g. pneumonia and bacterial enteritis) may also present in this manner. CSF may be normal in cerebral abscess and in the prodromal phase of bacterial meningitis.

Unexplained rash An unexplained rash in a febrile patient should be regarded as meningococcaemia until proved otherwise, even in the absence of headache or CSF pleocytosis.

Jaundice Jaundice in the febrile patient is associated with a greatly increased risk of death, admission to an intensive care unit (ICU) and a prolonged hospital stay.⁶ Jaundice in a febrile patient is unlikely to be due to viral hepatitis but occurs in serious bacterial infections, such as bacteraemia, cholangitis, pyogenic liver abscess and malaria.

Box 9.1.2 Clinical pointers: evolution of illness

- Those presenting early (<24 h)
- Those presenting with rapidly evolving symptoms
- Patients presenting to emergency department on more than one occasion over a 24- to 48-h period

Sore throat or dysphagia Severe sore throat or dysphagia with a normal-looking throat is frequently the presenting symptom of *Haemophilus influenzae* epiglottitis in adults.

Repeated rigors Although repeated rigors may occur in some viral infections, they should generally be regarded as indicators of sepsis, in particular abscesses, bacteraemia, endocarditis, cholangitis and pyelonephritis.

Clinical pointers: evolution of illness

How rapidly the illness evolves is often an indication of its severity. Previously healthy individuals do not seek medical attention unless they are worried. Notice should be taken of any person seeking help within 24 hours of the onset of illness or a person whose illness appears to have progressed rapidly within 24 to 48 hours (e.g. from being up and about to being bedridden). Similarly, the patient who presents to the ED on more than one occasion over a 24- to 48-hour period warrants a careful workup (Box 9.1.2).

Step 4: a final caveat

A major concern in the management of undifferentiated fever in adults is missing the diagnosis of meningococcal bacteraemia when the patient does not appear ill on presentation.

There are a number of infections that must be treated rapidly to minimize morbidity and mortality (Table 9.1.1). With the exception of meningococcal bacteraemia, there are usually some clues in the history or physical examination.

Meningococcal infection is peculiar in its wide spectrum of severity and variable rate of progression in different individuals. It may be fulminant and cause death within 12 hours or it may assume a chronic form that goes on for weeks.

Table 9.1.1 Infections requiring urgent treatment

Disease	Clues
Meningococcaemia	Myalgia, rash. May be none
Falciparum malaria	Travel history, blood film
Bacterial meningitis	Headache, change in conscious state, cerebrospinal fluid findings
Post-splenectomy sepsis	Past history, abdominal scar
Toxic shock syndromes	Presence of shock and usually a rash
Infections in febrile neutropaenia	Past history, blood film
Infective endocarditis	Past history, murmur, petechiae
Necrotizing soft tissue infections	Pain, tenderness, erythema and swelling in skin/muscle, toxicity
Space-occupying infection of head and neck	Localizing symptoms and signs
Focal intracranial infections	Headache, change in conscious state, neurological signs, computed tomography findings

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When a patient presents with fever and a petechial rash, meningococcaemia can easily be suspected if one remembers a golden rule of medicine that 'fever plus a petechial rash is meningococcaemia (or staphylococcal bacteraemia) until proved otherwise'. However, only 40% of meningococcal diseases present with a petechial rash.

It is less well known that the early meningococcaemic rash may be macular (i.e. one that blanches with pressure). This is the basis of another golden rule in infectious disease: early meningococcal rash may resemble a non-specific viral rash.

Rarely, meningococcal disease presents with symptoms and signs of a localized infection other than meningitis (e.g. pneumonia, pericarditis or urethritis). These presentations should not pose any management problems.

The risk of missing the diagnosis increases markedly when the patient with meningococcal disease presents with fever and non-specific symptoms without a rash. An abrupt onset of fever and generalized aches may be due to influenza, but it could also be due to meningococcaemia.

It is prudent to single out meningococcal disease and ask oneself, 'Could this patient have meningococcaemia?' If in doubt, the safest course is to take cultures, give antibiotics and admit.

Clinical investigations

Most febrile patients seen in the ED justify a fever workup.

Full blood examination is of limited use. White cell count ($>15 \times 10^9/L$), marked left shift, neutropaenia or thrombocytopaenia are pointers to a possible bacteraemia or occult bacterial infection, but they may also be seen in viral infections.¹⁵ Similarly, non-specific markers of inflammation, such as C-reactive protein and erythrocyte sedimentation rate, have not been shown to be useful in predicting outcomes for febrile patients in the ED.¹⁶

Urinalysis and urine culture should be done in febrile adults over the age of 50 years unless the pathology clearly lies in another body system. However, if the history does not suggest urinary sepsis and the dipstick urinalysis is normal, then urine cultures are usually negative.¹⁷

A chest x-ray is usually indicated unless a definite diagnosis has been made (e.g. chickenpox, tonsillitis).

Blood cultures should be done in anyone suspected of having bacteraemia, endocarditis or meningitis, in compromised patients with a fever, all febrile patients over the age of 50 years and, possibly, in anyone with an unexplained high fever. It should be noted that only 5% of

blood cultures in this setting will be positive and less than 2% will alter clinical management.¹⁸ In general, a patient considered 'sick enough' to warrant blood cultures should be admitted to hospital or followed up within 24 hours.

Disposition

Patients who have any of the following features are in need of resuscitation, followed by workup and admission: shock, coma/stupor, cyanosis, profound dyspnoea, continuous seizures and severe dehydration.

With few exceptions, the following groups of febrile adults should be investigated and admitted:

- Those over 50 years of age
- Patients with diabetes mellitus
- Alcoholic patients
- Injecting drug users
- Immunologically compromised patients
- Overseas travellers or visitors
- Those with 'alarm bells', as described in Step 3.

In general there should be close liaison with the admitting unit and the issue of empiric therapy for septic patients should be discussed. For the dangerously ill (e.g. those with septic shock or bacterial meningitis), antibiotics should be commenced almost immediately.

There is an increasing tendency to start antibiotics in the ED as soon as possible so as to reduce the length of hospital stay. Time to antibiotic therapy is used as a key performance indicator for the ED (e.g. for febrile immunocompromised patients).

Patients who do not require intervention after the basic workup in the ED are discharged home after a period of observation. Because of the time taken to interview the patient, perform investigations and wait for the results, the patient will usually have been observed for 1 to 2 hours and progression or lack of progression may help in deciding what to do. During observation one must be aware that the apparent improvement of the patient may be the result of pain relief or a fall in temperature due to administered antipyretics.

Arrangement must be made for the patient to be reviewed by his or her general practitioner or at the hospital. This is an essential component of the care of a febrile patient seen in an ED.

There is no easy way of detecting occult bacteraemic sepsis. The infectious process is a dynamic one and the doctor must maintain contact with the patient or family during the 24 to 72 hours following the initial visit.

Patients with fever above 39°C must be seen within 24 hours. Review by a doctor within 6 to 12 hours may be necessary in those who have had a lumbar puncture and is advisable in those who have had blood cultures ordered. A verified

phone number should be clearly recorded in the medical history.

All febrile patients discharged from the ED should be encouraged to seek review if there is any adverse change to their condition. A patient re-presenting to the ED provides an opportunity to ensure that he or she is being managed appropriately and to rectify any errors.

Fever due to most common viral infections will resolve by about 4 days. Many other infections will be diagnosed when new symptoms or signs appear.

If fever persists beyond 4 to 5 days without any localizing symptoms or signs, a less common infection or non-infective cause should be suspected and the patient thoroughly investigated. In this situation, the threshold of admission to hospital should be low.

The establishment of ED short-stay units allows fast-track treatment and observation, usually for 24 to 48 hours, for carefully selected febrile patients who are not suitable for immediate discharge home.

Future research directions

- The subject of undifferentiated fever of short duration in the adult has not been well studied. There are few data on the spectrum of diseases producing this clinical problem.

CONTROVERSIES

- Whether empirical antibiotics should be given to adult patients with undifferentiated fever of short duration in order to minimize the risk of death from unrecognized sepsis or meningitis. This is a perennial question and there are no algorithms capable of directing the management of this problem.
- The safe and ideal course of action is to admit for observation all those patients who are ill enough to warrant a blood culture or a lumbar puncture. The limitation of hospital beds precludes this policy and there will be unnecessary admissions. The introduction of ED short-stay units provides an alternative for selected patients.

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9.2 Meningitis

Andrew Singer

ESSENTIALS

- 1** Bacterial meningitis can be a rapidly progressive and fatal illness. A high level of suspicion is necessary, as well as rapid diagnosis and treatment.
- 2** Eighty-five percent of cases have headache, fever, meningism and mental obtundation, but these are often absent or diminished in very young or old patients, those partially treated with oral antibiotics and those with some form of immunocompromise.
- 3** Treatment should not be delayed if lumbar puncture cannot be performed within 20 minutes of arrival in the emergency department. Blood cultures should be taken prior to the first dose of antibiotics if at all possible.
- 4** The combination of a benzylpenicillin and a third-generation cephalosporin will treat most cases of suspected bacterial meningitis and should be given as soon as the diagnosis is suspected (benzylpenicillin is sufficient in the pre-hospital setting).
- 5** Steroids are potentially of benefit to both adults and children with bacterial meningitis, reducing the incidence of deafness and other neurological complications in *Haemophilus influenzae* and *Streptococcus pneumoniae* infections. They should be given either before or with the first dose of antibiotic.

Herpesviruses often cause meningitis as part of a more generalized infection of the brain (meningoencephalitis) or as part of an immune response to a systemic infection. A generalized viraemia may also cause aseptic meningitis owing to an immune reaction without direct infection.

Fungal

Fungal causes of meningitis, especially those due to *Cryptococcus neoformans*, tend to occur in immunocompromised patients, such as those with HIV/AIDS or those on immunosuppressant medication or cancer chemotherapy. It can occur in immunocompetent individuals as well, particularly the elderly.

Tuberculous

Tuberculous meningitis is rare in industrialized countries but can occur in all age groups. It tends to follow an insidious course, with a lack of classic signs and symptoms. Diagnosis is often difficult, owing to the low yield from CSF staining and the 4-week time frame required to culture the organism. Suspicion should be high in patients with immunocompromise or chronic illness. It tends to have a high mortality.

Spinal

Spinal meningitis is usually bacterial and due to direct spread from a localized infection in the spine.

Epidemiology

The epidemiology of meningitis is different for groups according to age as well as to immunocompetence.

- Neonates: Box 9.2.1 shows the main causes of bacterial meningitis in neonates. There is an overall incidence of 0.17 to 0.32 cases per 1000 live births. There is 26% mortality; it is even higher in premature infants.

Introduction

Definition

Meningitis is an inflammation of the leptomeninges, the membranes that line the central nervous system, as well as the cerebrospinal fluid (CSF) in the subarachnoid space. It is usually the result of an infection but can be due to an inflammatory response to a localized or systemic insult.

Classification

Meningitis is usually classified according to the aetiology or location as bacterial, aseptic (viral, tuberculous, fungal or chemical) or spinal (where the infection specifically affects the spinal meninges).

Aetiology

Bacterial

Bacterial meningitis is a serious cause of morbidity and mortality in all age groups. The causes vary according to age, as shown in (Box 9.2.1). Both *Neisseria meningitidis* and *Streptococcus pneumoniae* may be associated with a fulminant sepsis, including a purpuric rash and septic shock.

Aseptic

Aseptic meningitis may be due either to an immune response to a systemic infection (usually viral) or to a chemical insult.

Viral

Enteroviruses are the most common cause of meningitis, often in clusters of cases.

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Box 9.2.1 Causes of meningitis

Viral	Bacterial	Other
Echovirus 6, 9,11, 30	Neonates (<3 months old): Group B streptococcus (<i>Streptococcus agalactiae</i>) <i>Escherichia coli</i>	<i>Mycobacterium tuberculosis</i>
Coxsackieviruses A9, A16, B1, B5, B6	<i>Listeria monocytogenes</i> Coagulase-negative	<i>Cryptococcus neoformans</i> (especially in the immunocompromised)
Enterovirus 71 H	<i>Staphylococcus aureus</i>	Aseptic
Herpes simplex 1 and 2 viruses	<i>Pseudomonas aeruginosa</i>	
Cytomegalovirus		
Varicella zoster virus		
Epstein-Barr virus		
	Children (<6 years old): <i>Haemophilus influenzae</i> type b <i>Neisseria meningitidis</i> <i>S. pneumoniae</i>	
	Adults: <i>N. meningitidis</i> (especially in young adults) <i>S. pneumoniae</i> <i>L. monocytogenes</i> (especially in adults over age 50) <i>Klebsiella pneumoniae</i> <i>S. aureus</i> <i>E. coli</i> (in the immunocompromised)	

- Children: *Haemophilus influenzae* type b (Hib) used to be a common causative organism but immunization has significantly reduced its incidence. *N. meningitidis* has 13 serogroups. Six serogroups (A, B, C, W, X and Y) are associated with invasive disease. The incidence has declined significantly due to a number of factors including immunization (MenB in New Zealand and MenC in Australia). In Australia, there has been a recent increase in notifications of MenY.¹ Around 10% to 12% of isolates of *S. pneumoniae* are penicillin-resistant, especially in children.²
 - Adults: *N. meningitidis* and *S. pneumoniae* are common causes in all age groups, with *N. meningitidis* predominating in adults under 24 years of age. *Listeria monocytogenes* is more common in adults over 50 years and immunocompromised or alcoholic patients. The overall incidence in adults is 3.8 per 100,000 population. More unusual organisms occur in patients following neurosurgery or chronic illness, such as alcoholism, hepatic cirrhosis, chronic renal failure and connective tissue disease (gram negative rods [GNRs], coagulase-negative *Staphylococcus aureus*, *Mycobacterium tuberculosis*, *Klebsiella pneumoniae*).
 - Patients with HIV/AIDS: *C. neoformans* is relatively common, with an incidence of 5 per million of population or 10% of HIV-infected patients. Tuberculosis, *Listeria*, *Klebsiella* and syphilis are also causes of meningitis in this group, as well as viral causes of meningocephalitis.
- Tuberculous meningitis occurs in around 2% of patients with TB and around 10% of HIV-infected patients with TB. It has a poor prognosis, with 20% mortality.

Pathogenesis

Initially there is colonization of the infectious agent, commonly in the nasopharynx. Other infections, such as otitis media or sinusitis, may spread from already established foci. There is either haematogenous or local spread to the meninges and subarachnoid space, with inflammation of this area and the production of a purulent exudate approximately 2 hours after invasion of the area. The inflammatory response is initiated by bacterial subcapsular components, such as lipo-teichoic acid in *S. pneumoniae* and a lipo-oligosaccharide in *H. influenzae* and other gram negative endotoxins. These substances stimulate the release of cytokines, such as interleukin-1 and -6, tumour necrosis factor (TNF) and arachidonic acid metabolites as well as the complement cascade. There is a subsequent increase in neutrophil and platelet activity, with increased permeability of the blood-brain barrier. This response is often stronger after the initial destruction of bacteria by antibiotics. If the infection is left untreated, fibrosis of the meninges may occur. In viral and aseptic meningitis, there is a more limited inflammatory response, with mild to moderate infiltration of lymphocytes. In the more chronic cases, such as those due to fungi or tuberculosis, the exudate is fibrinous, the main cells being a mixture of lymphocytes, monocytes/macrophages and plasma cells. The base of the brain is most commonly affected.

Presentation

History

There are some differences in the history with different causes of meningitis, which may allow an early differential diagnosis to be made. There are no pathognomonic symptoms or signs for meningitis, so a high index of suspicion is necessary.

The combination of fever, headache, meningism and mental obtundation is found in approximately 85% of cases of bacterial meningitis; early in the course, however, symptoms may be subtle.³ It is also a common pattern in viral or aseptic meningitis, where obtundation is less of a feature. In fungal or tuberculous meningitis, these symptoms are much less common (seen in less than 40% of cases of cryptococcal meningitis). Elderly patients or those who have had recent neurosurgery may present with subtle or mild symptoms and lack a fever.

The headache is usually severe and unrelenting. It may be either global or located in a specific area. The main symptoms of meningism are nuchal rigidity (neck stiffness) and photophobia. The nuchal rigidity is clinically important when the patient complains of a painful restriction of movement in the sagittal plane (i.e. forwards and backwards only). Up to 35% of cases have associated nausea and vomiting.

As a general rule, the height of the fever is a poor indication of the possible cause, although the fever may often only be mild in tuberculous or fungal meningitis or in bacterial meningitis that has been partially treated by antibiotics. The spectrum of mental obtundation can range from mild confusion to bizarre behaviour, delirium or coma. The severity of obtundation is a good indication of the severity of the illness.

Focal neurological signs occur in around 10% to 20% of cases of bacterial meningitis but are also associated with cerebral mass lesions such as toxoplasmosis or brain abscess. They are also a feature of tuberculous meningitis. Seizures are relatively uncommon (13% to 30%) but may occasionally be the only sign of meningitis if the patient has been partially treated with oral antibiotics.

There may also be associated systemic symptoms. Myalgias and arthralgias are often associated with viral causes, but they may also be the sole presenting symptom in meningo-coccal meningitis. HIV/AIDS patients may show stigmata associated with that disease.

The course of the illness may also indicate the cause. Meningococcal or pneumococcal meningitis is frequently characterized by a rapid, fulminating course, often going from initial symptoms to death over an interval of hours. Viral causes tend to lead to a slower course over days. Fungal or tuberculous meningitis shows a more chronic course over days to weeks, with milder symptoms.

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Risk factors for meningitis include the extremes of age, pre-existing sinusitis or otitis media, recent neurosurgery, CSF shunts, splenectomy, immunological compromise and chronic diseases such as alcoholism, cancer, connective tissue disorders, chronic renal failure and hepatic cirrhosis.

Examination

The physical examination will often reflect symptoms elicited in the history, with fever, physical evidence of meningism, stigmata of AIDS, and so on.

As stated earlier, neck stiffness is clinically significant only when it occurs in the sagittal plane. There will be a restriction of both passive and active movement. Other tests to elicit meningism include the Kernig and Brudzinski signs, although these are present in only 50% of adult cases of bacterial meningitis. The Kernig sign is elicited by attempting to extend the knee of a leg that has been flexed at the hip with the patient lying supine and the other leg flat on the bed. The sign is positive if the knee cannot be fully extended due to spasm in the hamstrings. The test can be falsely positive in patients with shortening of the hamstrings or other problems involving the legs or lumbar spine. In the Brudzinski sign, flexing the head causes the thighs and knees to also flex. It can also be tested in children by the inability to touch the nose with the flexed hips and knees in the sitting position. These are both late signs.

Focal neurological signs should be a cause for concern as they can indicate a poorer prognosis.

Papilloedema is rare and late, as is a bulging fontanelle in infants; both should alert one to alternative diagnoses.

A rash, often starting as a macular or petechial rash on the limbs, is seen in sepsis due to *N. meningitidis* and *S. pneumoniae*. A petechial rash is a particularly serious sign and is an indication to start antibiotics immediately. A maculopapular rash is also a feature of viral causes.

Investigations

Lumbar puncture

A CSF sample via a lumbar puncture (LP) is an important source of information for making the diagnosis and determining the likely aetiology and treatment. Treatment should not be delayed if there will be more than a 20-minute delay before the LP is performed and there is a reasonable clinical suspicion that a bacterial cause is present. Blood cultures should be ordered prior to the administration of antibiotics.

Indications

- Symptoms suggestive of meningitis, especially the combination of fever, headache, neck stiffness and photophobia
- Any patient with fever and an altered level of consciousness
- Fever associated with seizures, especially in a neonate, older child or adult
- Seizures in any patient who has been on oral antibiotics

Precautions

- Deep coma: A patient with a Glasgow Coma Scale (GCS) score of 8 or less should have the LP delayed until he or she is stable and more conscious. A normal brain computed tomography (CT) scan does not exclude the risk of uncal herniation in this group.
- Focal neurological signs: The patient should have CT scan first, to exclude a space-occupying lesion; if present, it could increase the risk of cerebral herniation following the LP.
- Surgery to the lumbar spine.
- Local skin infection around the lumbar spine.

The main features to note during LP are the opening pressure and the physical appearance of the CSF. The sample should be sent for Gram stain, culture, sensitivities, polymerase chain reaction (PCR) analysis for bacteria and herpes simplex virus, a cell count and protein and

glucose levels. If fungal meningitis is suspected, an India-ink stain and cryptococcal antigen screen should be requested. If tuberculous meningitis is suspected, multiple 5-mL samples of CSF will be required to increase the likelihood of a positive result. If antibiotics have previously been administered, a bacterial antigen screen should also be requested.

Turbid CSF is indicative of a significant number of pus cells and is an indication for the immediate administration of antibiotics.

The pattern of cell counts and glucose and protein levels is shown in Table 9.2.1. This is only a guide and the clinician must also be guided by the complete clinical picture.

A white cell count (WCC) of more than 1000/ μ L with a predominantly neutrophilic pleocytosis is considered positive for bacterial meningitis. Ten percent of cases, especially early in the course of the illness, may have a predominance of lymphocytes. As a general rule, bacterial meningitis is characterized by a raised CSF protein and a low CSF glucose level. The ratio of CSF to serum glucose levels is also lowered. The combination of CSF glucose below 1.9 mmol/L, CSF:serum glucose ratio below 0.23, CSF protein above 2.2 g/L and either a total WCC above 2000/ μ L or a neutrophil count greater than 1180/ μ L has been shown to have a 99% certainty of diagnosing bacterial meningitis.⁴ Aseptic meningitis will often have cell counts near the normal range. This does not exclude infection with less common agents, such as herpesviruses or *L. monocytogenes*.

Computed tomography scan

CT scanning of the brain is indicated as a prelude to LP in the presence of focal neurological signs, mental obtundation or abnormal posturing. It must be noted, though, that a normal CT scan does not entirely exclude the risk of raised intracranial pressure in bacterial meningitis; therefore those with the mentioned signs should have LP delayed until they are conscious and stable.

Table 9.2.1 Expected cerebrospinal fluid values in meningitis

Parameter	Normal range	Bacterial	Viral	Fungal or TB
Pressure (cm H ₂ O)	5–20	>30	Normal or mildly raised	
Protein (g/L)	0.18–0.45	>1.0–5.0	<1.0	0.1–0.5
Glucose (mmol/L)	2.5–3.5	<2.2	Normal	1.6–2.5
Glucose ratio—CSF/serum	0.6 (0.8 in infants)	<0.4 (allow 2–4 h equilibration)	0.6	<0.4
White cell count/ μ L	<3, usually lymphocytes (if the tap is traumatic, allow 1 WBC for every 1000 RBC)	>500 (90% PMNs)	<1000, predominantly monocytes (10% are >90% PMNs, 30%–40% >50% PMNs)	100–500
Gram stain	No organisms	60%–90% positive	No organisms	

CSF, Cerebrospinal fluid; PMNs, polymorphonuclear leucocytes; RBC, Red Blood Cells; TB, tuberculosis; WBC, White Blood Cells.

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Microbiology

Apart from microscopy and culture of CSF, there are a number of other methods that may allow the causative organism to be identified.

Skin lesion aspirate

In cases where a petechial rash is present, a Gram stain or culture from some of the skin lesions may yield the causative organism. This has a reported sensitivity of 50%.⁵

Throat swab

Throat swabs are useful in identifying a bacterial cause spread by nasopharyngeal carriage; a throat swab should be obtained in a case of suspected bacterial meningitis.

Polymerase chain reaction

This potentially allows identification of the causative organism and even the serotype for organisms such as meningococcus. The test can be performed on CSF or ethylenediaminepentaacetic acid (EDTA) blood samples and may remain positive for up to 72 hours after the commencement of antibiotics. In CSF, the reported sensitivity is greater than 95%; in blood its sensitivity is 87%.⁵

Serology

Tests to detect Immunoglobulin M (IgM) to specific organisms are available for meningococcus and some viruses. For meningococcus, the test has a sensitivity and specificity of 97% and 95%, respectively, but it is reliable only in adults and in children over 4 years of age and takes 5 to 7 days after onset of the illness to reach diagnostic levels.

Antigenic studies

Latex agglutination, immune-electrophoresis or radioimmunoassay techniques can be used to screen for antigens from *S. pneumoniae*, Hib, group B streptococcus (*S. agalactiae*), *Escherichia coli* K1, *N. meningitidis* and *C. neoformans*. The tests can be performed on serum, CSF or urine. Serum or urine samples tend to allow greater sensitivities (around 96% to 99%) than CSF (82% to 99%). The test is no more sensitive than either a positive Gram stain or the presence of CSF pleocytosis in untreated cases. The main purpose of antigenic studies is to allow rapid identification of the causative organism in cases confirmed by the CSF findings or in cases where partial treatment with antibiotics renders the CSF sterile on culture. In many laboratories, these tests have been superseded by PCR methods.

General investigations

Full blood count (FBC), urea and electrolyte levels (UECs), blood cultures and C-reactive protein (CRP) can assist in assessment of the patient.

Blood cultures should be ordered prior to administering antibiotics. In most cases of

bacterial meningitis, a blood culture will grow the causative organism. Identification can be improved by a combination of blood culture, CSF Gram stain and PCR or antigen testing.

Differential diagnosis

- Generalized viral infections, with meningism as a feature.
- Encephalitis: This is a more generalized viral infection of the brain. Clinically, it may be indistinguishable from meningitis.
- Brain abscess: This tends to produce focal signs due to local pressure at the site of the abscess.
- Focal cerebral infections, such as those due to *Toxoplasma gondii* in HIV/AIDS patients.
- Subarachnoid haemorrhage: This will often produce identical symptoms of meningism, but generally without other evidence of infection, such as fever.
- Migraine and other vascular headaches: Again, photophobia and neck stiffness are common features.
- Severe pharyngitis with cervical lymphadenopathy causing neck stiffness.

Management

Management depends on the likely causative agent and the severity of the illness.

General

Patients should rest in bed, particularly following an LP. A quiet, darkened room will be beneficial to those with headache or photophobia. Simple analgesics with or without codeine may be used to treat the headache. Opiates may be required in severe headache.

Sedation may be necessary if the patient is very agitated or delirious. Suitable drugs are diazepam 5 to 10 mg IV or midazolam 2 to 10 mg IV or IM with or without the addition of an antipsychotic, such as droperidol 2.5 to 10 mg IV or IM or chlorpromazine 12.5 to 50 mg IV or IM.

Seizures should be treated appropriately, initially with a benzodiazepine, then maintained with phenytoin or phenobarbitone. Meningitis can occasionally be associated with status epilepticus, which should be treated in the standard way.

Patients with raised intracranial pressure may need pressure monitoring and measures to reduce the pressure, such as nursing the patient in a 30-degree head-up position and administering hyperosmotic agents such as mannitol or hypertonic saline. Obstructive hydrocephalus requires appropriate neurosurgical treatment with CSF shunting.

If septic shock has intervened, it should be treated in the usual way, with IV fluids and inotropes.

Antimicrobials

The choice of antimicrobial agent will be determined by the likely causative organism and is therefore determined primarily by age and immune status. It is important not to delay antibiotic therapy for investigations such as LP or CT and the antimicrobial should be administered as soon as the diagnosis is suspected. Table 9.2.2 shows the recommended choice of antimicrobial for different situations and organisms. Table 9.2.3 shows the recommended dosage of each. As a general rule, the combination of a third-generation cephalosporin and benzylpenicillin will cover most organisms in all age groups. It is important to note that there is emerging resistance to penicillins in *S. pneumoniae* (currently 10% to 12% of isolates in Australia). If gram positive diplococci are found or *S. pneumoniae* is identified on antigen or PCR testing, vancomycin should be added to the therapy.⁶

Steroids

Steroids have been shown to improve the prognosis of bacterial meningitis in both adults and children in high-income countries. They can lead to a reduction in complications, such as sensorineural deafness and short-term neurological deficits. The benefit appears to occur in infections from *H. influenzae* or *S. pneumoniae*. No benefit has been demonstrated with respect to mortality. Steroids are usually administered as dexamethasone 0.15 mg/kg (up to 10 mg) IV q6h, and are indicated only if they can be started before or with the first dose of antibiotics. They should then be continued for 4 days if one of the previously mentioned organisms is confirmed. The main adverse effect is gastrointestinal bleeding, which may be reduced by limiting treatment to 2 days.⁷

Disposition

All cases of bacterial meningitis will require admission for IV antibiotics as well as supportive therapy. They often require intensive therapy, especially if septic shock has supervened. Viral meningitis will usually require supportive therapy only, but this may necessitate admission. Mild cases of viral or aseptic meningitis with a clear diagnosis can safely be sent home.

Prognosis

Over the last 20 years the mortality of bacterial meningitis has ranged from 6% to 20%, and it is higher in the very young or very old. Meningitis in immunocompromised individuals carries a high mortality of up to 50%. Bacterial meningitis in children can lead to a number of long-term sequelae, such as sensorineural hearing loss, learning difficulties, motor problems, speech delay, hyperactivity, blindness, obstructive hydrocephalus and recurrent seizures. These sequelae are less common in adults.

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Table 9.2.2 Choice of antimicrobial in meningitis

Organism	First-line drug	Second-line drug	Duration
Pre-hospital	Benzylpenicillin	Ceftriaxone (if penicillin-allergic)	
Neonates	Cefotaxime plus ampicillin plus vancomycin (if MRSA suspected)		
Organism unknown	Cefotaxime or ceftriaxone plus benzylpenicillin (if <i>Listeria</i> suspected) plus vancomycin (if <i>Streptococcus</i> or <i>Staphylococcus</i> suspected)	Vancomycin plus ciprofloxacin or moxifloxacin (if penicillin-allergic)	7–10 days
<i>Haemophilus influenzae</i> type b	Cefotaxime or ceftriaxone	Benzylpenicillin or ciprofloxacin	7–10 days
<i>Neisseria meningitidis</i>	Benzylpenicillin or cefotaxime or ceftriaxone	Ciprofloxacin or chloramphenicol (particularly if penicillin-allergic)	5–7 days
<i>Streptococcus pneumoniae</i>	Benzylpenicillin (if susceptibility known)	Cefotaxime or ceftriaxone or vancomycin (if resistant to penicillin)	10 days
<i>Listeria monocytogenes</i>	Benzylpenicillin	Trimethoprim + sulfamethoxazole	3–6 weeks
<i>Cryptococcus neoformans</i>	Ampotericin plus flucytosine	Fluconazole	4–6 weeks
<i>Streptococcus agalactiae</i>	Benzylpenicillin		
Herpes simplex	Acyclovir		14 days

MRSA, Methicillin-resistant *Staphylococcus aureus*.

(Adapted from Therapeutic Guidelines Limited. *Therapeutic Guidelines: Antibiotic*, version 15; 2014.)

Table 9.2.3 Antibiotic doses in treating meningitis

Antibiotic	Adult dose	Child dose	Route	Frequency
Cefotaxime	2 g	50 mg/kg	IV	q6h
Ceftriaxone	4 g	100 mg/kg	IV	Daily
Benzylpenicillin	2.4 g	60 mg/kg	IV	q4h
Ampicillin		50 mg/kg	IV	q6h
Trimethoprim + sulphamethoxazole	160 + 800 mg	4 + 20 mg/kg	IV	q6h
Chloramphenicol	1 g	25 mg/kg	IV	q6h
Acyclovir	10 mg/kg	20 mg/kg in full-term neonates, 10 mg/kg otherwise	IV	q8h
Amphotericin B	1 mg/kg	1 mg/kg	IV	Daily
Flucytosine	25 mg/kg	25 mg/kg	IV or PO	q6h
Vancomycin	1.5 g (reduce dose to 1 g if renal impairment)	15 mg/kg	IV	q6h (reduce frequency in neonates)
Ciprofloxacin	400 mg	10 mg/kg	IV	q12h
Moxifloxacin	400 mg	10 mg/kg	IV	q12h

(Adapted from Therapeutic Guidelines Limited. *Therapeutic Guidelines: Antibiotic*, version 15; 2014.)

Prevention

Prophylaxis should be offered in cases of *N. meningitidis* or *H. influenzae* type b infection to the following persons:

- Household or household-like contacts: those who lived in the same house (or dormitory-type room) or were having an equivalent degree of contact with the case in the 7 days prior to the onset of the case's symptoms

until completion of 24 hours of appropriate antibiotic treatment. (In Hib, if less than 24 months old or less than 4 years and incompletely immunized against Hib).

- Passengers immediately adjacent to the index case on a trip of 8 hours' or longer duration.
- Any person who has potentially shared saliva (such as eating utensils or drink bottles) or had other intimate contact with the index case.

- Health care workers who have given mouth-to-mouth resuscitation to an index case or had unprotected close exposure to large-particle respiratory droplets during airway management.

Appropriate regimens for meningococcus are as follows:

- Ciprofloxacin 500 mg orally (250 mg for children over 5 and 30 mg/kg up to 125 mg for children under 5) as a single dose. This is

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preferred for adults, children and females on oral contraceptives.

- Ceftriaxone 250 mg (125 mg in children <12 years of age) IM in 1% lignocaine. This is preferred in pregnant women.
- Rifampicin 600 mg orally q12h for 2 days (5 mg/kg in neonates <1 month, 10 mg/kg in children). This is preferred in young children.
- Appropriate regimens for Hib are:
- Rifampicin 600 mg PO QD for 4 days (10 mg/kg in neonates <1 month, 20 mg/kg in children).
- Ceftriaxone 1 g IM QD for 2 days (50 mg/kg in children).

If the index case is less than 24 months old, Hib vaccination should be given as a full course as soon as possible after recovery. Unvaccinated contacts under 5 years of age should be immunized as soon as possible. Casual neighbourhood or hospital contacts are not required to receive prophylaxis.

Meningococcal vaccine should be considered in populations where cases are clustered. The vaccine is currently recommended for exposure to serogroups C, A, W or Y.

CONTROVERSIES

- Should all patients have a CT scan before lumbar puncture? CT is required only for patients with focal neurological signs or those who are comatose, where lumbar puncture should be delayed until they are more stable.
- When to use steroids? There is no demonstrated benefit of steroids outside of being given before or with the first dose of antibiotics in meningitis caused by *H. influenzae* b or *S. pneumoniae*.

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9.3 Septic arthritis

Christopher Carman

ESSENTIALS

- 1** Early diagnosis and treatment are critical for the prevention of irreversible joint destruction.
- 2** Diagnosis is based on clinical features and synovial fluid examination; imaging techniques have a role in difficult cases.
- 3** *Staphylococcus aureus*, *Streptococcus* and *Neisseria gonorrhoeae* are the most frequent pathogens in adults and older children. *Methicillin-resistant staphylococcus aureus* (MRSA) is an emerging problem, particularly among intravenous drug users. Fungal, mixed bacterial and exotic organisms are rarely seen outside of the intravenous drug using population.
- 4** Successful treatment hinges on rapid and complete joint lavage and high-dose parenteral antibiotics guided by culture results.
- 5** Outcomes are good in paediatric and gonococcal subgroups, but the presence of chronic arthritis or polyarticular involvement is associated with up to 15% mortality and 50% chronic joint morbidity.

Introduction

Septic arthritis is defined as bacterial infection of the synovial space. The knee is the most commonly affected joint in adults and the hip joint in the paediatric age group.¹ Intravenous drug users have a predisposition toward axial joint infections. Septic arthritis is commonly monoarticular and monomicrobial.

Aetiology, pathogenesis and pathology

Septic arthritis occurs as a consequence of a number of pathological processes: inoculation resulting from a penetrating injury or procedure, direct spread from an adjacent infective process such as osteomyelitis, cellulitis, bony or soft tissue abscess. Most commonly it may result

from haematogenous spread, as in sepsis or as a consequence of endocarditis. Once a joint is inoculated, an acute inflammatory reaction with hypersecretion of synovial serous or seropurulent exudate occurs. As the infection progresses, articular cartilage is eroded both through direct bacterial enzymatic destruction and as a consequence of the release by inflammatory and synovial cells of proteolytic enzymes. If the inflammation is not treated, loss of articular cartilage fluid eventually leads to healing by bony ankylosis or joint fibrosis.² Co-morbidity or deficient host defences are risk factors for infection³ and can be associated with more rapid and severe disease (Table 9.3.1).

The majority of cases are community acquired and occur in children and young adults.⁴ Prosthetic joint surgery and the invasive management of chronic arthritis are factors in the increased prevalence observed in older age groups.

Epidemiology

The incidence of proven and probable septic arthritis in Western Europe is 4 to 10 per 100,000 patients per year. This is more prevalent in lower socioeconomic groups in both Northern Europe and Australia.

The prevalence is 29 cases per 100,000 in the indigenous population, with a relative risk of 6.6 compared with the European Northern Territory Australian population.⁵

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Table 9.3.1 Risk factors for septic arthritis

Risk factors	Examples
Direct penetration	Trauma Medical (surgery, arthrocentesis), intravenous drug use
Joint disease	Chronic arthritis
Host immune deficit	Glucocorticoid or immunosuppressive therapy HIV infection Chronic illness Cancer

The incidence of septic arthritis is increasing and is linked to an increase in orthopaedic-related infection, an ageing population, more invasive procedures being undertaken and an enhanced use of immunosuppressive treatment.⁵

Clinical features

History

This will usually reveal the recent onset of a painful, hot, swollen joint, most commonly the hip or knee, although any joint may be affected. Systemic features of fever or rigors should be sought, plus the presence of any risk factors.

Examination

Typical findings include a hot, tender joint held in a position to minimize joint space pressure, with marked limitation of passive or active movement owing to pain. An effusion will be evident in most cases. A polyarticular presentation is more common in gonococcal infection or in the setting of chronic arthritis. In general, fever is low-grade and few patients will appear 'toxic' and unwell. The elderly and immunosuppressed may present non-specifically with anorexia, vomiting, lethargy or fever.

Differential diagnosis

Non-septic arthritis, crystalline arthritis or synovitis may be differentiated on clinical features and joint fluid analysis. Fractures will generally be evident on joint radiographs, but the detection of osteomyelitis may require more advanced imaging techniques, such as nuclear or computed tomography (CT) scanning. Rheumatic fever and brucellosis are rare causes.

Clinical investigations

Synovial fluid examination and culture

Aspiration should be performed promptly with local anaesthetic and a large-bore needle for

Table 9.3.2 Synovial fluid characteristics

Characteristic	Septic arthritis	Non-septic arthritis	Non-inflammatory effusion
Colour	Yellow/green	Yellow	Colourless
Turbidity	Purulent, turbid	Turbid	Clear
Leucocytes/ μ L	10–1 million	5–10,000	<1000
Predominant cell	PMN	PMN	Monocyte
	PMN, Polymorphonuclear leucocyte		

cell count, crystals, Gram stain and culture to confirm the diagnosis. Typical findings in septic arthritis and its differential diagnoses are shown in Table 9.3.2.⁶

Most infections are acute and bacterial (Table 9.3.3),⁶ although fungal and mycobacterial pathogens have been recognized in chronic and periprosthetic infections.

Other laboratory investigations

Blood cultures should always be ordered and may be positive in up to 50% of cases. Inflammatory markers (erythrocyte sedimentation rate [ESR] and C-reactive protein [CRP]) may be elevated, typically with a neutrophil-predominant leucocytosis. CRP may be negative if the infective organism is of low virulence.⁷ These are non-diagnostic investigations but aid in monitoring response to therapy. Further research may in future provide additional diagnostic aids (Box 9.3.1).

Imaging studies

Plain radiographs should be obtained in all cases prior to aspiration: they may reveal effusions or local oedema and help to exclude alternative conditions, particularly fracture and peri-articular malignancy. Ultrasound is very sensitive in detecting effusions and excellent for facilitating needle aspiration.

Fluoroscopy may also be used. Nuclear medical studies are very sensitive early but not specific for sepsis. CT and magnetic resonance imaging (MRI) have a small role in difficult joints (e.g. hip and sacroiliac).

Criteria for diagnosis

This depends on positive culture of synovial fluid from an affected joint, a positive Gram stain or blood culture in the context of an inflamed joint suspicious of sepsis, macroscopic pus aspirate and appropriate response to antibiotics.⁸

Management

Arthroscopic washout has gained increasing favour in both adults and children, offering a more rapid return to normal function, although

Table 9.3.3 Bacterial causes of septic arthritis

Age group	Typical bacteria
Children	<i>Staphylococcus aureus</i> Group A streptococci (B in neonates) <i>Haemophilus influenza</i>
Young adults	<i>Neisseria gonorrhoeae</i> <i>S. aureus</i>
Older adults	<i>S. aureus</i> Gram-negative species ^a Group A streptococci

^a*Pseudomonas* spp. and Enterobacteriaceae.

Box 9.3.1 Likely developments in the future

Synovial and haematologic cellular markers to distinguish septic arthritis from other sources of non-traumatic joint pain may become available to the emergency physician.

- Synovial fluid lactate assay
- Synovial probe based polymerase chain reaction technique to identify the bacterial pathogen
- Delta neutrophil index assay to determine burden of infection

From Carpenter CR, Schuur JD, Everett WW, Pines JM. Evidence-based diagnostics: adult septic arthritis. *Acad Emerg Med*. 2011;18:781–96.

See references 15 and 16.

arthrotomy and open washout is still utilized for severe and periprosthetic infections.^{9–11}

Antibiotic therapy is initiated after culture specimens have been obtained, with clinical presentation and Gram stain guiding the choice of agents. All regimens must include an anti-staphylococcal agent with gram negative cover as indicated by the clinical setting.

Suggested initial empiric regimen¹²

Flucloxacillin: 2 g (25 to 50 mg/kg up to 2 g) IV q6h. If gram-negative bacteria are suspected, add ceftriaxone 2 g IV. If methicillin resistance is suspected, add vancomycin 1 g (25 mg/kg) IV q12h. Confirmed gonococcal infections require the addition of a single dose of azithromycin 1g PO. Consult therapeutic guidelines in the context of penicillin hypersensitivity.

9.4 URINARY TRACT INFECTIONS

Definitive therapy will be tailored to later laboratory identification of the organism and its sensitivities.

The duration and route of therapy remain controversial but, in uncomplicated acute cases, parenteral antibiotics will be required for at least 3 days in children and 2 weeks in adults, with a total treatment duration of 3 to 6 weeks.^{13,14} Specific organisms, such as *Neisseria* spp., will respond more rapidly, whereas chronic infections and comorbidity will necessitate aggressive and more prolonged therapy.

General care—with initial joint rest, appropriate analgesia and physical therapy—is important. Admission is mandatory pending source control. Thereafter, ongoing therapy may be monitored on an outpatient basis or via domiciliary hospital services.

Prognosis

This depends upon the organism, patient comorbidity and the adequacy and rapidity of treatment. Gonococcal and paediatric infections have a generally good response, with low rates of ensuing joint morbidity. Polyarticular sepsis in rheumatoid arthritis has been associated with mortality rates of up to 15% and major morbidity in up to 50% of survivors.^{2,6,13}

Prevention

Safe sexual practice can reduce gonorrhoeal infections. Strict aseptic technique, good patient selection and prophylactic antibiotics help to prevent cases associated with invasive joint procedures. The overall incidence of infection after arthroplasty ranges from 0.5% to 2%.²

CONTROVERSIES

- The total duration of therapy has gradually been reduced, but the optimum duration is unclear, as is the balance between parenteral and oral routes.¹⁴
- Consensus has not been reached on the best method of joint drainage. Arthroscopic techniques provide the mainstay, although arthrotomy is still utilized, particularly in periprosthetic infections.^{9–11}
- Difficulties still exist in the differentiation of septic arthritis from new-onset non-septic arthritis, especially when polyarticular joint fluid analysis and medical imaging are used, but nuclear and CT scanning techniques may have difficulty in distinguishing infective from non-infective inflammation.

Full references are available at <http://expertconsult.inkling.com>

9.4 Urinary tract infections

Sean Arendse

ESSENTIALS

- 1** Urinary tract infection (UTI) is the most common bacterial infection.
- 2** By age 32, 50% of women will report at least one UTI.
- 3** Sexual activity is the most important risk factor in young women.
- 4** Most UTIs are caused by *Escherichia coli*, but *Staphylococcus saprophyticus* is responsible for up to 15% of infections in young, sexually active women.
- 5** There is a genetic predisposition in some women to recurrent UTI.
- 6** For the majority of outpatients with typical symptoms, urine culture is not necessary.
- 7** In hospitalized patients, urinary catheterization produces infection in 10% of patients per day.
- 8** Asymptomatic bacteriuria should not be sought or treated except in pregnant women and in patients about to undergo significant urological procedures.

Introduction

Urinary tract infections (UTIs) is the most common bacterial infection and the major cause of gram negative sepsis in hospitalized patients.^{1,2}

Definitions

Urinary tract infection

The term *urinary tract infection* is non-specific and may refer to a variety of clinical conditions,

including asymptomatic bacteriuria (ASB), urethritis, cystitis, female urethral syndrome and acute and chronic pyelonephritis. The most common clinical presentations are cystitis and acute pyelonephritis, although the clinical distinction between these diagnoses may not be as straightforward as the terms imply, with up to 50% of patients having unrecognized pyelonephritis.³

UTI is considered in two main groups: simple (or uncomplicated) and complicated. Simple UTI

occurs in an otherwise healthy person with a functionally and anatomically normal urinary tract, most commonly a young non-pregnant female. A complicated UTI is one associated with anatomical abnormality, urinary obstruction or incomplete bladder emptying due to any cause: instrumentation or catheterization, pregnancy or significant underlying disease, such as immunosuppression or diabetes mellitus.

Significant bacteriuria

Significant bacteriuria most commonly refers to more than 10^5 bacteria per millilitre of urine, reported as colony forming units per millilitre (cfu/mL). This usually represents infection as opposed to contamination (see 'Quantitative culture', further on), although there are significant exceptions to this generalization (see 'Urethral syndrome', later).

Asymptomatic bacteriuria

Asymptomatic bacteriuria refers to significant bacteriuria in the absence of symptoms of infection.

Epidemiology

UTI is very common, particularly in women, in whom age, degree of sexual activity and the form of contraception used are all factors that affect the incidence and prevalence of infection.

9.3 SEPTIC ARTHRITIS

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9.4 URINARY TRACT INFECTIONS

Although the overall rate of infection is difficult to estimate, since UTI is not a reportable disease, the self-reported incidence of UTI in a US health survey was 12.1% among women and 3% among men. By age 32, 50% of women will have had at least one UTI.⁴ In non-pregnant women aged 18 to 40 years, the rate of infection has been stated to be between 0.5 and 0.7 per person per year, with much higher rates in pregnancy.⁵

In males, the prevalence of bacteriuria beyond infancy is 0.1% or less. Between the ages of 21 and 50, infection rates may be as low as 0.6 to 0.8/1000.⁶ With increasing prostatic disease, the frequency of bacteriuria may rise to 3.5% in healthy men and to more than 15% in hospitalized men by age 70.⁷ Homosexual men are at increased risk of UTI.

In the presence of chronic disease and with institutionalization of the elderly, the incidence of bacteriuria may be as high as 50%, although this is most commonly asymptomatic.⁸

Aetiology

The aetiology of uncomplicated UTI has remained unchanged for decades, although increased antibiotic resistance in the bacteria responsible has been well documented. In community-acquired UTI, *Escherichia coli* accounts for 75% to 90% of cases, *Staphylococcus saprophyticus* accounts for 5% to 15% (especially in young, sexually active women), with enterococci and gram negative organisms, such as *Klebsiella* spp. and *Proteus mirabilis*, responsible for 5% to 10%.^{9,10} Which bacteria are isolated is influenced by factors such as whether the infection is initial or recurrent; the presence of obstruction, instrumentation or anatomical abnormalities; and whether the patient is an inpatient or outpatient. In simple acute cystitis, the most common presentation of UTI, a single organism is usually isolated. On the other hand, in complicated UTI, *E. coli* is isolated in 20% to 50% of cases and non-*E. coli* organisms, such as *Proteus* and *Klebsiella* species, are more commonly seen. In the presence of structural abnormalities, it is more common to isolate multiple organisms, and antibiotic resistance is frequently found.¹⁰

Pathogenesis

In healthy individuals, the perineum, vagina, vaginal introitus and urethra as well as periurethral areas each have their respective flora and are normally colonized by bacteria that differ from those commonly associated with UTI—that is, by non-pathogens. The periurethral area may become colonized by such UTI-causing (uropathogenic) bacteria, which then ascend via the urethra into the bladder and thence may ascend further to the kidney, causing

pyelonephritis. The reservoir for these bacteria is the gastrointestinal tract.⁴ There are host and bacterial mechanisms involved in determining whether a UTI will occur.

Host mechanisms

Anatomic considerations (men) and prostatic secretions

In males, the length of the urethra, its separation from the anus and the presence of prostatic secretions all contribute to the prevention of colonization and subsequent UTI.

Sexual activity, contraceptive practices, use of diaphragm/spermicides

Sexual activity is the most important risk factor for acute cystitis, with recent or frequent sexual activity increasing that risk. The use of a diaphragm with a spermicide (an inhibitor of normal vaginal flora) promotes vaginal colonization with uropathogenic bacteria and has also been shown to increase the risk of UTI.⁴

Secretor/non-secretor status

Blood group antigens are secreted in the body fluids by some women. The urethral and periurethral mucosae in women who do not secrete these antigens (non-secretors) in their body fluids have a higher affinity for bacterial adhesins (see later) than the mucosae of women who do. These non-secretors are more susceptible to recurrent infections.¹¹

Entry of bacteria into the bladder

Instrumentation of the bladder (see later) is a well-recognized mechanism by which bacteria are introduced into the bladder. Other factors have been considered but have not been conclusively demonstrated. These include frequency and timing of voiding, hormonal changes and personal hygiene habits.¹²

Bladder defence mechanisms

The healthy bladder can normally clear itself of bacteria. Three factors are involved: (1) voiding; (2) urinary bacteriostatic substances—such as organic acids, high urea concentrations and immunoglobulins; and (3) active resistance by the bladder mucosa to bacterial adherence.

Obstruction

This may be extrarenal (congenital anomalies, such as urethral valves, calculi, benign prostatic hypertrophy) or intrarenal (nephrocalcinosis, polycystic kidney disease, analgesic nephropathy). Complete obstruction of the urinary tract predisposes to infection by haematogenous spread. In the absence of such obstruction, haematogenous seeding of bacteria to the kidneys accounts for about 3% of infections. Partial obstruction does not have this effect.

Vesicoureteric reflux

Incompetence of the vesicoureteric valve is a congenital problem that is five times more common in boys than in girls but tends not to be a significant factor in adults. It allows infected urine to ascend to the kidney and is the most common factor predisposing to chronic pyelonephritic scarring.

Instrumentation

Although any instrumentation of the urinary tract predisposes to infection, catheterization is the most common of these. A single catheterization will result in UTI in 1% of ambulatory patients but, in hospitalized patients, 10% of women and 5% of men will develop a UTI after one catheterization. Once in place, catheters produce infection in up to 10% of patients per day and nearly all catheterized patients will be bacteriuric by 1 month.¹³ All chronically catheterized patients are bacteriuric.

Pregnancy

Changes to the urinary tract occur normally during pregnancy as a result of both anatomical alterations and hormonal effects: dilatation of the ureters and renal pelvis, decreased peristalsis in the ureters and decreased bladder tone. These changes begin before the end of the second month. The prevalence of bacteriuria rises with age and parity. A large proportion of asymptomatic bacteriuric women develop symptomatic pyelonephritis later in pregnancy, with significant increases in toxæmia and prematurity (see 'Asymptomatic bacteriuria', later).

Diabetes mellitus

The relationship between diabetes mellitus on the one hand and ASB and UTI on the other has been debated. Current evidence indicates that ASB is more common in diabetic women than in those who are not diabetic. The evidence in men is less clear. Good evidence from prospective studies for an increased incidence of symptomatic urinary tract infection in diabetics is lacking. What appears clear is that diabetes is a significant and independent risk factor for pyelonephritis, complicated UTI, urosepsis, hospitalization and other, often rare, complications (such as emphysematous pyelonephritis, papillary necrosis and candidal infections). The precise pathogenetic mechanism is unclear but involves many factors not necessarily related to glycaemic control.^{14–16}

Ageing

UTI is the most frequent bacterial infection in residents of long-term-care facilities. ASB is highly prevalent in residents of long-term-care facilities, with up to 30% of men and 50% of women showing such bacteriuria. The likelihood of bacteriuria correlates with the degree of functional

impairment. Several factors may be involved: chronic degenerative neurological diseases may impair bladder function as well as bladder and bowel continence, prostatic enlargement in men and oestrogen deficiency in women can both lead to incomplete bladder emptying, and the use of devices—such as indwelling catheters or condom drainage—predisposes to bacteriuria.⁸

Bacterial factors

A number of studies^{17–19} have shown that the strains of *E. coli* (and a number of other gram negative bacteria) that cause UTI are not just the most prevalent in the bowel of the patient at the time of the infection but have specific characteristics, termed virulence factors, that give them certain capabilities: increased intestinal carriage, persistence in the vagina and the ability to ascend and invade the normal urinary tract. Thus there are clearly uropathogenic strains of these bacteria. In cases of complicated UTI (e.g. those associated with reflux, obstruction or foreign body), these virulence factors are not significantly involved.

Presentation

History

A careful history should be taken in any patient presenting with symptoms of apparent UTI, looking for risk factors for complicated or recurrent infection (such as previous UTIs and their treatment, the presence of known anatomical abnormalities and investigations or instrumentation, the possibility of pregnancy and history of diabetes mellitus), as well as seeking to identify those patients with urethritis and vaginitis. In men, the most common cause of recurrent lower tract UTI is prostatitis. Therefore evidence of prostatitis, such as chills, dysuria and prostatic tenderness, should be sought.

Lower tract infections (cystitis) typically present with irritative micturition symptoms, such as dysuria and frequency, suprapubic discomfort and sometimes macroscopic haematuria. There is usually no fever. Women presenting with dysuria and frequency without vaginal discharge or irritation have a 90% probability of cystitis.²⁰ The classic symptom complex of loin pain, fever ($>38^{\circ}\text{C}$), chills and urinary symptoms is usually associated with pyelonephritis. Severe pain should raise suspicion of a ureteric calculus that, combined with infection, poses a greater risk of sepsis and of permanent injury to the kidney.

Patients with chronic indwelling catheters usually have no lower tract symptoms at all but may develop loin pain and fever.

In elderly patients, particularly those in long-term-care facilities, the long-held view that symptoms of increased confusion and reduced mobility in the absence of fever are due to urinary

tract infection has been cast into doubt (see 'Treatment of specific groups: elderly patients', further on).⁸

Examination

The clinical signs of lower UTI are few and non-specific; however, patients should be examined to exclude other causes for their symptoms, particularly vaginitis in women and prostatitis in men. The presence of renal angle tenderness associated with fever, chills and dysuria suggests pyelonephritis.

Investigations

The key step in the diagnosis of UTI is examination of the urine, most commonly a midstream specimen of urine (MSU). Catheterization is appropriate in patients with altered mental state or those who cannot void because of neurological or urological reasons. Suprapubic aspiration is commonly used in paediatric practice but can be used in adults if other techniques have failed or cannot be used.

The next step is to look for the presence of pyuria; subsequently the specimen may be sent for quantitative culture and antibiotic sensitivity testing. Testing for haematuria, proteinuria and nitrites may be of supportive value but the results are not diagnostic.

Reagent test strips

In considering the use of reagent strips in the diagnosis of UTI, it should be noted that variations in published sensitivity and specificity exist. These may be due to (1) the use of different brands of reagent strips; (2) the use of different 'gold standards' against which comparison is made (e.g. counting chamber or cells/high-power-field counts, 'cut-off' criterion of the test used); (3) the nature of the study (blinded, unblinded); (4) the reader of the test (lab worker, doctor, nurse); and, most importantly, (5) the clinical setting or target population (e.g. symptomatic ED patients rather than an asymptomatic population in a clinic or office environment)—in other words, the pre-test probability.

A reagent strip test for leucocyte esterase is now the most common screening test for pyuria (see later). Taken alone, this has a sensitivity of 48% to 86% and a specificity of 17% to 93% for detecting pyuria (as defined further on). A positive predictive value (in symptomatic individuals) of 50% and a negative predictive value of 92% make this a valuable test for screening the emergency department (ED) population. Most studies indicate that when the combination of leucocyte esterase and nitrite is considered, the sensitivity of the test is 68% to 88% and a negative test excludes the presence of infection.²¹ Recent work by Sultana and others has shown that

reagent strips significantly improve the clinician's accuracy in diagnosing UTI in symptomatic ED patients.²² The clinical probability of UTI must be considered when such screening tests are used. In the patient with typical urinary tract symptoms, such a test may provide an adequate screen. It should, however, be used with great caution in the presence of fever of unknown cause in the elderly, the patient with an indwelling catheter or the patient with an impaired mental state, as pyuria and the implied bacteriuria may not be the cause of the problem.

Pyuria

Pyuria indicates inflammation in the urinary tract and, as a sign of infection, is second only to bacteriuria determined by quantitative culture (see later). The 'gold standard' definition of pyuria is based on early work involving measurement of the rate of excretion of polymorphs in the urine. This work showed that excretion of 400,000 polymorphs per hour was always associated with infection and was also found to be represented by 10 polymorphs per cubic millimetre in a single (unspun) midstream urine (MSU).²³ Thus 'significant pyuria' was defined as 10,000 polymorphs per millilitre of urine. It was subsequently shown that more than 96% of symptomatic patients, defined as having significant bacteriuria, had significant pyuria and conversely that less than 1% of asymptomatic people without bacteriuria have this degree of pyuria. Other definitions of pyuria, such as more than 5 leucocytes per high-power field, are based on examination of either the urinary sediment or of centrifuged urine and are inherently inaccurate because they cannot be standardized but are nevertheless often used.²⁴ 'Sterile' pyuria indicates the presence of significant pyuria without the presence of bacterial growth in standard culture (Box 9.4.1).

Nitrites

This reagent strip-based test is dependent on the bacterial reduction of urinary nitrate to nitrite, a function of coliform bacteria but not of *Enterococcus* spp. or *Staphylococcus saprophyticus*. The test has a low sensitivity (45% to 60%), better specificity (85% to 98%) but a high false-negative rate (about 45% in many studies). False-negative results are likely if the infecting organism is gram positive

Box 9.4.1 Common causes of sterile pyuria

- Non-specific urethritis in males
- Prostatitis
- Renal tract neoplasm
- Renal calculi
- Catheterization
- Renal tuberculosis
- Previous antibiotic treatment

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or *Pseudomonas*, if the diet lacks nitrate or if there is diuresis or extreme frequency, as a period of bladder incubation is necessary to form nitrates.

Haematuria

Although a frequent accompaniment of UTI, this finding is non-specific, as there are many other causes of haematuria.

Proteinuria

Most commonly with UTI, protein excretion is less than 2 g/24 h. It is another common but non-specific finding.

Quantitative culture

Urine culture is not essential in the management of the pre-menopausal sexually active female with an uncomplicated UTI, as the probability of UTI in these patients is 90%.²⁰ Culture should always be performed in patients with recurrent infection, possible pyelonephritis, potentially complicated UTI, males, the elderly or in cases where the cause of infection is not clinically evident. In symptomatic patients, a single specimen with a bacterial count in urine of greater than 10^5 colony forming units (cfu) per millilitre has a 95% probability of representing infection.²⁵ However, it has been shown that 30% to 50% of women with symptoms of dysuria will have bacterial counts less than 10^5 cfu/mL.²⁶ Of these, about half have bacterial UTI with low numbers of bacteria. The rest may be considered in two groups; one group has urethritis due to *Chlamydia trachomatis* or *Neisseria gonorrhoeae* and the other has negative cultures and may have *Ureaplasma urealyticum* urethritis. In men, counts as low as 10^3 cfu/mL suggest infection.²⁷

In patients with indwelling urethral or suprapubic catheters or those who intermittently self-catheterize and have symptoms or signs of UTI, a colony count of $\geq 10^3$ cfu/mL of more than one bacterial species in a single catheter or MSU specimen if the catheter has been removed within the previous 48 hours does indicate UTI.²⁸

Blood cultures

Blood cultures are normally not taken in afebrile patients with symptoms of cystitis. Current evidence indicates that blood cultures do not alter management and are therefore unnecessary in the majority of cases of uncomplicated pyelonephritis since the infecting organism can be isolated from a urine specimen.^{29,30} Blood cultures should be taken in the following circumstances:

- Recent instrumentation
- Known anatomic abnormality
- Failure of empiric treatment
- Immunosuppression
- Significant co-morbidity, such as diabetes mellitus
- Major sepsis
- Fever of unclear cause

Imaging

Imaging is not required in cases of uncomplicated cystitis. In pyelonephritis, imaging should be performed if there is

- Pain suggestive of renal colic or obstruction
- Failure to defervesce within 72 hours
- Rapid relapse on cessation of antibiotic treatment or within 2 weeks
- Infection with an unusual organism

These circumstances have been shown to be associated with stones or renal scarring. Computed tomography (CT) scanning is the preferred modality as it has greater sensitivity for demonstrating not only stones and obstruction but also rare gas-forming infections, haemorrhage and inflammatory masses.

Management

Ideally, treatment of UTI should rapidly relieve symptoms and prevent short-term complications such as progression from cystitis to pyelonephritis and subsequent sepsis or long-term sequelae, such as renal scarring, and prevent recurrences by eliminating uropathogenic bacteria from vaginal and perineal reservoirs. Treatment should be cost-effective and have few or no side effects.

There is no evidence that non-specific treatments, such as pushing fluids or attempting to alter urinary pH, change the outcome of normal antibiotic treatment; however urinary alkalinizers should not be used with quinolones due to an increased risk of crystalluria.

Antibiotic treatment

Serum levels of antibiotics are largely irrelevant in the elimination of bacteriuria. Reduction in urinary bacterial numbers correlates with the sensitivity of the organism to the urinary concentration of the antibiotic. Inhibitory concentrations are usually achieved in the urine after oral doses of the commonly used antibiotics. On the other hand, blood levels are vitally important in the treatment of bacteraemic or septic patients or those with renal parenchymal infections. Worldwide the incidence of multi-drug-resistant *E. coli* is increasing, especially organisms with extended spectrum β -lactamase resistance (ESBL). In Australia these make up less than 3% of community UTI isolates, but they should be considered in high-risk groups such as

1. International travellers to antibiotic-resistant areas within the last 6 months
2. Those who have recently used antibiotics
3. Patients in long-term-care facilities
4. Cases where the first-line antibiotics have failed

Clinicians should always refer to the latest available guidelines. Empirically the choice of

antibiotic is based on the clinical presentation and the bacteria likely to be involved (Table 9.4.1).

We should also keep in mind that in community-acquired UTI approximately 20% of the *E. coli* organisms isolated are resistant to trimethoprim and that if the patient has had trimethoprim in the last 3 months we should consider an alternative antibiotic.

Management of specific groups

Frequency dysuria syndrome: presumed simple cystitis

A non-pregnant, non-diabetic woman first presenting from the community with typical lower urinary symptoms should have vulvo-vaginitis excluded and an MSU taken and examined or tested by dipstick for pyuria. If pyuria is confirmed, culture of the urine specimen is not necessary and treatment should be commenced empirically (Fig. 9.4.1).

There is now good evidence that short-course treatment in this group of patients is effective in both treating the infection and eradicating uropathogenic strains of bacteria from reservoirs. Three-day treatment is superior to a single dose in eradicating the reservoirs of uropathogenic organisms, thereby reducing the incidence of recurrence. Longer courses have an increased incidence of side effects but not higher cure rates. The antibiotic of choice for 3-day treatment is trimethoprim.^{31,32} The emergence of trimethoprim-resistant uropathogens has been well documented in some communities. The subsequent overuse of fluoroquinolones as first-line agents has resulted in a rapid rate of development of resistance to these agents in parts of Europe and North America.^{34,35} In general fluoroquinolones should not be used as first-line agents for simple cystitis.³¹ Awareness of local antibiotic resistance patterns is thus an important factor in choice of the most appropriate antibiotic.

Amoxicillin/clavulanic acid, nitrofurantoin and cephalexin are suitable for 5-day therapy, but amoxicillin alone should not be used as there is a high incidence of resistant *E. coli* in community-acquired UTI. If there is no clinical response, MSU should be sent for culture and, in sexually active women, treatment for *C. trachomatis* commenced (doxycycline 100 mg bid). In non-sexually active women, further treatment is guided by the results of sensitivity testing. Short-course treatment is inappropriate in women who are at risk for UTI (despite lower tract symptoms), which includes those with a history of previous infections due to resistant organisms, with symptoms for more than 1 week or those with diabetes mellitus.

Males with UTI should be investigated for urinary tract abnormality and associated prostatic or epididymal infection. Such individuals must

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Table 9.4.1 Choice of treatment depending on bacteria involved (see text)

Condition	Bacteria involved	Suggested treatment ^{31,32}
Acute simple cystitis	<i>Escherichia coli</i> , <i>Enterococcus faecalis</i> , <i>Staphylococcus saprophyticus</i> , <i>enterococci</i> , <i>Proteus</i> spp., <i>Klebsiella</i> spp., <i>Pseudomonas</i> spp.	1. Trimethoprim 300 mg qd for 10–14 days ^a , OR 2. Cephalexin 500 mg q6h for 5 days OR 3. Amoxicillin/clavulanate 875/125 mg q8h for 5 days, OR 4. Nitrofurantoin 100 mg q12h for 5 days in women only ^b Males or patients with recurrent infection should be treated for up to 14 days. Norfloxacin 400 mg q12h for 7 days in resistant infection only
Acute uncomplicated pyelonephritis	<i>E. coli</i> , <i>E. faecalis</i> , <i>S. saprophyticus</i> , <i>enterococci</i> , <i>Proteus</i> spp., <i>Klebsiella</i> spp., <i>Pseudomonas</i> spp.	Mild infection: oral treatment Amoxicillin/clavulanate 875/125 mg q12h for 10–14 days, OR 1. Cephalexin 500 mg q6h for 10–14 days, OR 2. Trimethoprim 300 mg/day for 10–14 days Severe infection iv Gentamicin PLUS Amoxy/ampicillin 2 g IV, 6 hourly, OR patients with penicillin hypersensitivity Ceftriaxone 1g iv daily, OR Cefotaxime 1g IV 8 hourly
UTI with structural abnormalities (complicated) and in inpatients	Increased frequency of <i>Proteus</i> spp., <i>Pseudomonas</i> spp., <i>Klebsiella</i> spp., <i>enterococci</i> , <i>staphylococci</i>	Treatment should be guided by culture and sensitivity testing. The following are a general indication only³³:
Catheter-associated UTI	<i>E. coli</i> , <i>Proteus</i> spp., <i>Klebsiella</i> spp., <i>Pseudomonas</i> spp., <i>enterococci</i> , <i>staphylococci</i>	Treat only if symptomatic Change catheter Treat as for 'complicated UTI'
Dysuria with low bacterial numbers (urethral syndrome)	<i>Ureaplasma urealyticum</i> ^c	Doxycycline in young women
Prophylaxis in patients with recurrent infections		Trimethoprim 150 mg at night OR Cephalexin 250 mg at night

^aContraindicated in pregnancy.

^bIn men, nitrofurantoin does not achieve reliable concentrations and is therefore not recommended.

^cNB: may have chlamydial or gonococcal urethritis.

UTI, Urinary tract infection

have a urine culture initially and should have at least 14 days of treatment with any of the agents used for treatment of young women with simple cystitis (see Table 9.4.1).³¹ In men over 50 years of age, there is a high probability of invasion of prostatic tissue and treatment may have to be continued for 4 to 6 weeks.

Recurrent urinary tract infection

Recurrent UTI is defined as a symptomatic UTI that follows resolution of a previous UTI. These may be re-infections (with the same organism or another) or relapses (regrowth of the same organism within 2 weeks of treatment). Re-infections are more common than relapses, but the two may be indistinguishable.³⁶ It is important to consider the risk factors specific to the age and gender of the patient (e.g. sexual activity and use of spermicides in the young pre-menopausal woman or the higher rate of ASB in the older patient). A careful search for causes and reversible factors (e.g. of complicated UTI due to stone or obstruction, previously undiagnosed diabetes mellitus, prostatitis in males) should be made together with urine culture and sensitivity testing. Treatment is generally as for pyelonephritis, with an appropriate antibiotic guided by the results of sensitivity tests for at least 10 to 14 days. Female patients may benefit from post-intercourse or maintenance prophylaxis with, for example, cephalexin 250 mg or trimethoprim 150 mg at

night for several months. There has recently been burgeoning interest in the use of cranberry juice, either as juice or in tablet form, for UTI prophylaxis. Evidence is variable, but a recent Cochrane review of 24 studies concluded that cranberry juice cannot be recommended for UTI prevention.³⁷

Acute pyelonephritis

Patients presenting with the typical symptoms of pyelonephritis are at risk for bacteraemia or sepsis syndrome and therefore must rapidly have adequate concentrations of appropriate antibiotics delivered to both the blood and urine. In order to meet this requirement, particularly in patients who are vomiting, parenteral (intravenous) treatment is usually required initially but seldom for longer than 24 to 48 hours, by which time the patient is usually afebrile and not vomiting.

The choice of antibiotics is of necessity empirical at this stage. In cases of mild infection in patients who are not vomiting, 10-day treatment with one of the antimicrobials used for simple cystitis is appropriate, with ciprofloxacin or norfloxacin reserved for resistant organisms or proven *Pseudomonas aeruginosa*. For severe infections, parenteral ampicillin or amoxycillin (2 g q6h) together with gentamicin (4–6 mg/kg and up to 7 mg/kg as the initial dose for severe sepsis) are appropriate, with a third-generation cephalosporin as an alternative to gentamicin

when the use of aminoglycosides is contraindicated. In patients with hospital-acquired infections and suspected gram negative sepsis or infections with *Pseudomonas aeruginosa*, broader-spectrum agents—such as ceftazidime, piperacillin/tazobactam, ticarcillin/clavulanic acid and imipenem—perhaps in combination with aminoglycosides, may be required. Parenteral treatment is followed by oral therapy for 2 weeks.

The use of short-stay observation units is now a standard part of the practice of emergency medicine. The safety and efficacy of treatment of pyelonephritis in such units with intravenous antibiotics and fluid administration, followed by oral therapy, is widely accepted.³⁸ 'Hospital in the Home (HITH)' programmes are also now commonplace, allowing close supervision of these patients by hospital-based staff and once- or twice-daily intravenous antibiotic administration at home. The efficacy and safety of HITH is well established but requires careful patient selection to exclude those at risk for complicated infections. Appropriate follow-up is essential, although repeat urine cultures are not recommended in asymptomatic patients following simple pyelonephritis.^{39,40}

Pregnancy

UTIs in pregnancy are associated with an increased incidence of premature delivery and low-birth-weight infants. This has also been

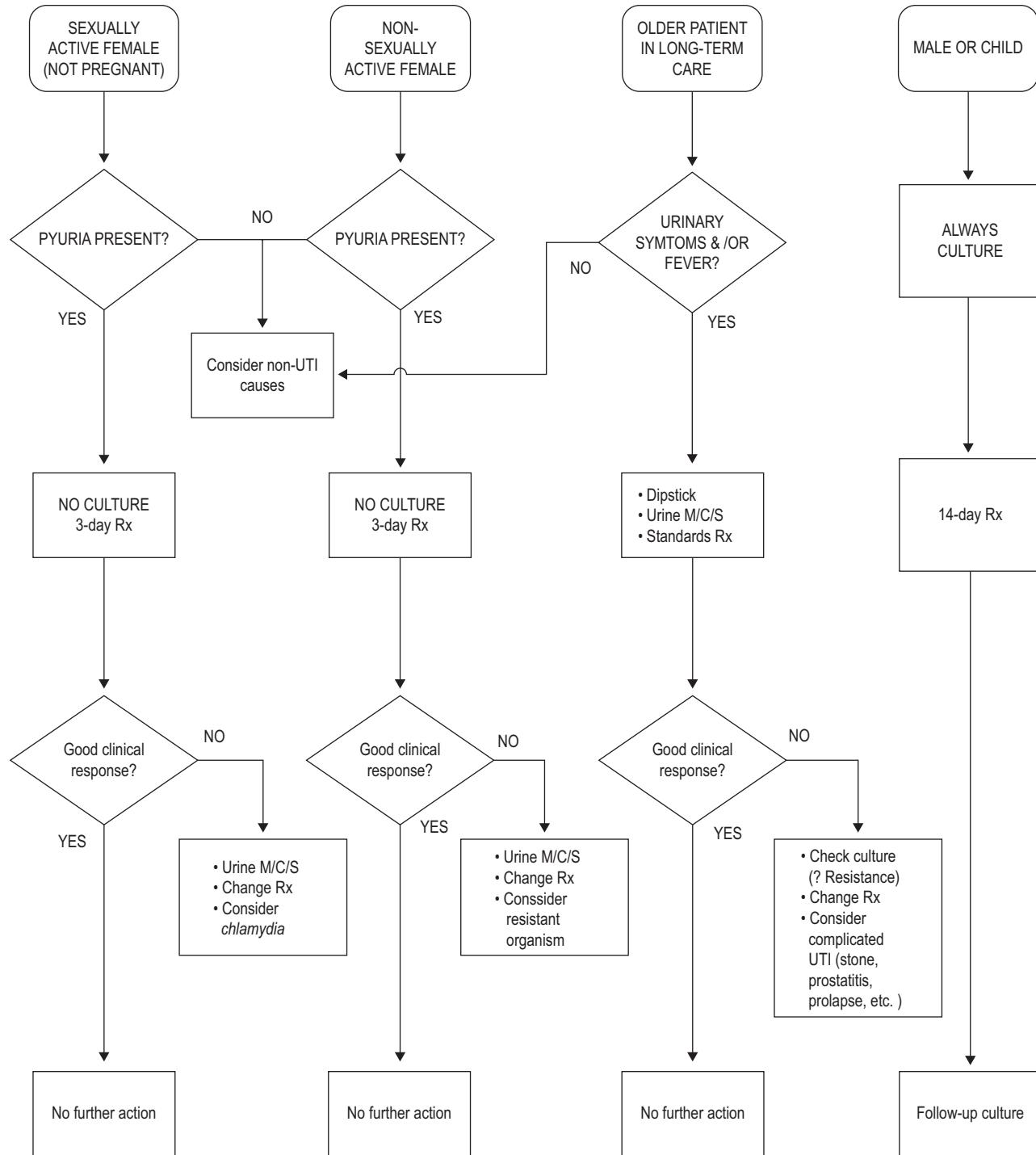


FIG. 9.4.1 Suggested flowchart for the management of simple cystitis.

demonstrated to occur with ASB, although up to 40% of asymptomatic women develop acute pyelonephritis later in pregnancy. Therefore screening for bacteriuria and treatment of pregnant women is essential and urine must be sent for culture and antibiotic sensitivity testing. Three-day courses of treatment are not widely recommended, although it may be reasonable to use them with close follow-up in an effort to reduce antibiotic usage. However, 10-day

treatment courses are the norm. Cephalexin, nitrofurantoin or amoxycillin/clavulanate are appropriate for use in pregnancy, Sulpha drugs and trimethoprim being contraindicated.³¹

Complicated urinary tract infection

As there is a greater range of organisms causing infection in these circumstances and a higher probability of antibiotic resistance, urine culture is essential and initial empiric treatment must cover

the broader spectrum of organisms potentially involved. If possible, antibiotic treatment should be delayed until the results of urine culture and antibiotic sensitivities are known. If empirical therapy is instituted, management should be reviewed as soon as such results are available.³³ Trimethoprim or a quinolone is appropriate for mild infections. More serious infections may need combinations of agents, such as aminoglycosides with amoxicillin or imipenem/cilastatin.

Catheter-associated urinary tract infection

Catheter-associated UTIs (CA-UTI) are the most common nosocomial infections. In patients with short-term catheters who develop infection, the catheter must be removed or changed and treatment instituted as for complicated UTI. For those with chronic indwelling catheters (such as patients with spinal injuries), bacteriuria is universal and treatment is indicated only in the presence of symptoms such as fever, chills or loin pain. Patients with chronic spinal injuries may present with autonomic dysreflexia syndrome, the symptoms of which include sudden hypertension, muscle spasm and sweating with or without fever. Antibiotic selection should again be based on culture or empirically as for complicated UTI. The most important strategy for the prevention of CA-UTI is minimizing catheter use and duration whenever possible. Preventive strategies based on use of methenamine, cranberry juice or prophylactic antibiotics at time of catheterization or catheter change are not supported by evidence.^{28,31}

Elderly patients

As previously stated, ASB and UTI are very common in older patients and more so with increasing functional impairment. Symptomatic infection is a significant cause of morbidity and mortality, as this age group also has a higher incidence of bacteraemia associated with pyelonephritis, and septic shock commonly follows. Given the high rate of ASB, the diagnosis of UTI in such individuals is difficult. The traditional view that non-specific symptoms—such as increased confusion (without fever), falling or deteriorating mobility—are due to UTI has been called into question. Evidence indicates that UTI should be considered only in patients with fever or specific genitourinary symptoms or both. In patients with non-specific symptoms, non-infective causes should be sought; in the case of fever alone, other potential sources of infection must be considered.⁸

Antibiotic treatment of symptomatic UTI in the elderly patient is no different initially from that of younger patients; however, it should be borne in mind that a greater variety of organisms may be cultured in this age group and urine for culture should be obtained at the outset whenever possible.

Asymptomatic bacteriuria

ASB is defined as the presence of significant bacteriuria (as previously defined) in a person without signs or symptoms of UTI. The presence of pyuria per se should not be taken to indicate bacteriuria; a quantitative culture is essential for the diagnosis. Current evidence indicates that many patient groups may be harmed or at least

may not benefit from antibiotic treatment for ASB. Antibiotics should therefore not be given to the following:

- Pre-menopausal, non-pregnant women
 - Diabetic women
 - Older people either living in the community or in institutions
 - Patients with long-term indwelling catheters
- Conversely, two significant groups receive clear benefit from antibiotic treatment for ASB: pregnant women and patients about to undergo urological procedures in which mucosal bleeding is anticipated (e.g. Transurethral resection of the prostate [TURP]).

Pregnant women with ASB have a 20- to 30-fold increased risk of developing pyelonephritis during pregnancy, with consequent premature delivery and low-birth-weight infants. Therefore pregnant women should be actively screened for ASB in early pregnancy and treated as for uncomplicated cystitis (without nitrofuranoin), with repeat cultures to confirm bacterial clearance. Periodic re-testing is recommended.

Patients who undergo urological procedures with mucosal bleeding (e.g. TURP) have a 60% rate of bacteraemia, with sepsis in 6% to 10%. These patients should be screened for ASB prior to the procedure and antibiotic treatment commenced shortly prior to the procedure and continued until after the procedure or removal of the post-procedure catheter.⁴¹

Disposition

Patients with simple UTI should have follow-up to confirm clinical cure. Failure of symptomatic improvement in 48 hours may indicate antibiotic resistance, which requires urine culture to elucidate. Recurrence of symptoms within 1 to 2 weeks may indicate occult renal infection and necessitates urine culture and at least 7 days' treatment.

Prognosis

In adults with normal urinary tracts, UTI does not cause long-term sequelae. In the presence of urinary tract abnormalities, infection may be a factor in producing renal damage or altering its rate of onset. Imaging of adults as part of their follow-up should detect this group of patients.

CONTROVERSIES

- The level of bacteriuria representing infection—traditional 10^5 cfu/mL or lower counts, such as 10^2 cfu/mL.
- Best first-line treatment of uncomplicated cystitis in the face of emerging resistance of uropathogens to common antibiotics such as trimethoprim and fluoroquinolones.

- The role of blood cultures as part of the investigation of pyelonephritis. Although traditionally used, they add little to the diagnosis and management.
- Asymptomatic bacteriuria in older, institutionalized patients—differentiation from symptomatic infection and appropriate management.

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9.5 Skin and soft-tissue infections

Cecil S. Johnny

ESSENTIALS

- 1** The time-honoured principles of soft tissue infection management and judicious evidence-based use of antibiotics remain the basis of treatment and the prevention of further complications.
- 2** These infections are common and range from mild to rapidly progressive and life threatening; early clinical recognition and treatment are paramount in reducing morbidity and mortality.
- 3** Deep soft tissue infections have high morbidity and mortality and, unless treated aggressively, can rapidly result in loss of a limb or the death of the patient.
- 4** Unusual organisms, including organisms not usually considered to be pathogenic, frequently cause serious infections in the immunocompromised, diabetic individuals and patients with hepatic disease.
- 5** There has been an increasing worldwide prevalence of community-acquired methicillin-resistant *Staphylococcus aureus* (CAMRSA) associated with skin and soft tissue infections (SSTIs) in the last decade.

Introduction

Skin and soft tissue infections (SSTIs) are among the most common reasons for emergency department (ED) presentations and admissions to the hospital. SSTIs are a diverse group of etiologically and anatomically distinct infections, with bacteria responsible for the majority of presentations in the ED. The pathogenesis of these infections usually involves the direct inoculation of bacteria as a result of violation of the skin or its defences, although infection may also spread from a distant source via the haematogenous

or lymphatic systems. The severity of infections encountered may range from mild to life threatening. Most recommendations for the diagnosis and treatment of SSTIs are based on tradition or consensus, as there are few randomized clinical trials on the subject. Some of the challenges to the emergency physician include the following:

- Early and accurate diagnosis of the type of infection, based on clinical judgement and limited use of laboratory and radiological investigations
- Early identification of potentially high-risk situations when the initial presentation is

seemingly innocuous by looking at patient factors (e.g. diabetes, immunosuppression) and local factors (bite wounds, site of infection, e.g. orbital cellulitis)

- Role of antibiotics: (1) appropriate choice of pharmacotherapeutic agent where indicated, taking into account the emergence of new infections and changing bacterial resistance patterns; (2) optimal route of delivery (i.e. topical versus oral versus initial intravenous or intramuscular bolus, followed by oral antibiotics versus intravenous therapy); (3) duration of the antibiotic treatment
- Need for surgical intervention (e.g. drainage of abscess, early debridement in necrotizing fasciitis)
- Disposition: outpatient versus inpatient care

Epidemiology and aetiology

The incidence of SSTIs has recently increased worldwide, mainly due to expansion of the aging population, comorbidities and the emergence of community-acquired methicillin-resistant *Staphylococcus aureus* (CAMRSA). The majority of SSTIs are caused by aerobic gram positive bacteria, commonly *Staphylococcus aureus* and group A streptococcus. gram negative, anaerobic or mixed organisms usually cause deeper, more complicated infections, commonly seen in the immunocompromised host. The increased prevalence of CAMRSA associated with SSTIs poses a challenge because there are high rates of treatment failure and relapse ([Table 9.5.1](#)).^{1,2}

Table 9.5.1 Causes of skin and soft tissue infections

Risk factor/setting	Expected pathogen
Simple cutaneous infection	<i>Staphylococcus aureus</i> . Also <i>S. epidermidis</i> , <i>S. hominis</i> , <i>S. viridans</i>
Perianal, genital, buttocks, ungual and cervical areas	<i>Bacteroides fragilis</i> , <i>Escherichia coli</i> , <i>Klebsiella</i> and <i>Proteus</i>
Immunocompromised host	<i>Cryptococcus neoformans</i> , <i>Coccidioides</i> , <i>Aspergillus</i> , <i>M. kansasii</i> , <i>M. tuberculosis</i> and <i>Yersinia enterocolitica</i>
Human bite	<i>Eikenella corrodens</i> , <i>Fusobacterium</i> , <i>Prevotella</i> , streptococci
Dog bite	<i>Pasteurella multocida</i> , <i>Capnocytophaga canimorsus</i>
Cat bite	<i>P. multocida</i>
Injection drug abuse	<i>S. aureus</i> , <i>Clostridium</i> spp., <i>E. corrodens</i> , <i>Staphylococcus pyogenes</i>
Body piercing	<i>S. aureus</i> , <i>S. pyogenes</i> , <i>P. aeruginosa</i> , <i>Clostridium tetani</i>
Hot tub/wading pool	<i>Pseudomonas aeruginosa</i>
Freshwater injury	<i>Aeromonas hydrophila</i>
Saltwater injury	<i>Vibrio vulnificus</i>
Fish tank exposure	<i>Mycobacterium marinum</i>

Examination

History

When a history is being taken, it is important to elicit the following:

- Any event leading to a breach in skin integrity, which may precipitate an infection (e.g. human, insect or animal bite, 'clenched fist' injury, excoriation, fungal infection or puncture wound). This is important because it will help in determining the likely pathogen and choice of antibiotics as well as the need to rule out any potential foreign body that may be embedded in the wound.
- The speed with which the infection has progressed, which serves to indicate how aggressive the infection is and the urgency of needed treatment.
- Patient factors that may complicate treatment of the infection, such as
 - History of immunosuppression (e.g. diabetes, steroid use, chronic liver disease, alcoholism, malnourishment, HIV, oncology patients on chemotherapy, nephrotic syndrome).
 - Recent use of antibiotics, (i.e. failed treatment).
 - History of prosthetic heart valves, mitral valve prolapse with regurgitation, previous history of endocarditis.
 - Chronic venous stasis or lymphoedema in limbs; surgery that includes lymph node dissection or saphenous vein resection.
 - Intravenous drug use (IVDU).
 - Tetanus immunization status.
 - Contamination with soil or water, which would suggest unusual pathogens as the cause of the infection.

Physical examination

- Identification of signs of sepsis: haemodynamic instability, pyrexia, 'toxic'-looking patient.
- Specific features of the infection to help narrow down the diagnosis (e.g. raised erythematous margins in erysipelas; presence of bullae and crepitus or tenderness out of proportion to physical signs, which are suggestive of necrotizing fasciitis; fetid odour, suggesting anaerobic infection; green exudates typical of *Pseudomonas* spp.).
- The extent of the infection (e.g. mapping areas of erythema to track progress, fluctuance that indicates a likely abscess, or lymphangitic spread).
- Location of the infection, as involvement of certain critical areas (e.g. head, face, hands, perineum) may require more intensive inpatient management and specialist consultation.
- Complicating factors that might impair successful treatment (e.g. IVDU, the presence of prosthetic heart valves).

Investigations

The diagnosis of SSTIs is essentially clinical. Laboratory and radiological investigations play a secondary and limited role in routine evaluation but may be useful in the ED management of immunocompromised patients or those with signs and symptoms of severe sepsis. In such situations, the following parameters should be considered:³

- Full blood examination with differential: Marked leucocytosis, leucopaenia or an extreme left shift in the white cell differential; new-onset anaemia or thrombocytopenia may suggest sepsis syndrome.

- Urea/creatinine: Elevated levels suggest intravascular volume depletion or renal failure.
- Creatine kinase: Elevated levels may indicate myonecrosis caused by necrotizing fasciitis.
- Tests to rule out diabetes mellitus: There is a strong association between SSTI and diabetes as well as a higher rate of complications.
- Blood cultures: These are recommended only in patients with systemic toxicity and wound cultures indicating severe purulent and deep soft tissue infection. The yield from blood cultures is less than 10% and may be compounded by false-positive results.⁴

Patients with a chronic, recurrent or unusual infection should have their immune status checked, including serology for HIV. Soft tissue radiographs may demonstrate a foreign body or gas in deep tissues. Ultrasonography is extremely useful in evaluating soft tissue infections for the presence of abscesses as well as for guiding drainage and the removal of foreign bodies. Computed tomography (CT) or magnetic resonance imaging (MRI) may be needed to define the depth and extent of the infective process in deep soft tissue infection.

Management

Key points in the management of SSTIs include the following:

- Appropriate use of antibiotics and timely surgical intervention
- Analgesia and supportive measure such as limb elevation
- Tetanus prophylaxis if indicated.
- Disposition

Analgesia

Oral or parenteral analgesia should be prescribed, as most patients with SSTIs will present with pain. Simple measures—such as immobilization, elevation, heat or moist warm packs—should not be overlooked, as they may help to alleviate pain in cellulitis. Abscess pain is best resolved by timely incision and drainage.

Antibiotic therapy

Antibiotics are recommended for patients with signs of systemic toxicity, high fever, tachycardia, for those who look unwell or are immunocompromised. They are also needed for infection in high-risk areas (hands, perineal region or face) and where deep tissue infection is suspected.

It is important for the emergency physician to recognize patients with serious SSTIs and to initiate timely and appropriate care. The choice of antibiotic is often empiric and thus must be guided by the patient's history, record of recent hospitalization and knowledge of the typical range of pathogens associated with each type

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of infection and their resistance patterns. The antibiotic of choice is the one that has proven efficacy against the range of expected pathogens is associated with minimal toxicity and is cost-effective. Where possible, narrow-spectrum antibiotics should be used in preference to broad-spectrum ones.⁵ Guidelines on antibiotic therapy are often deliberately non-prescriptive, reflecting the wide variety between differing patient populations, resistance patterns, risk for methicillin-resistant *Staphylococcus aureus* (MRSA) and local governance policies. It is also prudent to remember that SSTI clinical trials often exclude the most severely ill patients and may be powered to demonstrate non-inferiority only. The Infectious Diseases Society of America has released guidelines for treating SSTIs, including CAMRSA infections.⁶ Unlike those in inpatient or chronic care settings, emergency physicians more frequently have to initiate empiric antibiotics based on clinical judgement and prevailing anti-biograms due to the absence of culture and susceptibility results.

Current agents active against the common pathogens including MRSA and licensed for treating complicated SSTIs include linezolid, daptomycin and tigecycline. Novel approaches like phage therapy and novel antimicrobial therapy (oritavancin and tedizolid), which has equal efficacy with a better safety profile and shorter regimen, are under investigation.⁷

Surgical intervention

Effective treatment of abscesses and carbuncles and large furuncles entails incision, drainage of pus and breaking up of loculations, followed by regular dressings. Necrotizing fasciitis requires early aggressive surgical debridement together with broad-spectrum antibiotics in order to achieve a good outcome.⁶

Tetanus and other prophylaxis

All traumatic wounds should be considered to be tetanus-prone and treated accordingly. The patient's immunization status should be confirmed and, where appropriate, tetanus toxoid plus tetanus immunoglobulin should be administered. Rabies prophylaxis should be considered for all feral and wild animal bites and in geographical areas where there is a high prevalence of rabies.

In cases involving human bites, consideration should also be given to screening for blood-borne pathogens such as hepatitis B virus, hepatitis C virus, HIV and *Neisseria gonorrhoea*.

Disposition

Good candidates for the observation/short-stay unit include patients likely to respond to empirical therapy as well as those with a low likelihood

of infection or with unusual and/or resistant organisms.

Patients who have signs of systemic toxicity, involvement of vital structures (fingers, hands, face and neck; genitourinary, scrotal and anal regions), who are unable to take oral medication, and/or have failed outpatient therapy or who are immunocompromised are highly likely to require admission. Other prognostic factors include low serum bicarbonate, elevated creatinine, elevated creatine kinase and marked left shift polymorphonuclear neutrophils. The emergency physician must also be alert to scenarios requiring not just inpatient care but also urgent subspecialty consultation (e.g. necrotizing fasciitis).

Superficial skin infections

Clinical presentation

Patients usually present with complaints of localized pain, erythema and swelling. They may be on oral antibiotics and have not responded to them. The patient may present with signs of cellulitis and regional lymphadenopathy. Frequently an indurated fluctuant swelling may be elicited, indicating the presence of an abscess. If the patient is febrile or there is systemic involvement, his or her immune status must be examined. A diligent history should be taken to assess whether a foreign body associated with an abscess may be present. Ultrasonography is extremely useful in identifying this in such cases.

Impetigo

Impetigo is the commonest bacterial skin infection in children, usually caused by *Staphylococcus pyogenes* or *S. aureus*. It is highly contagious and there are two types: nonbullous (70%) and bullous (30%). Local wound care with a topical antibiotic (mupirocin) often suffices, but oral antibiotics (first-generation cephalosporin or erythromycin) may be needed in cases with extensive or bullous lesions.

Folliculitis

Folliculitis is a superficial, purulent infection of the hair follicles. Most cases are caused by *S. aureus*, but *Pseudomonas aeruginosa* infection can occur when folliculitis is associated with specific exposures (e.g. hot tubs and spas). Treatment is supportive with topical therapy. Removal of the hair in limited infections usually results in rapid resolution.

Furuncle and carbuncle

A furuncle is a purulent infection of hair follicles that involves the subcutaneous tissue. Furuncles most commonly occur on the back, in the axillae or on the lower extremities. When the infection extends to involve several adjacent follicles, resulting in a coalescent inflammatory mass, the lesion

is termed a carbuncle. Furuncles are often seen in patients with poorly controlled diabetes mellitus and in the immunocompromised. Small furuncles are best treated with moist heat. Larger furuncles and all carbuncles require incision and drainage.

Antibiotics are indicated if there is extensive surrounding cellulitis, the patient has a fever or diabetes or if he or she is immunocompromised, in which case di(flu)cloxacillin (500 mg q6h PO), cephalexin (500 mg q6h) or clindamycin (450 mg q8h PO) can be used.

Erysipelas

Erysipelas is an acute infection involving the cutaneous lymphatics of the superficial layers of the skin. The lesion is inflamed, indurated and elevated with a well-demarcated margin. It is often preceded by prodromal symptoms such as malaise, generalized aches, chills and high fever (5% of these patients will have bacteraemia). It is most often caused by Group A streptococci, with streptococcal toxins playing a part in the inflammatory response (other causes are non-group A streptococci, *Haemophilus influenzae*, *S. aureus* and *Streptococcus pneumoniae*). Contrary to popular belief, the commonest presentations involve the lower limbs, followed by the face and arms. Common risk factors include obesity, chronic oedema, previous leg surgery, leg ulcers, intertrigo, increasing age and medical comorbidities like hypertension, diabetes and peripheral vascular disease. Erysipelas may rapidly progress to cellulitis, abscess formation and, occasionally, fasciitis. Bullous erysipelas occurs in about 5% of the cases and is common in women and patients with renal or liver disease. It is associated with higher rates of MRSA infection.

Penicillin is the first line of therapy, followed by first-generation cephalosporins, macrolides and vancomycin (MRSA infections). Treatment includes elevation of the affected part, analgesia and the management of a possible underlying cause.

Herpetic whitlow

Herpetic whitlow is a superficial infection commonly affecting the fingers and characterized by intense pain, erythema and vesicle formation. It is caused by the herpes simplex virus (type 1 or 2). It commonly affects children and young adults and is often an occupational hazard for health workers. Diagnosis is usually clinical, and treatment is mainly supportive. Use of antivirals may reduce the duration of symptoms. Incision and drainage is contraindicated as this may cause bacterial superinfection or systemic spread.

Cellulitis

Cellulitis is an acute infection of the epidermis, dermis and subcutaneous fat, and it has a propensity to spread. In an immunocompetent

individual, infection is caused by bacteria that normally colonize the skin, principally *S. aureus* and group A β-haemolytic streptococci. Predisposing factors include conditions leading to a disrupted cutaneous barrier and/or impaired local host defences, such as trauma and inflammatory dermatoses (e.g. eczema, oedema from venous insufficiency or lymphatic obstruction).

Despite its common occurrence, there is a paucity of published research on issues such as criteria for antibiotics, admission and severity assessment. The presence of an underlying abscess should be considered if there is no response to antibiotic therapy. Bedside soft tissue ultrasonography is a useful tool that is increasingly available in EDs.

Treatment is guided by the site and extent of infection, clinical comorbidities and sometimes also social circumstances. Supportive care, such as elevation of the affected part and analgesia, is important.

Recommended antibiotics include penicillin such as diflucloxacillin (2 g q6h IV) or a first-generation cephalosporin such as cephazolin (2 g q8h IV) and vancomycin in suspected MRSA infection.

Broad-spectrum antibiotics may be required in special settings, such as in patients with diabetes, or infection in particular anatomical areas. Anaerobes or gram negative organisms have been identified in 95% of affected diabetic foot ulcers, with *S. aureus* found in approximately 33%.

Infections that originate from wounds involving the feet may be due to *P. aeruginosa*; they are also associated with osteomyelitis of the foot. Antibiotic treatment should consist of an antipseudomonal β-lactam such as carbenicillin or a third-generation cephalosporin such as ceftriaxone and an aminoglycoside.

Cellulitis is a well-known complication in women who have undergone axillary lymph node dissection and surgery for breast cancer. The major mechanism is thought to be an altered lymphatic and/or venous circulation related to the surgical procedure and to radiation therapy. Empiric antibiotic therapy is again targeted at *S. aureus* and β-haemolytic streptococci. If the patient has received recent chemotherapy and is neutropaenic, then the antibiotic regimen must be broadened to include coverage for aerobic gram negative bacilli, including *P. aeruginosa*.

Facial cellulitis, including periorbital and orbital cellulitis, is a serious infection occurring in both adults and children. The causal organisms include *S. aureus*, *H. influenzae* type b and *S. pneumoniae*. They may arise from an infected paranasal sinus, direct inoculation or haematogenous spread. Radiological evaluation, including CT scanning, may be necessary to identify the extent of infection, which may serve to guide treatment. The antibiotic of choice is flucloxacillin 2 g q6h IV plus ceftriaxone 2 g daily in case of suspected orbital cellulitis.

Abscesses

Pilonidal abscess

Pilonidal abscesses occur in the natal cleft and arise from disruption of the epithelium, causing the formation of a pit lined with epithelial cells; this may become plugged with hair and keratin, leading to inflammation and abscess formation. Treatment involves incision and drainage, usually in the operating theatre, although smaller abscesses can be drained in the ED. They are usually associated with mixed organisms, both aerobic and anaerobic.

Hidradenitis suppurativa

This is a chronic inflammatory skin disease of the upper apocrine sweat glands in the groin and axillae, resulting in recurrent nodule formation, inflammation and abscesses. Risk factors include female sex, obesity, smoking and follicular occlusion disorders. Organisms include *S. aureus*, *S. viridans* and *Proteus* spp. Treatment includes both medical and surgical management as indicated. Due to the chronic nature of the disease, the treatment is best coordinated by a specialist surgeon.

Bartholin abscess

This abscess occurs due to the obstruction of a Bartholin duct and the resulting inflammation. Isolates are usually polymicrobial, including both aerobes and anaerobes. *N. gonorrhoeae* and *C. trachomatis* may also be involved. Treatment is incision, drainage and marsupialization of the cyst in the operating theatre.

Acute paronychia

This is a superficial infection of the lateral aspect of the nail, which may proceed to abscess formation. Common organisms involved are *S. aureus* and streptococcal species. Incision and drainage is required in case of abscess formation.

Perianal abscess

These are the commonest of the anorectal abscesses (60%), which arise from the anal crypts and are located near the anal verge. Patients frequently complain of pain on defaecation and sitting. Perianal abscesses may be associated with inflammatory bowel disease and fistula formation. Treatment should be incision and drainage in the operating theatre under general anaesthesia. When the abscess is superficial and 'pointing', drainage in the ED is possible.

Infected cutaneous cysts

These are quite common, affecting around 20% of adults. They can occur anywhere on the body except the palms and soles.

Treatment

Incision and drainage of cutaneous abscesses is the key to treatment. Some patients require antibiotic therapy. Patients who are immunosuppressed or who have diabetes mellitus should be treated empirically with appropriate antibiotic therapy. Patients at risk of developing bacterial endocarditis require prophylactic antibiotics prior to incision and drainage. The treatment of superficial skin abscesses has in recent years been complicated by the emergence of MRSA. Proponents of the practice of 'routine culture' of abscess fluid say that surveillance of antimicrobial susceptibility allows therapeutic adjustment. Detractors point out that for simple abscesses, incision and drainage without antibiotics is usually sufficient; thus, if antibiotics are not considered clinically useful, it is unlikely that culture results will alter the management.

Deep soft tissue infections

Necrotizing fasciitis

Necrotizing fasciitis is a rare, rapidly progressing and life-threatening infectious process involving primarily the superficial fascia (i.e. all the tissue between the skin and underlying muscles, that is, the subcutaneous tissue). Patients usually present with the triad of exquisite pain—often out of proportion to initial physical findings—swelling and fever. Early diagnosis is sometimes thwarted by the paucity of cutaneous findings early in the course of the disease. The clinician should have a high index of suspicion based on the clinical presentation as well as the patient's underlying co-morbidities (diabetes, alcoholism and immunosuppression).

Numbness of the involved area is characteristic of advanced necrotizing fasciitis; this is a result of infarction of the cutaneous nerves. Eighty percent of cases show clear origins for an accompanying skin lesion (insect bite, minor abrasion, furuncle, and IVDU injection site); in the remaining 20%, however, no skin lesion can be found.^{8,9}

Patients appear extremely toxic with high fever, tachycardia and malaise. Pathognomonic features include extensive undermining of the skin and subcutaneous tissues, with separation of the tissue planes. The subcutaneous tissues may have a hard, wooden feel. Bullous lesions and skin ecchymoses may also be evident. Crepitus may be clinically evident and gas may be visualized on x-ray in some 80% of patients. The gas is typically layered along fascial planes. CT or MRI may aid in confirming the clinical suspicion. Laboratory values may be used in risk scoring (e.g. the Laboratory Risk Indicator for Necrotizing Fasciitis [LRINEC], which has been validated prospectively and has a high sensitivity and positive predictive value of 92% in patients with scores

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of 6 points and above). Patients with scores of 5 points and below are considered at low risk of necrotizing fasciitis.^{10,11}

Bacteria involved in this infection are usually mixed: *S. aureus*, haemolytic streptococci, gram negative rods and anaerobes. Sometimes only group A streptococci, either alone or in combination with *S. aureus*, are found. Aggressive therapy is essential, as mortality approaches 50%. Immediate extensive surgical intervention to open and debride the wound is required, as myonecrosis may be present.¹² Appropriate antimicrobial therapy should be commenced immediately: meropenem (1 g q8h IV) plus clindamycin (600 mg q8h IV) plus vancomycin 15–20 mg/kg/dose q8–12h IV. Hyperbaric oxygen therapy should be considered.

Fournier gangrene is a form of necrotizing fasciitis involving the scrotum, penis or vulva and is usually seen in diabetic patients. It usually originates from perianal or urinary tract infections (which extend into the periurethral glands) and can progress rapidly. The management is early recognition and surgical debridement as well as intravenous antibiotics.

Gas gangrene

Gas gangrene is an acute life- and limb-threatening deep tissue infection, also known as clostridial myonecrosis. Aetiological agents include *Clostridium perfringens*, *C. histolyticum*, *C. septicum* and *C. novyi*. *C. perfringens* is the most common cause in traumatic gas gangrene, whereas spontaneous gangrene is principally associated with *C. septicum*. This infection is characterized by the rapid development (often within hours) of intense pain in the region of a wound, followed by local swelling and a haemoserous exudate. A characteristic foul smell is also a good indication of the diagnosis. The area becomes tense and may develop a bluish and bronze or dusky discolouration. The presence of gas is typical, although that may be a late finding. It is frequently found on x-ray, where it has a feathered pattern as gas develops within the muscle itself. Aggressive treatment is required, as the patient may present in an advanced stage with tachycardia, altered mental status, shock and haemolytic anaemia.

Classically, the gas gangrene occurs in extensive and/or deep wounds with predisposing factors, including vascular compromise, diabetes and the presence of foreign bodies. Gram stain frequently reveals relatively few white blood cells and large numbers of club-shaped gram positive rods.

Early surgical intervention is essential, including wide debridement of necrotic muscle and other tissues, administration of high-dose penicillin (benzylpenicillin 2.4 g q4h IV), clindamycin (600 mg q6h IV) and hyperbaric oxygen therapy.

Early hyperbaric oxygen therapy has been shown to lead to an improved outcome.^{6,10–14}

It should be noted that the presence of gas certainly raises the suspicion of a deep tissue infection, including gas gangrene but that it may also be present because of previous wound manipulation, self-injection of air, localized gas abscess or other gas-producing organisms, including anaerobes, *E. coli*, streptococci and staphylococci.

Pyomyositis

Pyomyositis is the presence of pus within individual muscle groups; the usual culprit is *S. aureus*. A positive blood culture yield is found in only 5% to 30% of cases. Typical presenting symptoms include localized pain in a single muscle group, usually in an extremity, and fever. Ultrasonography or CT may be warranted to differentiate the condition from a suspected deep vein thrombosis.

Toxic complications of wound infections

A number of bacteria produce toxins that result in systemic symptoms.

Tetanus

Tetanus, albeit rare in developed countries, still occurs despite the fact that immunization is completely effective in preventing it. All wounds should be treated as tetanus-prone. Tetanus can occur with trivial wounds that may not even be apparent. The incubation period is variable, ranging from 3 days to several weeks after inoculation, and the disease is more severe at the extremes of age. Difficulty in swallowing and a fever with progression to stiffness and trismus is pathognomonic. Tetanus is also associated with autonomic nervous system dysfunction. Occasionally localized tetanus may occur with muscle spasm in the area adjacent to the wound. This is sometimes associated with cranial nerve dysfunction. Treatment is largely supportive, often requiring deep sedation, paralysis and ventilation for prolonged periods. Antibiotic therapy with high-dose penicillin should also be given in addition to tetanus immunization and tetanus immunoglobulin.¹⁵

Toxic shock syndrome

Toxic shock syndrome (TSS) is a life-threatening multisystem disease caused by an inflammatory immune responses to toxigenic strains of *S. aureus*. TSS has been classically associated with the use of tampons, although 10% to 40% of cases are not related to menstruation. Non-menstrual cases occur after childbirth, abortions, in bone and skin infections including postoperative wound infections, burns, mastitis

and varicella-related cellulitis. The wound itself may look insignificant. There is a rapid onset of fever, usually above 38.9°C, hypotension and an initial diffuse and later desquamating erythematous rash. Multi-organ involvement may include muscular (myalgia), neurological (headache, altered sensorium) and gastrointestinal (nausea, diarrhoea) symptoms. Occasionally *S. aureus* can be cultured locally, although blood cultures are rarely positive. Antibiotics do not affect the course of TSS but may lower the recurrence rate by 59% to 73%. An anti-staphylococcal agent should be given with an aminoglycoside. Patients are frequently haemodynamically compromised, requiring aggressive fluid resuscitation and inotropic support. Debridement of necrotic wounds, if present, and elimination of the source of infections (e.g. removal of the tampon) should be carried out urgently. A similar syndrome can develop due to infection with group A β-haemolytic streptococci. This is known as 'wound' or 'surgical' scarlet fever. Treatment is the same as for TSS.

Special infections

Human bites

Human bite wounds may occur as a result of an accident, deliberate biting or closed-fist injuries. The bacteriology reflects the normal oral flora of the biter: streptococci in 50% to 80% of wounds, staphylococci, *Eikenella corrodens* and anaerobic organisms. Therapy consists of irrigation and topical wound cleansing; prophylactic antibiotics should be initiated as early as possible in all patients regardless of the appearance of the wound.

Clenched-fist injuries over the metacarpophalangeal joint warrant hospitalization for formal washout and intravenous antibiotics. Appropriate antibiotic choices include amoxicillin-clavulanate (875 + 125 mg q12h PO) or piperacillin-tazobactum (4+0.5 g q8h IV). In cases of penicillin allergy, metronidazole plus doxycycline or ciprofloxacin may be used.

Animal bites

Most such bites are from dogs (80%) or cats, but bites from exotic pets and feral animals also occur. *Pasteurella* and *Bacteriodes* spp. are the most common bacterial isolates and *Capnocytophaga canimorsus* can cause bacteraemia and fatal sepsis, especially in patients with underlying liver disease or asplenia. Infected bites presenting less than 12 hours after injury are more likely to be infected with *Pasteurella* spp., whereas those presenting after 24 hours are more likely to be infected with staphylococci or anaerobes. Wounds should be cleansed with sterile normal saline and infected wounds should not be closed. Cat bite wounds have less crush injury and

wound trauma than dog bites but lead to a higher proportion of osteomyelitis and septic arthritis. The oral agent of choice for both dog and cat bites is amoxicillin/clavulanate, with clindamycin plus ciprofloxacin as an alternative. Intravenous options include second-generation cephalosporins, piperacillin/tazobactam and carbapenems. Established infection usually responds to 7 to 10 days of therapy. Rabies prophylaxis should be considered for all feral and wild animal bites and in geographic areas where there is a high prevalence of rabies.

Water-related infections

Water-related infections may be caused by unusual organisms. *Vibrio vulnificus*, *Vibrio alginolyticus* and other non-cholera vibrios are found in salt and brackish water and can result in serious and life-threatening infections, especially in patients with hepatic disease. Aggressive infection can progress rapidly over 2 to 4 hours. It is associated with saltwater exposure or the ingestion of raw shellfish. Infections can mimic gas gangrene, with rapid progression and tissue destruction; septicaemia may occur and can be fatal. If parenteral therapy is required, a third-generation cephalosporin can be combined with an aminoglycoside and/or doxycycline.

Exposure to fresh or brackish water (rivers, mud, caving) can result in infection with the gram-negative bacillus *Aeromonas hydrophila*.¹⁶ *Aeromonas* infections can result in superficial skin infections, myositis and septicaemia. Treatment consists of administration of ciprofloxacin 500 mg q12h PO.

Mycobacterium marinum, *M. ulcerans*, *M. chelonei*, *M. gordanae* and *M. fortuitum* are found in fish tanks and can result in 'fish fancier's finger'. After 2 to 6 weeks of incubation, an ulcerating granuloma develops. Treatment options include clarithromycin, trimethoprim/sulfamethoxazole or a combination of ethambutol and rifampicin. Systemic infection is uncommon.

Handlers of saltwater fish may develop infections due to *Erysipelothrix rhusiopathiae*; this causes erysipeloid, a type of cellulitis.¹⁷ It also causes infections in people handling fish, poultry, meat and hides. Coral cuts are often infected with *Streptococcus pyogenes*; other marine pathogens may be involved (including *Vibrio* species). Treatment should consist of penicillin or ciprofloxacin.

Mastitis

Infections of the breast can occur in both sexes and in patients of all ages; however, breast infections are most common in nursing mothers. The prevalence in Australia is estimated at 20%.¹⁸ *S. aureus* is the most common pathogen in infective mastitis.

Treatment consists of regular emptying of the breast. If breastfeeding must be stopped because of the severity of the infection or the risk to the neonate, a pump or manual expression methods should be employed (at least temporarily). If symptoms are not resolving within 12 to 24 hours of effective milk removal and analgesia, antibiotic treatment should be commenced to prevent abscess formation. Around 11% of these patients will have abscess formation if not appropriately treated. Options include di(flu) cloxacillin (500 mg q6h PO) or cephalexin (500 mg q6h PO) or clindamycin (450 mg q8h PO) for at least 5 days. Severe infections may require parenteral or more prolonged therapy. Local care to the region is also important, including warm compresses, breast support, analgesia and the application of a moisturizing cream to the nipple and areolar region. Patients who develop an abscess will require percutaneous aspiration or open drainage.¹⁹

Decubitus ulcers

These are cutaneous ulcers caused by prolonged pressure resulting in ischaemic necrosis of the skin and underlying soft tissue. They are most commonly found in patients who are bedbound, particularly elderly nursing home patients and patients with sensory deficits. Immobility, compounded by vascular insufficiency and neuropathy, results in ulcer formation; Unless these lesions are treated aggressively, serious complications can follow.²⁰ Complications include cellulitis and deep soft tissue necrosis, osteomyelitis, septic thrombophlebitis, bacteraemia and sepsis. Culture of the ulcer invariably reveals a mixed bacterial flora of both aerobes and anaerobes, which do not distinguish between colonization and tissue infection. The most common organisms found are staphylococci, streptococci, coliforms and a variety of anaerobes. Antibiotics are required for patients with clinical signs of sepsis or osteomyelitis.

Varicose ulcers

These are superficial ulcers of the lower limbs caused by oedema and poor tissue drainage as a result of dysfunction of the venous system. They are more common in the elderly and obese and may be chronic, therefore healing is often difficult. Complications include cellulitis and occasionally bacteraemia. Culture of the ulcer variably reveals a mixed bacterial flora of both aerobes and anaerobes that cannot help to distinguish colonization from tissue infection. The most common organisms found are staphylococci, streptococci, coliforms and a variety of anaerobes.

Treatment consists of debridement of necrotic tissue, pressure area and general nursing care, as well as treatment of infection if present. Antibiotic treatment is indicated only where there is

systemic evidence of infection or a complicating infection, such as osteomyelitis or bacteraemia. Surgical debridement is frequently as important if not more important than antibiotic therapy, particularly where the bacterial infection is localized.

Diabetic foot infections

Foot infections are a common complication of diabetes and require both local (foot) treatment and systemic (metabolic) optimization, which is best undertaken by a multidisciplinary team including surgeons, podiatry services and the endocrinologist or physician.

The peripheral neuropathy associated with diabetes leads to the loss of protective pain sensation and results in repetitive injuries followed by the development of ulcers that become infected. Vascular insufficiency and impaired immune function contribute to the increased risk of acute and chronic infection. Infections in foot ulcers are often polymicrobial, and both the number of bacterial groups and bacterial density are thought to affect healing.¹⁷ Aerobes include *S. aureus*, coagulase-negative staphylococci and streptococci. Enterobacteriaceae and *Corynebacterium* are common. Anaerobes, which have been isolated from up to 48% of patients, include *Bacteroides* and *Clostridium* spp. The presence of anaerobes is associated with a high frequency of fever, foul-smelling lesions and the presence of an ulcer. Cultures obtained using curettage following debridement should be used in preference to wound swabs to identify causative organisms and sensitivities.

Local signs and symptoms predominate and include those secondary to infection, vasculopathy and neuropathy. Pain and tenderness are often minimal due to the neuropathy and pulses are frequently reduced or absent. Wound infections must be diagnosed clinically on the basis of local (and occasionally systemic) signs and symptoms of inflammation. Laboratory (including microbiological) investigations are of limited use for diagnosing infection except in cases of osteomyelitis. Radiography and/or a bone scan may be warranted to exclude osteomyelitis.

A systematic review²¹ reported that there is no strong evidence for any particular antimicrobial agent in the prevention of amputation, resolution of infection or ulcer healing. For mild to moderate infections with no evidence of osteomyelitis or septic arthritis, consider amoxicillin/clavulanate (875 + 125 mg q12h PO) for at least 5 days. Alternatives include ciprofloxacin 500 mg q12h with clindamycin 600 mg q8h. For severe limb- or life-threatening infections, intravenous piperacillin/tazobactam 4+0.5 g q8h or ticarcillin/clavulanate 3 + 0.1 g q6h are acceptable for empiric therapy. Prolonged use of antibiotics may be required, especially in the setting of osteomyelitis or septic arthritis.

9.6 HEPATITIS

Surgical-site/postoperative wound infection

They are the most commonly occurring adverse events in patients who have undergone surgery, accounting for as much as 38% of nosocomial infections in postoperative patients. Surgical-site infections are usually diagnosed by the usual features of inflammation, which may manifest late in morbidly obese patients or those with deep wounds. Most bacterial wound infections present with fever only after 48 hours. Earlier symptoms may be seen in *S. pyogenes* and clostridial infections.

The treatment generally requires opening of the sutures, evacuation of any collection and ordering wound cultures. However, the physician should be mindful of the type and site of surgery and should always involve the concerned surgical team. There has been a paucity of evidence regarding the use of antibiotics combined with drainage,²² but expert consensus generally advocates the use of empirical antibiotics for patients with temperature above 38.5°C and/or a pulse rate greater than 100/min in the presence of obvious wound infection.⁶

Post-traumatic wound infection

The goals of wound care are to avoid infection and to achieve a functional and cosmetically acceptable outcome. Adequate wound management requires a thorough history, with particular attention directed at factors adversely affecting healing. Factors such as the extremes of age, diabetes, chronic renal failure, malnutrition, alcoholism, obesity and patients on immunosuppressive agents lead to an increased risk of infection and impaired wound healing. Wounds located in highly vascular areas, such as the scalp

or face, are less likely to become infected than wounds in less vascular areas.

In order to reduce the incidence and severity of infection, wounds must be thoroughly cleansed and irrigated. Devitalized tissue should be debrided, injuries to associated structures excluded and the wound closed appropriately. The method of closure depends on the location of the wound, the level of contamination and the age of the wound. Wounds that should not be closed because of a high risk of infection, such as heavily contaminated wounds, should be treated by delayed primary closure. Where primary closure is possible, the wound should be closed and a protective non-adherent dressing applied for a minimum of 24 to 48 hours, with both the wound and the dressing kept dry.²³

The use of prophylactic antibiotics is not recommended except where there is significant bacterial contamination, foreign bodies, the patient is immunosuppressed or the wound is the result of a bite (human or animal) or associated with an open fracture. Most wounds can be treated with amoxicillin/clavulanate (875 + 125 mg q12h PO) or metronidazole (400 mg q12h PO) plus di(flu)cloxacillin (500 mg q6h PO). Broad-spectrum antibiotics should be limited to heavily contaminated lesions and bite wounds and to immunosuppressed patients.

Intravenous drug users

Intravenous drug users frequently develop SSTIs at injection sites and at times may be polymicrobial. The reasons include contaminated drug paraphernalia, alteration of skin flora, poor nutrition and immune function (many have hepatitis B, C and HIV), injection under the skin (skin popping),

extravasation and tissue necrosis.²⁴ Intravenous drug users frequently have mixed gram-positive and gram-negative infections, particularly anaerobes including *Klebsiella*, *Enterobacter*, *Serratia* and *Proteus*. Some develop fungal infections, including candidaemia. Subacute bacterial endocarditis and endocarditis must be considered in IV drug users presenting to the ED. If endocarditis is not suspected, treatment should consist of flucloxacillin 2 g IV q6h and gentamicin 5 to 7 mg/kg/day as a single daily dose.

CONTROVERSIES

- The timing and method of closure of contaminated or 'old' (more than 6 hours since injury) wounds.
- The prophylactic use of antibiotics in patients with 'clean' wounds.
- Choice of antibiotics in treating skin and soft tissue infections: narrow-spectrum first-generation cephalosporin or broad-spectrum third-generation cephalosporin? Should antibiotics be used to cover gram negative, gram positive organisms, anaerobes and aerobes?
- Can more patients be treated as outpatients using parenteral therapy or after early discharge once the acute toxic phase is over?
- Management of cutaneous abscesses: are antibiotics necessary after incision and drainage? Are cultures of the abscess fluid needed?

Full references are available at <http://expertconsult.inkling.com>

9.6 Hepatitis

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ESSENTIALS

- 1** Acute and chronic viral hepatitis is of global public health importance.
- 2** Definitive diagnosis may be delayed in the emergency setting.
- 3** Supportive care is fundamental in the acute management of hepatitis.
- 4** Prevention of viral hepatitis is possible via the introduction of public health programmes that include appropriate education regarding high-risk practices.

Introduction

Hepatitis is a non-specific clinicopathological term that encompasses all disorders characterized by hepatocellular injury and histological evidence of a necroinflammatory response. An important distinction is that between acute and chronic viral hepatitis. *Acute viral hepatitis* is a process of self-limited liver injury of less than 6 months' duration.¹ *Chronic viral hepatitis* is diagnosed on pathological criteria and is characterized by a duration of more than 6 months.

9.5 SKIN AND SOFT-TISSUE INFECTIONS

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Clinical presentations of viral hepatitis

Patients with acute viral hepatitis may be asymptomatic; those with only mildly deranged liver function tests (LFTs) may be symptomatic with or without jaundice or may present with fulminant disease (severe liver failure, which develops within 8 weeks of symptom onset).

Various clinical phases characterize acute viral hepatitis. The incubation phase is the time between the original infection and the initial symptoms during which viral replication occurs, providing laboratory evidence of hepatitis. During the pre-icteric phase, non-specific symptoms evolve, such as malaise, fatigue, anorexia, nausea, vomiting, myalgias, arthralgias and abdominal discomfort. If fever is present, it is generally of low grade. Cough, coryza, pharyngitis and a distaste for alcohol and tobacco smoke may be evident. Meningoencephalitis may rarely occur.

The icteric phase features a variable degree of jaundice, dark urine (bilirubinuria), pale stools (absence of bile pigment in the stool), pruritus, hepatomegaly and splenomegaly. During the convalescent phase, symptoms resolve, as do liver enzyme abnormalities. In patients presenting to the emergency department (ED) during the pre-icteric phase, the diagnosis may be challenging given the non-specific symptomatology. If a patient presents during the icteric phase, focused history taking, examination and the appropriate investigations should result in a definitive diagnosis.

Laboratory investigations

Blood test abnormalities are a prominent aspect of acute viral hepatitis. Serum transaminases are typically elevated at greater than 500 U/L and often more than 1000 U/L.² Alanine aminotransferase (ALT) may characteristically test higher than aspartate aminotransferase (AST). Alkaline phosphatase may be normal or mildly elevated. Serum bilirubin is variably elevated and is usually divided between conjugated and unconjugated fractions. Albumin and the prothrombin time should be normal unless hepatic synthetic function is significantly impaired. Neutropaenia and lymphopaenia may be transient. Severe acute hepatitis may cause hypoglycaemia.

Management

In cases of acute viral hepatitis, the fundamental management is supportive care. Many of these patients can be managed on an outpatient basis. Patients require hospitalization when they have intractable vomiting with inadequate oral intake and demonstrate clinical features of liver failure. A well-balanced diet is beneficial. It is recommended that alcohol be avoided during the acute phase, but there is no definitive evidence

that alcohol consumption post-recovery causes either relapses or progression to chronic disease. Given that the liver is involved in the metabolism of a plethora of drugs, all medications must be prescribed with special care to patients with acute hepatitis.

In managing fulminant hepatic failure, it is imperative that potential patients be identified as early as possible. In the emergency setting, intubation and the concomitant critical care may be necessary for patients with progressive encephalopathy.

Prevention and immunization

Prevention of viral hepatitis is possible via the introduction of public health programmes, improved sanitation and vaccination programmes. Post-exposure prophylactic regimens are particularly relevant to health care workers.

Hepatitis A virus

As the most common cause of viral hepatitis, hepatitis A virus (HAV) contributes significantly to the global burden of disease. Multiple genotypes exist and infection with one genotype confers immunity against others. (See Table 9.6.1 for virology.)

Epidemiology

HAV is highly endemic in developing countries and can often be traced to contaminated water or food.

Natural history

Virus is excreted in the stool of the infected person for 1 to 2 weeks prior to and for 1 week after the onset of symptoms. A non-specific prodrome may be followed by jaundice and tender hepatomegaly.

The clinical severity of the illness increases with age, with more than 80% of children being asymptomatic. HAV has been associated with extrahepatic features, such as cutaneous vasculitis, renal failure, pancreatitis, bradycardia and, rarely, convulsions, transverse myelitis and aplastic anaemia. Relapsing hepatitis has been described in 20% of those with HAV infection. Relapses are generally benign and may occur 4 to 15 weeks after the original illness. Complete recovery is the typical outcome. Fulminant hepatic failure occurs in less than 1% of cases.¹ Chronic infection never ensues.

Laboratory investigations

Serum antibody is present from the onset of HAV disease in both Immunoglobulin M (IgM) and Immunoglobulin G (IgG) forms. After approximately 3 to 12 months, anti-HAV IgM disappears and anti-HAV IgG persists, thereby conferring lifelong immunity against re-infection.

Management

Supportive management is of primary importance. Potentially hepatotoxic medications must be ceased. Alcohol should not be consumed during acute episodes because of its direct nephrotoxic effects.

Prevention and immunization

General measures are imperative—safe water supplies, proper sewage disposal and careful hand washing. HAV vaccines can prevent HAV infection and, importantly, have excellent safety profiles. Persons who have been exposed to HAV and who have not been previously vaccinated should receive the vaccine within 2 weeks of exposure. Travellers to endemic areas require inactivated hepatitis vaccine, which confers long-term immunity to more than 90% of persons.

Table 9.6.1 Characteristics of the main hepatitis viruses

	HAV	HBV	HCV	HDV	HEV
Family	Picornavirus	Hepadnavirus	Flavivirus	Incomplete	Calicivirus
Nucleic acid	RNA	DNA	RNA	RNA	RNA
Diameter (nm)	27	42	32	36	34
Incubation period (weeks)	2–6	6–24	2–26	6–9	2–10
Spread					
Faeces	Yes	No	No	No	Yes
Blood	Uncommon	Yes	Yes	Yes	No
Sexual	Uncommon	Yes	Uncommon	Yes	?
Vertical	No	Yes	Uncommon	Yes	No
Chronic infection	No	Yes	Yes	Yes	No
Vaccine	Available	Available	Nil	Nil	Nil

HAV, Hepatitis A virus; HBV, hepatitis B virus; HCV, hepatitis C virus; HDV, hepatitis D virus; HEV, hepatitis E virus.

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Hepatitis B virus

Of the viral causes of hepatitis, few are of greater global importance than hepatitis B virus (HBV). HBV infection is endemic in certain parts of the world—Southeast Asia, China and sub-Saharan Africa. It is estimated that there are 350 million carriers worldwide. By 2020, it is estimated there will be a two- to threefold increase in the number of hepatitis B–induced liver cancer cases and a marked increase in the number of deaths attributable to hepatitis B under current treatment patterns in Australia. (See Table 9.6.1 for virology.)

Epidemiology

Transmission occurs by percutaneous and mucosal exposure to infected blood products and bodily fluids; hence unprotected sexual contact with infected individuals, the use of contaminated paraphernalia during intravenous drug use and vertical transmission from mother to infant are commonly implicated. In the last decade, several factors have changed the worldwide dynamics of hepatitis B epidemiology, including massive population migrations from highly endemic areas and the implementation of preventive strategies, screening policies and public education.

Natural history

Many acute HBV infections are asymptomatic, particularly in younger patients. The non-specific symptoms of the acute episode may be preceded by a serum-sickness syndrome with fevers, urticaria and arthralgias.

Approximately 90% of patients completely recover from an acute episode of HBV infection. Fulminant hepatic failure may develop in 1% of patients and has a mortality rate of up to 80%.

Progression to chronic HBV infection occurs in 5% to 10% of cases, with 90% of these experiencing an asymptomatic carrier state and the remaining 10% proceeding to cirrhosis and hepatocellular carcinoma. The risk of developing chronic disease is related to the age at which HBV infection is first contracted—there is a greater than 90% risk of developing chronic HBV infection in neonates and a less than 5% risk in immunocompetent adults. Although chronic HBV infection is generally a lifelong condition, a small percentage of infected individuals will experience complete viral eradication. In chronic HBV infection, the incidence of cirrhosis is about 2% to 3% per year. Variables associated with progression to cirrhosis are persistence of viral replication, older age, elevation of ALT levels and HBeAg positivity.³

Laboratory investigations

The diagnosis of HBV infection is currently based on the detection of serological markers, including Hepatitis B Surface Antigen (HbsAg),

anti-HBs antibodies, anti-HBc antibodies (total or IgM), HBeAg, and anti-HBe antibodies, and on the detection and quantification of HBV DNA in peripheral blood. The diagnosis of acute hepatitis B is based on the concomitant presence of HBsAg and anti-HBc IgM (Table 9.6.2). In chronic HBsAg carriers, the presence or absence of HBeAg, the HBV DNA level, and the ALT level help diagnose the phase of chronic infection.⁴

Management

Supportive care is the primary aim of management. Household contacts require adequate education. In cases of chronic HBV infection, the aims are to suppress HBV replication and to reduce liver injury. Interferon alpha (IFN- α) has antiviral, antiproliferative and immunomodulatory effects and is an effective treatment option against HBV infection. Patients with normal serum ALT levels have a poor response to IFN- α because the lack of hepatic dysfunction is suggestive of low immune-mediated hepatic inflammation. The limiting factor in the use of IFN- α is the side-effect profile, which includes an influenza-like illness, gastrointestinal symptoms, psychological sequelae (particularly depression), bone marrow suppression, thyroid dysfunction and possible birth defects. Lamivudine is an oral nucleoside analogue that potently inhibits HBV DNA synthesis. New antiviral approaches that target various steps and components of the HBV life cycle, including covalently closed circular DNA (cccDNA), are currently being investigated in the hope of achieving functional cure of infection or, if possible, complete viral eradication. These approaches include HBV entry inhibitors, such as Mycludex B, cytokines or sequence-specific nucleases that damage or destroy cccDNA and monoclonal antibodies that decrease circulating HBsAg load.

Prevention and immunization

The pre-exposure administration of HBV vaccine is fundamental to immunoprophylaxis. The vaccine is protective in over 90% of individuals. Current recommendations include all infants at birth and individuals with high exposure risk, such as health care personnel, injecting drug users and high-risk sexual workers. Antibody titres may decrease with time but the protective effects persist. The risk of HBV infection in the occupational setting is related primarily to the degree of contact with blood and to the HBeAg status of the donor. In needle-stick injuries, the risk of developing clinical hepatitis if the blood is both HBsAg- and HBeAg-positive has been estimated to be up to 30%. Post-exposure prophylaxis involves the administration of hepatitis B immunoglobulin in addition to the recombinant vaccine series.

Hepatitis C virus

International studies estimate that up to 3% of the world's population is infected with hepatitis C virus. International studies estimate that up to 3% of the world's population is infected with hepatitis C virus (HCV).⁵ (See Table 9.6.1 for virology.) The identification of six major genotypes of the HCV has important clinical implications in that such genomic sequence variation makes vaccine development extremely difficult.

Epidemiology

Parenteral exposure leads to HCV infection, the use of contaminated needles and syringes being a predominant factor. Sexual and perinatal transmission of HCV is negligible. Transfusion-related HCV transmission has essentially been eradicated via donor screening. Up to 10% of HCV cases do not have an identifiable source of infection.

Natural history

A pre-icteric phase featuring non-specific symptoms develops in 15% to 20% of patients. When the icteric phase develops, it typically lasts for 1 to 2 weeks. Fulminant hepatic failure rarely results from acute HCV infection.

Following an acute episode, 75% to 85% of adults and 55% of children will enter a chronic phase. There is a high proportion of subclinical chronic HCV infection; hence patients may not manifest any pathology until incidental blood tests or end-stage liver disease many years after the initial infection. Approximately 20% to 30% of patients with chronic HCV develop cirrhosis, with subsequent hepatocellular carcinoma occurring in up to 20% of the latter group.

Laboratory investigations

A fluctuating titre of HCV RNA is detectable within days to weeks of the initial HCV infection. The rate at which HCV antibodies develop is variable. Notably, HCV antibodies are neither neutralizing nor protective. It may not be possible to distinguish between acute and chronic HCV infection given that the same laboratory markers can be present in both conditions. Further specific laboratory tests for viral hepatitis are presented in Table 9.6.2.

Management

Supportive management is fundamental in addressing HCV infection. Relevant education and counselling regarding high-risk behaviours and referrals to appropriate support networks are necessary. Avoidance of alcohol is advisable. Standard therapy for HCV infection has consisted of a combination of pegylated IFN- α and ribavirin. However, the combination therapy leads to cure in only about 50% of cases. Direct-acting antiviral agents target specific steps within the HCV life cycle and disrupt viral replication in an attempt

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Table 9.6.2 Laboratory tests in viral hepatitis

Test	Interpretation of positive test	Clinical significance
Tests for HAV		
Anti-HAV IgM	Recently acquired HAV	Acute hepatic illness
Anti-HAV IgG	Previous infection/vaccination	Immunity
Tests for HBV		
HBsAg (surface Ag)	Current/chronic infection	Structural viral component
Anti-HBsAg (surface Ab)	Previous infection/vaccination	Immunity
Anti-HBcIgM (core Ab)	Recently acquired HBV	Test for acute HBV
HBeAg	Marker of viral replication	High infectivity
Anti-HBeAg	No viral replication	Low infectivity
HBV DNA	Complete virus present	High infectivity
Tests for HCV		
Anti-HCV	HCV exposure	Variable infectivity
HCV RNA	Virus present	
Tests for HDV		
Anti-HDV IgG/IgM	HDV exposure	Acute or chronic HDV
Delta Ag	HDV present	Acute or chronic HDV
Tests for HEV		
Anti-HEV IgM	Recently acquired HEV	Acute hepatic illness
Anti-HEV IgG	Previous exposure	

HAV, Hepatitis A virus; HBV, hepatitis B virus; HCV, hepatitis C virus; HDV, hepatitis D virus; HEV, hepatitis E virus.
 (Modified with permission from Talley N, Martin C. *Clinical Gastroenterology: A Practical Problem-based Approach*. 2nd ed. Edinburgh: Churchill Livingstone; 2006.)

to terminate that cycle before its completion.⁶ Rapid development of directly acting antiviral drugs against HCV has led to the reality of interferon-free regimens being available for the treatment of HCV. These regimens have a short course, are easily tolerated and are equally successful in HIV-positive and negative individuals. Major national collaborative ventures with the ultimate aim of controlling and eliminating HCV infection in Australia by 2026 are currently in place. Programs such as Control and Elimination within Australia of Hepatitis C from people living with HIV (CEASE), directed toward the Australian HIV-positive population, have been developed with the specific aim of evaluating the feasibility of rapid scale-up of interferon-free direct-acting antiviral agent (DAA) treatments.⁷

Prevention and immunization

Currently no effective vaccination is available against HCV infection, nor is there any specific post-exposure prophylactic regimen. Vaccination against HAV and HBV is advisable. HCV is not transmitted efficiently through occupational exposures to blood. The average incidence of anti-HCV seroconversion after accidental exposure from an HCV-positive source is less than 2%.

Hepatitis D virus

Hepatitis D virus (HDV) infection leads to the most severe form of chronic viral hepatitis. As a defective virus, HDV requires the presence of HBV for virion assembly and viral replication. (See Table 9.6.1 for virology.)

Epidemiology

Only patients with acute or chronic HBV infection are susceptible to infection with HDV. An estimated 5% of HBV carriers are infected with HDV worldwide. Parenteral exposure is the primary transmission mode. HDV infection can occur as a co-infection with acute HBV (acquired at the same time) or as a superinfection in chronic HBV carriers.

Natural history

In cases of HDV and HBV co-infection, acute HDV infection generally presents as a benign acute hepatitis with subsequent resolution in up to 80% to 95% of patients. Chronic HDV/HBV infection may occur in 5% to 10% of patients. HDV superinfection results in progression to chronic HDV/HBV in 70% to 80% of cases. Chronic HDV/HBV infection manifests as a chronic

healthy carrier state or severe liver disease. HDV superinfection may result in fulminant hepatitis in 2% to 20% of cases. Chronic HDV infection leads to more severe liver disease than HBV mono-infection and is associated with an accelerated progression of fibrosis, earlier hepatic decompensation and an increased risk for the development of hepatocellular carcinoma.

Laboratory investigations

HBsAg must be detected to diagnose acute HDV/HBV co-infection. Anti-HDV IgM is transiently present in acute infections. Anti-HDV IgG appears late in acute infections.

Management

The management of CHD has not changed in over 30 years and consists of treatment with IFNs. The only modification in therapy is the switch from conventional to pegylated IFN (peg-IFN), which probably has not led to better viral response rates but is more convenient for patients, with once-weekly dosing compared with the thrice-weekly schedule of conventional IFNs.⁸ Hepatocyte entry inhibitors and prenylation inhibitors give hope to patients suffering from chronic hepatitis D.

Prevention and immunization

Currently there is no vaccine for preventing HDV infection. HBV immunization has been shown to provide protection against the development of HDV.

Hepatitis E virus

See Table 9.6.1 for virology.

Epidemiology

Hepatitis E virus (HEV) is endemic in developing countries, such as Southeast and Central Asia and the Indian subcontinent. The primary mode of transmission is via the faecal-oral route, with contaminated drinking water and food supplies being primary sources of infection. Young adults are often predominantly affected.

Natural history

The clinical course is similar to that of acute HAV infection. Full recovery from the acute HEV infection is the norm. There have not been any recorded cases of chronic HEV infection.

Overall mortality from acute HEV infection is about 5%. For reasons that remain unclear, fulminant hepatic failure with a subsequent high mortality rate occurs in 25% of women with HEV infection during the third trimester of pregnancy. Liver transplant recipients may be at a greater risk for HEV infection, which can lead to chronic hepatitis.

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Laboratory investigations

Anti-HEV IgM appears between 1 week and 6 months after illness onset. Anti-HEV IgG is evident during the convalescent phase or post-exposure.

Management

Supportive management is the key.

Prevention and immunization

Disease control depends on good personal hygiene and improved environmental sanitation. There is no effective vaccine.

Hepatitis G virus

Exposure to blood products is a recognized route of acquisition of hepatitis G virus (HGV) infection in humans. Chronic viraemia results and the reported prevalence of HGV infection ranges from 1% to 3% in most populations, figures that are higher than those for either HBV or HCV in these populations. A causal relationship between the prevalence of HGV and hepatitis, however, has not been proven. HGV RNA may persist in the serum of patients acutely infected with HGV for as long as 16 years; however, in about 90% of these patients persistence is not accompanied by evidence of hepatocellular injury. Currently there should be no need to test for HGV in the emergency setting.

Non-hepatotrophic viruses

Several non-ABCDE viruses cause viral hepatitis. The cytomegalovirus (CMV) and Epstein-Barr virus (EBV) commonly contribute to abnormal LFTs, and icteric hepatitis may also occasionally be noted. In immunocompromised patients, herpes simplex may lead to a hepatic picture. Progression to chronic hepatitis has not been demonstrated with any of these viruses.

Non-viral hepatitis

Of the causes of non-viral hepatitis, the following are important in the emergency setting: alcoholic hepatitis, non-alcoholic steatohepatitis (NASH), drug-induced hepatitis and autoimmune hepatitis.

Alcoholic hepatitis

Alcoholic hepatitis is an important clinical syndrome that is variably characterized by anorexia,

nausea, jaundice, hepatomegaly and features of portal hypertension, such as ascites and encephalopathy. Cirrhosis and death are possible sequelae if the patients do not cease their alcohol consumption.

Non-alcoholic steatohepatitis

Defects in the processing of fatty acids through the liver may cause steatosis-induced inflammation (steatohepatitis). Ten to 50% of patients with this condition are at risk of developing cirrhosis.

Drug-induced hepatitis

Toxic exposure to certain medications, vitamins, herbal remedies and food supplements may result in a drug-induced hepatitis. This may occur as an expected consequence of a drug's toxicity profile or as an idiosyncratic reaction to a standard dose. Hepatotoxic agents result in variable clinicopathological patterns of liver injury via toxic and immune mechanisms. The formation of reactive hepatotoxic metabolites is often the primary underlying mechanism. Extensive lists of hepatotoxic drugs can be found in the literature. Acute liver injury may be necro-inflammatory (e.g. from paracetamol), cholestatic (e.g. from chlorpromazine) or of a mixed type. Table 9.6.3 lists drugs that may induce hepatitis and are encountered in the emergency setting.²

Autoimmune hepatitis

Autoimmune hepatitis is a self-perpetuating hepatocellular inflammation of unknown cause associated with hypergammaglobulinaemia and serum antibodies. Fatigue, anorexia and jaundice may progress to liver failure. Corticosteroids are the basis of treatment.⁹

Future directions

- Global emphasis on adequate public health schemes, including vaccination programmes, to control the transmission of viral hepatitis
- Emphasis on public education regarding high-risk practices
- Surveillance of the long-term immunity conferred by the hepatitis A and B vaccinations
- Development of a vaccine for hepatitis C
- Optimization of the management algorithms for chronic viral hepatitis

Table 9.6.3 Hepatitis-inducing drugs

Drug	Pathology
Allopurinol	Hepatic granulomas
Cloxacillin	Lobular hepatitis
Chlorpromazine	Cholestatic hepatitis
Dantrolene	Cytolytic hepatitis
Erythromycin	Cholestasis with hepatitis
Flucloxacillin	Cholestatic hepatitis
Halothane	Hepatocellular injury
Isoniazid	Cytolytic hepatitis
Non-steriodals	Primarily cholestasis
Paracetamol	Cytolytic hepatitis
Phenothiazines	Cholestatic hepatitis
Phenytoin	Non-caseating granulomas
Sulphonamides	Cytolytic hepatitis

(Modified from Thomas DL, Astemborski J, Rai RM, et al. The natural history of hepatitis C virus infection. *JAMA* 2000;284:450–456; and Friedman L, Keeffe E, Schiff E. *Handbook of Liver Disease*. 2nd ed. Edinburgh: Churchill Livingstone; 2004.)

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9.7 Human immunodeficiency virus and acquired immune deficiency syndrome

Carl Luckhoff

ESSENTIALS

- 1** Patients with previously undiagnosed human immunodeficiency virus (HIV) infection may present to the emergency department at any time during the course of infection, from early (seroconversion) to late acquired immune deficiency syndrome ([AIDS]-defining illness) stages.
- 2** Patients with previously diagnosed HIV infection may present with complications of anti-retroviral therapy or, if therapy has failed or is not taken, with a range of HIV-related clinical syndromes.
- 3** Globally, heterosexual transmission accounts for most HIV infections; in Australia, however, HIV infection remains predominantly a disease of men who have sex with men (MSM).
- 4** Most AIDS-defining illnesses occur when the CD4 T-lymphocyte count is below 200/ μL (bacterial pneumonia and tuberculosis are exceptions).
- 5** Serious non-AIDS events that are not classically associated with HIV infection—such as cardiovascular disease, bone disease, renal disease and cognitive impairment—cause significant morbidity, may occur at higher CD4 cell counts and are possibly related to chronic inflammation.
- 6** Combination anti-retroviral therapy with well-tolerated and potent once-daily regimens dramatically reduces HIV mortality and morbidity, reduces the risk of HIV transmission from the infected individual to his or her partner and may decrease HIV transmission at a population level (treatment as prevention).
- 7** Close liaison between emergency department staff and the patient's hospital or local doctor is vital for optimal management of HIV-infected patients.

Introduction

HIV medicine is a complex and specialized field and emergency physicians are not the usual primary care providers for people with HIV infection. However, the emergency department (ED) is often the first point of contact for patients presenting with acute HIV-related complications, whether or not they have already been diagnosed with HIV.

Emergency medicine physicians do not need to be HIV experts, but they should develop knowledge and skills in the following areas:

- The natural history and clinical manifestations of HIV infection
- The principles of HIV diagnosis, including the ability to engage patients in discussions about HIV testing and test results
- The principles of early management of patients with common HIV-related disease syndromes

- Knowledge of the antiretroviral agents in current use, including toxicity and drug interactions
- The first cases of AIDS were recognized in the United States in 1981 and in Australia in 1982. The causative agent, human immunodeficiency virus (HIV), was discovered in 1984 and a diagnostic blood test was developed soon thereafter. In 1986, the first effective antiretroviral drug (azidothymidine [AZT], later renamed zidovudine) became available. Since the late 1990s, the use of combination antiretroviral therapy (ART) has led to dramatic reductions in HIV-associated morbidity and mortality in resource-rich countries. Antiretroviral use is rapidly increasing in developing countries, with AIDS-related deaths having decreased by 43% since 2010. The world's most affected region remains eastern and southern Africa. Worldwide 2.1 million infections were reported in 2015, adding up to a total of 36.7 million people living with HIV.¹

Epidemiology

The great majority of HIV infections globally arise as a result of heterosexual transmission. In developed countries, injecting drug use and men who have sex with men (MSM) account for a greater proportion of HIV infections, although the contribution of specific behaviours to overall transmission varies greatly within and between countries and over time.

In 2016 it was estimated that 26,444 people were living with HIV in Australia. The number of newly diagnosed cases remained stable between 2011 and 2016, with approximately 1000 new cases per year. Seventy-five percent of people infected with HIV report male-to-male sex, 20% become infected through heterosexual transmission and the rest occurred in other groups, including injecting drug users and recipients of contaminated blood or blood products. Women account for 9% of HIV-infected people and children less than 1%.² Compared with some other countries, the prevalence of HIV infection in injecting drug users in Australia has remained low, in the order of 1% to 2%.

In 2016, an estimated 11% of all people living with HIV in Australia were unaware of their HIV status.²

Pathogenesis

Once HIV infection becomes established, huge numbers of HIV virus particles are produced, chiefly in lymph nodes and other lymphoid tissue, accompanied by the daily turnover of up to 1 billion CD4 T lymphocytes. The number of CD4 cells falls secondary to mechanisms such as immune activation and direct infection of CD4 cells, resulting in reduced helper function for cell-mediated and humoral immunity.³

HIV replication occurs at a relatively constant rate, producing a stable level of HIV in the blood; this can be measured with quantitative HIV RNA detection tests. The HIV viral load in combination with blood cell counts is used as a prognostic marker (because it is associated with the rate at which CD4 T lymphocytes are lost) and to monitor the efficacy of anti-retroviral therapy (ART).

The peripheral blood CD4 T-lymphocyte count is an accurate indicator of the degree of immunosuppression. The normal count is 500 to 1500 cells/ μL ; susceptibility to opportunistic infection and to most other serious HIV-related

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complications is greatest when the CD4 cell count is less than 200 cells/ μL . In untreated patients the rate of decline in CD4 cells follow a skewed distribution, with progressive decline in CD4 cell count following HIV infection.²⁰

A wide variety of chronic medical conditions not previously associated with HIV infection—such as cardiovascular, bone and kidney disease, mild cognitive impairment and non-HIV related cancers—are more common in HIV-infected patients.⁴ Predisposition to these serious non-AIDS events results from a complex interplay between an ageing HIV-infected population, traditional risk factors, side effects of some anti-retroviral agents and HIV infection itself. Chronic inflammation induced by HIV infection, which may persist despite effective ART, is thought to mediate some of the direct HIV effects.

Classification and natural history

HIV infection can be divided into the following stages:

- Viral transmission
- Acute HIV infection
- Seroconversion
- Chronic HIV infection
 - Asymptomatic
 - Early symptomatic HIV infection
 - AIDS, characterized by a CD4 cell count below 200 cells/ μL or the presence of any AIDS-defining condition
 - Advanced HIV infection characterized by a CD4 cell count below 50 cells/ μL

Patients are categorized as having AIDS when they develop an AIDS-defining condition regardless of the CD4 count, a CD4 cell count below 200 cells/ μL , an HIV-related malignancy, a wasting syndrome or AIDS dementia complex.

Presentation

Patients with underlying HIV infection who present to the ED fall into three distinct groups. First, they may present with a manifestation of previously unrecognized HIV infection. To identify these patients, the physician must know who is potentially at risk of HIV infection (see 'Epidemiology', earlier) and be aware of the many different ways in which previously undiagnosed HIV infection may present. Prompt consideration of the possibility of HIV infection is important because the differential diagnosis of the presenting problem will broaden to encompass a variety of other conditions, some of which may be life threatening and require a different approach to initial investigation and treatment.

The second group includes those who are already known to be HIV-infected. Many of these patients will have been started on ART; serious HIV-related infections or malignancies are uncommon in this group, but ED presentations may

be related to complications of therapy or to the chronic medical conditions associated with HIV infection discussed in the previous section. A smaller group of patients have developed resistance to or are intolerant of antiretroviral agents or decline to start or remain on treatment; these patients usually present with one of a limited number of classic HIV-related clinical syndromes, such as fever and cough or shortness of breath, diarrhoea, unexplained fever or neurological symptoms. The initial diagnostic and treatment approach is based on knowledge of the differential diagnosis for each of these syndromes.

Finally, there will be patients whose ED presentation is not related to an HIV complication at all but who have clinically silent, 'incidental' HIV infection. Readily identifiable groups who may be in this category are patients with a sexually transmitted infection (STI) and those with hepatitis B or hepatitis C infection. Otherwise a brief history including a sexual history is required to elicit HIV risk factors. Presentation of these patients to the ED offers an important opportunity to explore HIV risk factors and to discuss the benefits of early HIV diagnosis and the desirability of HIV testing.

Previously undiagnosed HIV infection

Acute seroconversion illness (Box 9.7.1)

The proportion of patients suffering from symptoms of acute infection varies greatly and 10% to 60% patients do not experience any symptoms at all. For those patients suffering from acute retroviral syndrome, the symptom duration and severity may vary widely. The highest frequency of symptoms and signs is observed just prior to peak viraemia, usually 2 weeks after the initial detection of viral RNA.⁶ The most common features are fever, fatigue, myalgia, rash, headache, lymphadenopathy and/or diarrhoea. Prolonged duration of any of these and the presence of mucocutaneous ulcers are suggestive of acute retroviral syndrome. The diagnosis is often missed at this stage; patients may be thought to have a 'viral illness', such as infectious mononucleosis or, if a patient develops a complication, more common causes (e.g. herpes simplex virus in a patient with encephalitis) and not HIV are considered.⁵

Chronic HIV Infection

Asymptomatic infection People are generally healthy during this phase. Thrombocytopaenia may occur; therefore HIV infection should be considered in appropriate patients with idiopathic thrombocytopenia.

Early symptomatic human immunodeficiency virus infection

This is a phase when previously undiagnosed HIV-infected patients often present with HIV-related conditions, but the clues may not be recognized as such and the underlying diagnosis can be missed. Manifestations that will alert the astute clinician include the following:

- Minor infections: shingles, severe or very frequent orolabial or genital herpes, oral thrush
- Skin conditions: extensive seborrhoeic dermatitis, worsening psoriasis
- Constitutional symptoms: fever, weight loss, diarrhoea
- Generalized lymphadenopathy
- More serious complications: bacterial pneumonia (especially recurrent), tuberculosis and, rarely, Kaposi sarcoma or non-Hodgkin lymphoma

AIDS characterized by a CD4 cell count below 200 cells/ μL or AIDS-defining condition

It is often not appreciated that patients may remain completely well during the early and intermediate stages of HIV infection and present only when they develop a serious HIV-related complication, such as an opportunistic infection. The ED may be the first point of medical care for such patients. If the history reveals risk factors for HIV infection, HIV testing can be performed and initial investigations directed at specific HIV-related complications. However, if the patient does not volunteer this information, is not specifically asked about HIV risk factors or does not belong to a 'conventional' HIV risk group, diagnosis of the presenting illness and the underlying HIV infection is often delayed.

The following clinical situations (discussed in more detail in the following section) should

Box 9.7.1 Manifestations of primary HIV infection

Common (present in >30% of patients)	Less common	Complications
Fever	Diarrhoea	Aseptic meningitis
Rash	Generalized lymphadenopathy	Guillain-Barré syndrome
Myalgia/arthritis	Painful swallowing	Encephalitis
Headache	Abdominal pain	Interstitial pneumonitis
Pharyngitis	Cough	Rhabdomyolysis
Cervical lymphadenopathy	Photophobia	Haemophagocytic syndrome
Mouth ulcers	Tonsillitis	

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prompt consideration of the possibility of underlying HIV infection:

- Diffuse bilateral pulmonary infiltrates (as a manifestation of *Pneumocystis jiroveci* pneumonia [PJP]): This is the commonest serious opportunistic infection in patients with previously undiagnosed HIV infection. It is often misdiagnosed as atypical pneumonia, leading to incorrect initial treatment with a macrolide agent or doxycycline.
- Ring-enhancing space-occupying cerebral lesion: In non-HIV-positive patients, the usual cause is a tumour or bacterial brain abscess, and brain biopsy is required. In the setting of HIV infection, cerebral toxoplasmosis is the most likely diagnosis and brain biopsy can usually be avoided.
- Tuberculosis: Although the overlap between those at risk for HIV and tuberculosis is not as great in Australia as in resource-poor countries with a high HIV burden, all patients with tuberculosis should be encouraged to undergo HIV testing after appropriate counselling.
- Kaposi sarcoma: Well-developed lesions (purple, oval and nodular) are easy to recognize, but early lesions are often non-descript (brown or pink and flat) and biopsy may be required for diagnosis.
- Other presentations: Unexplained cytopenias (anaemia or pancytopenia) and other AIDS-defining conditions such as non-Hodgkin lymphoma, cryptococcal meningitis, chronic cryptosporidial diarrhoea or AIDS dementia complex (manifesting as impaired cognition and motor performance) are occasionally the first manifestation of previously unsuspected HIV infection.

Previously diagnosed HIV infection⁷

Patients with known HIV infection are less likely to present with the classic AIDS-related clinical syndromes indicative of advanced immunodeficiency. However, previously diagnosed patients may fail ART or elect not to start or continue treatment and are still susceptible to AIDS-defining conditions. (Otherwise these presentations involve patients with previously unrecognized HIV infection, as discussed in the preceding section.) Patients with known HIV infection may also present with complications of ART, with chronic medical conditions not associated with HIV and of course with an acute problem not related to HIV at all.

Cough, shortness of breath, fever

Respiratory pathogens are listed in Box 9.7.2. The most important issue is to decide whether the patient has PJP or not, because this complication is common and potentially serious. Tuberculosis

Box 9.7.2 Respiratory complications in HIV-infected patients

Common	Uncommon
<i>Pneumocystis jiroveci</i> pneumonia (PJP)	Infectious:
Bacterial pneumonia: <i>Streptococcus pneumoniae</i>	Tuberculosis
<i>Haemophilus influenzae</i>	Atypical mycobacteria
Bronchitis	<i>Aspergillus</i> pneumonia
	Other infectious:
	<i>Rhodococcus equi</i> , cytomegalovirus (CMV)
	Non-infectious:
	Pulmonary Kaposi's sarcoma
	Lymphoma

must also be considered because of the need to place the patient in respiratory isolation.

- PJP (strongly suspected in patients with CD4 cell count <200 cells/ μ L): The presentation is subacute or chronic, with a non-productive cough, dyspnoea, fever and chest tightness. Physical examination may reveal fever, tachypnoea and reduced chest expansion, but chest auscultation is often normal. PJP is unlikely in patients taking regular co-trimoxazole (a trimethoprim/sulphamethoxazole combination).
- Bacterial pneumonia: Patients usually present with a short history, a productive cough and sometimes pleuritic chest pain. Physical examination may be normal or reveal signs of consolidation, a pleural rub or pleural effusion.
- Patients who are immunosuppressed secondary to HIV have a high incidence of invasive streptococcal infection, although the availability of multi-valent pneumococcal vaccines has helped to decrease the incidence of these infections.
- Tuberculosis: The clinical features vary according to the degree of immunosuppression. Patients with otherwise asymptomatic HIV infection usually present with typical symptoms and signs of tuberculosis (chronic cough, haemoptysis, fever and weight loss). However, in late-stage HIV infection, atypical manifestations such as disseminated disease are common and diagnosis is more difficult.

Investigations If the CD4 cell count is above 200 cells/ μ L, most patients can be managed as if they did not have HIV infection. Investigations required for patients with suspected bacterial pneumonia or tuberculosis include a chest x-ray, full blood examination, sputum examination and blood cultures.

If the CD4 cell count is below 200 cells/ μ L, investigation is almost always indicated. Its extent will be guided by the patient's condition and the likely diagnostic possibilities.

Investigations may include some or all of the following:

- Chest x-ray
- Blood cultures
- Sputum Gram stain, culture and acid-fast bacillus (AFB) smear and culture
- Induced sputum for detection (by microscopy or polymerase chain reaction [PCR]) of PJP
- Bronchoscopy, usually during inpatient admission.

A high index of suspicion for tuberculosis must be maintained; the diagnosis is generally suggested by one or more suggestive epidemiological, clinical or radiological features.

Management Any person with suspected pulmonary tuberculosis must be placed in respiratory isolation until the diagnosis is excluded. Otherwise, on the basis of the initial diagnostic evaluation, patients can be categorized and management can proceed as follows:

- Significant infection unlikely: no treatment.
- Possible PJP: empirical PJP therapy with co-trimoxazole, and corticosteroids if saturation levels are below 93% at rest on room air oxygen.
- Possible bacterial pneumonia:
 - Non-severe, outpatient—treat as for community-acquired pneumonia in immunocompetent patient.
 - Non-severe, inpatient—treat as for community-acquired pneumonia in immunocompetent patient.
 - Severe—consider community-acquired pneumonia regimens plus HIV-related opportunistic infections.
- Possible tuberculosis—admission and respiratory isolation; treatment with isoniazid, rifampicin, pyrazinamide and ethambutol according to local guidelines if diagnosis confirmed; empirical therapy is sometimes necessary depending on clinical circumstances (e.g. suspected coexisting tuberculous meningitis).

Focal neurological signs, convulsions or altered conscious state

These features generally indicate the presence of an intracerebral space-occupying lesion, the most common causes of which are as follows:

- Cerebral toxoplasmosis: This infection occurs when the CD4 cell count is below 200 cells/ μ L. The specific focal features depend on the site of the usually multiple lesions and may include hemiparesis, visual field defects, personality change and/or cerebellar signs.
- Primary intracerebral lymphoma: This complication occurs with advanced HIV infection (CD4 cell count usually below 500 cells/ μ L) and manifested in 2% to 3% of AIDS patients

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prior to the development of effective ART. It is associated with Epstein-Barr virus (EBV) infection. Clinical presentation is indistinguishable from that of cerebral toxoplasmosis.

- Progressive multifocal leucoencephalopathy: Caused by JC virus (a polyomavirus). Patients present with cognitive decline or focal signs. Seizures are relatively uncommon. Differentiation from cerebral toxoplasmosis and primary cerebral lymphoma requires computed tomography (CT) or magnetic resonance imaging (MRI) (see later).

Investigations A brain CT scan (with contrast) should be done in all patients, often as a matter of some urgency and should always precede a lumbar puncture. MRI will often provide additional important information. The commonest causes of focal lesions are cerebral toxoplasmosis and primary intracerebral lymphoma. A *Toxoplasma gondii* IgG test will usually have been performed in those with previously diagnosed HIV infection; if positive, this indicates prior infection and a predisposition to the development of cerebral toxoplasmosis; if negative, toxoplasmosis is much less likely. Diagnosis of cerebral lymphoma is primarily based on non-response to empiric treatment for cerebral toxoplasmosis; cerebrospinal fluid (CSF) cytology, detection of EBV DNA in CSF by polymerase chain reaction (PCR) or, occasionally, brain biopsy will be required for a specific diagnosis. Progressive multi-focal leucoencephalopathy manifests as focal white matter lesions visible on T2-weighted MRI scans.

Management Treatment is guided by the results of the brain CT scan. If a space-occupying lesion is found, the patient is treated empirically for cerebral toxoplasmosis with sulphadiazine and pyrimethamine. The CT scan is repeated after 2 to 3 weeks; if no response is evident, a brain biopsy might be considered in selected patients to diagnose cerebral lymphoma. If the CT scan is normal or non-diagnostic, MRI scanning is usually indicated and supplemented by lumbar puncture.

Diarrhoea, with or without abdominal pain or fever

A wide range of gastrointestinal (GI) pathogens cause diarrhoea in HIV-infected patients (Box 9.7.3). Patients should be asked about recent travel or antibiotic use. Bloody, small-volume diarrhoea with cramping lower abdominal pain is suggestive of a large bowel pathogen, such as cytomegalovirus (CMV), *Entamoeba histolytica* or *Clostridium difficile*, whereas profuse watery diarrhoea suggests an infection of the small bowel, such as cryptosporidiosis. Clinical features are, however, of limited diagnostic value and the specific diagnosis rests on identification of the pathogen in a faecal or biopsy specimen. Prominent anal pain or tenesmus

Box 9.7.3 Gastrointestinal pathogens in HIV-infected patients

Bacterial	Protozoal
<i>Salmonella</i>	<i>Cryptosporidium</i>
<i>Campylobacter</i>	<i>Giardia</i>
<i>Clostridium difficile</i>	<i>Entamoeba histolytica</i>
<i>Mycobacterium avium complex</i> (MAC)	<i>Microsporidium</i>
Viral	Non-infective
<i>Cytomegalovirus</i> (CMV)	Lactose intolerance Gastrointestinal Kaposi sarcoma Lymphoma

should alert the clinician to the possibility of proctitis due to a sexually acquired infection, such as gonorrhoea, *Chlamydia trachomatis* (including lymphogranuloma venereum) or herpes.

Investigations Faecal examination (preferably two to three fresh specimens collected on different days) for the following:

- Microscopy for ova, cysts and parasites
- *Cryptosporidium* antigen test or stain, *Microsporidium* stain
- culture for *Salmonella*, *Campylobacter* and *Shigella*
- *Clostridium difficile* culture and toxin, especially if there has been recent antibiotic therapy

Selected patients with diarrhoea may require colonoscopy or upper GI endoscopy if infections such as CMV, MAC or microsporidiosis are suspected. Endoscopy is generally reserved for those in whom no specific cause is identified on initial evaluation and whose diarrhoea persists despite antimotility therapy.

Swabs for gonorrhoea, *Chlamydia* and herpes should be taken from patients with symptoms of proctitis.

Management Any infection identified on initial faecal examination is treated on its merits. Symptomatic treatment with an anti-motility agent such as loperamide is contraindicated if bloody diarrhoea and fever are present; otherwise it can be given safely to most patients.

Fever without localizing features

This is chiefly a problem in those with a CD4 cell count below 200 cells/ μ L.

The differential diagnosis is extensive, the major causes being as follows:

- Disseminated opportunistic infections: disseminated MAC, disseminated tuberculosis, disseminated histoplasmosis (the United States and South America), *Salmonella* bacteraemia, CMV
- Focal opportunistic infections with non-focal presentation: PJP, cryptococcal meningitis, tuberculosis

- Bacterial infections: sinusitis, bacterial pneumonia, primary bacteraemia (especially in patients with an indwelling long-term intravenous device or neutropaenia)
- Non-HIV-specific infections: right-sided endocarditis, secondary syphilis
- Non-infectious causes: non-Hodgkin lymphoma, drug fever

Investigations If the CD4 cell count is greater than 200 cells/ μ L, serious HIV-related causes are uncommon; therefore investigation will be guided by clinical features, severity of illness and other salient clinical findings. If the CD4 cell count is below 200 cells/ μ L, most patients will need investigation, beginning with the following:

- Blood cultures, including mycobacterial blood cultures if CD4 cell count <500 cells/ μ L
- Chest x-ray
- Serum cryptococcal antigen

Additional tests for selected patients include faecal examination, sputum examination, abdominal ultrasonography or CT scanning and, occasionally, bone marrow or liver biopsy.

Management Empirical antibacterial therapy (with an anti-pseudomonal agent such as piperacillin/tazobactam with or without an aminoglycoside or vancomycin) is indicated for patients with an absolute neutrophil count below 500 cells/ μ L; otherwise the need for specific treatment is guided by the condition of the patient and the results of the diagnostic workup. Any long-term intravenous access device should be removed if infection of the device is suspected on clinical or microbiological grounds or if diagnostic evaluation reveals no other focus of infection. Treatment for disseminated MAC (with clarithromycin and ethambutol with or without rifabutin) is generally given only after the organism has been isolated, although occasional patients with debilitating fevers, weight loss and no other diagnosis may be treated empirically.

Difficult or painful swallowing

This is usually due to *Candida* oesophagitis, in which case coexisting oral candidiasis is often present. Other causes include CMV oesophagitis, herpes simplex oesophagitis and idiopathic aphthous ulceration.

Investigation Oesophagoscopy and biopsy are reserved for those who fail an empiric course of antifungal therapy (see later).

Management Empirical antifungal therapy is started with an azole agent, usually oral fluconazole. Patients with resistant *Candida* infections need treatment with an alternative azole agent, such as posaconazole, or a short course of

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intravenous amphotericin B. Patients undergo endoscopy if they do not respond to antifungal treatment; the results of histology and cultures determine subsequent treatment.

Headache, fever, neck stiffness

Cryptococcal meningitis is the most common cause of this syndrome, although headache may be mild and signs of meningism subtle or absent. Less common causes include tuberculous meningitis, syphilitic meningitis, HIV itself and lymphomatous meningitis.

Investigation The serum cryptococcal antigen test is a useful screening test for cryptococcal meningitis because a negative result effectively excludes the diagnosis. A lumbar puncture should be performed only after a CT brain scan and if the CT does not show a space-occupying lesion or evidence of increased intracranial pressure. CSF should be routinely sent for the following:

- Protein and glucose
- Gram stain and culture (and AFB smear and culture if tuberculosis is suspected)
- India ink stain and cryptococcal antigen
- Cytology
- Venereal Disease Research Laboratory (VDRL) or rapid plasma reagins (RPR) test –indicated only if serum syphilis serology is positive

Management Patients with confirmed cryptococcal meningitis are treated with a combination of intravenous amphotericin B and oral 5-fluorocytosine for 2 weeks; they then remain on suppressive therapy with oral fluconazole. If tuberculous meningitis is suspected, empirical therapy should be started immediately while awaiting the results of CSF cultures.

Specific treatment of other infections

- CMV infections: Intravenous ganciclovir or intravenous foscarnet
- *Salmonella* infections (non-enteric fever): Ciprofloxacin

Complications of antiretroviral therapy

Antiretroviral drugs are discussed in more detail further on and drug side effects are outlined in Table 9.7.1. Examples of more serious side effects and treatment complications that may prompt presentation to the ED include the following:

- Pancreatitis—didanosine^a
- Hepatitis—nevirapine
- Drug rash—nevirapine, abacavir, fosamprenavir,^a efavirenz
- Renal calculi—indinavir,^a atazanavir
- Lactic acidosis—zidovudine
- Renal impairment—tenofovir
- Anaemia—zidovudine

^aThese agents are no longer in widespread use in Australia

Table 9.7.1 Side effects of antiretroviral agents

Agent	Side effect
Nucleoside/nucleotide reverse transcriptase inhibitors (NRTI)	
Zidovudine	Nausea, headache, myalgia, anaemia, neutropaenia
Lamivudine (β TC)	Abnormal liver function, neutropaenia, pancreatitis (all uncommon)
Emtricitabine (FTC)	Skin pigmentation
Abacavir	Hypersensitivity reaction (challenge contraindicated); associated with HLA-B*5701 (8% of Caucasian populations), perform HLA B locus typing pre-therapy
Tenofovir	Renal tubular dysfunction, renal impairment, reduced bone mineral density
Non-nucleoside reverse transcriptase inhibitors (NNRTI)	
Nevirapine	Rash, hepatitis, fever
Efavirenz	Neuropsychological symptoms (vivid dreams, insomnia, difficulty concentrating, light-headedness, sleeping difficulty), rash, abnormal liver function, teratogenic in animals
Etravirine	Rash, abnormal liver function
Rilpivirine	Abnormal liver function, depression and other neuropsychological effects
Protease inhibitors (PIs)	
Class effects (variable between individual agents)	Hyperglycaemia, hyperlipidaemia, redistribution of body fat, abnormal liver function, gastrointestinal symptoms
Lopinavir	Diarrhoea, nausea
Atazanavir	Hyperbilirubinaemia, renal calculi
Fosamprenavir	Rash, diarrhoea, nausea
Darunavir	Rash
Tipranavir	Rash, myalgia
Integrase inhibitors	
Raltegravir	Myalgia, abnormal liver function
Entry inhibitors	
Enfuvirtide	Injection-site reactions, hypersensitivity
Maraviroc	Gastrointestinal symptoms, myalgia, respiratory infections
Drugs that are licensed in Australia but are no longer commonly used have been omitted.	
<ul style="list-style-type: none"> • Jaundice—atazanavir (unconjugated hyperbilirubinaemia) • Immune reconstitution inflammatory syndrome—patients who commence ART with very low CD4 cell counts may develop an exacerbation of symptoms and signs of a recently diagnosed opportunistic infection or a previously unrecognized infection may be ‘unmasked’; this occurs with mycobacterial infections (notably tuberculosis) and a range of other infections. 	
<ul style="list-style-type: none"> • Abdominal pain: Pancreatitis due to ART, HIV cholangiopathy, intra-abdominal lymphadenopathy secondary to MAC or lymphoma, lactic acidosis and hepatic steatosis associated with ART • Neuropsychiatric manifestations: Depression, mania, cognitive decline • HIV-associated neurocognitive disorders (HAND): Changes in memory, concentration, attention and motor skills that are not clearly attributable to a cause other than HIV are collectively classified as HAND. These disorders broadly include three levels of neuropsychological test performance impairment and associated functional impairment including asymptomatic neurocognitive impairment (ANI), mild neurocognitive disorder (MND) and HIV-associated dementia (HAD). 	
Other presentations	
<ul style="list-style-type: none"> • Cutaneous manifestations: Kaposi sarcoma, infections (e.g. secondary syphilis, herpes zoster, warts, molluscum contagiosum and crusted scabies), eosinophilic folliculitis, drug rashes 	

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- Visual complaints: CMV retinitis (when the CD4 cell count is below 500 cells/ μL), syphilitic uveitis or chorioretinitis and rarely toxoplasma or cryptococcal chorioretinitis.

Clinically silent HIV infection with risk factors

Sexually transmitted infections

Perianal or rectal STIs in men are obvious markers of HIV infection risk and should prompt testing for infection. However, STIs often 'hunt in packs', so any patient diagnosed with gonorrhoea, *Chlamydia*, syphilis, genital warts, genital herpes or another STI should also be investigated for HIV.

Other risk groups

Other patients who present with a problem unrelated to HIV but with whom the desirability of HIV testing should be discussed include those with the following risk factors:

- Men who have sex with men, especially if intercourse is unprotected
- Sharing of injecting equipment
- Being from a country with a high HIV prevalence
- Being the sexual partner of either an HIV-positive person or a person at risk of HIV

Investigations

Requesting an HIV test

In Australia, doctors who request an HIV test are obliged to provide patients with information about the medical, psychological and social consequences of a positive or negative HIV test (pre-test counselling) and to provide the result to the patient in person. More detailed information about HIV testing can be found in guidelines issued by Australian authorities.⁸

Unfortunately, practical issues mean that the ED is usually not an ideal setting for HIV testing. First, discussion about sensitive personal information, such as sexual history (especially if it has to be obtained via an interpreter) is difficult in an open-design, crowded, noisy ED. Second, many EDs do not have a mechanism for the follow-up of patients to provide test results. For these reasons, a more appropriate arrangement may be to refer patients who are discharged from the ED to their local doctor or local sexual health clinic for testing, whereas testing of patients admitted to hospital can be the responsibility of the admitting unit.

Widespread 'opt out' HIV testing of hospital patients is recommended in the United States but has not been adopted in Australia. However, if the 'treatment as prevention' approach is to be effective, increasing rates of testing among groups at risk of HIV will be necessary in order

to reduce the number of undiagnosed HIV infections and increase the acceptance of HIV treatment. Rapid point-of-care HIV tests are now licensed in Australia and do not require a follow-up visit, but whether these tests will have a role in settings such as EDs is currently unclear.

Primary HIV infection

- Full blood examination, heterophile antibody test
- HIV antibody/p24 antigen enzyme immunoassay (EIA) test: may be negative initially, in which case it is vital to repeat the test in 2, 4 and 6 weeks. A positive EIA is confirmed with a positive Western blot test.
- HIV RNA (viral load) test: not generally recommended for diagnosis of primary HIV infection because false positives may occur (although with a low viral load, whereas true positives usually have a very high viral load).

Previously unrecognized HIV infection (not including acute HIV infection)

The HIV antibody/antigen EIA test will be positive in all infected patients; other tests are not needed for diagnosis.

Antiretrovirals in the management of HIV infection

ART aims to reduce HIV-related morbidity and mortality and to prevent transmission of HIV. It should be offered to all HIV-infected persons regardless of immune status, although evidence for ART in untreated patients with preserved CD4 cell counts and undetectable HIV RNA (non-progressors) is lacking. Combination ART has transformed the lives of people living with HIV infection by improving their quality of life and reducing the incidence of HIV-related complications and deaths by 80% or more. More than 90% of patients starting treatment with one of the currently recommended antiretroviral regimens will achieve a non-detectable plasma HIV viral load and a substantial increase in CD4 cell count. In the great majority of patients, these benefits are sustained in the long term.⁹ Modern antiretroviral regimens are much more convenient, less toxic and more potent than earlier combination ART, but ART is not without its costs: difficulty in maintaining life-long adherence, short- and long-term toxicities of antiretroviral agents and the potential development of antiretroviral resistance remain challenges.

Effective treatment is also available for patients failing therapy because of drug resistance or intolerance, using antiretroviral agents that belong to the same classes of drugs used for initial therapy or that have novel mechanisms of action. Examples include 'new-generation' protease inhibitors (tipranavir and darunavir) and

non-nucleoside reverse transcriptase inhibitors (etravirine), inhibitors of CCR5 (maraviroc), a host chemokine receptor involved in HIV cell entry and the fusion inhibitor enfuvirtide.¹⁰

The emergency physician does not require a detailed knowledge of ART but should be aware of the agents in current use, their side effects and the potential for clinically significant drug-drug interactions. More detailed information can be referenced in regularly updated antiretroviral guidelines; examples are those produced by a panel of the US Department of Health and Human Services with an added Australian commentary, accessible at <http://www.ashm.org.au/aust-guidelines/> and British HIV treatment guidelines, accessible at <http://www.bhiva.org/>.

Indications

Advances in treatment options and improved side-effect profiles have led to a general approach of initiating ART in all HIV-infected individuals with detectable viraemia regardless of their CD4 cell count.¹¹⁻¹³

Classes of drug^b

- Nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs): tenofovir, emtricitabine (FTC), abacavir, lamivudine (3TC), zidovudine (ZDV or AZT)
- Non-nucleoside reverse transcriptase inhibitors (NNRTIs): nevirapine, efavirenz, etravirine, rilpivirine
- Protease inhibitors (PIs): atazanavir, lopinavir, fosamprenavir, tipranavir, indinavir, darunavir (all co-administered with low-dose ritonavir)
- Integrase strand transfer inhibitors (INSTIs): raltegravir, dolutegravir
- Fusion inhibitors: enfuvirtide
- Entry (chemokine receptor 5 [CCR5]) antagonist: maraviroc

The first four classes of drugs mentioned in the preceding list are typically used in initial regimens. The CCR5 antagonist is also available but is generally not used in treatment-naïve patients. The fusion inhibitor is generally reserved for patients with multi-drug-resistant virus.

Initial regimens—at least three drugs

- Two NRTIs plus one NNRTI: examples are tenofovir plus FTC plus efavirenz (Atripla) OR abacavir plus 3TC (Kivexa) plus efavirenz OR tenofovir plus FTC plus rilpivirine (Epivlera)
- Two NRTIs (as listed earlier) plus one PI (atazanavir) boosted with low-dose ritonavir
- Two NRTIs (as listed earlier) plus raltegravir

^bDrugs that are licensed but are no longer in common use in Australia have been omitted.

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Side effects¹⁴ (see Table 9.7.1)

If an antiretroviral drug is suspected or known to be the cause of a serious side effect, the patient's treating HIV doctor or a hospital HIV doctor should be consulted. In the interim, or unless advised otherwise by the treating or hospital doctor, all antiretroviral medications and not just the incriminating drug should be withheld to reduce the risk of development of resistance on a less than fully suppressive therapy.

Drug-drug interactions

Some commonly used drugs metabolized by or that induce hepatic cytochrome P450 oxidases are contraindicated with certain PIs or NNRTIs; in addition, many other drugs will require dose modification or closer monitoring. Always check before prescribing any new drug to a patient on ART; a very useful website (from the University of Liverpool, UK) is www.hiv-druginteractions.org.

Disposition

Patients with newly diagnosed HIV infection should be referred to a specialized HIV clinic or to a doctor with expertise in HIV medicine.

HIV medicine is a complex and rapidly changing field. For this reason the management of patients with known HIV infection presenting to the ED should always involve consultation with a hospital doctor knowledgeable about HIV infection, such as an infectious diseases physician or immunologist. The patient's usual HIV doctor (a hospital specialist, sexual health physician or general practitioner with a high HIV case load) can be contacted to obtain important details such as recent CD4 cell count and current antiretroviral agents. In general, patients with a suspected or confirmed serious opportunistic infection will have to be admitted for investigation and management. Patients in the final stages of AIDS (fortunately an uncommon group in Australia) or those with less serious complications can often be managed in the community, in which case liaison with the local doctor, home-care nurses or community-care agencies is vital.

Prognosis

Prior to the widespread use of opportunistic infection prophylaxis and effective ART, 50% of patients developed AIDS 10 years after becoming HIV-infected and 75% of patients did so after 13 years. Following an AIDS-defining illness, the median survival was 12 to 24 months. Long-term non-progressors who have normal CD4 cell counts and no HIV-related

complications without ART after 10 or more years of HIV infection comprise less than 5% of patient cohorts.

Most AIDS-defining infections, such as PJP, now have low mortality and high 1-year survival rates if the infection is treated appropriately and patients are started promptly on combination ART. However, survival rates following the diagnosis of disseminated MAC and CMV end-organ disease are lower because these two opportunistic infections usually occur at a very advanced stage of HIV infection. Combination ART has reduced the mortality and incidence of opportunistic infections by over 80%.

Data from several large cohort studies indicate that average life expectancy in developed countries for patients on long-term ART is close to but still lower than that of the HIV-uninfected population.¹⁵ This difference is partly accounted for by an excess of deaths due to chronic conditions not typically associated with HIV infection, such as cardiovascular disease, non-HIV associated malignancy and renal disease (discussed earlier in the chapter); classic HIV complications, such as opportunistic infections or HIV-related malignancies, still occur but do not contribute substantially to this difference.

Prevention

Prevention of HIV transmission

- Public health and educational efforts to encourage the adoption of safer sex practices
- HIV screening of blood, blood products and tissue donors
- Non-sharing and use of clean needles and syringes by injecting drug users
- Observance of standard precautions by workers in health care settings
- Use of antiretroviral therapy and avoidance of breastfeeding to prevent transmission from an HIV-infected mother to baby
- Use of ART to prevent transmission from an infected individual to an uninfected partner¹⁶
- Use of anti-retroviral prophylaxis after significant occupational exposure (see Chapter 9.10) or sexual exposure to HIV (post-exposure prophylaxis)
- Use of anti-retroviral prophylaxis by an uninfected individual before HIV exposure (pre-exposure prophylaxis)¹⁷
- Male circumcision—shown to reduce the acquisition of HIV infection by 60% in studies in sub-Saharan Africa¹⁸

Prevention of HIV-related complications¹⁹ (Table 9.7.2)

Table 9.7.2 Prevention of HIV-related complications

Infection	Preventive measure
Pneumococcal pneumonia	Pneumococcal vaccination
Latent tuberculous infection	Isoniazid
<i>Pneumocystis jiroveci</i> pneumonia	Co-trimoxazole
Toxoplasmosis	Co-trimoxazole
<i>Mycobacterium avium</i> complex (MAC)	Azithromycin or rifabutin

CONTROVERSIES

- Will the 'treatment as prevention' approach (broadening treatment indications for people already known to be HIV-infected and increasing testing rates in at-risk groups in order to diagnose and then treat people with unrecognized HIV) lead to a reduction in HIV transmission at the population level?
- What is the role of other preventive measures that are known to be effective, such as pre-exposure prophylaxis and male circumcision?
- What is the relative contribution of HIV infection, antiretroviral therapy and standard risk factors to the risk of developing chronic medical conditions that are responsible for most of the morbidity and mortality in patients on effective antiretroviral therapy, and what is the nature of the association?
- Can an effective HIV vaccine be developed?

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9.8 Sexually transmitted infections

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ESSENTIALS

- 1** Sexually transmitted infections (STIs) are among the commonest infections worldwide and account for a significant number of emergency department (ED) visits per year. ED staff should be competent to screen, diagnose and treat STIs and to notify and improve future sexual health through advice and referral.
- 2** Emergency physicians should aim to provide effective, confidential, non-judgemental and culturally appropriate care. The sexual history, where appropriate, should be normalized as part of the medical history.
- 3** Patients may be asymptomatic or may present at any stage of the STI and with multiple co-existent STIs; if missed or undertreated, these can result in chronic infection and infertility.
- 4** Constantly evolving antimicrobial resistance renders treatment regimens eventually ineffective; therefore knowledge of current local treatment guidelines is essential, as is effective treatment that is easily taken with a low side-effect profile.
- 5** The essentials of the sexual history can be summed up by the five Ps: Partners, Practices, Pregnancy, Protection, Past STIs.
- 6** Empirical treatment may have to be commenced in the ED, as screening results are rarely available at presentation; syndromic treatment in areas of high prevalence may also have to be commenced. Highly sensitive point-of care-testing is becoming more widespread.
- 7** Emerging behavioural and medical factors, such as social media-related sexual encounters as well as pre-exposure prophylaxis, may further alter the profile of STIs during the next decade.

Introduction

Sexually transmitted infections (STIs) are among the commonest infections worldwide and continue to be a major public health problem.

Over 340 million people per year contract an STI according to World Health Organization figures.¹ STIs account for a significant number of emergency department (ED) visits per year and notification rates in Australia,² the United

Kingdom,³ and the United States⁴ currently show a year-on-year increase. However, the true incidence is difficult to ascertain in view of likely under-reporting.

EDs should aim to provide effective and confidential care in a sensitive and non-judgemental environment for patients who are unable to access a specialist STI clinic. This may be a challenge for a busy, noisy department with multiple simultaneous care priorities.

Patients will continue to use EDs to access help for their health care needs, therefore emergency physicians (EPs) must have a sound working knowledge of STI management, including screening, diagnosis, treatment, advice and notification to public health. This may be the only opportunity to intervene.

Patients may present at any stage of their disease and with multiple coexistent, STIs. A detailed and specific sexual history should be normalized within the context of the general medical history and with consideration of the individual's cultural background, using skilled interpreters where necessary.

STIs may be asymptomatic, missed or undertreated, leading to complications that may include ectopic pregnancy, chronic infection and infertility.

EPs should maintain a high index of suspicion, avoid stereotyping patients, and be prepared to treat empirically, especially in areas of high prevalence.

Patients should be referred for follow-up, including HIV and hepatitis screening.

ED patients may have high rates of asymptomatic STIs,⁵ and around half of females presenting

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with chlamydial infection or gonorrhoea are discharged without adequate treatment.³ Conversely, most females presenting with vaginal discharge do not have STIs and are more likely to have candidiasis or bacterial vaginosis. Debates around whether to screen for STIs and HIV in EDs versus specialist clinics continue. The cost of screening—especially if adequate and accessible specialized facilities exist nearby and the potential for increasing antibiotic resistance with empiric treatment—must be weighed against the consequences of missed infections and the significant public health, social and economic burden of undiagnosed and untreated STIs. Alternative facilities may not be accessible at the time of presentation. There is, therefore, an important opportunity for the EP to intervene and capture these patients at presentation.

Epidemiology

STIs are increasing worldwide. There are several well-documented high-risk groups for STIs and some newly emerging patient groups. Those known to be high-risk include young people in the 15- to 24-year age group, individuals who exchange sex for money or drugs (also known as transactional sex), pregnant women and men who have sex with men (MSM). Users of erectile dysfunction medication and widowers may also be at risk.⁶ STIs can affect any sexually active person and be transmitted in utero and at birth, therefore stereotyping should be avoided.

The commonest STI in Australia, the United Kingdom and the United States is infection with *Chlamydia trachomatis* (commonly called simply chlamydia), with an increase in Australia from 103 to 409 cases per 100,000 population between 2001 and 2016. The next commonest is gonorrhoea, with an increase from 31 to 101 cases per 100,000 in the same period.²

Syphilis is currently increasing overall in Australia, as in the United Kingdom³ and the United States,⁴ with 659 reported cases in Australia in 2005, which increased to 1285 cases in 2011.² Donovanosis is now rare in Australia following a successful eradication programme, although cases are still occasionally seen in Papua New Guinea, South Africa and India.

Prevention

Public health campaigns have been active around STI prevention, although rates of infection continue to increase. It is not clear whether this is linked to increased awareness and reporting, and possibly in some urban areas to newly emerging behaviours such as the rise of social media—facilitated sexual encounters.⁷ Advice should include discussion around high-risk behaviour and safe sex practices. This should include

effective barrier contraception in the form of latex condoms, the need to abstain from sex until STI treatment is complete and the need for regular STI screening, especially in high-risk groups. Pre-exposure prophylaxis (PrEP) is another new field that may affect rates of STI transmission over the next decade.

History

Effective communication is especially important within the context of a sexual history, and patients are often embarrassed and anxious. The sexual history should take the form of a comprehensive and holistic risk screening. Wherever possible, a private, clean, comfortable cubicle with a door that closes should be used for taking the sexual history. Thought is required around the initial greeting, appropriate body language, eye contact, skilled interpreters where needed and non-verbal cues from the patient. Be prepared that this may take a little longer than the focused history often used in EDs. It may be necessary for the EP to reflect on his or her own personal attitudes toward sexual behaviour in order to normalize the sexual history within the overall medical history and make an objective assessment. Communication must take into account language, hearing difficulty and cultural context; these should be addressed.

Efforts should be made to reinforce the confidential nature of the interview in order to encourage candour. It may help to display local STI clinic posters and literature within the ED. Students and observers will need the consent of the patient to be present, and such consent is not always given owing to the sensitive nature of the interview and the need for confidentiality. A detailed and specific history is important to identify at-risk patients and ascertain which anatomic sites should be focus on for screening. The history may start with open statements and questions, such as telling the patient that it is important to ask questions around his or her sexual behaviour, and then progressing to closed questions around specifics of the five Ps of the history, as outlined further on. It may be necessary to explain clearly the need to ask certain questions in order to avoid offence. For example, explaining that asking about the gender of a partner and details of sexual practices is needed in order to offer appropriate screening tests, and that questions around partners are necessary to allow contact tracing and follow-up. The history often opens with the presenting symptoms, including discharge or genital ulcers. Further questions should ask about the characteristics of any discharge, abdominal and pelvic pain, dyspareunia, dysuria, joint and eye symptoms, bowel or urinary symptoms and skin rashes. The history should look for risk factors for STI in

general and for specific features of STIs; it should also screen for complicated, disseminated or recurrent infection. A previous history of STI or partner infection and treatment and the possibility of pregnancy should be explored. It is important to adapt the questioning style to the cultural context, as many patients will be unfamiliar and uncomfortable with discussing the details of their sexual practices.

The sexual history can be summarized in terms of the five Ps: Partners, Practices, Pregnancy, Protection and Past STIs (Table 9.8.1). The skill of taking a focused sexual history, including the following points, in the time available in ED takes practice.

Partners

Ask how many in the past year and how many in the past 3 months, what gender, current length of relationship, risk factors of partners (e.g. intravenous drug use), seroconcordance if HIV is confirmed in the patient or partners, and other partners outside the relationship. The practice of multiple sexual partners over several days, often accompanied by recreational drug ingestion—known as 'chemsex'—is becoming recognized as a new risk factor for STIs among MSM.⁷

Practices

Number and genders of recent partners within the past 3 months, whether condoms are used (always, sometimes, never); whether sexual acts are vaginal, anal insertive, anal receptive or oral; other practices and with whom.⁷ A history of recent travel may identify infections in areas where specific pathogens or antibiotic resistance are known.

Table 9.8.1 Essentials of the sexual history

<i>The five Ps of the sexual history</i>	<i>Essential points to cover</i>
Partners	Last 3 months who, how many, where from, risk factors in partners?
Practices	Is sexual contact vaginal, oral, anal and with whom? Are condoms used sometimes, always, never?
Protection	How is risk reduced (e.g. monogamy, condoms)?
Pregnancy	Plans around becoming or preventing pregnancy and details of contraception used
Past STIs	In patient and partners—what infections, when and how were they treated, how were they followed up? Screening since?

STIs, Sexually transmitted infections.

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Pregnancy

Assess for current risk of pregnancy, which may affect treatment options and follow-up, whether contraception is used or not and what type, any pregnancy-related symptoms, including last menstrual period. All females of childbearing age should have a pregnancy test. The need for emergency contraception should be assessed and a cervical cytology history taken.

Protection

It is useful to ask what the patient does to protect himself or herself from STIs and HIV, including monogamy, condoms, safer sexual practices, PreP; also to gauge the patient's perception of his or her own and the partners' risks.

Past sexually transmitted infections

Previous STIs may indicate higher-risk behaviour and also repeat infection. Ask specifically whether the patient has ever had or been treated for gonorrhoea, chlamydia or any other STI, including HIV testing and results, and about hepatitis testing and results.

General principles of examination and screening

Following the full sexual history, a comprehensive STI check should be offered.

A chaperone should be available for all intimate examinations. Examination should be performed in a comfortable private cubicle with a door that closes and, preferably, with screens available for additional privacy. A good light source is essential and swabs and specimen pots should be readily available.

General physical examination—including the mouth, pharynx, lymph nodes and skin—should then be followed by genital examination. This should include palpation for inguinal lymph nodes, careful inspection of the genital and perianal areas for discharge, papules, ulcers, warts, lice or nits; and signs of local trauma. Examination beneath the foreskin in the male is important, as is inspection of the urethral meatus for lesions and discharge. The scrotum, testes and epididymis should be examined for lesions and tenderness and the anorectal area examined, including a digital exam and proctoscopy considered in patients at risk of rectal disease or presenting with anorectal symptoms.

Examination of the vulva, Bartholin glands, vagina, cervix and perianal area is important in the female and should include bimanual pelvic examination to assess for tenderness and masses. A pregnancy test should be performed on all women of childbearing age.

It is important to confirm with the laboratory which specimen tubes and transport media are needed for which tests and how specimens

should be stored; for example gonorrhoea swabs should be kept at room temperature. A ready-made testing pack supplied by the laboratory is useful and will generally include swabs with charcoal transport medium for urethral and high vaginal smear and culture, glass slides for high vaginal or urethral smear, wire cotton-tipped swabs with a plastic shaft tube for chlamydia, gonorrhoea and herpes. The nucleic acid amplification test (NAAT) is now becoming highly accurate and may replace other testing methods in time. Clotted blood tubes are used for serological tests. Specimen collection is a specialist skill upon which the diagnosis rests, and advice from laboratory staff prior to collection is invaluable. Swabs should be taken from the appropriate areas, as detailed further on, for microscopy, culture and sensitivity (M, C and S) and NAAT for chlamydia, gonorrhoea, trichomonas and other organisms as indicated. This may include the genital area, anorectal area and pharynx. Best practice in specimen collection may require extra training and updates by genitourinary medicine clinicians. A badly collected and transported specimen is unhelpful and even harmful if treatment is incorrect as a result. Current local guidelines should be used for specimen collection, transport and storage.

Urine should be sent as first void specimen for M, C and S and NAAT testing for specific organisms and a midstream specimen for general M, C and S. Swab or lesion scrapings should be sent if ulcers are present. Blood should be taken for syphilis, HIV and hepatitis serology.

Clinical features of specific infections

STIs may be asymptomatic or may present with constitutional or focal symptoms (Table 9.8.2). Focal symptoms are commonly those

of urethritis, cervicitis or genital ulcers. Disseminated infection may present with skin rash or with joint or eye symptoms. Not considering an STI in the differential diagnosis of a skin, joint, bowel or other generalized presentations will lead to missed diagnoses. One or more STIs may coexist and, as the clinical features may be indistinguishable, empirical treatment, especially in males in areas of high prevalence, is indicated. Syndromic treatment, according to symptoms, has been shown to be neither sensitive nor specific in females presenting with vaginal discharge because most cases of vaginal discharge are not caused by STIs and many STIs in females are asymptomatic. In areas of high prevalence, a judgement should be made as to whether symptoms are likely to be STI-related and whether treatment is indicated prior to results. Around one-third of cases of vaginal discharge presenting to ED remain undiagnosed pathologically,⁸ which may reflect inadequate specimen sampling or possibly other non-infective physiological causes.

Infections presenting with discharge, urethritis and cervicitis

These symptoms may be caused by chlamydia, gonococcus, *Trichomonas vaginalis*, *Ureaplasma urealyticum* and *Mycoplasma genitalium* (MG). Occasionally genital herpes may cause discharge, although this is seldom the only symptom. *Candida* and bacterial vaginosis also present with discharge, although these are not classically STIs.

Chlamydia

Chlamydia is the most common STI in Australia, the United Kingdom and the United States. It is caused by the organism *Chlamydia trachomatis* and often coexists with gonorrhoea and other STIs. Chlamydia is often asymptomatic, especially in women,^{3,9} and may be carried at extra-genital

Table 9.8.2 Clinical presentation of sexually transmitted infections and differential diagnosis

Symptoms	Differential diagnosis
Vaginal discharge	<i>Candida albicans</i> <i>Trichomonas vaginalis</i> <i>Neisseria gonorrhoeae</i> <i>Chlamydia trachomatis</i> Herpes simplex Bacterial vaginosis
Urethritis or cervicitis	<i>Neisseria gonorrhoeae</i> <i>Chlamydia trachomatis</i> <i>Mycoplasma genitalium</i> <i>Ureaplasma urealyticum</i> <i>Trichomonas vaginalis</i>
Genital ulcers	Syphilis Chancroid LGV Donovanosis Herpesvirus

LGV, Lymphogranuloma venereum.

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sites in asymptomatic MSM.⁷ This leads to under-diagnosis and under-treatment, which may result in long-term complications, including pelvic inflammatory disease (PID) and infertility. Screening in sexually active females under 25 years of age and in older females with new or multiple sexual partners as well as in other high-risk groups is advised.⁷ Symptoms and signs, if present, are most commonly a mucopurulent cervical, urethral or vaginal discharge, intermenstrual bleeding and dysuria in females, or symptoms of urethritis, proctitis and epididymitis in males, including urethral discharge, itching, dysuria and sterile pyuria. Males may present with Reiter syndrome.

Diagnosis is made by NAAT and Gram stain of discharge or first voided urine for NAAT.

Treatment for uncomplicated infection is with azithromycin 1 g oral as a single dose. If PID is likely, ceftriaxone 500 mg IM once and

metronidazole 400 mg oral bd for 14 days should be added. Antibiotic resistance and regional sensitivities may alter and current local guidelines should always guide treatment.

Gonorrhoea

Gonococcal infections are increasing and are the second most common STI in Australia,² the United Kingdom³ and the United States.⁴ Of the 24,000 new diagnoses in Australia in 2016, most were in young men in the 20- to 29-year age group. They are caused by the gram-negative intracellular diplococcus *Neisseria gonorrhoeae*, which has an incubation period of 10 to 14 days. Infection in females is often asymptomatic and may coexist with chlamydia. Untreated gonococcal infection may lead to PID and ectopic pregnancy in females and epididymitis and prostatitis in males. Symptomatic presentation is usually with purulent penile discharge in males and pelvic

discomfort and mucopurulent cervicitis in females. Rectal infection is seen in up to 50% of females and is more common in MSM,⁷ as is pharyngeal gonorrhoea, which is often asymptomatic. Gonococcal infections may disseminate to cause constitutional symptoms of fever and malaise as well as focal signs of septic arthritis, tenosynovitis and a distinctive skin rash of pustular lesions on an erythematous base on the palms and fingers.

Diagnosis is by NAAT testing of swabs and urine, with swabs taken also at extra-genital sites according to the history. A suggested treatment regimen may be found in Table 9.8.3, although local sensitivities and antibiotic resistance mandates current local knowledge and microbiology advice. Gonococcal antibiotic sensitivities change rapidly, with fluoroquinolone resistance widely documented, and some regions, for example the Northern Territory of Australia and Southeast Asia, have penicillin-sensitive strains.

Table 9.8.3 Treatment guideline summary

Clinical diagnosis and pathogen	Recommended treatment	Alternative choice treatment
Chlamydia (uncomplicated)	Azithromycin 1 g PO once	Doxycycline 100 mg bd oral 7 days
Gonorrhoea Genital, pharyngeal, rectal	Ceftriaxone 500 mg IM once plus azithromycin 1 g PO once	If acquired from Top End or Central Australia, amoxicillin 3 g plus probenecid 1 g PO once
Trichomoniasis	Metronidazole 2 g PO once OR tinidazole (not in pregnancy) 2 g PO once	
Pelvic inflammatory disease	Ceftriaxone 500 mg IM once PLUS Azithromycin 1 g PO once PLUS Metronidazole 400 mg PO, bd for 14 days PLUS Doxycycline 100 mg oral bd for 14 days	
Bacterial vaginosis	Metronidazole 400 mg PO bd for 7 days	
Urethritis, dysuria, urethral discharge	Ceftriaxone 500 mg IM once PLUS Azithromycin 1 g PO once OR Doxycycline 100 mg PO bd for 7 days	Erythromycin 500 mg PO qds for 7 days
Chancroid	Azithromycin 1 g PO once OR Ceftriaxone 500 mg IM once	Ciprofloxacin 500 mg PO, bd for 3 days
Lymphogranuloma venereum	Doxycycline (not in pregnancy) 100 mg PO, bd for 21 days	Erythromycin 500 mg oral qid for 21 days OR Azithromycin 1 g PO 1 dose weekly for 3 weeks
Donovanosis	Azithromycin 1 g PO once weekly or 500 mg qd for 3 weeks or until lesions have healed	Co-trimoxazole 160/800 mg bd PO 3 weeks
Mycobacterium G	Doxycycline, azithromycin and moxifloxacin	
Herpes Anogenital, primary episode	Valacyclovir 500 mg PO, bd for 7–10 days	
Anogenital, recurrent episode	Valacyclovir 500 mg PO, bd for 3 days	
Severe, disseminated infection	Acyclovir 5–10 mg/kg IV q 8 h for 5–10 days	
Genital warts		
External genital and perianal	Podophyllin 0.5% lotion topical tds for 3 days, then no treatment for 4 days, repeat 4 cycles or until resolution	
Mucosal warts	Cryotherapy or trichloroacetic acid 80% topical weekly for 2 weeks	Podophyllin resin 25% in benzoin topical for urethral meatus warts once weekly for 2 weeks
Syphilis		
Primary, secondary, early latent, late latent or >2 years' duration	Benzathine penicillin G 2.4 million U IM, with 2 mL 1% lignocaine once	

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Trichomoniasis

This infection occurs mainly in females and is caused by the protozoan *Trichomonas vaginalis*. The incubation period is up to 1 month. Infection may be asymptomatic or may present with genital irritation and vaginal discharge or urethritis in males. The discharge is rarely frothy and green-coloured but, more commonly, clear and offensive. Other symptoms may include dysuria, dyspareunia and pelvic pain. Untreated trichomoniasis may cause PID. Diagnosis is by visualization of the protozoa within 20 minutes if a wet mount is readily available, but more accurate diagnostic methods include high vaginal or urethral swabs for NAAT. Treatment is with metronidazole 2 g PO as a single dose or tinidazole 2 g PO if the patient is female and not pregnant. PID should be treated with combination antibiotics, as described previously. Antibiotic resistance and regional sensitivities may alter and current local guidelines should always be consulted.

Mycoplasma genitalium

This organism was identified in the 1980s; it is slow-growing and difficult to culture. MG is thought to account for up to 30% of persistent urethritis in men and PID in women. NAAT testing of urine, urethral and vaginal swabs is currently preferred for MG. In view of the difficulty isolating and diagnosing MG, treatment may have to be syndromic as part of urethritis or PID treatment. Treatment with azithromycin 1g as a single dose may be effective, although resistance is high and moxifloxacin and doxycycline may be used as second-line therapy. Current local treatment guidelines should always be considered.

Urethritis or urethral discharge in males

This is usually caused by gonorrhoea or chlamydia but may also be due to *U. urealyticum*, MG, *T. vaginalis* or herpesvirus. Diagnosis is made by the clinical history (although this will not indicate the causative organism) plus urethral swab and first void urine specimen for NAAT, culture and cell count. Midstream urine should be sent for general M, C and S, as UTI, especially in older males, may be the cause. Consider swabbing extra-genital sites also, depending on the history. Treat empirically if the STI is likely to be gonorrhoea and/or chlamydia, as per current local guidelines.

Candidiasis

Vaginal candidiasis may feature in the differential diagnosis of STIs causing irritation and discharge but it is generally not a STI. It is caused by the fungus *Candida albicans* in most cases and characterized by an itchy white, curd-like discharge. Swabs for Gram stain or wet mount specimens may confirm the diagnosis by visible yeasts and pseudohyphae. Treat with clotrimazole 500 mg as a single-dose vaginal pessary or fluconazole 150 mg PO single dose.

Bacterial vaginosis

Bacterial vaginosis is not caused by any one specific organism and may occur in women who are not sexually active. It is associated with having multiple sexual partners and is a differential diagnosis of STI-related vaginal discharge. It is characterized by an overgrowth of normal vaginal flora by anaerobic bacteria and may be asymptomatic or present with discharge. Diagnosis is by Gram stain, combined with the characteristic thin, offensive discharge and clue cells on microscopy. Treat with metronidazole 400 mg bd PO for 7 days.

Infections presenting with genital ulcers

Genital ulceration may be caused by the herpesvirus, syphilis and, rarely, chancroid, lymphogranuloma venereum (LGV) and lymphogranuloma inguinale (Donovanosis). These infections have higher rates of HIV co-transmission. Genital ulceration may rarely be caused by malignancy and referral should be made for any lesion that does not respond to treatment. There are reports of an increase in vulval cancer in young indigenous Australian females.¹⁰

Herpes simplex (e-Fig. 9.8.1)

The widespread introduction of the herpes simplex virus (HSV) vaccination programme for schoolgirls in 2007 and schoolboys in 2013 has seen a 90% reduction in HSV-related genital lesion presentations from 2007 to 2016 in Australia and the United Kingdom, with similar programmes internationally.^{2,3}

HSV infections are still common worldwide, although most are asymptomatic. Genital ulceration is more commonly caused by HSV type 2 and occurs in up to one-quarter of patients who are seropositive for the virus. HSV type 1 generally causes oro-labial blisters but may also cause genital ulceration identical to HSV-2. Subclinical infections may spread by viral shedding during sex. The primary outbreak of genital ulceration is usually accompanied by constitutional symptoms of fever, malaise, headache and painful bilateral regional lymphadenopathy, which may precede the ulceration by 1 or 2 days. Prodromal tingling or paresthesia in the affected dermatomes may occur. The lesions are initially vesicular with an itchy, erythematous base; they then become ulcerated before forming a scab. They may occur around the vulva, anus, thighs or buttocks in women and on or around the penis, perianal area, thighs and buttocks in males. They are usually very painful, and adequate analgesia is important. Females may experience urinary retention due to the pain of voiding and sacral radiculopathy and may require admission for catheterization and intravenous anti-viral treatment. The virus

is shed for up to 2 weeks after the rash appears and lesions usually heal within 3 weeks. Recurrent episodes are generally less severe. Genital herpes is diagnosed by the characteristic clinical features and confirmation may be possible from viral swabs of lesion fluid, although treatment should be commenced empirically. Severe or disseminated infection should be treated by high-dose intravenous anti-virals with a duration adequate to ensure lesion healing. The patient should be informed that treatment does not cure and that there may be recurrent episodes. Future episodes can be attenuated if treatment is commenced at the onset of symptoms. Frequent recurrences (more than six per year) may indicate the need for prophylactic antiviral therapy. Diagnosis is clinical and confirmation is by dry swab of the ulcer base or blister fluid for NAAT. Treatment is with valacyclovir 500 mg bd for 7 to 10 days for the primary episode or 3 days for recurrent episodes. Local guidelines should be followed for current drug regimens.

Chancroid

Chancroid is a disease seen mainly in Asia, Africa and the Caribbean, with few cases reported in the developed world. There have been very few reports in Australia for the decade up to 2016. It is caused by the gram negative bacillus *Haemophilus ducreyi* and presents with painful genital ulcers up to 2 cm diameter. Painful inguinal lymph nodes may go on to suppurate if the infection is untreated. Chancroid may coexist with other genital ulcerating infections including syphilis and HSV. Unlike herpes, chancroid is rarely accompanied by constitutional symptoms and is rarely recurrent. Diagnosis is generally clinical, although lesion swabs for culture and NAAT may confirm the diagnosis. Treatment may be with azithromycin 1 g PO single dose or ceftriaxone 500 mg IM single dose and should follow current local guidelines.

Lymphogranuloma venereum

LGV is caused by *Chlamydia trachomatis* and is endemic in parts of Africa, South America, India, Southeast Asia and the Caribbean. It is rarely seen in the developed world with the exception of sporadic outbreaks since 2003, predominantly among MSM who are HIV-positive. It presents either with proctitis or may be asymptomatic. There are three clinical stages. The initial presentation with a painless ulcer or papule may be missed. The second stage involves painful inguinal lymphadenopathy, which is commonly unilateral. The third stage involves strictures, fistulae and scarring around the perianal area. Diagnosis is clinical and by NAAT of vulvovaginal swabs in females or urethral swabs in males or NAAT of first-catch early morning urine in both.

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Treatment is according to current local guidelines, with a suggested regimen of doxycycline 100 mg PO bid for 21 days or erythromycin 500 mg qid for 21 days.

Donovanosis

This is now a rare infection, although there are pockets of increased prevalence in desert areas of central Australia and in rural tropical and subtropical areas including Southeast India, South Africa, Papua New Guinea and the Caribbean. Only two cases have been reported in Australia since 2011.² It is caused by *Klebsiella granulomatis* and is seen more commonly in males. The incubation period is up to 12 weeks. Red papules in the genital and perianal areas evolve into nodules of friable granulation tissue that bleed easily. The initial lesions may resemble chancroid and progress to spread and necrose; if untreated, there may be loss of genital tissue and depigmentation. Diagnosis is generally clinical and may be confirmed by lesion swab or scraping for NAAT, although specialized laboratory services may be required for testing. Treat according to current local guidelines, which may include azithromycin 1 g PO weekly for at least 4 weeks or until the lesions are fully healed.

Syphilis (e-Figs. 9.8.2-9.8.4)

Syphilis is currently increasing worldwide in Australia, the United Kingdom and the United States, especially among MSM. The causative organism is the spirochaete *Treponema pallidum*. Patients may present with symptoms in any of the three stages of primary, secondary or tertiary infection or may present in the latent phase. Primary syphilis has an incubation period of up to 90 days, which is thought to be dose dependent, with larger inoculations presenting sooner.⁷ It classically presents with a painless genital ulcer known as the primary chancre. This may last for up to 6 weeks and is not accompanied by constitutional symptoms. If untreated, the primary stage may evolve into the secondary stage within 6 weeks, characterized by the distinctive macular pink rash that may resemble pityriasis rosea. It may be present on the flexor surfaces, trunk, palms and soles. The secondary stage is often accompanied by constitutional symptoms of fever, malaise and headache. Tertiary syphilis occurs up to 20 years after the primary infection in around one-third of patients with untreated secondary syphilis. The presentation includes widespread granulomas, known as gummas, or may present with meningitis, dementia, thoracic aneurysm or neuropathy, known as tabes dorsalis. There may be extensive involvement of the cardiovascular and nervous systems.

Diagnosis depends on serological confirmation of treponemal or non-treponemal tests. Treponemal tests remain positive for life. Non-treponemal tests respond to treatment.

An NAAT for syphilis may be requested from swabs or scrapings from rash or ulcers. Treatment is according to current local guidelines, typically including benzathine penicillin 2.4 million units IM as a single dose if the infection is under 2 years in duration or three doses at weekly intervals if over 2 years in duration. There is no documented treponemal resistance as yet to penicillin, although treatment failures have occurred occasionally and are thought to be either re-infection or individual variation in decline of the non-treponemal test titres in response to treatment.

Notification of cases should be sent to the regional syphilis register.

Genital warts

Genital warts are caused by the human papillomavirus. Since 2003, new diagnoses have fallen by over 90% among the immunized population of young adults. Up to three-quarters of non-immunized sexually active adults are infected, although most infections are subclinical. Multiple warts, which may cluster, are seen over the vulva and penis. Internal warts may be seen in the rectum and around the cervix. Diagnosis is clinical and the differential diagnosis of molluscum contagiosum, secondary syphilis (condylomata) and carcinoma must be considered. Treatment is with podophyllin 0.5% lotion applied twice daily to lesions for 3 days, then no treatment for 4 days, and repeat until lesions resolve. This may take four or more cycles of treatment.

Principles of clinical investigations

Diagnosis is initially clinical and treatment may need to be empirical. Attempts should be made to confirm the diagnosis by laboratory analysis of swabs and urine, and it is important to communicate with laboratory staff to discuss the collection, transport and testing of specimens and the specific type of swab, transport medium and temperature for each organism. All specimens should be correctly labeled with patients' details in leakproof containers. NAAT is now seen as the gold standard for confirmation of many STIs and has the advantage of first-voided early-morning urine collection. Swabs from possible affected areas for M, C and S and swabs and urine for NAAT should be taken. Serum for syphilis, HIV and hepatitis serology should be sent and referral should be considered for cervical cytology in females.

If lesions are suggestive, scraping the lesion for syphilis microscopy and specialist swabs for HSV and *H. ducreyi* may be helpful.

Overall, it is unlikely that most emergency medicine clinicians will become expert STI specimen collectors without additional training;

either modular training delivered in the ED or specialist clinic rotation may increase the yield of diagnostically useful ED specimens.

Treatment

See Table 9.8.3 for an example summary guideline.

Treatment is subject to current local guidelines and sensitivities and may vary according to regional strains and sensitivities. Where the infection likely originated is an important part of the history. Always refer to current local guidelines.

Follow-up

Referral to a local STI clinic for follow-up, contact tracing and treatment of partners is essential to stop the spread of STIs.

The patient should be advised of the need for partner treatment and abstinence from sex until the infection has been treated adequately. The opportunity for health education around safer sexual practices and STI prevention should be taken. Notifiable diseases include chlamydia, gonorrhoea, syphilis, chancroid, LGV and Donovanosis.

CONTROVERSIES AND FUTURE DIRECTIONS

- There are conflicting views over whether the ED is the right place to screen for STIs including HIV, although in some cases an ED visit may offer the only opportunity for diagnosis and treatment.
- Debate continues over whether to treat infections empirically and the potential for increasing antibiotic resistance versus the burden of untreated disease. Syndromic treatment in areas of low prevalence may be more effective in males, as most cases of vaginal discharge in females are not STI-related.
- Highly sensitive point-of-care testing is becoming more readily available and will shorten time to diagnosis and treatment.
- The rise of social media-facilitated sexual encounters, mainly in major cities among MSM over the past few years, is a new high-risk sexual behaviour for STI transmission⁷
- Pre-exposure prophylaxis for HIV and STIs is gaining momentum and is likely to alter the landscape of STI transmission and sexual habits over the next decade.
- Constantly changing antibiotic sensitivities mandate the consideration of current local treatment guidelines and close liaison with colleagues in sexual health, infectious disease, microbiology and virology.

9.9 ANTIBIOTICS IN THE EMERGENCY DEPARTMENT

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Further reading

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9.9 Antibiotics in the emergency department

John Vinen

ESSENTIALS

- 1** Patients with infections and infectious diseases commonly present to emergency departments.
- 2** There are also changing patterns of infectious disease, largely due to immunosuppression from chemotherapy, continuing development of bacterial resistance, HIV-associated infections and new and emerging infections.
- 3** Many bacteria are becoming increasingly resistant to available antimicrobials, with some resistant to multiple agents including many community-acquired infections.
- 4** The growing world trade in wildlife, factory farming, increasing air travel and increased population density increases the risk of infectious disease transmission.
- 5** There are relatively few new antimicrobials to counter these changing patterns of resistance.
- 6** Antimicrobial prescribing should follow evidence-based guidelines or infectious disease consultant advice.
- 7** Some patients with infection can be treated wholly as outpatients using parenteral therapy or after early discharge once the acute toxic phase is over.
- 8** Early administration of guideline-based antibiotics combined with supportive therapy is the key to a good outcome in patients with serious infections.
- 9** The increasing incidence of terrorism may result in patients presenting with novel, unusual or clusters of infections caused by biological agents.

Principles of antimicrobial therapy

Antibiotic stewardship

The first decision to be made regarding antimicrobial therapy is whether the administration of these agents is truly indicated. The growing incidence of antibiotic resistance is rapidly increasing. In many cases, antibiotics are administered without clear indications. This practice is potentially dangerous, as some agents can cause serious

toxicity or allergic reactions, diagnoses may be masked if appropriate cultures are not taken prior to therapy, serious adverse events can result and microorganism resistance may emerge.

Ideally, antibiotic therapy is determined by the isolation of the organism(s) involved and determination of the antibiotic susceptibility pattern. As this information is rarely available, it is necessary to make treatment decisions without precise knowledge of the infectious source or

microbial species, in which case empiric treatment is commenced based on the type of infection (if known) and the likely organisms involved utilizing recognized guidelines.

In specific situations (e.g. suspected meningitis, meningococcal infection, necrotizing fasciitis, sepsis, peritonitis, febrile neutropaenia and pneumonia), early empiric therapy can be lifesaving.

The choice of an appropriate antimicrobial agent requires consideration of the following factors.

The microorganism

The identity of the infecting organism(s) needs to be identified or suspected. In the emergency department (ED) setting, almost all antimicrobial decisions will be made without the benefit of cultures, with treatment commencing based on the most likely to cause infection in a given clinical setting.¹ However, certain 'rapid methods' of microbial identification may be employed. These include Gram-stain preparations (bacterial, some fungal and leucocyte identification) and immunological methods for antigen detection (enzyme-linked immunoabsorbent assay, latex agglutination, polymerase chain reactions).

Another way of guiding appropriate use and prescription of antibiotics is to use defined criteria, examples are shown in Box 9.9.1.

Other examples include:

- Systemic inflammatory response syndrome (SIRS), Sepsis and Septic Shock Criteria
- Renal, age, purulence, infection source, and dietary factors (RAPID) for pleural infection

Microorganism susceptibility

This information is unlikely to be available and therapeutic decisions will generally be based on evidence-based guidelines and a knowledge of likely susceptibilities.¹ For example, group A streptococci remain susceptible to the penicillins

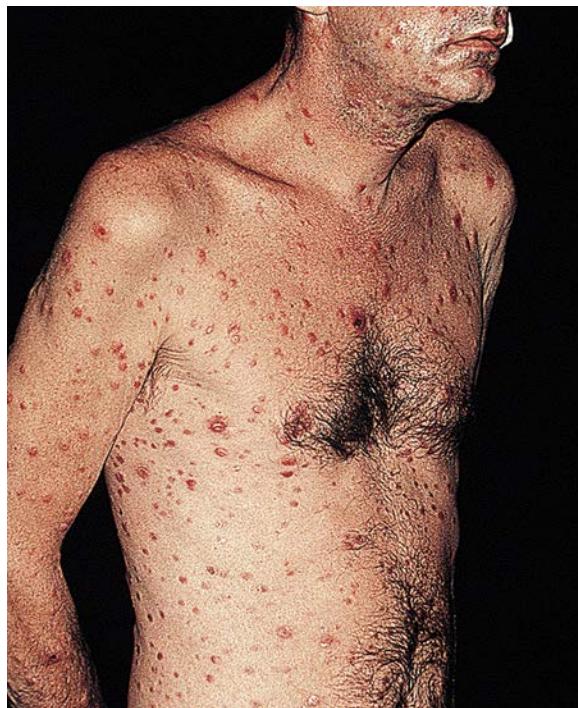
9.8 SEXUALLY TRANSMITTED INFECTIONS



E-FIG. 9.8.1 Genital herpes rash, primary attack. (Reproduced with permission from Campbell JL, Chapman MS, Dinulos JGH, Zug KA. Chapter 7: Skin disease: diagnosis and treatment. *Sexually Transmitted Infections*. 3rd ed. Elsevier Inc. 2011;184–209.)



E-FIG. 9.8.2 Syphilis primary chancre. (Reproduced with permission from Campbell JL, Chapman MS, Dinulos JGH, Zug KA. Chapter 7: Skin disease: diagnosis and treatment. *Sexually Transmitted Infections*. 3rd ed. Elsevier Inc. 2011;184–209.)



E-FIG. 9.8.3 Secondary syphilis rash. (Reproduced with permission from Campbell JL, Chapman MS, Dinulos JGH, Zug KA. Chapter 7: Skin disease: diagnosis and treatment. *Sexually Transmitted Infections*. 3rd ed. Elsevier Inc. 2011;184–209.)



E-FIG. 9.8.4 Secondary syphilis rash. (Reproduced with permission from Campbell JL, Chapman MS, Dinulos JGH, Zug KA. Chapter 7: Skin disease: diagnosis and treatment. *Sexually Transmitted Infections*. 3rd ed. Elsevier Inc. 2011;184–209.)

9.9 ANTIBIOTICS IN THE EMERGENCY DEPARTMENT

Box 9.9.1 Diagnostic Criteria for Community-Acquired Pneumonia

- Clinical features suggest pneumonia + consolidation on CXR → Pneumonia likely
- CAP score—determine if CAP score 'severe' using CORB^a or SMART-COP^b
- Admit to hospital or discharge with antibiotic treatment based on CORB or SMART-COP

^aCORB (C-confusion, O-Oxygen saturation 90% or less, R-RR 30 bpm or greater, B-SBP <90 mm Hg or DBP 60 mm Hg or less)

^bSMART-COP (SBP <90 mm Hg, M-multilobar involvement on CXR, A-albumin <35 g/L, R-RR 25 bpm or greater, T-tachycardia 125 bpm or greater, C-confusion [acute], O-PaO₂ <70 mm Hg, or O₂ saturation 93% or less, or PaO₂/FiO₂ less than 333, P-pH <7.35)

Reference: Therapeutic Guidelines Antibiotic.

and cephalosporins, and virtually all anaerobes (except *Bacteroides* spp.) are susceptible to penicillin G. However, when the identity or susceptibility of the infecting organism is sufficiently in doubt, the patient's clinical condition is atypical, serious or potentially serious or where antimicrobial resistance is suspected, it is good practice to obtain appropriate specimens for culture and susceptibility testing prior to empirical broad-spectrum antimicrobial therapy (Table 9.9.1).

Host factors

An adequate history of drug allergies must be obtained to prevent the administration of an antimicrobial that may have serious or fatal

consequences. Where this is not possible, avoid the administration of penicillin and associated antimicrobials. The age of the patient may have clinically significant effects on drug absorption (e.g. penicillin absorption is increased in the young and the elderly),² metabolism (e.g. reduced chloramphenicol metabolism in the neonate)² and excretion (e.g. declining renal function with age³ may reduce the excretion of penicillins, cephalosporins and aminoglycosides). Furthermore, tetracyclines bind and discolour the developing bone and tooth structures in children aged 8 years or less.² Pregnant women and nursing mothers may pose certain problems in the selection of appropriate

Table 9.9.1 Antimicrobial agents of choice in selected infections

Microorganism	Diseases	First choice	Second choice
Gram positive cocci			
<i>Staphylococcus aureus</i> ^a	Abscesses penicillinase-negative: Osteomyelitis	Benzylpenicillin (penicillin G), phenoxymethyl penicillin (penicillin V)	Cephalosporin (G1), clindamycin
	Bacteraemia penicillinase-positive:	Nafcillin, oxacillin	Cephalosporin (G1)
	Endocarditis		Vancomycin, clindamycin
	Pneumonia methicillin-resistant:	Vancomycin ± rifampicin	Co-trimoxazole + rifampicin
	Cellulitis		Ciprofloxacin + rifampicin
<i>Streptococcus</i> (A, B, C, G and bovis)	Pharyngitis, scarlet fever, otitis media, cellulitis, erysipelas, pneumonia, bacteraemia, endocarditis, meningitis	Benzylpenicillin (penicillin G), phenoxymethylpenicillin (penicillin V), ampicillin	Erythromycin Cephalosporin (G1) Vancomycin
<i>Streptococcus pneumoniae</i> ^a	Pneumonia, arthritis, sinusitis, otitis media, meningitis, endocarditis	Benzylpenicillin (penicillin G), phenoxymethylpenicillin (penicillin V), ampicillin, penicillin G	Erythromycin, cephalosporin (G1–3) Vancomycin + rifampicin Ceftriaxone
<i>Streptococcus viridians</i> ^a	Bacteraemia, endocarditis	Benzylpenicillin (penicillin G) ± gentamicin	Ceftriaxone, vancomycin ± gentamicin
<i>Enterococcus</i>	Bacteraemia, endocarditis, urinary tract infection	Ampicillin + gentamicin, benzylpenicillin (penicillin G) + gentamicin	Vancomycin + gentamicin, nitrofurantoin Fluoroquinolone, ampicillin + clavulanic acid
Gram negative cocci			
<i>Moraxella catarrhalis</i>	Otitis, sinusitis, pneumonia	Co-trimoxazole	Cephalosporin (G2,3)
		Amoxicillin + clavulanic acid	Erythromycin, tetracycline
<i>Neisseria gonorrhoeae</i>	Gonorrhoea, disseminated disease	Ceftriaxone, ampicillin + probenecid	Ciprofloxacin, doxycycline spectinomycin
<i>Neisseria meningitidis</i>	Meningitis, carrier state	Benzylpenicillin (penicillin G) rifampicin	Cephalosporin (G3), chloramphenicol
Gram positive bacilli			
<i>Clostridium perfringens</i> ^a	Gas gangrene Tetanus	Benzylpenicillin (penicillin G)	Clindamycin, metronidazole, cephalosporin
<i>Clostridium tetani</i>	Tetanus	Benzylpenicillin (penicillin G), vancomycin	Doxycycline, clindamycin
<i>Clostridium difficile</i>	Antimicrobial-associated colitis	Metronidazole (oral)	Vancomycin (oral)
<i>Corynebacterium diphtheriae</i>	Pharyngitis, tracheitis, pneumonia	Erythromycin	Benzylpenicillin (penicillin G), clindamycin
<i>Listeria monocytogenes</i>	Meningitis, bacteraemia	Ampicillin ± gentamicin	Co-trimoxazole, erythromycin

9.9 ANTIBIOTICS IN THE EMERGENCY DEPARTMENT

Table 9.9.1 Antimicrobial agents of choice in selected infections—cont'd

Microorganism	Diseases	First choice	Second choice
Gram negative bacilli			
Brucella	Brucellosis	Doxycycline + gentamicin	Co-trimoxazole + gentamicin/rifampicin
<i>Campylobacter jejuni</i> ^a	Enteritis	Fluoroquinolone	Erythromycin, azithromycin
<i>Escherichia coli</i> ^a	Urinary tract infection, bacteraemia	Ampicillin, co-trimoxazole, cephalosporin (G1)	Ampicillin + gentamicin
<i>Enterobacter</i> species	Urinary tract and other infections	Fluoroquinolone imipenem	Gentamicin + broad-spectrum penicillin, co-trimoxazole
<i>Haemophilus influenzae</i> ^a	Otitis, sinusitis, pneumonia	Co-trimoxazole, ampicillin, amoxicillin	Amoxicillin + clavulanic acid, azithromycin, Cefuroxime
	Epiglottitis, meningitis	Cephalosporin (G3)	Chloramphenicol
<i>Klebsiella pneumoniae</i> ^a	Urinary tract infection, pneumonia	Cephalosporin ± gentamicin	Co-trimoxazole, fluoroquinolone
<i>Legionella pneumophila</i>	Legionnaires disease	Erythromycin ± rifampicin	Ciprofloxacin, azithromycin, co-trimoxazole
<i>Pasteurella multocida</i>	Animal bite infections, abscesses, bacteraemia, meningitis	Benzylpenicillin (penicillin G) amoxicillin + clavulanic acid	Doxycycline, cephalosporin
<i>Proteus mirabilis</i> ^a	Urinary tract and other infections	Ampicillin, amoxicillin	Cephalosporin, co-trimoxazole, gentamicin
<i>Proteus</i> (other species) ^a	Urinary tract and other infections	Cephalosporin (G3), gentamicin	Co-trimoxazole, fluoroquinolone
<i>Pseudomonas aeruginosa</i> ^a	Urinary tract infection, pneumonia, bacteraemia	Broad-spectrum penicillin ± gentamicin	Ceftazidime ± gentamicin Fluoroquinolone ± gentamicin
<i>Salmonella</i> species ^a	Typhoid fever, paratyphoid fever, bacteraemia, gastroenteritis	Fluoroquinolone, ceftriaxone	Amoxicillin, co-trimoxazole, chloramphenicol
<i>Shigella</i> ^a	Acute gastroenteritis	Fluoroquinolone	Amoxicillin, co-trimoxazole
<i>Vibrio cholera</i>	Cholera	Doxycycline, fluoroquinolone	Co-trimoxazole
Miscellaneous agents			
<i>Chlamydia</i> species	Pneumonia, trachoma, urethritis, cervicitis	Doxycycline	Azithromycin, erythromycin
<i>Mycoplasma pneumonia</i>	Atypical pneumonia	Erythromycin, doxycycline	Azithromycin
<i>Pneumocystis carinii</i>	Pneumonia in impaired host	Co-trimoxazole	Trimethoprim + dapsone, pentamidine
<i>Rickettsia</i>	Typhus fever, Q fever, Rocky Mountain spotted fever	Doxycycline	Chloramphenicol
<i>Treponema pallidum</i>	Syphilis	Benzylpenicillin (penicillin G)	Ceftriaxone, doxycycline

^aGi, First-generation cephalosporin; G2, second-generation cephalosporin; G3, third-generation cephalosporin. All strains should be examined *in vitro* for sensitivity to various antimicrobial agents.

antimicrobial agents, as all of these agents cross the placenta to varying degrees. The administration of antibiotics to pregnant patients must be based on guidelines.⁴ Whether or not antibiotic use has an effect on the efficacy of combined oral contraceptive pills (OCPs) has been a matter of controversy. A significant pharmacokinetic interaction between combined OCPs and antibiotics, apart from rifampicin and griseofulvin, has not been proven. It has been suggested that if an interaction does exist, it is likely that it occurs in a small number of predisposed individuals. It is not possible at this time to predict who is at risk

for potential interaction.⁵ Other host factors that may require consideration include the patient's renal and hepatic function, their genetic (e.g. liver acetylation rate) or metabolic abnormalities (e.g. diabetes mellitus) and the site of the infection.⁶

Route of administration

In general, the oral route is chosen for infections that are mild and can be managed on an outpatient basis. In this situation, consideration needs to be given to compliance with treatment, the variability of absorption with food in the stomach and interaction of the agent

with concomitant medications.⁷ The parenteral route is used for agents that are inefficiently absorbed from the gastrointestinal tract and for the treatment of patients with serious infections in whom high concentrations of antimicrobial agents are required.⁷ Intramuscular administration (not in patients on anticoagulants or who are coagulopathic) will provide adequate serum concentrations for most infections and may be appropriate where antimicrobial depots are desirable; for example, procaine penicillin injections where patient compliance with oral medication is doubtful. Intravenous administration allows

9.9 ANTIBIOTICS IN THE EMERGENCY DEPARTMENT

large doses of drugs to be given with a minimal amount of discomfort to the patient; for example, infection prophylaxis in compound fractures, life-threatening infections and shock. For intravenous administration, large veins should be used followed by saline flushing of the veins to help to minimize the incidence of venous irritation and phlebitis.

Supportive care

Supportive care in association with antimicrobial therapy is essential in many infections, fluid resuscitation, vasopressors and compliance with sepsis guidelines being essential for a good outcome in suspected sepsis/sepsis.⁸

Adverse drug events involving antibiotics

Antibiotics are one of the top medication classes resulting in ED visits for adverse drug events.

There is a 1:1000 risk that an individual prescribed an antibiotic will require a visit to the ED because of an antibiotic side effect.

Antibiotics are responsible for 19% of ED visits for adverse drug events:

- in children (<18 years), antibiotics are the most common cause of ED visits for adverse drug events
- 79% of ED visits for documented antibiotic-associated adverse drug events are due to allergic reactions.⁹

Antibiotic resistance

Bacteria can be resistant to an antimicrobial agent because the drug fails to reach the target or is inactivated or because the target is altered.^{10–12} Bacteria may produce enzymes that inactivate the drug or have cell membranes impermeable to the drug. Having gained entry into the microorganism, the drug must exert a deleterious effect. Natural variation or acquired changes at the target site that prevent drug binding or action can lead to resistance.

Resistance is most commonly acquired by the horizontal transfer of resistance determinants from a donor cell, often of another bacterial species, by transformation, transduction or conjugation. Resistance also may be acquired by mutation and passed vertically by selection to daughter cells. Antimicrobial agents can affect the emergence of resistance by exerting strong selective pressures on bacterial populations favouring those organisms capable of resisting them.¹³

The increasing emergence of antibiotic resistance is a very serious development that threatens the end of the antibiotic era. Penicillin-resistant strains of pneumococci account for >50% of isolates in some European countries. The worldwide emergence of *Haemophilus* and

gonococci that produce β-lactamase is a major therapeutic problem.¹⁴ Methicillin-resistant strains of *Staphylococcus aureus* (MRSA) are widely distributed among hospitals and are increasingly being isolated from community-acquired infections.¹⁵ There are now strains of enterococci (vancomycin-resistant Enterococcus), *Pseudomonas* and enterobacters that are resistant to all known drugs.¹⁶ Epidemics of multiple drug-resistant strains of *Mycobacterium tuberculosis* are increasingly being reported.¹⁶

A more responsible approach to the use of antimicrobial agents is essential to slow the development of multidrug-resistant organisms. Their use is unnecessary in viral infections; their use in prophylaxis and in established bacterial infections must be on evidence-based guidelines.¹ The use of narrow-spectrum antimicrobial agents to which the organism is susceptible is encouraged and, in certain circumstances, the use of combinations of agents may prevent the emergence of resistant mutants during therapy.

Prophylactic use of antibiotics

Antimicrobial prophylaxis is the use of antimicrobial agents in order to prevent infection developing. It is indicated in many circumstances, including the prevention of recurrent rheumatic fever, endocarditis, meningitis, tuberculosis and urinary tract and surgical infections.¹ Antimicrobial prophylaxis in the ED is usually indicated to prevent trauma-related infection following contamination of soft tissue, crush injuries, bites, clenched fist injuries and compound fractures. Other risk factors for wound infection include 'old' wounds (>18 hours),¹⁷ penetrating injuries, contaminated wounds, co-morbid illness, shock, colon injury and massive haemorrhage.¹⁸

Antimicrobial prophylaxis should be considered where there is a significant risk of infection, but cannot be relied upon to overcome excessive soiling, damage to tissues, inadequate debridement or poor surgical technique. Adequate wound care, with splinting and elevation of the affected area as indicated, will continue to be important factors in trauma-related infection prophylaxis.

Antimicrobial prophylaxis should be directed against the likely causative organism(s). However, an effective regimen need not necessarily include antimicrobials that are active against every potential pathogen. Regimens that only reduce the total number of organisms may assist host defences and prevent infection.¹ The type, dose, duration and route of administration of antimicrobial therapy will vary according to the nature, site and aetiology of the injury, as well as host factors, and should be based on established guidelines. In all cases of open traumatic injury, no matter how trivial, tetanus prophylaxis must be considered.

Penicillins

Chemistry and mechanism of action

The penicillins constitute one of the most important groups of antimicrobial agents and remain the drugs of choice for a large number of infectious diseases. The basic structure of the penicillins consists of a thiazolidine ring connected to a β-lactam ring, and a side chain. The penicillin nucleus is the chief structural requirement for biological activity, whereas the side chain determines many of the antibacterial and pharmacological characteristics of the particular type of penicillin.

Peptidoglycan is an essential component of the bacterial cell wall and provides mechanical stability by virtue of its highly cross-linked lattice-work structure. Penicillin is thought to acetylate and inhibit a transpeptidase enzyme responsible for the final cross-linking of peptidoglycan layers. Penicillin also binds to penicillin-binding proteins (PBPs), causing further interference with cell wall synthesis and cell morphology. The lysis of bacteria is ultimately dependent on the activity of cell wall autolytic enzymes: autolyses and murein hydrolases. Although the relationship between the inhibition of PBP activity and the activation of autolysins is unclear, the interference with peptidoglycan assembly in the face of ongoing autolysis activity might well lead to cell lysis and death.

Bacterial resistance to penicillins

Microorganisms may be intrinsically resistant to the penicillins because of structural differences in PBPs. Resistance may be acquired by the development of high molecular weight PBPs that have reduced affinity for the antibiotic.¹² Bacterial resistance also can be caused by the inability of the agent to penetrate to its site of action. Unlike gram positive bacteria, gram negative bacteria have an outer membrane of lipopolysaccharide which functions as an impenetrable barrier to some antibiotics. However, some broader-spectrum penicillins, such as ampicillin and amoxicillin, can diffuse through aqueous channels (porins) of this outer membrane to reach their sites of action.

Bacteria can destroy penicillins enzymatically. Different bacteria elaborate a number of different β-lactamases and individual penicillins vary in their susceptibility to these enzymes. In general, gram positive bacteria produce a large amount of β-lactamase, which is secreted extracellularly. Most of these enzymes are penicillinases, which disrupt the β-lactam ring and inactivate the drug. In gram negative bacteria, β-lactamases are found in relatively small amounts strategically located between the inner and outer bacterial membranes for maximal protection.

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Classification of penicillins

Benzylpenicillin (penicillin G) and phenoxyethyl penicillin (penicillin V)

These drugs are the so-called 'natural penicillins'. The antimicrobial spectra of benzyl penicillin (penicillin G) and phenoxyethyl penicillin (penicillin V) are very similar for aerobic gram positive microorganisms. Benzyl penicillin is the drug of choice against many gram positive cocci (streptococci, penicillin-sensitive staphylococci), gram negative cocci (*Neisseria meningitidis* and *Neisseria gonorrhoeae*), gram positive bacilli (*Bacillus anthracis*, *Corynebacterium diphtheriae*), anaerobes (*peptostreptococcus*, *Actinomyces israelii*, *Clostridium* and some *Bacteroides*), *Pasteurella multocida* and *Treponema pallidum*. Phenoxyethyl penicillin is an acceptable alternative for *Streptococcus pneumoniae*, *Streptococcus pyogenes* (A) and *Actinomyces israelii*.

The sole virtue of benzylpenicillin compared to phenoxyethyl penicillin is that it is more stable in an acid medium and therefore much better absorbed from the gastrointestinal tract. Benzylpenicillin is administered parenterally but has a half-life of only 30 minutes. Accordingly, repository preparations (penicillin G procaine, penicillin G benzathine) are often used, and probenecid may be administered concurrently to block the renal tubular secretion of the drug. Once absorbed, both penicillins are distributed widely throughout the body. Significant amounts appear in the liver, bile, kidney, semen, joint fluid, lymph and intestine. Importantly, penicillin does not readily enter the cerebrospinal fluid (CSF) when the meninges are normal. However, when the meninges are acutely inflamed, penicillin penetrates into the CSF more easily. Under normal circumstances, penicillin is eliminated unchanged by the kidney, mainly by tubular secretion.

The penicillinase-resistant penicillins

These drugs remain the agents of choice for most staphylococcal disease. Methicillin is a penicillin resistant to staphylococcal β -lactamase, although the increasing incidence of isolates of methicillin-resistant microorganisms is cause for concern. MRSA contain a high molecular weight PBP with a very low affinity for β -lactam antibiotics.¹² From 40% to 60% of strains of *Staphylococcus epidermidis* are also resistant to penicillinase-resistant penicillins by the same mechanism. As bacterial sensitivities are usually not known in the ED, methicillin is rarely administered in this setting.

The isoxazolyl penicillins (oxacillin, cloxacillin, dicloxacillin and flucloxacillin) are congenic semisynthetic penicillins that are pharmacologically similar. All are relatively stable in an acid medium and are adequately absorbed after oral administration. These penicillins undergo

some metabolism but are excreted primarily by the kidney with some biliary excretion. All are remarkably resistant to cleavage by penicillinase and inhibit both penicillin-sensitive and some penicillin-resistant staphylococci. Methicillin-resistant staphylococci are resistant to these penicillins. Isoxazolyl penicillins inhibit streptococci and pneumococci but are virtually inactive against gram negative bacilli.

The aminopenicillins

Ampicillin is the prototypical agent in this group. It is stable in acid medium and, although well absorbed orally, is often administered parenterally. Amoxicillin is a close chemical and pharmacological relative of ampicillin. The drug is stable in acid and was designed for oral use. It is more rapidly and completely absorbed from the gastrointestinal tract than is ampicillin. The antimicrobial spectra of these agents are essentially identical, with the important exception that amoxicillin appears to be less effective for shigellosis. Ampicillin is the penicillin of choice for many gram negative bacilli (*Haemophilus influenzae*, *Escherichia coli*, *Proteus mirabilis*, *Salmonella typhi* and *Salmonella* spp.), some gram positive bacilli (*Listeria monocytogenes*) and some gram positive cocci (*Enterococcus faecalis*). It also has activity against *Pneumococcus* spp., *Neisseria* spp., *Peptostreptococcus*, *Fusobacterium*, *Clostridium* and *Erysipelothrix*.

Bacterial resistance to these drugs is becoming an increasing problem. Many pneumococcal isolates have varying levels of resistance to ampicillin. *H. influenzae* and the viridans group of streptococci are usually inhibited by very low concentrations of ampicillin. However, strains of *H. influenzae* (type b) that are highly resistant to ampicillin have been recovered from children with meningitis. It is estimated that 30% or more cases of *H. influenzae* meningitis are now caused by ampicillin-resistant strains. Similarly, ampicillin-resistant strains of *H. influenzae* have been increasingly isolated from cases of acute otitis media. An increasing percentage of *N. gonorrhoeae*, *E. coli*, *P. mirabilis*, *Salmonella* and *Shigella* are now resistant to ampicillin and practically all species of *Enterobacter* are now insensitive.

β -Lactamase inhibitors have been introduced to combat many penicillin-resistant microorganisms. These molecules bind to β -lactamases and inactivate them, thereby preventing the destruction of β -lactamase antibiotics. Clavulanic acid binds to the β -lactamases produced by a wide range of gram positive and gram negative microorganisms. It is well absorbed orally and can be given parenterally. It has been combined with amoxicillin as an oral preparation (Augmentin) and with ticarcillin (a carboxypenicillin) as a parenteral preparation (Timentin). Augmentin

is effective for β -lactamase-producing strains of staphylococci, *H. influenzae*, gonococci and *E. coli*. Sulbactam is another β -lactamase inhibitor, which also can be administered orally or parenterally. In combination with ampicillin (Unasyn), good coverage is provided for gram positive cocci (including β -lactamase-producing strains of *Staph. aureus*), gram negative anaerobes (but not *Pseudomonas*) and anaerobes.

Adverse reactions to penicillin

Hypersensitivity reactions are the major adverse effects of penicillins. Penicillins are capable of acting as haptens to combine with proteins contaminating the solution or with human protein after the penicillin has been administered. Penilloyl and penicillanic derivatives are the major determinants of penicillin allergy. All acute hypersensitivity reactions to penicillin are mediated by the immunoglobulin (Ig)E antibody and range in severity from rash to anaphylaxis. Anaphylactic reactions are uncommon, occurring in only 0.2% of 1000 courses of treatment, with 0.001% out of 100,000 courses resulting in death.¹⁹ Morbilliform eruptions that develop after penicillin therapy are likely to be mediated by IgM antibodies and the uncommon serum sickness is likely to be mediated by IgG antibodies. All forms of penicillin are best avoided in patients with a history of penicillin allergy.

Otherwise, the penicillins are generally well tolerated. Central nervous system (CNS) toxicity, in the form of myoclonic seizures, can follow the administration of massive doses of benzylpenicillin (penicillin G), ampicillin or methicillin. Massive doses have also been associated with hypokalaemia. Haematological toxicity—usually neutropaenia—and nephrotoxicity have also been reported. Gastrointestinal disturbances have followed the use of all oral penicillins, but have been most pronounced with ampicillin. Enterocolitis due to the overgrowth of *Clostridium difficile* is well documented, and abnormalities in liver function have been reported, especially with flucloxacillin.²⁰

Cephalosporins

The antimicrobial activity of cephalosporins, like that of other β -lactam antibiotics, results at least in part from their ability to interfere with the synthesis of the peptidoglycan component of the bacterial cell wall. However, the exact bactericidal and lytic effects of cephalosporins are not completely understood.

Classification and uses

The first-generation compounds (cephalothin, cefazolin, cefalexin) have a relatively narrow spectrum of activity focused primarily on the gram positive cocci, especially penicillin-sensitive

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streptococci and methicillin-sensitive *Staph. aureus*. These compounds have modest activity against gram negative organisms, including *E. coli* and *Klebsiella* spp. Cefaclor has extended gram negative activity and is active against *H. influenzae* and *M. catarrhalis*.

The second generation of cephalosporins (cefuroxime, cefamandole) are more stable against gram negative β -lactamases. They have variable activity against gram positive cocci, but have increased activity against gram negative bacteria (*E. coli*, *Proteus*, *Klebsiella*). In spite of relatively increased potency against gram negative aerobic and anaerobic bacilli (*Bacteroides fragilis*), the cephamycins (cefoxitin, cefotetan) are included in this generation.

The third-generation cephalosporins (ceftaxime, ceftriaxone, cefazidime, cefpirome) have very marked activity against gram negative bacteria. Most are useful against *Ps. aeruginosa*, *Serratia* and *Neisseria* species and some Enterobacteriaceae. Some of these compounds have limited activity against gram positive cocci, particularly methicillin-sensitive *Staph. aureus*. This generation of cephalosporins is particularly effective in meningitis because of their better penetration into the CSF and higher intrinsic activity. However, as these third-generation drugs are more expensive and have a wide antimicrobial spectrum, their use should be based on established guidelines.

Recently, several compounds have been considered as possibly meriting classification as a fourth generation. Cefepime has activity against gram positive cocci and a broad array of gram negative bacteria, including *Ps. aeruginosa* and many of the Enterobacteriaceae with inducible chromosomal β -lactamases.

Adverse reactions

Hypersensitivity reactions are the most common side effects of the cephalosporins and all compounds have been implicated. The reactions appear to be identical to those caused by the penicillins. Immediate reactions, such as anaphylaxis, bronchospasm, angio-oedema and urticaria, have been reported. More commonly, a maculopapular rash develops, usually after several days of therapy. Because of the similarity in structure between the penicillins and the cephalosporins, patients allergic to one class of agents may manifest cross-reactivity when a member of the other class is administered. Studies indicate that about 0.5% of patients allergic to penicillin will demonstrate a clinically apparent reaction when a first-generation cephalosporin is administered (0% for second- and third-generation cephalosporins).²¹ Patients with a mild or temporarily distant reaction to penicillin appear to be at low risk of rash or other allergic reactions following the administration of

a cephalosporin. However, subjects with a recent history of an immediate reaction to penicillin should not be given a cephalosporin. Other reactions to cephalosporins are uncommon and include diarrhoea, nephrotoxicity, intolerance of alcohol and bleeding disorders.

Penicillin allergy cross-reactivity with cephalosporins is significantly overstated. Cross-reactivity between penicillins and cephalosporins is much less than the 10% commonly cited. Cephalothin, cephalexin, cefadroxil and cefazolin confer an increased risk of allergic reaction among patients with penicillin allergy.

Cefuroxime, cefpodoxime, cefazidime and ceftriaxone do not increase risk of an allergic reaction.

No cross-reactivity exists between penicillins and third-generation cephalosporins. However, if a patient has known anaphylaxis to penicillin, caution with cephalosporin use is still warranted.

Bacterial resistance

The most prevalent mechanism for resistance to cephalosporins is their destruction by β -lactamase hydrolysis. The cephalosporins have variable susceptibility to β -lactamase, with the later-generation compounds being more resistant to the β -lactamases produced by gram negative bacteria. However, third-generation cephalosporins are susceptible to hydrolysis by inducible, chromosomally encoded (type 1) β -lactamases. The induction of type 1 β -lactamases by treatment of infections due to many aerobic gram negative bacilli with second- or third-generation cephalosporins may result in resistance to all third-generation cephalosporins.

Macrolides

Erythromycin was originally isolated from soil bacteria and contains a many-membered lactone ring to which are attached one or more deoxy sugars. Clarithromycin, azithromycin and roxithromycin are new semisynthetic derivatives of erythromycin. Clarithromycin differs only by methylation of a hydroxyl group and azithromycin contains a methyl-substituted nitrogen atom in the lactone ring. Roxithromycin is a good alternative to oral erythromycin and has good oral bioavailability, but is more expensive. The macrolides are usually bacteriostatic and inhibit protein synthesis by binding reversibly to 50S ribosomal subunits of sensitive microorganisms. They are thought to inhibit the translocation step wherein a newly synthesized peptidyl tRNA molecule moves from the acceptor site on the ribosome to the peptidyl (donor) site.

Clinical uses

Erythromycin is most effective against aerobic gram positive cocci and bacilli. It is active against

Strep. pyogenes, *Strep. pneumoniae*, *Clostridium perfringens*, *C. diphtheriae*, *L. monocytogenes* and some staphylococci. Useful activity has also been seen with *P. multocida*, *Borrelia* spp., *B. pertussis*, *Campylobacter jejuni*, *Legionella pneumophila*, *M. pneumoniae*, *C. trachomatis* and some atypical mycobacteria. It has modest activity *in vitro* against some gram negative organisms, including *H. influenzae* and *N. meningitidis* and excellent activity against most strains of *N. gonorrhoeae*.

Clarithromycin is more potent against erythromycin-sensitive strains of streptococci and staphylococci, but has only modest activity against *H. influenzae* and *N. gonorrhoeae*. However, it has good activity against *M. catarrhalis*, *Chlamydia* spp., *L. pneumophila* and *Mycoplasma pneumoniae*. Azithromycin is generally less active than erythromycin against the gram positive organisms and is more active than the other two macrolides against *H. influenzae* and *Campylobacter* spp. Azithromycin is very active against *M. catarrhalis*, *P. multocida*, *Chlamydia* spp., *M. pneumoniae*, *L. pneumophila* and *N. gonorrhoeae*.

Adverse reactions

Erythromycin is one of the safest antibiotics and causes serious adverse effects only rarely. Dose-related abdominal cramps, nausea, vomiting, diarrhoea and flatulence occur, but are uncommon in children and young adults. Allergic reactions observed include fever, eosinophilia and skin eruptions. Cholestatic hepatitis, transient hearing loss, polymorphic ventricular tachycardia, superinfection of the gastrointestinal tract and pseudomembranous colitis have been reported. Intravenous use of erythromycin is often associated with thrombophlebitis, but the incidence of this complication can be reduced with appropriate dilution of the dose. Adverse reactions to the other macrolides, at the usual dose, are rare and usually confined to the gastrointestinal tract. For this reason, roxithromycin is often prescribed instead of erythromycin.

Erythromycin and, to a lesser extent, the other macrolides, has been reported to cause clinically significant drug interactions.²² Erythromycin has been reported to potentiate astemizole, terfenadine, carbamazepine, corticosteroids, digoxin, theophylline, valproate and warfarin, probably by interfering with cytochrome P450-mediated drug metabolism. Care should be used in the concurrent administration of the macrolides with these drugs.

Bacterial resistance

Resistance to erythromycin may be the result of reduced permeability through the cell envelope. This form of resistance is exhibited by the Enterobacteriaceae and *Pseudomonas* spp.

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Alteration of ribosomal proteins, especially the 50S protein, often affects binding of the drug and has led to the emergence of resistant strains of *B. subtilis*, *Strep. pyogenes* and *Strep. pneumoniae*, *Campylobacter* spp., *E. coli*, *Staph. aureus*, *Cl. perfringens*, *Listeria* spp. and *Legionella* spp. Finally, enzymatic degradation of the drug has conferred high-level resistance among strains of Enterobacteriaceae.

Tetracycline

Tetracyclines are generally bacteriostatic and are thought to inhibit bacterial protein synthesis by binding to the 30S bacterial ribosome and preventing access of aminoacyl tRNA to its acceptor site.

Clinical uses

The antimicrobial spectra of all the tetracyclines are almost identical. They possess a wide range of antimicrobial activity against aerobic and anaerobic gram positive and gram negative bacteria. Clinically, the tetracyclines are useful against *Strep. pneumoniae*, *H. influenzae*, *Neisseria* spp., *E. coli*, *Brucella* spp., *H. ducreyi*, *Vibrio cholerae*, *Campylobacter* spp. and some *Shigella* and *Mycobacterium* spp. Many pathogenic spirochaetes are susceptible, including *Borrelia burgdorferi*. They are also effective against some microorganisms that are resistant to cell-wall active antimicrobial agents, such as *Rickettsia*, *Coxiella burnetii*, *Mycoplasma pneumoniae*, *Chlamydia* spp., *Legionella* spp. and *Plasmodium* spp.

Adverse reactions

The tetracyclines all produce gastrointestinal irritation in some individuals, although doxycycline is usually well tolerated. Epigastric discomfort, nausea, vomiting and diarrhoea are commonly reported. Renal and liver toxicity and photosensitivity may occur. Tetracyclines are deposited in the skeleton and teeth during gestation and childhood and can cause abnormalities of bone growth and discolouration of the teeth. It is therefore essential not to administer these agents to pregnant women or children under 8 years of age. Hypersensitivity reactions, including skin reactions, burning of the eyes, pruritus ani, vaginitis, angio-oedema and anaphylaxis, are rarely seen.

Bacterial resistance

Bacteria develop resistance to the tetracyclines mainly by preventing the accumulation of the drug within the cell. This is accomplished by reducing the influx or increasing the ability of the cell to export the antibiotic. Rarely, the tetracyclines are inactivated biologically or inhibited in their ribosomal attachment.²³ Resistance to one tetracycline usually means resistance to all.

Clinically, most strains of enterococci are now resistant to tetracycline; group B streptococci are 50% susceptible and only 65% of *Staph. aureus* remain susceptible. Resistant pneumococci are now found in many geographical areas and many strains of *Neisseria* spp. are now resistant.

Aminoglycosides

Each aminoglycoside demonstrates concentration-dependent bactericidal activity against susceptible microorganisms. Gentamicin is the most commonly administered aminoglycoside in the ED and is a mixture of three closely related constituents. It binds to a specific area on the interface between the smaller (30S) and the larger (50S) bacterial ribosomal subunits, causing an increase in the misreading of messenger RNA and a measurable decrease in protein synthesis. However, these effects do not provide a complete explanation for the rapidly lethal effect of gentamicin on bacteria.

Clinical uses

The antibacterial activity of gentamicin is directed primarily against aerobic and facultative gram negative bacilli. It has little activity against anaerobic microorganisms and facultative bacteria under anaerobic conditions and its activity against most gram positive bacteria is very limited. Gentamicin is clinically effective against *Pseudomonas aeruginosa*, *P. mirabilis*, *Klebsiella pneumoniae*, *E. coli*, *Enterobacter* spp. and *Serratia* spp. It is particularly effective when used in combination with cell-wall active antimicrobial agents (e.g. penicillin, cephalosporin). Interactions between these agents result in synergistic effects on bacterial death and may be useful against enterococci, *Strep. pyogenes*, some staphylococci, Enterobacteriaceae and *Pseudomonas aeruginosa*.

Adverse reactions

Like most other aminoglycosides, gentamicin has the potential to cause injury to the renal proximal convoluted tubules, damage to the cochlear and/or vestibular apparatus and neuromuscular blockade. As the drug is eliminated almost entirely by glomerular filtration, gentamicin dosing in renal failure must be undertaken with care and drug-level monitoring is recommended. Gentamicin has little allergenic potential. Anaphylaxis, rash and other hypersensitivity reactions are unusual.

Bacterial resistance

Bacteria defend themselves against the aminoglycosides by a combination of alteration of uptake, synthesis of modifying enzymes and a change of ribosomal binding sites.

In several centres, a significant percentage of clinical isolates are highly resistant to all

aminoglycosides. At present, other widespread bacterial resistance to the aminoglycosides remains limited. However, there are reports of resistance emerging among some strains of *Ps. aeruginosa*, Enterobacteriaceae, *E. coli*, *Serratia* spp. and *Staph. aureus*.

Metronidazole

The toxicity of metronidazole is due to short-lived intermediate compounds or free radicals that produce damage by interaction with DNA and possibly other macromolecules.

Clinical uses

Metronidazole is active against a wide variety of anaerobic protozoal parasites. It is directly trichomonicidal. Sensitive strains of *Trichomonas vaginalis* are killed by very low concentrations of the drug under anaerobic conditions. The drug also has potent amoebicidal activity against *Entamoeba histolytica*, even in mixed culture, and substantial activity against the trophozoites of *Giardia lamblia*. Metronidazole manifests antibacterial activity against all anaerobic cocci and both anaerobic gram negative bacilli and anaerobic spore-forming gram positive bacilli. *Bacteroides*, *Clostridium*, *Helicobacter*, *Fusobacterium*, *Peptococcus* and *Peptostreptococcus* spp. are all susceptible.

Adverse reactions

In general, metronidazole is well tolerated. The most common side effects are headache, nausea, dry mouth and a metallic taste. Vomiting, diarrhoea and abdominal distress are occasionally experienced.²⁴ Furry tongue, glossitis and stomatitis may occur during therapy and are associated with a sudden intensification of moniliasis. Of clinical importance is metronidazole's well-documented disulfiram-like effect (Antabuse). Some patients experience abdominal distress, vomiting, flushing or headache if they drink alcohol during therapy with this drug.

Bacterial resistance

Fortunately, very few strains of *Bacteroides* spp. have demonstrated resistance. Some resistant strains of *T. vaginalis* have been isolated from patients with refractory cases of trichomoniasis, but these patients have usually responded to higher doses of metronidazole and prolonged courses of therapy.²⁵

Co-trimoxazole

Co-trimoxazole is a combination of sulphamethoxazole, a sulphonamide antibiotic, and trimethoprim, a diaminopyrimidine. The antimicrobial activity of this combination results from actions on two steps of the enzymatic

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pathway for the synthesis of tetrahydrofolic acid. Sulphamethoxazole inhibits the incorporation of Para-aminobenzoic acid (PABA) into folic acid and trimethoprim prevents the reduction of dihydrofolate to tetrahydrofolate. The latter is the form of folate essential to bacteria for one-carbon transfer reactions. Mammalian cells utilize preformed folate from the diet and do not synthesize this compound. This combination has been associated with serious sulphonamide-induced side effects. It has been recommended that the combination product be restricted to the few situations where combined use is the treatment of choice.¹

Clinical uses

Trimethoprim is effective in the treatment of most urinary tract infections and should be used alone for this indication. However, co-trimoxazole is active against a wide range of gram positive and gram negative microorganisms. *C. diphtheriae* and *N. meningitidis* are susceptible, as are most strains of *Strep. pneumoniae*. From 50% to 95% of strains of *H. influenzae*, *Staph. aureus* and *epidermidis*, *Strep. pyogenes* and *viridans*, *E. coli*, *Proteus mirabilis*, *Enterobacter spp.*, *Salmonella*, *Shigella* and *Serratia* are inhibited. Also sensitive are *Klebsiella spp.*, *Brucella abortis*, *Pasteurella haemolytica* and *Yersinia spp.* Co-trimoxazole has an important place in the treatment and prophylaxis of *P. carinii* infection and the treatment of *L. monocytogenes* and *Nocardia* infection.

Adverse reactions

In routine use, the combination appears to produce little toxicity. About 75% of adverse reactions involve the skin. These reactions are typical of those produced by sulphonamides and include a wide variety of rashes, erythema nodosum, erythema multiforme and Stevens–Johnson syndrome, exfoliative dermatitis and photosensitivity. Severe reactions tend to be more common among the elderly and HIV-infected patients. Gastrointestinal reactions include nausea and vomiting, but rarely diarrhoea. Glossitis and stomatitis are relatively common. CNS reactions (headache, depression and hallucinations) and haematologic disorders (anaemias, coagulation disorders and granulocytopenia) have been reported.

Bacterial resistance

The frequency of development of bacterial resistance to co-trimoxazole is lower than it is to either of the constituent compounds alone. Resistance to sulphamethoxazole is presumed to originate by random mutation and selection or by transfer of resistance by plasmids. Such resistance is usually persistent and irreversible. Resistance to all sulphonamides is now becoming widespread in both community and nosocomial strains of bacteria, including streptococci,

staphylococci, Enterobacteriaceae, *Neisseria spp.* and *Pseudomonas spp.* Trimethoprim-resistant microorganisms may arise by mutation, but resistance in gram negative bacteria is often associated with the acquisition of a plasmid that codes for an altered dihydrofolate reductase. Increasing incidences of resistance have been found in Enterobacteriaceae, *Ps. aeruginosa*, *Staph. aureus*, *E. coli*, *Salmonella* and *Shigella*.

Quinolones

The 4-quinolones, including nalidixic acid, are a family of compounds that contain a carboxylic acid moiety attached to a basic ring structure. The newer fluoroquinolones also contain a fluorine substituent, for example, ciprofloxacin, and ofloxacin. Some may also contain a piperazine moiety. Bacterial DNA gyrase is an essential enzyme involved in DNA function. The quinolones inhibit the enzymatic activities of DNA gyrase and promote the cleavage of DNA within the enzyme–DNA complex.

Clinical uses

The early quinolones are most active against aerobic gram negative bacilli, particularly Enterobacteriaceae and *Haemophilus spp.* and against gram negative cocci, such as *Neisseria spp.* and *M. catarrhalis*. The fluoroquinolones are significantly more potent and have a much broader spectrum of antimicrobial activity. Relative to nalidixic acid, the fluoroquinolones also have additional activity against *Ps. aeruginosa* and some staphylococci. Ciprofloxacin remains the most potent fluoroquinolone against gram negative bacteria. Several intracellular bacteria are inhibited by the fluoroquinolones, including *Chlamydia*, *Mycoplasma*, *Legionella*, *Brucella* and some mycobacteria. Recently, a new drug, moxifloxacin, has been released, which is useful for sinusitis, community-acquired pneumonia and acute bronchitis.

Adverse reactions

Generally, these drugs are well tolerated. Gastrointestinal symptoms of anorexia, nausea, vomiting, diarrhoea and abdominal discomfort are commonly seen, particularly with the older quinolones. Headache, dizziness, insomnia and alteration in mood are the next most commonly reported symptoms. Allergic and skin reactions, including phototoxicity, may occur. Rarely, arthralgias and joint swelling, leucopaenia, eosinophilia, thrombocytopenia and haemolysis are reported.

Bacterial resistance

Resistance patterns over time have indicated that resistance increased following the introduction of fluoroquinolones and occurred most often

with *Pseudomonas spp.* and staphylococci, and in soft-tissue infections and infections associated with foreign bodies. Possibly reflecting the pressures of extensive use, increasing fluoroquinolone resistance has been reported among strains of *Cl. jejuni* and *E. coli*. Focused quinolone use should be considered to avoid compromising the utility of the fluoroquinolones.

Nitrofurantoin

The mechanism of action is poorly understood, but activity in many cases appears to require enzymatic reduction within the bacterial cell.²⁶ The reduced derivatives are thought to bind to and damage intracellular proteins, including DNA, and inhibit bacterial respiration, pyruvate metabolism and the synthesis of inducible enzymes.

Clinical uses

Nitrofurantoin is active against over 90% of clinical strains of *E. coli*, *Citrobacter spp.*, *Staph. saprophyticus* and *E. faecalis*. However, most species of *Proteus*, *Pseudomonas*, *Serratia*, *Providencia*, *Morganella* and many *Enterobacter* and *Klebsiella spp.* are resistant. Given its spectrum of activity and concentration in the urine, nitrofurantoin is usually administered for the treatment of urinary tract infections or for urinary antisepsis. However, it may have activity against bacteria not usually associated with urinary tract infections, including *Salmonella*, *Shigella*, *Staph. aureus*, *Strep. pneumoniae* and *pyogenes* and *Bacteroides*. Fortunately, bacteria that are susceptible to nitrofurantoin rarely become resistant during therapy.

Adverse reactions

Gastrointestinal upsets, particularly nausea, vomiting and diarrhoea, are the commonest side effects of nitrofurantoin. The frequency of these symptoms may be reduced if the macro-crystalline formulation is administered. Rashes, presumably allergic in nature, have been seen quite commonly. Cholestatic jaundice, acute and chronic hepatitis, pulmonary and haematologic reactions and peripheral neuropathies have all been reported.

Colistin Link Parenteral

Colistin Link Parenteral has activity against gram negative bacilli: *Enterobacter aerogenes*, *E. coli*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*.

Serious infection due to strains of *Pseudomonas aeruginosa* that exhibit resistance to all common antipseudomonal antimicrobials is an increasingly serious problem.

Pseudomonas aeruginosa is the gram negative pathogen that most commonly causes nosocomial pneumonia and is associated with the

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highest rates of crude and attributable mortality, even among patients who receive appropriate antimicrobial therapy.

Colistin Link Parenteral is eliminated mainly by renal excretion; it should be used with caution when the possibility of impaired renal function exists. The decline in renal function with advanced age should be taken into consideration; it can also cause nephrotoxicity. The maximum daily dose should not exceed 5 mg/kg/day with normal renal function.²⁷

Antiviral drugs

Several antiviral drugs are available, although famciclovir, acyclovir and valacyclovir (prodrug of acyclovir that requires a lower dosage frequency) are the most frequently prescribed. Their mechanism of action is similar. Each drug targets virus-infected cells and inhibits viral DNA polymerase. Consequently, viral DNA synthesis and therefore viral replication are inhibited.

Clinical uses

These drugs are primarily used for the management of herpes zoster (within 72 hours of rash onset), treatment and suppression of genital herpes and the management of patients with advanced symptomatic HIV disease. Famciclovir is well absorbed in the gut and has the advantage of a three times daily dosage compared to five times daily for acyclovir.

Acyclovir is also used to treat herpes simplex encephalitis (HSE).

HSE needs to be distinguished from herpes simplex meningitis, which is more commonly caused by the herpes simplex virus (HSV)-2 than by HSV-1 and which often occurs in association with a concurrent herpetic genital infection.

Empiric treatment with acyclovir is essential in patients with suspected HSE pending confirmation of the diagnosis because acyclovir is the drug of choice and is relatively non-toxic and, if commencement of treatment is delayed, the prognosis for untreated HSE is poor.

Adverse reactions

These drugs are generally well tolerated. However, headache, gastrointestinal disturbance, dizziness and fatigue have been reported. Adverse effects are generally mild.

Antiviral agents for influenza

Zanamivir and oseltamivir are related antiviral medications known as neuraminidase inhibitors. These two medications are active against both influenza A and B viruses. They differ in pharmacokinetics, safety profiles, route of administration, approved age groups and recommended dosages.

The two other drugs used to treat influenza, amantadine and rimantadine are related antiviral drugs classified as adamantanes. These medications are active against influenza A viruses but not influenza B viruses. Widespread adamantane resistance among influenza A (H3N2) virus strains has made this class of medications less useful clinically.

Early antiviral treatment can shorten the duration of fever and symptoms and may reduce the risk of complications from influenza (e.g. otitis media in young children, pneumonia, respiratory failure) and death, and shorten the duration of hospitalization. Clinical benefit is greatest when antiviral treatment is administered early, especially within 48 hours of influenza illness onset.

Antiretroviral drugs

Emergency physicians are unlikely to initiate these drugs as they form the basis of HIV treatment.

The only exception is prophylaxis following needle stick injury or body fluid exposure where close adherence to the hospital's policy is essential.

However, an appreciation of their uses and side effects is useful. Furthermore, the management of patients with HIV disease can be difficult, and advice from an appropriate specialist source is essential.

Standard antiretroviral therapy consists of the combination of at least three antiretroviral (ARV) drugs to suppress maximally the HIV virus and to stop the progression of HIV disease.

Clinical uses

The ARVs are used in the treatment of established HIV infection. This includes patients with HIV-associated illnesses (e.g. CNS disease, malignancies, opportunistic diseases) and asymptomatic patients with low CD4 cell counts and/or high HIV viral loads. The drugs are also of use in the prevention of maternofoetal transmission and as post-exposure prophylaxis for significant exposure from a known HIV-infected source.

Three major classes of ARV drugs are available. For initial therapy, two to three drugs are generally used in combination (see Chapter 9.2).

Post-exposure prophylaxis [PEP] has been recently introduced. PEP is a 4-week course of anti-HIV medication effective in preventing HIV infection if commenced within 72 hours of exposure. Jurisdictional guidelines are available.²⁸

Antifungal agents

Systemic fungal infections are becoming more and more common. Candidiasis and aspergillosis are the most common infections; other systemic fungal infections include histoplasmosis, blastomycosis, coccidioidomycosis.

Severe systemic fungal infection in hospitals are commonly seen in:

- neutropenic patients following chemotherapy and other oncology patients with immune suppression
- persons that are immune compromised due to acquired immune deficiency syndrome caused by HIV infection
- patients in intensive care (ICU), who are not necessarily neutropenic but are compromised due to the presence of long-term intravascular lines or other breaches in their integument, severe systemic illness or burns and prolonged broad-spectrum antibiotic therapy. Other predisposing factors include:
- Acute physiology and chronic health evaluation (APACHE) score >10
- renal dysfunction
- haemodialysis
- surgery for acute pancreatitis, splenectomy
- recurrent gastrointestinal perforation
- Hickmann catheters.

Systemic fungal infections cause ≈25% of infection-related deaths in patients with leukaemia. Infections due to *Candida* species are the fourth most important cause of nosocomial bloodstream infection.

The mainstay of antifungal therapy for severe systemic mycoses is amphotericin B.

Cryptococcal meningitis

Cryptococcus neoformans is an encapsulated yeast. The most serious infections usually develop in patients with defective cell-mediated immunity including, patients with:

- AIDS
- organ transplantation
- reticuloendothelial malignancy
- corticosteroid treatment
- sarcoidosis.

The incidence of cryptococcosis is increasing and now represents a major life-threatening fungal infection in AIDS patients.

Occupational risk factors for the infection include arborists and those exposed to bird droppings.

The initial site or sites of infection (pulmonary, CNS, and disseminated disease) determine the medical history of patients with symptomatic cryptococcal disease.

Patients with CNS infections, which are usually subacute or chronic in nature, present with headaches, neck pain, confusion, lethargy, malaise, and then – as the untreated infection progresses – focal neurological defects and decreased Loss of consciousness (LOC). Fever, nausea and vomiting are not uncommon.

Treatment

Amphotericin B at 0.7 to 1 mg/kg/day for 2 weeks, with or without 2 weeks of flucytosine at 100 mg/kg/day in four divided doses, followed by

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fluconazole at 400 mg/day for a minimum of 8 to 10 weeks.

Initial therapy should be considered successful only after CSF culture is negative for cryptococcal organisms and the patient has had significant clinical improvement.

Initial therapy of fluconazole 400 to 800 mg followed by maintenance therapy using fluconazole at 200 mg/day for life.

Amphotericin B

Amphotericin B is useful in the treatment of infection with *Blastomyces*, *Coccidioides*, *Histoplasma*, *Paracoccidioides*, *Candida* and *Cryptococcus*, but does have substantial risk of toxicity. It is a 'polyene' and works on fungi by binding to ergosterol in the fungal cell membrane, disrupting the membrane and killing the fungus.

Other antifungal agents include fluconazole, which is mainly used for *C. albicans* infection (and some other susceptible *Candida* spp. but not *C. krusei*, and has variable activity against *C. glabrata*). *C. albicans* may acquire resistance, especially with chronic or recurrent treatment in AIDS patients. Fluconazole may be effective against *Cryptococcus neoformans* meningitis and coccidioidomycosis.

Outpatient parenteral antibiotic therapy

Outpatient parenteral antibiotic therapy (OPAT) has been widely used for the treatment of moderate to serious infections, either as an alternative to hospitalization or following initial hospitalization and early discharge once the patient is over the toxic phase of the infection. A wide range of infections are suitable for OPAT therapy (Box 9.9.2).

Significant savings, both in terms of direct and indirect costs, are possible utilizing OPAT. Appropriate patient selection is essential for safe and effective outpatient parenteral therapy (Boxes 9.9.3 and 9.9.4). Patients should be clinically stable, be willing to participate and be physically and mentally capable of being treated at home (see Box 9.9.4).

Some patients require initial hospitalization (Box 9.9.5), following which they may be suitable for early discharge to continue treatment at home.

Once patients comply with predefined discharge criteria (Box 9.9.6), they may be able to be discharged into an outpatient parenteral therapy programme.

Close patient monitoring is essential, with daily reviews by a nurse either by telephone or face to face while patients are in the programme. Patients should be reviewed at least weekly by a physician.

The benefits of OPAT include a reduction in the overall costs of patient care through avoidance

Box 9.9.2 Conditions that can be treated on an outpatient basis with parenteral antibiotic therapy

AIDS	Soft-tissue infections
Associated infections	Cellulitis Wound infections/abscesses
Cardiac	Bone and joint infections
Endocarditis Prosthetic-valve infections	Osteomyelitis Septic arthritis Prosthetic infections Neurological infections Meningitis
Genitourinary	Other infections
Pyelonephritis Complicated urinary tract infections Prostatitis Pelvic inflammatory disease	Bacteraemia Mastoiditis
Respiratory	
Pneumonia Lung abscess	

Box 9.9.3 Patient selection process

Condition suitable for outpatient therapy
Patient does not fulfil need to admit criteria (see Box 9.9.5)
OR
Patient meets discharge criteria (see Box 9.9.6)
Home environment suitable
Patient/family consent

Box 9.9.4 Patient selection criteria

Able to give consent
Adequate social support at home
The antibiotic(s) chosen is/are appropriate for OPAT use
Patient's condition is stable
Concurrent illness does not require hospital care
Adequate venous access can be maintained; patient is mobile
The infection is amenable to outpatient parenteral therapy
Adequate monitoring by the treating medical team is possible

OPAT, Outpatient parenteral antibiotic therapy.

or reduction in hospitalization, reduction of the costs associated with the hazards of hospitalization and increased patient satisfaction.^{29,30}

Other issues

The risks associated with bioterrorism need to be taken into account with every patient presenting with a febrile illness or signs and symptoms of infection.

Box 9.9.5 Criteria for admission to hospital

Confused
Persistent high fever
Systolic blood pressure <100 mm Hg
Respiratory rate >30/min
Pulse rate >100/min
Requires specialized nursing care assistance with activities of daily living
Hypoxic on room air ($\text{PaO}_2 <80 \text{ mm Hg}$)
Concurrent illness requiring inpatient care
Personal or social reasons
Pneumonic consolidation in more than one lobe

Box 9.9.6 Discharge criteria

Medical
Afebrile
Clinical improvement
No specialized nursing care required
Stable
Bacterial pathogens identified
Response to inpatient therapy
Complications unlikely

Social
Parents interested and motivated
Parents capable
Home environment acceptable
Telephone and transport access

Numerous bacterial agents and bacterial toxins have been identified as potential biological agents. Patients presenting in clusters or with unusual or uncommon infections—particularly those that can be used as biological agents—should be quarantined, with staff utilizing post-exposure prophylaxis and strict infection control procedures. It may be necessary to activate the hospital's Mass Casualty Incident Plan when biological agents are suspected.³¹

Recent updates from the medical literature

In August 2012, the Centers for Disease Control and Prevention (CDC) announced changes to the 2010 sexually transmitted disease guidelines for gonorrhoea treatment. The Gonococcal Isolate Surveillance Project (GISP) described a decline in cefixime susceptibility among urethral *N. gonorrhoeae* isolates in the United States from 2006 to 2011. Because of cefixime's lower susceptibility, new guidelines were issued that no longer recommend oral cephalosporins for first-line gonococcal infection treatment.³²

The incidence of untreatable gonorrhoea is increasing.

Likely developments over the next 5 to 10 years

The most important challenge regarding infectious disease in the future will be:

- The containment of and management of antimicrobial resistance patterns. In part, these patterns have emerged as a result of poor prescribing habits.³³
- Fewer new antimicrobial drugs are being developed, with the result that with

developing resistance patterns there will be very few effective antibiotics available for use against infection.⁹

- The implementation of prescribing guidelines based on scientific evidence will form the basis of all antibiotic prescribing.
- Human behaviour, wildlife trade, factory farming, poor hygiene, global warming and increasing travel will increase the risk of pandemics, evolution and the spread of new and old infections.^{34,35}

Detailed descriptions of the drugs described above are available on the Internet by accessing MIMS Online and Antibiotic Guidelines.¹

Full references are available at <http://expertconsult.inkling.com>

9.10 Needlestic injuries and related blood and body fluid exposures

Sean Arendse

ESSENTIALS

- 1** Avoiding blood and other body fluid exposure remains the primary means of preventing occupationally acquired blood-borne virus infections.
- 2** The risks of acquiring infection after occupational exposure to blood-borne viruses are human immunodeficiency virus (HIV) 0.3%, hepatitis B virus (HBV) 12% to 30%, hepatitis C virus (HCV) 1.8%.
- 3** HBV immunization is an integral part of workplace safety.
- 4** Effective post-exposure prophylaxis (PEP) is available for both HBV and HIV, but not HCV.
- 5** Significant emotional distress often complicates needlestick and related occupational injuries.

Introduction

Management of the health care worker who sustains an occupational exposure to blood or other potentially infectious body fluids (e.g. semen, vaginal secretions, cerebrospinal fluid [CSF] and fluids containing visible blood) is an important issue for the emergency department (ED) doctor. Overall, 16,000 hepatitis C virus (HCV), 66,000 hepatitis B virus (HBV), and 1000 human immunodeficiency virus (HIV) infections may have occurred in the year 2000 worldwide among Health Care Workers (HCWs) due to their occupational exposure to percutaneous injuries. The fraction of infections with HCV, HBV and HIV in HCWs attributable to occupational exposure to percutaneous injuries fraction reaches 39%, 37%, and 4.4%, respectively.¹ This figure is a conservative estimate as many needlestick injuries go unreported. HBV, HCV and HIV are the most important occupationally acquired blood-borne pathogens;

however, many other organisms, including malaria, syphilis, cytomegalovirus and possibly the prion diseases (e.g. Creutzfeldt–Jakob disease) also may be transmissible via this route.

When evaluating health care providers (HCPs) at risk for occupational infection with HIV, 'exposure' is defined as contact with potentially infectious blood, tissue or body fluids in a manner that allows for possible transmission of HIV, and therefore requires consideration of post-exposure prophylaxis (PEP).

Such potentially infectious contacts are:

- a percutaneous injury (e.g. a needlestick or cut with a sharp object)
- contact of mucous membrane or non-intact skin (e.g. exposed skin that is chapped, abraded or afflicted with dermatitis).

Body fluids of concern include:

- body fluids implicated in the transmission of HIV: blood, semen, vaginal secretions, other body fluids contaminated with visible blood

- potentially infectious body fluids (undetermined risk for transmitting HIV): cerebrospinal, synovial, pleural, peritoneal, pericardial and amniotic fluids.

Fluids that are not considered infectious unless they contain blood include faeces, nasal secretions, saliva, gastric secretions, sputum, sweat, tears, urine and vomitus.

In addition, any direct contact (i.e. without barrier protection) to concentrated HIV in a research laboratory or production facility is considered an 'exposure' that requires clinical evaluation and consideration of PEP.

Intact skin is an effective barrier against HIV infection. Contamination of intact skin with blood or other potentially contaminated fluids is not considered an exposure and does not require PEP.

Most exposures do not result in infection and the risk of infection following significant exposure varies with factors such as:

- the pathogen involved (hepatitis B, hepatitis C or HIV)
- the fluid involved—blood is generally the most infectious body fluid
- the type of exposure—percutaneous or mucous membrane/non-intact skin
- the amount of blood or other infectious body fluid involved in the exposure
- the amount of virus in the patient's blood at the time of exposure.

General issues

Prevention of needlestick injuries

The old adage 'prevention is better than cure' certainly rings true when considering needlestick

9.9 ANTIBIOTICS IN THE EMERGENCY DEPARTMENT

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injuries, as the cost of managing one needlestick injury exposure can range from 376 USD to 2456 USD.²

The potentially infectious nature of all blood and bodily fluids necessitates the implementation of infection control practices. The universal application of standard precautions should be the minimum level of infection control when treating patients to prevent blood-borne virus transmission. The important elements of standard precautions are:

- the use of gloves when contact with blood, body fluids or secretions is anticipated
- the use of masks and protective eyewear during procedures that have the potential to generate splashes or sprays of blood or bodily fluids
- the use of gowns to protect skin and clothing from soiling by blood and other bodily fluids
- correct handling and disposal of needles and other sharp instruments:
 - disposal of sharps directly from patient immediately into sharps bins
 - locating sharps bins conveniently to reduce the unnecessary transportation of uncapped devices
 - avoiding overfilling sharps containers
 - never re-sheathing or re-capping needles
 - 100% attention when handling sharps.

More than 50 products with features designed to prevent needlestick injuries are currently available and fall broadly into two categories: those providing 'passive' or automatic protection, and those with a safety mechanism that the user must activate.

It has been demonstrated that most needlestick injuries are preventable³ and that the use of safety-engineered devices reduces needlestick injuries.^{3,4} The passive devices are most effective in preventing needlestick injuries.⁵

Hospital systems

Hospitals need to have appropriate policies and procedures to deal with occupational exposures to blood and body fluids; these are best implemented through a comprehensive and coordinated occupational exposure programme. Depending on the individual institution, such a programme is usually managed by infection control personnel and involves staff health, occupational health, laboratory services, the ED and the infectious diseases service.

Staff needs to be aware of the appropriate steps to take in the event that they sustain an exposure, such as who to notify, incident reporting requirements, and where and how to seek medical evaluation. The programme should develop processes for consent and testing of the source individual (including situations where the individual refuses or is unable to give consent),

prompt blood-borne virus testing and communication of results to the exposed person. Clear written guidelines and clinical pathways should be accessible to medical staff involved in managing these exposures (including specific recommendations for exposures involving a blood-borne virus positive source and antiretroviral PEP).

Management

The initial management of all needlestick injuries is the same: first aid measures, documentation of the event, determining the status of the source and counselling of the exposed worker.

Initial management

Occupational exposure to blood or other potentially infectious body fluids should be considered a medical emergency to ensure timely management. Following exposure, the exposed person should be removed from the area and general first aid measures applied:

- for skin exposures: wash the exposed area well with soap and water; if no water is available, use an alcohol-based antiseptic. Other antiseptics, such as iodophors, chloroxylenol (PCMX) and chlorhexidine (CHG) also inactivate HIV. (Do not squeeze the needle stick injury site.)
- for eye exposures: remove contact lenses if present and irrigate eyes with copious amounts of water or saline.
- for oral mucous membrane exposures: spit out contaminating material and rinse the mouth with water several times.

Documentation

Clinical information on the source patient for the exposure and the recipient HCP should be documented. This includes risk factors and serological tests for HIV and hepatitis B and C. The nature and time of the exposure should also be described. The exposure should be evaluated and documented on the basis of the definition of exposure given above. All potential exposures to blood or contaminated body fluids as defined above should be promptly evaluated. The following information should be obtained by trained medical personnel:

- name and identification of the source
- time and date of the exposure
- nature of the exposure (i.e. non-intact skin, mucosal, or percutaneous exposure, human bite); type of fluid (i.e. blood, blood-contaminated fluid or other contaminated fluid)
- body location of the exposure and contact time with the contaminated fluid
- infective status of the source (i.e. HIV, HCV, hepatitis B surface antigen [HBsAg]), if known, including date of test

- when the source is HIV positive, selection of the PEP regimen should consider the comparative risk represented by the exposure and information about the exposure source, including the history of and the response to antiretroviral therapy based on clinical response, CD4 cell counts, viral load measurements and current disease stage
- for percutaneous injuries, a description of the injury (depth of wound, solid vs hollow needle, sharp use in source patient).

The injured HCP should be questioned about the circumstances of the exposure (activity, time, device type, availability of Personal protective equipment [PPE]). The following information should be obtained from the injured person and verified from their medical/occupational health record:

- dates of hepatitis B immunizations
- post-immunization titre, if known
- previous testing (if available) for HIV, HBV and HCV
- tetanus immunization status
- current medications
- current or underlying medical conditions that might influence drug selection (e.g. pregnancy, breastfeeding, renal or hepatic disease).

Determining status of the source

All source cases should be tested for HBsAg, HCV and HIV, unless the source is known to be infectious. If feasible, a system should be devised to allow HIV test results to be obtained as soon as possible (i.e. within 24 hours). The rapid HIV test should be used to make an initial determination of the source patient's HIV status and has the advantage that results are available in less than 60 minutes.⁶ All positive tests should be confirmed by Western blot. Negative tests do not require confirmation. Determination of HBsAg status should be obtained as soon as possible, but not later than 7 days. Local and state laws regarding consent and counselling prior to HIV testing should be followed.

Clinicians should also be aware of rare case reports where the source patient tested HIV seronegative and was later found to have primary HIV infection⁷; these rare events do not alter guidelines for routine antibody testing but do highlight the importance of testing for HIV RNA if clinically indicated.

Counselling of exposed worker

Risk assessment is particularly important for the HCP to make educated decisions about PEP since the consequences are huge and the stress is extraordinary. They should also be well informed of the benefits and risks of PEP and of the importance of close follow-up. Specifically, the following issues should be discussed with the exposed HCP:

9.10 NEEDLESTICK INJURIES AND RELATED BLOOD AND BODY FLUID EXPOSURES

- The HCP should be informed of the risk associated with the specific exposure experienced.
- The efficacy and side effects of PEP should be discussed.
- Risk reduction strategies should be employed to prevent transmission of HIV should the HCP acquire infection. In the event of HIV infection post-exposure, the greatest risk of transmission to other individuals is in the first 6 to 12 weeks. The exposed HCP should be instructed on condom use or abstinence from sex and refraining from blood, plasma, organ, tissue and semen donation until the 6-month serological test is negative. There is no need to modify an HCP's patient-care responsibilities after an exposure.
- Follow-up is important to identify HIV infection or adverse effects of the PEP regimen, if administered.
- Specific counselling is warranted for women of childbearing age. Data from an HIV pregnancy registry suggest overall safety of antiretroviral drugs.⁸ Temporary discontinuation of breastfeeding following exposure until the 6-month serological test is negative should be considered.

Hepatitis B

Hepatitis B vaccination is recommended for all health care workers who are involved in direct patient care or who handle human blood or tissues,⁹ and is an important infection control and occupational health strategy. Health care workers should be aware of their HBV immunization status and should undergo antibody testing 4 to 8 weeks after the last dose of the HBV vaccine to ascertain their immune status.

The risk of acquiring HBV from occupational blood/body fluid exposure from a patient positive for HBsAg is well recognized and related primarily to the degree of contact with blood and the hepatitis B e-antigen (HBeAg) status of the source. Following contact with a source positive for HBeAg, the risk of clinical hepatitis is 22% to 31% and serological evidence of HBV infection develops in 37% to 62% of exposed, non-immune individuals. In contrast, after exposure to HBeAg-negative blood, there is a 1% to 6% risk of clinical hepatitis and a 23% to 37% risk of serological evidence of HBV infection.¹⁰ The average time from exposure to the development of symptoms is 10 weeks (range 4 to 26 weeks). Routine vaccination against HBV has been recommended for health care workers since the early 1980s,¹¹ with a consequent marked reduction in the incidence of infection in this population.

Post-exposure management following an occupational blood/body fluid exposure to HBV requires evaluation of the source's HBsAg status and the HBV vaccination and vaccine response status of the exposed person.^{12,13} HB immunoglobulin (HBIG) is indicated for people who are non-immune (either because of no prior vaccination or because of vaccine non-responsiveness) and are exposed to blood or other infectious body fluids from an HBsAg-positive source. HBIG is prepared from human plasma (screened for blood-borne viruses) known to contain a high titre of antibody to HBsAg (antiHBs). The dose of HBIG is 400 IU, given intramuscularly. Concomitantly, the HBV vaccination should be injected at a separate site and a full course completed. Table 9.10.1 provides more detailed information about specific indications for HBIG and hepatitis B vaccination following occupational exposures. The exposed person does not need to take any special precautions to prevent secondary transmission.¹⁴

There are no apparent risks for adverse effects to developing foetuses when hepatitis B vaccine is administered to pregnant women.¹⁵ The vaccine contains non-infectious HBsAg particles, which should pose no risk to the foetus. HBV infection during pregnancy might result in severe disease for the mother and chronic infection for the newborn.

Therefore neither pregnancy nor lactation should be considered a contraindication to the vaccination of women. HBIG is also not contraindicated for pregnant or lactating women.¹⁶

Hepatitis C

The risk associated with occupational exposure to hepatitis C following a parenteral injury is estimated to range between 1.8% and 10%.

Transmission to health care workers has never been documented from skin contamination and rarely from mucous membrane exposure. In contrast to HBV, environmental contamination is not significant.¹⁷

If the source HCV antibody test is positive, then polymerase chain reaction (PCR) testing for HCV RNA should be performed. Transmission is much less likely to occur from a source who is PCR negative, and the exposed individual can be reassured that the transmission of HCV in this case is negligible. If the source is positive for HCV RNA, a baseline serum from the exposed person is tested for HCV RNA by PCR, anti-HCV antibody testing by enzyme-linked immunosorbent assay (ELISA) and alanine aminotransferase (ALT) with follow-up testing as shown in Table 9.10.2. HCV viraemia can be detected by PCR between 10 days and 6 weeks after infection.^{18,19} Since 2016 in Australia, direct-acting antivirals have been available on the Pharmaceutical Benefits Scheme (PBS), which are over 90% effective in curing HCV. The standard treatment time is

Table 9.10.1 Hepatitis B virus post exposure prophylaxis following occupational exposure

Vaccination and antibody response status of exposed	Treatment when source		
	HBsAg positive	HBsAg negative	Unknown status
Unvaccinated	HBIG, initiate HB vaccine series	HB vaccine series	Vaccine series, consider HBIG
Vaccinated and known responder ^a	Reassure	Reassure	Reassure
Vaccinated and known non-responder ^a	HBIG, initiate HB vaccine series	Reassure, consider revaccine	If high-risk source, treat as HBsAg positive
Vaccinated and unknown response ^a	Test exposed person for anti-HBs	Reassure	Test exposed person for anti-HBs
	If adequate ^a , reassure		If adequate ^a , reassure
	If inadequate ^a , HBIG and course of vaccination		If inadequate ^a , HBIG and course of vaccination

^aA responder is a person with adequate levels of serum antibody to HBsAg (i.e., anti HB_s equal to/o mkl/ml).

anti-HBsAg, Antibody to hepatitis B surface antigen; HBIG, hepatitis B immunoglobulin; HBsAg, hepatitis B surface antigen.

(From US Public Health Service. Updated U.S. Public Health Service guidelines for the management of occupational exposures to HBV, HCV, and HIV and recommendations for postexposure prophylaxis. MMWR Recomm Rep. 29 June 2001;50(11):1–452; and Centers for Disease Control and Prevention (CDC). Testing for HCV infection: an update of guidance for clinicians and laboratorians. MMWR. 2013;62(18):362–365.)

9.10 NEEDLESTICK INJURIES AND RELATED BLOOD AND BODY FLUID EXPOSURES

8 to 12 weeks, but this can be extended to 24 weeks and may also involve the addition of older medications such as interferon in resistant cases. Usually the exact drug regimen prescribed will be decided in consultation with the infectious disease consultant and is dependent on the genotype of HCV, whether the patient has sustained or has any pre-existing liver damage, and other co-morbidities. Examples of these drugs include daclatasvir and sofosbuvir.

Currently, no recommendations exist to restrict professional activities of health care workers with HCV infection. As recommended for all health care workers, those who are HCV-positive should follow strict aseptic techniques and standard precautions, including the appropriate use of hand washing, protective barriers and care in the use and disposal of needles and other sharp instruments.¹⁴

Human immunodeficiency virus

The average risk of acquiring HIV infection from all types of reported percutaneous exposure to HIV-infected blood is 0.3%.²⁰ This is increased for exposures considered as high risk involving:

- a deep injury
- visible blood on the device causing the injury

- a device previously placed in the artery or vein of the source patient
- a source with terminal AIDS or who has died as a result of AIDS within 60 days of the exposure and thus is presumed to have a high titre of HIV.²¹

These factors are also probably significant for mucous membrane and skin exposures to HIV-infected blood, where the average risk of HIV transmission is approximately 0.09% and <0.09%, respectively.²² Prolonged or extensive skin contact or visibly compromised skin integrity would also suggest a higher risk.

Recommendations for PEP with antiretroviral agents have been guided by a better understanding of the pathogenesis of primary HIV infection, which indicates that HIV infection does not become established immediately; this leaves a brief window of opportunity during which post-exposure antiretroviral intervention might modify or prevent viral replication. An early case-control study demonstrated that use of zidovudine decreased the risk of occupational HIV seroconversion by 81%,²³ and it is likely (but not proven) that combination antiretroviral therapy provides even greater protection. Animal data also support the use of antiretroviral prophylaxis after exposure to HIV, provided prophylaxis is administered

promptly and for an adequate period. Failures of HIV PEP are well documented with both single drug and combination drug regimens.²⁴

HIV PEP should be initiated promptly, preferably within 2 hours of the exposure, although it may still be effective for up to 72 hours. Given the complexity of choosing and administering HIV PEP, whenever possible, consultation with an infectious diseases consultant or another physician who has experience with antiretroviral agents is recommended, but it should not delay timely initiation of PEP. There is a slight variability in the selection of drugs by different authorities. For the sake of simplicity and ease of understanding, a three-drug regimen is generally recommended for all high-risk injuries, as shown in Table 9.10.3. The preferred PEP regimen is tenofovir + emtricitabine (lamivudine may be used in place of emtricitabine) plus dolutegravir. Zidovudine is no longer recommended in the preferred PEP regimen. The recommended duration of PEP is 28 days. A 3- to 5-day supply of PEP antiretroviral agents (a 'starter pack') should be kept in the ED.

This regimen is now the preferred combination because of its excellent tolerability, proven efficacy, fewer side effects and drug–drug interactions, and ease of administration. Studies have shown increased rates of adherence

Table 9.10.2 Serology testing for needle stick injury exposed person

		Time			
		At exposure	4–6 weeks	3 months	6 months
Low-risk source and negative serology		Anti-HBsAg antigen antibody		HIV and HCV antibodies testing may be offered	
High-risk source or positive serology	HBV	Anti-HBsAg antibody			
	HCV	HCV RNA PCR, Anti-HCV antibody by ELISA	HCV RNA PCR	HCV RNA PCR, Anti-HCV antibody by ELISA	HCV RNA PCR
		ALT, AST	ALT, AST	ALT, AST	
	HIV	Anti-HIV antibodies	Anti-HIV antibodies	Anti-HIV antibodies	
Unknown source, serology results not available		Anti-HBsAg, anti HCV and HIV antibodies		HIV and HCV antibodies	HIV and HCV antibodies

ALT, Alanine amino transferase; AST, aspartate amino transferase; ELISA, enzyme linked immunosorbent assay; HBsAg, hepatitis B surface antigen; HCV RNA PCR, hepatitis C virus RNA by polymerase chain reaction; HIV, human immunodeficiency virus; PEP, post exposure prophylaxis.

Table 9.10.3 Post exposure prophylaxis drug recommendations based on exposure

Exposure to HIV positive source	Estimated transmission risk	VL (<50 copies/mL) undetectable on ART	VL unknown on ART	VL detectable or new HIV diagnosis not on ART	VL detectable on ART
Percutaneous NSI	Extremely low	No PEP or 2 drugs depending on exposure Tenofovir DPO4 + emtricitabine	2 drugs Tenofovir DPO4 + emtricitabine	3 drugs Tenofovir DPO4 + emtricitabine + dolutegravir	Presumed resistance—call HIV specialist for advice
Mucous membrane or non-intact skin	<1/1,000	No drugs	2 drugs Tenofovir DPO4 + emtricitabine	3 drugs Tenofovir DPO4 + emtricitabine + dolutegravir	Presumed resistance—call HIV specialist for advice

ART, Antiretroviral treatment; NSI, Needle Stick Injury; PEP, Post exposure prophylaxis; VL, Viral load.

9.10 NEEDLESTICK INJURIES AND RELATED BLOOD AND BODY FLUID EXPOSURES

and regimen completion when tenofovir plus either emtricitabine or lamivudine have been used as components of the PEP regimen.^{25–31} Zidovudine is not a 'must' inclusion in the newer regimens, as it has no clear advantages in efficacy over tenofovir and it has significant treatment-limiting side effects. Efavirenz should not be used in pregnant women or women of childbearing age. Nevirapine, abacavir and didanosine should not be used as PEP because of significant side effects.

Most occupational exposures do not result in the transmission of HIV and the potential benefits of PEP need to be carefully weighed against the toxicity of the drugs involved. Nearly 50% of health care workers taking HIV PEP experience adverse symptoms (e.g. nausea, malaise, headache, diarrhoea and anorexia) and approximately 33% cease taking drugs because of side effects.^{32,33} In some other studies, adherence to PEP has been estimated to be around 40% to 60%.^{33–35} The importance of completing the prescribed regimen needs to be stressed and measures taken to minimize side effects.

The emotional effect of an occupational HIV exposure is substantial³⁶ and often underestimated. The exposed person may need time off work, short-term use of a night-time sedative or even referral for formal psychological or psychiatric counselling. Patients should be advised of measures to prevent secondary transmission (e.g. safer sexual practices) during the follow-up period, especially the first 6 to 12 weeks.

Maintaining confidentiality for the staff member sustaining exposure is a priority, as it may have lasting implications both personally and professionally.

The circumstances surrounding the exposure should be reviewed as part of the hospital's occupational exposure policy and appropriate preventive and educational measures taken if indicated.

Exposures that occur in the community

Blood or body fluid exposures may be sustained in the community, as well as in health care settings; examples include needlestick injuries from improperly discarded needles and syringes or blood splashes to the eye or mouth in the course of an altercation. The exposed person may be a member of the public or of an emergency service, such as a policeman or ambulance officer. These exposures are usually managed in the ED.

Although the principles of management are broadly similar to those for occupational exposures, there are some important differences. First, the source is almost never available for testing. (If the source syringe has been retrieved by the exposed person, this should *not* be tested for blood-borne viruses because such testing is only validated on serum.) Second, needlestick exposures almost always involve old dried blood; this is much less infectious than fresh blood because the viral titre falls with time and dried blood does not pass easily from the lumen of the needle into the exposed person's subcutaneous tissue. Third, these exposures often provoke a considerable degree of distress in the affected person and there may be considerable pressure from the exposed person, a family member or a colleague to 'do something'. Some of these incidents even attract media attention.

In Australia, only 1% to 2% of injecting drug users are HIV infected, so the risk of HIV transmission from a discarded needlestick injury is negligible, for example, 1:100 (risk source is HIV positive) times 1:300 (risk of HIV transmission after needlestick) times undefined factor to account for old dried blood (say 1:5)—or approximately 1 in 150,000. Similar calculations show a potentially higher risk of HBV and HCV transmission but, in reality, documented instances of blood-borne virus infection resulting from these community exposures are extremely rare and people should be reassured about this.

In Australia, antiretroviral prophylaxis is not recommended for these exposures unless there are particularly compelling epidemiological circumstances to indicate a high HIV risk in the source.

People not previously vaccinated against HBV should be given HBIG and the first dose of a hepatitis B vaccination course. Despite the low risk of blood-borne virus transmission, many patients feel more reassured if they are offered baseline and follow-up testing. As with exposures in the hospital setting, the attending doctor needs to provide the affected person with information, support and a sympathetic ear!

Pre-exposure prophylaxis

PrEP is where anti-retroviral agents are prescribed to uninfected individuals who are at high risk for contracting the HIV virus, such as those whose condom use is inconsistent and who engage in high-risk sexual activities. PrEP may be taken orally (tenofovir and emtricitabine) or topically as a vaginal gel (tenofovir).

The efficacy of oral tenofovir based PrEP regimens has been well established by randomized control trials involving both heterosexual and homosexual individuals, as well as intravenous drug users, and in 2015 the World Health Organization recommended that those at substantial risk should be offered PrEP as part of a comprehensive prevention program.^{37,38}

Provision of antiretroviral prophylaxis following sexual exposures in the community is a highly specialized field and is outside the scope of this chapter; advice should be sought from a doctor with HIV expertise. Interested readers are referred to guidelines produced by the Australian Department of Health and Ageing, available at <http://www.ashm.org.au/pep-guidelines/>.

Full references are available at <http://expertconsult.inkling.com>

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9.11 TROPICAL INFECTIOUS DISEASES

9.11 Tropical infectious diseases

Sander Manders

ESSENTIALS

- 1** Tropical diseases are a major cause of morbidity and mortality worldwide.
- 2** Due to climate change and increasing population mobility (migration and travel), health practitioners in non-tropical areas will increasingly have to diagnose and treat tropical diseases.
- 3** A significant proportion of northern Australia has a tropical climate and several tropical diseases occur in this area. Vigilant public health surveillance, case tracking and vector control are instrumental in controlling incursions of non-endemic tropical diseases into Australia.
- 4** Indigenous Australians are disproportionately affected by infections in tropical Australia.
- 5** Within tropical areas, the aetiological spectrum of common diseases is different from that in temperate areas. This is due to different local prevalences of common pathogens, as well as the existence of specific tropical agents. Knowledge of local protocols is important in choosing appropriate antibiotic cover for the treatment of common diseases in the tropics.
- 6** In travellers who have returned from the tropics and present to the emergency department, common infections not specific to the tropics should not be forgotten as likely causes. A good history and systematic approach may aid in the correct identification of tropical diseases. Expert consultation may be of great benefit and public health notification is essential.

Introduction

Tropical diseases cause an enormous burden of disease worldwide, and many other diseases that are not specific to the tropics disproportionately affect people in developing countries.

Returned travellers or migrants may present to health practitioners with signs and symptoms of tropical diseases. Due to climate change and increasing population mobility (travel and migration), health practitioners in non-tropical areas will increasingly need to diagnose and treat tropical diseases. A high index of suspicion, a systematic approach and expert consultation contribute to the appropriate investigation and management of these cases.

Significant areas of northern Australia have a tropical climate, including the Top End (around Darwin), Far North Queensland (north of Cairns) and the Kimberley (in Western Australia). Several tropical diseases are endemic there, with others occurring only infrequently. Indigenous Australians are disproportionately affected by both tropical and non-tropical disease.

Diseases common to temperate climates also occur in the tropics, and it is important to

recognize that these may have different aetiologies there. Community-acquired pneumonia in tropical Australia, for instance, is most commonly caused by *Streptococcus pneumoniae*; but in severe cases, organisms such as *Burkholderia pseudomallei* and *Acinetobacter baumannii* should also be covered. *Cryptococcus gattii* should be considered in meningitis or subacute pneumonia. In undifferentiated sepsis, melioidosis is an important differential diagnosis. Knowledge of protocols based on specific local circumstances is important.

Vigilant public health systems are in place to help prevent the spread of disease from endemic areas into non-endemic areas. Many of the diseases discussed in this chapter are notifiable in both Australia and New Zealand. An appropriate public health response may include case surveillance, contact tracing and vector control.

Parasitic tropical diseases

Malaria

Introduction and epidemiology

Malaria is often considered the most important tropical disease worldwide. Half of the world's

population is at risk, with over 200 million cases annually. An estimated 429,000 deaths occurred in 2015, of which 92% were in sub-Saharan Africa.¹ A substantial number of malaria infections occur in South America, Southeast Asia and the Pacific.

In Australia, malaria was officially considered eradicated only in 1981, and there are ongoing concerns regarding the potential re-establishment of the disease due to the widespread presence of appropriate vectors and geographic proximity to endemic areas (particularly Indonesia and Papua New Guinea). Around 400 to 500 cases are reported in Australia each year in travellers and migrants.

Malaria is caused by the protozoan parasite *Plasmodium*, of which six species are currently known to infect humans (Table 9.11.1). They have a complex life cycle and are transmitted by *Anopheles* mosquitoes, which bite from dusk to dawn. Less commonly, malaria can also be transmitted vertically. The parasites enter the blood and spread to the liver, where they replicate and are periodically released back into the bloodstream and then invade red blood cells.

The majority of malaria cases are caused by *P. falciparum*, which is the most severe and lethal form. Groups at particular risk include young children, pregnant women, immunocompromised patients (including those with HIV/AIDS) and travellers (due to a lack of immunity). Conversely, some genetic red blood cell variations—including sickle cell trait, thalassaemia trait, G6PD deficiency² and Melanesian ovalocytosis—provide some resistance against malaria.

Prevention

A large number of national and international organizations are involved in malaria prevention. Measures include vector control programmes, indoor residual spraying, insecticide-treated nets and intermittent preventative treatment for pregnant women. Travellers to endemic areas should use appropriate chemoprophylaxis tailored to the locally occurring *Plasmodium* species and drug resistance patterns and avoid mosquito exposure. Efforts to develop a malaria vaccine are ongoing.

Clinical features

The incubation period is typically 10 days to 4 weeks, but it can be longer. Mild cases of acute malaria are characterized by paroxysmal fevers caused by periodic parasitaemia. Rigors herald 6 to 10 hours of high fever ($>40^{\circ}\text{C}$), after which a relatively asymptomatic period follows. The rigors recur after approximately 40 hours ('tertian'

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fever) with *P. vivax* and *P. ovale* or approximately 64 hours ('quartan fever') with *P. malariae*. In *P. falciparum* malaria, fevers are less predictable and may be continuous. Additionally, there may be flu-like symptoms, diarrhoea and mild jaundice.

Chronic malaria occurs when low-level parasitaemia persists, causing recurrent attacks and anaemia, hepatosplenomegaly and increased susceptibility to other infections. Secondary complications include massive splenomegaly, malarial nephropathy and Burkitt lymphoma.

Severe malaria is almost exclusively caused by *P. falciparum*. Important features are summarized in Table 9.11.2. The World Health Organisation

(WHO) has published case definitions for severe malaria.⁴ The prognosis is poor, especially in children. Non-falciparum malaria is usually more benign, but death due to splenic rupture can occur.

Diagnosis

Clinical findings are of limited utility in diagnosing malaria⁵; microscopic examination of thick and thin blood smears⁶ remains essential. A thick smear (drop of blood on a slide) is used to detect the presence of parasites and a thin smear (drop of blood spread thin on a slide) may help to identify the *Plasmodium* species.

One negative smear does not exclude malaria; usually three sets are obtained at 12- to 24-hour intervals. Rapid dipstick immunoassay tests exist but can be falsely negative with low or very high levels of parasitaemia. *Plasmodium*-specific polymerase chain reaction (PCR) tests are sensitive and specific but not widely available in endemic areas. Many other laboratory abnormalities, such as thrombocytopenia and hyperbilirubinaemia, can be seen in malaria, but these are not specific enough to make the diagnosis. Before the diagnosis of cerebral malaria can be made, bacterial meningitis should be ruled out by lumbar puncture.

Treatment

Early treatment reduces morbidity, mortality and malaria transmission. Emerging resistance to antimalarial drugs (chloroquine and sulfadoxine-pyrimethamine) is a recurring problem worldwide. Artemisinin, a compound derived from wormwood, combined with another agent (artemisinin combination therapy) is the best currently available treatment for *P. falciparum* malaria.^{7,8} It is given orally for uncomplicated cases and intravenously for severe cases. Various regimens are available to treat other *Plasmodium* species. For travellers diagnosed with malaria, different drugs should be used for treatment than were taken for prophylaxis. Initial hospitalization with the consultation of an infectious disease specialist is recommended for all cases.

Table 9.11.1 *Plasmodium* species that cause malaria in humans

<i>Plasmodium</i> species	Area	Notes
<i>P. falciparum</i> ($\pm 75\%$)	Africa, South America, Southeast Asia	Responsible for most severe cases and deaths
<i>P. malariae</i> ($\pm 20\%$)	Africa, Southeast Asia, Pacific, South America	Quartan malaria
<i>P. ovale curtisi</i> <i>P. ovale wallikeri</i>	West Africa, Southeast Asia	Two subspecies of <i>P. ovale</i> have been described ²
<i>P. vivax</i>	United States, South America, Asia, Africa	Relatively benign
<i>P. knowlesi</i>	Southeast Asia (Malaysia)	Can cause severe cases; macaques are a reservoir

Table 9.11.2 Features of severe malaria

Feature	Causes	Signs and symptoms
Cerebral malaria	Microvascular obstruction with parasite-containing red blood cells	Drowsiness, confusion, coma Delirium, transient psychosis Seizures Focal neurological signs (rare) Usually absent meningeal signs
Respiratory distress	Direct capillary damage (ARDS) Respiratory compensation of metabolic acidosis Intercurrent chest infection Anaemia	Increased work of breathing Kussmaul breathing pattern
Severe anaemia	Increased RBC clearance (both infected and non-infected RBCs) Hypersplenism and immunological causes Haemolysis Failing bone marrow erythropoiesis	Pallor Fatigue, prostration Failure to thrive Jaundice Haemoglobinuria ('blackwater fever')
Acute renal failure	Pre-renal (dehydration, hypovolaemia) Renal (microvascular obstruction, glomerulonephritis)	Oliguria, anuria
Acidosis	Lactic acidosis	Hyperpnoea (respiratory compensation)
Hypoglycaemia	Abnormal liver function Hyperinsulinaemia from quinine/quinidine administration	Anxiety, diaphoresis Drowsiness, coma Hypothermia
Disseminated intravascular coagulation (DIC)	Inappropriate coagulation cascade activation	Bleeding complications Relatively rare (<10% of severe malaria)

ARDS, Acute respiratory distress syndrome; RBC, red blood cell

(From Trampuz A, Jereb M, Muzlovic I, Prabhu RM. Clinical review: severe malaria. *Critical Care*. 2003;7:315–323.)

Schistosomiasis (bilharzia)

This parasitic disease affects more than 200 million people worldwide, with more than 90% of infections occurring in Africa. Its global impact is second only to malaria, with an estimated 200,000 deaths per year and significant chronic morbidity in survivors.

Infected freshwater snails release free-swimming larvae (cercariae) into surface waters, which can penetrate the skin of humans who come into contact with the water. Schistosomula then circulate in the blood and replicate in the portal vessels. Subsequently they migrate to blood vessels in other parts of the body and release their eggs, some of which are shed in human faeces and end up back in the surface waters. The eggs hatch in the water and produce miracidia, which enter suitable freshwater snails. After multiplying inside the snail, cercariae are released into the water, awaiting a new human host. The species of *Schistosoma* responsible for human infections are listed in Table 9.11.3; mixed infections also occur.

Acute infections are more likely to cause symptoms among non-residents of endemic areas. A pruritic rash in response to cercariae entering the skin (swimmers' itch) can occur within a day, usually subsiding within 10 days. Acute toxæmic

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schistosomiasis (Katayama fever) is an uncommon but often severe seroconversion illness that may occur 1 to 3 months after the primary infection. Symptoms include fever, malaise, urticaria, cough, diarrhoea, hepatosplenomegaly and lymphadenopathy. It may last several weeks.

In chronic infection, the parasites migrate to species-specific areas in the host body, where their eggs induce a localized inflammatory response with fibrosis. This causes a high burden of disease^{9,10}; common symptoms are listed in Box 9.11.1.

Prevention includes improving sewage management and using personal protection, such as rubber boots. Freshwater exposure should be avoided where possible. Vaccine development has proved challenging.

The diagnosis is made by a history of freshwater exposure and the demonstration of eggs in the urine or faeces. During Katayama fever, no eggs may be seen. Serological tests are available. Abdominal x-rays may show bladder calcification in chronic genitourinary schistosomiasis.

Praziquantel (40 to 60 mg/kg in two divided doses) is an effective treatment but, due to the high rate of re-infection, it may be difficult to achieve a cure in endemic areas. During Katayama fever, prednisone may be given to suppress the acute reaction and a repeat dose of praziquantel is recommended after 1 to 2

Table 9.11.3 Schistosoma species that infect humans

<i>Schistosoma mansoni</i>	Latin America, Africa, Middle East
<i>S. haematobium</i>	Africa, Middle East, Turkey, India
<i>S. japonicum</i>	East Asia, Pacific
<i>S. intercalatum</i> ($\pm 1\%$)	Sub-Saharan Africa
<i>S. mekongi</i> (<1%)	Cambodia, Laos (Mekong river basin)

Box 9.11.1 Symptoms of chronic schistosomiasis

<i>Schistosoma mansoni</i>	<i>S. haematobium</i>	Neuroschistosomiasis
<i>S. japonicum</i>		<i>S. japonicum</i>
<i>S. intercalatum</i>		Meningoencephalitis
<i>S. mekongi</i>		Focal seizures
Hepatosplenic schistosomiasis (hepatic periportal fibrosis)		<i>S. mansoni</i> , <i>S. haematobium</i>
Hepatomegaly		Cauda equina syndrome, paraplegia, bladder dysfunction
Portal hypertension		
Splenomegaly		
Pancytopenia		
Intestinal schistosomiasis		Pulmonary schistosomiasis
Intermittent bloody diarrhoea		<i>S. haematobium</i>
Tenesmus		Pulmonary hypertension
Anaemia		Right heart failure, tricuspid incompetence
Hypoalbuminaemia		
Intussusception		

months. Community treatment programmes exist in endemic areas.

Leishmaniasis

Various species of *Leishmania* protozoa occur in South America, Africa, the Middle East and India as well as in southern Europe.¹¹ They are transmitted by sandflies from human and canine reservoirs. Preventative measures include diethyltoluamide (DEET)-containing insect repellents, covering exposed skin and insecticide spraying inside houses. Sandflies are so small that they will pass through the mazes of bed nets that have not been treated with insecticide.

Leishmania infections can have cutaneous or systemic manifestations depending on parasite species and host factors, and they can remain asymptomatic. HIV co-infection predisposes to severe or recurrent disease. The incubation period is usually 1 to 2 weeks to 6 months, but there can be a latent period of up to 3 years.

Cutaneous leishmaniasis manifests with skin ulcers, which are usually painless unless a secondary bacterial infection occurs. Most lesions heal spontaneously over a few months, leaving a scar. A mucocutaneous form of the disease causes destruction of the mucous membranes of the nose, mouth, throat and surrounding tissues and can occasionally be fatal.

Visceral leishmaniasis (also known as kala-azar) manifests as fever with rigors, malaise, anorexia, lymphadenopathy and non-tender hepatosplenomegaly. Malnutrition and anaemia occur as the disease becomes chronic. The mortality is very high within 2 years if the disease remains untreated, although milder chronic forms also occur.

The diagnosis can be confirmed by microscopy, culture or PCR. Treatment of leishmaniasis varies by clinical manifestation and geographic region; pentavalent antimony-containing preparations are often the most effective drugs.

Post-kala-azar dermal leishmaniasis (PKDL) can occur several months to years after recovery

from visceral leishmaniasis and consists of maculopapular lesions that spread from around the mouth. It typically disappears within a year without treatment but may require several months of treatment in some regions. PKDL patients can be long-term reservoirs of infection.

Trypanosomiasis

American trypanosomiasis (Chagas disease)

A major public health concern in Latin and South America, Chagas disease is caused by the flagellate protozoan *Trypanosoma cruzi*. It is spread to humans and other mammals by the faeces of insects of the Triatominae subfamily ('kissing bugs'). Additionally, it can be spread vertically or by the administration of blood products. Prevention focuses on vector control, including the improvement of housing conditions and the use of insecticides and mosquito nets. Blood products and organ donors in the Americas are screened for *T. cruzi*.

The acute phase of the infection may cause no or non-specific flu-like symptoms, but it can be fatal in children. Swelling around the site of inoculation in the face or around the eye (Romaña sign) is well described. The infection becomes asymptomatic within approximately 2 months. In the chronic phase, the parasites invade the myocardium and intestinal smooth muscle. The development of cardiomyopathy leads to congestive heart failure and arrhythmias and is fatal in 30% of patients. Dilatation of the oesophagus and colon (10%) and neurological involvement may also occur.

The diagnosis can be made by direct visualization of the parasites in blood smears or by serological testing. Benznidazole and nifurtimox are effective treatments if given soon after the infection occurs. Treatment for chronic infections is difficult and side effects are common. Supportive treatment for cardiac and gastrointestinal complications is important.

African trypanosomiasis (sleeping sickness)

This disease of sub-Saharan Africa is caused by *Trypanosoma brucei*, which is spread by bites of the tsetse fly. Several major epidemics have occurred in the last century and vector control programmes have been successful in reducing the number of cases reported.

Approximately 95% of cases are caused by *Trypanosoma brucei gambiense* (West and Central Africa). A chancre may develop at the site of inoculation, followed by an asymptomatic stage which can last months to years. Symptomatic infection then begins with the haemolymphatic stage, characterized by fever, arthralgias and pruritus. Posterior cervical lymphadenopathy (Winterbottom sign) is common. The neurological stage begins when the trypanosomes invade

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the central nervous system, causing headaches, personality changes, psychosis and focal motor, extrapyramidal and/or cerebellar signs. The final stages of the disease are characterized by daytime somnolence, seizures, coma and death.

A second type of the disease is caused by *Trypanosoma brucei rhodesiense* (5%), which occurs in southeastern Africa. Its course is more fulminant, with early multiple organ failure and death.

The diagnosis can be made by direct microscopic observation of the trypanosomes. Several serological screening tests (card agglutination trypanosoma test) exist for Gambian trypanosomiasis. The treatment is complex and depends on parasite subtype, regional drug resistance and the stage of the disease.

Filariasis

This variable disease is caused by a number of helminth species (worms) that occur throughout the (sub)tropics and are spread by mosquitoes and black flies. Lymphatic filariasis is the most common form; the worms develop in the lymphatic system and cause lymphoedema. Elephantiasis is the most extreme manifestation of this disease. Subcutaneous filariasis is caused by different species of helminths, producing a rash and arthritis. *Onchocerca volvulus* inhabits the eyes and is the world's second cause of blindness ('river blindness'). The diagnosis can be made with thick and thin blood smears obtained on a species-specific time of the day or by PCR. Treatment is with diethyl-carbamazine or ivermectin and albendazole; sequelae often remain chronic.

Gastrointestinal parasites

A variety of gastrointestinal infections are prevalent throughout the tropics (Box 9.11.2); they represent a major cause of morbidity and childhood mortality. Most are transmitted by the faecal-oral route; prevention therefore includes improving sanitation and access to safe drinking water. The most important feature of management is appropriate oral or intravenous rehydration; specific antimicrobial therapy is secondary.

Protozoa

Giardia lamblia is a protozoan parasite with worldwide distribution, including Australia and New Zealand. It can survive for a long time in freshwater lakes and streams contaminated with animal or human faeces. Mild infections can be asymptomatic, but it often causes foul-smelling, loose stools that may become fatty and float on water. It is usually self-limiting (7 to 10 days) but can become more chronic and contribute to malnutrition. The diagnosis is made by microscopy and treatment is with oral metronidazole (30 mg/kg up to 2 g qd for 3 days) or tinidazole (50 mg/kg up to 2 g as a single dose).

Entamoeba histolytica infection is often asymptomatic or causes only mild diarrhoea, but it may lead to severe diarrhoea with mucus, pus and blood in the stools (dysentery). Complications include peritonitis from intestinal perforation and amoebal liver abscesses. Microscopy must often be repeated to make the diagnosis. Supportive treatment is important; the specific treatment is oral metronidazole (15 mg/kg up to 600 mg q8h for 7 to 10 days) or tinidazole (50 mg/kg up to 2 g qd for 3 days).

Several species of *Cryptosporidium* occur worldwide (including in Australia and New Zealand), causing self-limiting watery diarrhoea. Special microscopic techniques are required to make the diagnosis. Specific treatment is required only in immunocompromised patients (particularly those with AIDS), as this illness may become severe, even life-threatening in this group.

Helminths (worms)

Soil-transmitted helminths infect humans when their eggs are ingested (*Ascaris*, *Trichuris*) or by active penetration of the skin by larvae (hookworms, *Strongyloides*). Most helminthic infections cause chronic abdominal discomfort without significant diarrhoea. Complications include intestinal obstruction (*Ascaris*), chronic diarrhoea (*Trichuris*) and iron deficiency anaemia (hookworms). The eggs and larvae of these species can be distinguished by microscopy. Benzimidazoles (albendazole, mebendazole) as a single dose or short course are effective treatment.

Strongyloides occurs worldwide but it is hyper-endemic in rural and remote indigenous communities in northern Australia with a reported prevalence of up to 60%. Due to a cycle of auto-infection, *Strongyloides* infection can be lifelong if untreated.^{12,13} Clinical features of strongyloidiasis are summarized in Box 9.11.3. Immunocompromised patients, including those given corticosteroids, may develop disseminated strongyloidiasis, which carries a high mortality. The diagnosis can be made by the detection of larvae in stool or serology in specialized laboratories. Treatment is with ivermectin (200 µg/kg as a single dose) or albendazole (400 mg qd for 3 days); some authors advocate repeat treatments.

Box 9.11.2 Common gastrointestinal pathogens in tropical areas

Parasites	Bacteria	Viruses
Protozoa		
<i>Giardia lamblia</i>	<i>Salmonella</i>	Rotavirus
<i>Entamoeba histolytica</i>	<i>Shigella</i>	Norovirus
<i>Cryptosporidium parvum</i> , <i>Cryptosporidium hominis</i>	<i>Yersinia enterocolitica</i>	Adenovirus
	<i>Campylobacter jejuni</i>	Astrovirus
	<i>Escherichia coli</i> (enterotoxigenic)	
	<i>Staphylococcus aureus</i>	
	<i>Clostridium difficile</i>	
	<i>Clostridium botulinum</i>	
	<i>Vibrio cholerae</i>	
Helminths		
<i>Ascaris lumbricoides</i> (roundworm)		
Hookworms		
<i>Ancylostoma duodenale</i>		
<i>Necator americanus</i>		
<i>Trichuris trichuria</i> (whipworm)		
<i>Enterobius vermicularis</i> (threadworm)		
<i>Strongyloides stercoralis</i> (pinworm)		

In Australia, *Strongyloides* is sometimes called 'roundworm'; In American English, 'pinworm' refers to *Enterobius* and 'threadworm' to *Strongyloides*.

Box 9.11.3 Clinical features of strongyloidiasis

Acute strongyloidiasis

- Diarrhoea
- Hypoproteinaemia
- Hypokalaemia

Chronic uncomplicated strongyloidiasis

- Recurrent diarrhoea
- Epigastric pain
- Cutaneous manifestations
- Urticaria
- Transient, migratory, linear erythema (larva migrans)
- Respiratory symptoms
- Cough, haemoptysis
- Pneumonia, pulmonary abscess

Disseminated strongyloidiasis (hyperinfective syndrome)

- Sepsis (from enteric bacteria spread by migrating larvae)
- Severe diarrhoea
- Paralytic ileus
- Pneumonia, pulmonary haemorrhage

See references 12 and 13.

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Viral tropical diseases

Many tropical viral infections are arthropod-borne (arboviruses), with flaviviruses being the most important subgroup (Table 9.11.4). Alphaviruses also cause some important infections in tropical and temperate areas.

Yellow fever

In acute yellow fever, a flu-like syndrome develops after 3 to 6 days' incubation and improves after another 3 to 4 days. In 15% of cases, a 'toxic phase' then develops, with high fever and liver dysfunction causing jaundice and haemorrhage; there may also be renal impairment. Mortality in this group is approximately 50%; survivors recover without significant sequelae. There is no specific treatment, but an effective vaccine exists. Evidence of vaccination is required by health authorities in many countries for travellers returning from endemic areas.

Dengue

Four distinct serotypes of the dengue virus occur in most tropical areas of the world; most cases occur in Southeast Asia. In Australia, occasional outbreaks occur, mostly in Far North Queensland. Most cases remain asymptomatic. Dengue fever may develop after 3 to 14 days' incubation; it lasts for 2 to 7 days. Arthralgias are often severe. The rash resembles that of measles. The most feared complication is dengue haemorrhagic fever (DHF), which may develop if a subsequent infection with another dengue serotype occurs. Features are summarized in Box 9.11.4. Laboratory diagnosis can be made with PCR testing. Supportive management with adequate hydration and analgesia is important; no specific therapy exists. A vaccine against all four serotypes is in an advanced stage of development.¹⁴

Arboviral encephalitis

Various arboviruses cause encephalitis and, although the vast majority of infections remain

asymptomatic, potentially devastating sequelae occur in symptomatic patients. Clinical symptoms do not reliably differentiate between various arboviral causes of encephalitis; a definitive diagnosis can be obtained by serological testing.

In recent years, the West Nile virus (WNV) has been successful in extending its range into temperate areas including North America, Europe and Australia. Kunjin virus is a subtype of WNV endemic to Australia and Papua New Guinea.¹⁵ The Murray Valley encephalitis virus is also endemic to northern Australia and Papua New Guinea and epidemics in the southern states of Australia have been well described.¹⁶ Japanese encephalitis virus sporadically occurs on the Torres Strait Islands and the northernmost tip of Queensland.

In the presence of symptoms, these viruses may cause fever with a flu-like syndrome, rash, meningeal signs, convulsions and decreased level of consciousness. Encephalitis, meningitis or a poliomylitis-like illness with flaccid paralysis have all been described. Disease progression is variable, ranging from full recovery to death. Long-term neuropsychiatric sequelae occur in a large proportion of survivors. Treatment is supportive. A vaccine exists for the Japanese encephalitis virus.

Alphaviruses

Several thousand cases of Ross River virus (RRV) and Barmah Forest virus (BFV) infections are seen annually in Australia. They cause flu-like symptoms with arthralgia and a widespread maculopapular rash in 50% of cases. Arthritis, myalgia and fatigue can last for 6 months or longer. IgM serological tests for RRV or BFV may be false positive in patients with other infections such as malaria and dengue. The closely related chikungunya virus occurs in Africa and Southeast Asia and causes similar symptoms. There is no specific treatment.

Viral haemorrhagic fevers

Several families of viruses can cause fever with a haemorrhagic diathesis (Table 9.11.5). They are carried by vectors, but person-to-person spread is mostly responsible for outbreaks. Dengue, yellow fever and certain other flaviviruses occasionally cause haemorrhagic fever as well.

The clinical presentation of viral haemorrhagic fevers is variable but usually includes a flu-like prodrome with respiratory and sometimes central nervous system symptoms. The disease progresses to multiple organ failure with disseminated intravascular coagulopathy. Case fatality rates are high, up to 90%. Treatment is supportive; no specific antiviral agents are available.

A large outbreak of Ebola virus disease¹⁷ in West Africa (Liberia, Sierra Leone and Guinea) between 2013 and 2016 caused immense global

Table 9.11.4 Major viral tropical diseases

Disease and virus ^a	Areas of common occurrence	Vector
Flaviviruses		
• Yellow fever (YFV)	South America, Africa	Mosquitoes (<i>Aedes aegypti</i>)
• Dengue (DENV)	Latin and South America, Africa, South and Southeast Asia	
• Zika virus disease (ZIKV)	Equatorial Africa and Asia ^b	
• West Nile encephalitis (WNV)	Africa, Middle East, Central Asia, North America, Europe, Australia	Mosquitoes (<i>Culex spp.</i>)
• Kunjin (KUNV)	Australia, Pacific	
• Japanese encephalitis (JEV)	Southeast and Far East Asia	
• Murray Valley encephalitis (MVEV)	Northern Australia, PNG	
Alphaviruses		
• Ross River fever (RRV)	Australia, PNG, South Pacific	Mosquitoes (<i>Aedes spp.</i>)
• Barmah Forest fever (BFV)	Australia	
• Chikungunya (CHIKV)	Africa, South and Southeast Asia	

^aCommonly used abbreviation to indicate the causative virus.

^bThe 2015 to 2016 Zika virus epidemic spread the virus to parts of the Pacific and much of the Americas and the Caribbean. PNG, Papua New Guinea.

Box 9.11.4 World Health Organization case definitions for dengue

Dengue fever (DF)	Dengue haemorrhagic fever (DHF)	Dengue shock syndrome (DSS)
Acute febrile illness with ≥ 2 of:	ALL of the following:	All criteria for DHF plus evidence of circulatory failure:
<ul style="list-style-type: none"> • Headache • Retro-orbital pain • Myalgia • Arthralgia • Rash • Haemorrhagic manifestations (not meeting DHF criteria) • Leukopenia and • Supportive serology 	<ul style="list-style-type: none"> • Febrile illness lasting 2–7 days • Haemorrhagic tendencies • Positive tourniquet test • Petechiae, ecchymoses or purpura • Bleeding from the mucosa, Gastro-intestinal (GI) tract, injection sites or other • Haematemesis or melena • Thrombocytopenia ($\leq 100,000/\text{mm}^3$) • Evidence of increased vascular permeability • Rise in haematocrit $\geq 20\%$ • Drop in haematocrit $\geq 20\%$ after rehydration • Signs of plasma leakage (pleural effusion, ascites, hypoproteinæmia) 	<ul style="list-style-type: none"> • Rapid, weak pulse • Narrow pulse pressure (≤ 20 mm Hg) • Hypotension • Cold, clammy skin and restlessness

Note: The World Health Organisation is currently re-evaluating these clinical case definitions.

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Table 9.11.5 Important viral haemorrhagic fevers

Virus	Areas of common occurrence	Vector
Arenaviridae • Lassavirus	West Africa	Rats
Bunyaviridae • Hantaviruses	South and North America, South Asia, Europe	Rodents (rats, mice)
• Crimean–Congo haemorrhagic fever virus	Africa	Ticks (<i>Hyalomma</i>)
• Rift Valley fever virus	Africa	Mosquitoes (<i>Aedes</i> and <i>Culex</i> spp.)
Filoviridae		
• Ebola virus	Central Africa	Bats
• Marburg virus	Equatorial Africa	Bats

concern. The international response was slow initially, but eventually plans were deployed to fight the outbreak locally and limit its spread internationally. Screening systems were set up at international borders and at points of entry into health services (e.g. ambulance services and emergency departments). Persons who had arrived from affected areas within the preceding 21 days with fever, flu-like symptoms or gastroenteritis, were isolated and screened for Ebola. Rigorous protocols were set up for handling patients and contaminated materials. Ultimately over 28,000 people were infected, of whom 11,000 died; only 7 patients were identified outside of West Africa. A newly developed vaccine was reported to be highly effective.¹⁸

Viral hepatitis

A high incidence of hepatitis A and B (HAV, HBV) occurs in developing countries. HAV is spread via the faecal-oral route, whereas HBV is spread via contaminated blood and other bodily fluids. Vaccinations are recommended for travellers to endemic areas.

The hepatitis C virus (HCV) is a non-arthropod-borne flavivirus. Transmission via non-sterilized medical equipment is a concern in certain countries and recommendations for travellers may include carrying their own needles; no vaccine is available.

Hepatitis E (HEV) causes a self-limiting disease similar to hepatitis A except during pregnancy, when fatal hepatitis has been well documented.

Bacterial tropical diseases

Tuberculosis

Introduction

Approximately one-third of the world's human population is infected by *Mycobacterium tuberculosis*, making it a major worldwide public health concern. Tuberculosis is by no means exclusively

a tropical disease but it disproportionately affects people in developing countries. Risk factors include HIV infection and other causes of immune suppression, diabetes, pulmonary disease and malnutrition. It is transmitted via the inhalation of droplets produced by a person with tuberculosis when he or she coughs. Mortality if untreated is around 50%.

Screening and prevention

For screening purposes, the Mantoux (tuberculin) skin test and interferon-gamma release assays (IGRAs) are commonly used. When positive, these tests indicate prior exposure to tuberculosis but do not prove active disease. False-negative and false-positive test results are a concern. The Bacillus Calmette-Guérin (BCG) vaccination offers some protection to people at high risk of contracting tuberculosis; it may cause a false-positive Mantoux test.

Symptoms

Tuberculosis can be asymptomatic but may also produce non-specific symptoms including fever, night sweats, anorexia and cachexia.

The most common presentation is pulmonary tuberculosis, which causes a productive cough, haemoptysis, chest pain and dyspnoea. An exudative pleural effusion may occur. Chronic complications include bronchiectasis and pulmonary fibrosis.

Non-pulmonary tuberculosis can occur in virtually any part of the body, including lymph nodes, bones, meninges, pericardium, abdomen and genitourinary tract. Miliary tuberculosis is an aggressive form of haematogenously disseminated tuberculosis that occurs in infants and immunocompromised patients.

Latent tuberculosis occurs when mycobacteria persist intracellularly; patients are asymptomatic and not infectious. The disease can reactivate later—for example, when the patient becomes immunocompromised.

Box 9.11.5 Chest x-ray findings associated with pulmonary tuberculosis

Consolidation
Hilar lymphadenopathy
Ghon focus (calcified nodule that remains after resolution of initial consolidation)
Cavitating lesions
Fibrosis (dominant in upper lobes)
Calcifications
Miliary pattern (small nodules throughout lungs)
Tuberculoma (well-defined tuberculosis mass)

Diagnosis

Pulmonary tuberculosis may be suggested by chest x-ray appearance (Box 9.11.5). Mycobacteria can be demonstrated on acid-fast (Ziehl-Neelsen) staining of sputum or broncho-alveolar lavage fluid. Culture confirms the diagnosis by identifying the species of mycobacteria; it also enables drug susceptibility testing. For non-pulmonary tuberculosis, samples appropriate to the site should be obtained and tested.¹⁹

Management

Within an emergency department or other hospital setting, patients suspected to have infective tuberculosis should be held in a negative-pressure room; staff and visitors should wear appropriate N95 face masks (aerosol precautions).

Treatment of any form of tuberculosis requires expert consultation. Public health reporting with appropriate contact tracing is essential. A 6-month treatment regimen with four drugs initially ('HRZE', i.e. isoniazid, rifampicin, pyrazinamide, ethambutol) is often used to treat uncomplicated tuberculosis. Emerging multi-drug resistance is of increasing concern worldwide.^{20,21}

Melioidosis

Introduction

The gram negative bacterium *Burkholderia pseudomallei* is the cause of melioidosis.²² It is found throughout Southeast Asia and India and is highly endemic in northeast Thailand, Malaysia, Singapore and northern Australia (with sporadic cases seen further south). The bacteria live in the soil during the dry season but can be found in surface water and mud after a heavy rainfall; they may also become airborne. Transmission occurs through the skin (cuts and sores), inhaled airborne dust or droplets and, rarely, through the ingestion of contaminated water. Person-to-person transmission is extremely rare.

The most important risk factors are diabetes, renal disease, alcohol excess and chronic lung disease. Indigenous Australians are disproportionately affected. Healthy people can become infected while working in wet, muddy conditions without adequate hand and foot protection.

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Symptoms

The most common presentation of melioidosis is pneumonia, which may be severe.²³ It can also cause multiple abscesses in the skin, prostate, spleen, kidney and liver. Septic arthritis, osteomyelitis and neurological disease also occur. In endemic areas, melioidosis is an important differential diagnostic consideration in community-acquired sepsis. Septic shock develops in approximately 20% of patients and carries a high mortality. Unusual features of melioidosis include the development of sepsis after a long initial period of subclinical infection and its potential for recurrence after apparently appropriate antibiotic treatment.

Diagnosis and management

Melioidosis should be treated empirically when the diagnosis is suspected in endemic areas. Serological tests are of limited utility in populations with high background rates of infection. Cultures of blood, sputum, urine or swabs from an abscess or skin ulcer (in Ashdown selective medium) can confirm the diagnosis. A chest x-ray should be obtained in all suspected cases and a computed tomography scan of the abdomen and pelvis is recommended to seek abscesses in any culture-positive case.

B. pseudomallei is resistant to penicillins, most cephalosporins and aminoglycosides. It has some susceptibility to ceftriaxone (2 g IV is recommended initially for adults). However, to treat melioidosis definitively, meropenem (25 mg/kg up to 1 g, q8h), imipenem (25 mg/kg up to 1 g q6h) or ceftazidime (50 mg/kg up to 2 g q6h) must be given. Intravenous antibiotic therapy should be continued for at least 14 days and be followed by oral therapy (usually with sulfamethoxazole/trimethoprim) for 3 to 6 months. Abscesses should be drained and septic joints washed out. Expert consultation is recommended.

Leptospirosis

The zoonotic spirochaete bacteria of the *Leptospira* genus have a worldwide distribution (including Australia and New Zealand), with a higher prevalence in wet and humid tropical areas. Transmission occurs via the urine of infected animals; people with occupational or recreational exposure to animals or their urine are at particular risk.

Leptospira organisms enter the body through damaged skin or mucous membranes, circulate in the blood and then invade the kidneys, lungs and liver. The incubation period is 2 to 20 days. The initial (spiraemic) phase produces non-specific flu-like symptoms with conjunctivitis and occasional jaundice and hepatosplenomegaly. This is followed by a second (immune) phase that may include renal and hepatic failure, aseptic

meningitis and pulmonary haemorrhage. Multi-organ failure can lead to death.

The diagnosis is usually made by leptospirosis serology (micro-agglutination test). However, initial serology is often negative, necessitating a convalescent serum sample for diagnosis. PCR tests are also available. Cultures may become positive only after several weeks of incubation. Members of the *Leptospira* genus are sensitive to a wide variety of antibiotics, including doxycycline (100 mg PO q12h for 5 to 7 days). For more severe disease, intravenous benzylpenicillin (30 mg/kg up to 1.2 g IV q6h for 5 to 7 days) or ceftriaxone (25 mg/kg up to 1 g qd for 5 to 7 days) are recommended.

Rickettsia

The rickettsiae comprise a group of pleomorphic, gram negative, obligate intracellular bacteria, with various species occurring in different areas throughout the world. They are spread by ticks and several other vectors.

Spotted fever

This group of rickettsial diseases includes Rocky Mountain spotted fever (RMSF), African tick bite fever, Mediterranean spotted fever, Australian tick typhus and others. The disease typically begins with fever, nausea and vomiting, myalgia and headaches. After a few days, a maculopapular rash appears in the majority of cases. RMSF in particular can progress to severe disease with vasculitis involving the lungs, intra-abdominal organs, central nervous system and skin (petechial rash). Treatment with oral or intravenous doxycycline (100 mg q12h for 7 to 10 days) should be commenced when there is sufficient clinical suspicion; confirmation from serological tests should not be awaited.

Typhus

Caused by rickettsiae that are spread by lice and fleas, epidemics occur after natural or human-made disasters. Symptoms include a high fever with rigors, cough, myalgias and delirium. After a few days, a centrifugal rash may be seen. Treatment with doxycycline (dosing as earlier) or azithromycin (500 mg PO on day 1, then 250 mg qd for a further 4 days) may be lifesaving.

Scrub typhus

This disease is caused by *Orientia* species, which are bacteria similar to rickettsiae. It is endemic to East and Southeast Asia and northern Australia and is spread by larval stages of mites that occur in dense scrub vegetation. Symptoms include fever with chills, headache, cough, lymphadenopathy and sometimes a rash. An eschar (macule with black scab) often develops when the bite site ulcerates, usually in the groin, on the buttocks or in the axillae. Multi-organ failure

can develop and fatal cases within Australia have been described. It is treated with doxycycline or azithromycin (dosing as earlier).

Enteric fever

Salmonella enterica, serovar Typhi causes a severe, acute febrile illness known as typhoid fever. Paratyphoid fever is a similar but usually less severe disease caused by serovar Paratyphi. Together these entities are referred to as enteric fever. The causative bacteria occur throughout tropical areas of the world, with the majority of cases occurring in South Asia (India, Pakistan, Bangladesh). They are spread via the faecal-oral route, often via contaminated food or water. Oral and intramuscular vaccines are available but are not completely effective.

Enteric fever is a systemic illness, different from the 'simple' gastroenteritis caused by non-typhoid *Salmonella* serovars. Initial symptoms include high fever for more than 2 days with malaise, headache, cough and constipation. After a week, prostration and high fevers with relative bradycardia become prominent. A rash (rose spots) and hepatosplenomegaly can occur. Delirium and profuse diarrhoea often develop in the third week. Most mortality is caused by complications, including intestinal haemorrhage or perforation, septicaemia, encephalitis and the formation of secondary abscesses. Survivors slowly improve over another week or so.

The diagnosis can be made from blood or stool cultures. Management is complicated by increasing rates of antibiotic resistance, with multi-drug resistance particularly problematic in Southeast Asia. Fluoroquinolones or third-generation cephalosporins are still largely effective treatments; azithromycin is recommended for Southeast Asia. For infections acquired in areas with less antibiotic resistance, other options may include chloramphenicol, amoxicillin and co-trimoxazole; expert consultation is recommended. Dexamethasone may reduce mortality in septic shock from enteric fever, and good supportive management is essential.

Cholera

The flagellated gram negative bacterium *Vibrio cholerae* secretes a toxin that causes profuse, watery diarrhoea.²⁴ It is transmitted via the faecal-oral route and occurs throughout sub-Saharan Africa, South Asia and South America. Oral vaccines are available.

Cholera causes high-volume watery diarrhoea ('rice water'), leading to dehydration with electrolyte loss, metabolic acidosis and hypoglycaemia. Vomiting occurs in the majority of cases. Shock, renal failure and cardiac arrhythmias are the main causes of mortality.

In the event of an outbreak, the diagnosis is often made on clinical grounds alone. V.

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cholerae may be demonstrated on microscopy, and cultures in selective media can confirm the diagnosis.

The cornerstone of management is rehydration (oral or intravenous fluids) with electrolyte replacement. In severe cases, antibiotics reduce the duration and severity of diarrhoea. Doxycycline and azithromycin (20 mg/kg up to 1 g PO as a single dose) are most commonly used; other antibiotics may also be effective, such as ciprofloxacin (25 mg/kg up to 1 g PO as a single dose).

Approach to the returned traveller

People returning from tropical areas may present to health care providers with a variety of symptoms. A systematic approach is important to appropriately investigate and manage these patients. Ordered lists of common presenting symptoms, incubation times and geographical distributions can be found widely on the internet²⁵. Up-to-date information on endemic tropical diseases in the area of the patient's travel should be sought, including any current outbreaks of tropical or non-tropical diseases. Recent outbreaks have included novel influenza viruses, severe acute respiratory syndrome (SARS), Middle Eastern respiratory syndrome (MERS), and Zika virus. It is essential that common non-tropical diseases, such as influenza or meningococcal meningitis, be included in the differential diagnosis.

History

Obtain a detailed previous medical history, including any predisposing factors such as immune compromise, splenectomy and pregnancy as well as a list of medications and known adverse drug reactions.

The travel history should include the following:

- The exact locations, duration and dates of stay, including any stopovers
- The nature of the accommodation (e.g. air-conditioned hotel or camping), use of bed nets and insect repellents
- Vaccination history (routine and travel-related) and adherence to preventative medication (such as antimalarial drugs)
- Any behaviour that may have led to disease exposure: known insect or tick bites, contact with sick people, animals, fresh water (including leisure activities), potentially unsafe food or water and sexual or needle exposures

The history of the presenting complaint should include fever patterns (including rigors) and associated symptoms (e.g. respiratory, cutaneous, gastrointestinal and other symptoms). Ask about the appearance and frequency of stools and whether they contained blood or mucus (dysentery).

Examination

The physical examination is often non-specific but can sometimes provide important clues to the diagnosis. Careful examination of the

respiratory system, lymph nodes and skin is important (Table 9.11.6). Look for hepatosplenomegaly, jaundice and bleeding.

Investigations

Potential non-tropical causes for the patient's condition should be investigated as usual (e.g. chest x-ray for respiratory infections or a lumbar puncture for meningitis).

If the history and examination have raised suspicion for conditions for which specific tests (such as serology or cultures) are available, these should be sent off. Keep in mind that many of these will take days or longer to come back. Stool samples for culture, ova and parasites may be helpful. Specific tests for *Giardia*, *Cryptosporidium* and *Entamoeba histolytica* can be requested.

Routine blood tests may provide support for certain conditions, but they are rarely diagnostic. There should be a low threshold for obtaining three sets of thick and thin smears for malaria. Malaria rapid antigen detection tests are also very helpful, although because of the relatively low sensitivity of these kits, three blood films are still required to rule out malaria in any traveller with persisting fever who has returned from a malaria-endemic location. Eosinophilia is usually associated with parasitic (helminth) infection but also with several other infections including HIV, Human T-cell lymphotropic virus (HTLV) and tuberculosis. Evidence of haemolysis or coagulopathy may correlate with worse outcome.

Table 9.11.6 Common differential diagnoses of fever in the returned traveller

Fever plus:	Non-specific systemic symptoms	Respiratory symptoms	CNS involvement	Cutaneous involvement
Tropical or travel-related causes (consider dependent on travel history):	<ul style="list-style-type: none"> • Malaria • Arboviral infections (e.g. dengue, chikungunya, Zika) • Enteric fever • Infectious hepatitis (HAV) • Rickettsial diseases • Tuberculosis • Trypanosomiasis • Leptospirosis • Viral haemorrhagic fevers 	<ul style="list-style-type: none"> • Epidemic respiratory viruses (e.g. influenza, SARS, MERS) • Pneumonia from tropical pathogen (e.g. <i>Burkholderia pseudomallei</i>, <i>Cryptococcus gattii</i>) • Q fever • Pertussis • Malaria • Leptospirosis • Tularaemia • Pneumonic plague 	<ul style="list-style-type: none"> • Arboviral encephalitis (e.g. WNV, JEV) • Cerebral malaria • Meningitis/encephalitis from other tropical cause (e.g. <i>Cryptococcus gattii</i>) • Trypanosomiasis • Rabies 	<ul style="list-style-type: none"> • Arboviral infections (e.g. dengue, chikungunya, Zika) • Alphaviral infections (BFS, RRV) • Measles • Rickettsial diseases • Enteric fever • Rheumatic fever • Lyme disease • Scabies • Diphtheria • Leishmaniasis • Schistosomiasis • Cutaneous larva migrans (hookworms) • Filariasis
Non-tropical causes (do not forget):	<ul style="list-style-type: none"> • Seasonal influenza • Atypical pneumonia (e.g. <i>Legionella pneumophila</i>) • Bacterial sepsis (e.g. <i>Neisseria meningitidis</i>) • Urinary tract infection • Infra-abdominal infections • Acute HIV infection • Osteomyelitis • Endocarditis • Auto-immune diseases 	<ul style="list-style-type: none"> • Seasonal influenza • Bacterial pneumonia from non-tropical pathogens (typical, atypical, hospital-acquired) • Pulmonary embolism 	<ul style="list-style-type: none"> • Bacterial meningitis/encephalitis from non-tropical pathogens (e.g. <i>Neisseria meningitidis</i>) • Viral meningitis/encephalitis • Intracranial haemorrhage • Seizures 	<ul style="list-style-type: none"> • Infectious mononucleosis • Varicella • Viral myocarditis • Endocarditis • Acute HIV infection • Syphilis • Childhood viral infections (e.g. parvovirus B19) • Henoch-Schönlein purpura (HSP) • Allergic reaction or drug rash

(Modified from Fairley JK. General Approach to the Returned Traveler. Centers for Disease Control; 2017. <https://wwwnc.cdc.gov/travel/yellowbook/2018/post-travel-evaluation/general-approach-to-theReturned-traveler>. Accessed December 24, 2017 and other sources.)

BFS, Barmah Forest virus; HAV, hepatitis A virus; HIV, human immunodeficiency virus; JEV, Japanese encephalitis virus; MERS, Middle East respiratory syndrome; RRV, Ross River virus; SARS, severe acute respiratory syndrome; WNV, West Nile virus.

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Management

Specific treatment may be commenced if available, depending on the likely diagnosis. This may have to be done without the benefit of laboratory confirmation. A low threshold for expert consultation is recommended to help guide investigations and management. Supportive treatment is very important and may include analgesia, fever-control measures and the maintenance of adequate hydration and electrolyte replacement.

Patients who are unwell or suspected to have a high-risk condition should be admitted to the hospital. Consideration can be given to discharging low-risk patients provided that adequate follow-up can be arranged, including the results of any outstanding tests. Public health notification of any suspected or proven notifiable diseases is essential.

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The author strongly recommends checking all drug doses and regimens carefully. The latest version of the Australian Therapeutic Guidelines (Antibiotic) or other appropriate local guidelines should be consulted.

It is the responsibility of the prescriber to check their patient's particular circumstances +/- check with their infectious disease specialist and/or local protocols.

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SECTION 10

GENITOURINARY EMERGENCIES

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10.1 Acute kidney injury 457

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10.3 Renal colic 469

10.1 Acute kidney injury

Nicholas Adams

ESSENTIALS

- 1 Acute kidney injury (AKI) is defined as a rapid reduction in the glomerular filtration rate marked by an acute increase in the serum creatinine (SCr) concentration.
- 2 The early stages of AKI are usually asymptomatic and the diagnosis is based on a decrease in urine output or an elevated SCr. It may take 24 hours or more for an initially normal SCr concentration definitely to increase and up to 48 hours to distinguish between early AKI and renal failure.
- 3 The basic processes causing AKI are renal hypoperfusion (prerenal causes); damage to glomeruli, tubules, interstitium or blood vessels (renal causes); or obstruction to urine flow (post-renal causes).
- 4 Prerenal factors are present in about 40% of persons with AKI. They include hypovolaemia, hypotension, oedematous states with a reduced 'effective' circulating volume, renal hypoperfusion and drugs.
- 5 Bedside correction of hypovolaemia should be based on the cardiovascular response to passive leg raise and the urine output response to intravenous fluid resuscitation.
- 6 Renal factors are present in about 50% of persons with AKI. Acute tubular necrosis (ATN) is the most common pathological process causing ARF and is classified as ischaemic ATN or ATN due to damage by toxins (e.g. myoglobin) or drugs. No therapeutic intervention has hastened the recovery of renal function in established ATN.
- 7 Obstruction is present in about 10% of persons with AKI. Hydronephrosis can occur in the absence of obstruction, and some persons with obstruction do not have a dilated urinary collecting system.
- 8 Urine output usually decreases in AKI and the patient may be oliguric (less than 400 mL/day) or anuric (less than 100 mL/day). Only a few conditions cause anuria: complete urinary tract obstruction, vascular lesions, severe ATN or rapidly progressive glomerulonephritis.
- 9 Intravenous mannitol and sodium bicarbonate to produce an alkaline diuresis as a means of preventing ATN in severe rhabdomyolysis has not been shown to be effective.

Introduction

The basic process in acute kidney injury (AKI) is a rapid (hours to days) reduction in the glomerular filtration rate (GFR) due to renal hypoperfusion; damage to glomeruli, tubules, interstitium or blood vessels; or obstruction to urine flow. The GFR is inversely related to the serum creatinine (SCr) concentration and the diagnosis of AKI is made when there is an acute increase in the SCr concentration with or without a decrease in the urine output. A simple definition of μ AKI is an acute and sustained (lasting for 48 hours or more) increase in the SCr of 44 μ mol/L if the baseline is less than 221 μ mol/L or an increase in the SCr of more than 20% if the baseline is more than 221 μ mol/L. A more comprehensive definition (the RIFLE system) is used to classify persons with acute impairment of renal function (Table 10.1).¹

Aetiology and pathogenesis

The causes of AKI are grouped according to the source of renal injury: prerenal (hypoperfusion), renal (parenchymal) and post-renal (obstructive). More than one cause can be present simultaneously.

Pre-renal acute kidney injury

Prerenal AKI is initially an adaptive response to severe volume depletion and hypotension in structurally intact nephrons. Prerenal AKI that is prolonged or inadequately treated can be followed by parenchymal renal damage (acute tubular necrosis [ATN]). Prerenal AKI is a potentially reversible cause of acute renal failure (ARF).

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Reductions in renal blood flow (RBF) and GFR occur in the setting of hypovolaemia, hypotension, oedematous states with a reduced 'effective' circulating volume (cardiac failure, hepatic cirrhosis, nephrotic syndrome) or impaired

renal perfusion (renal artery stenosis, hepatorenal syndrome). Drugs that interfere with renal autoregulation (e.g. prostaglandin inhibitors, angiotensin-converting enzyme [ACE] inhibitors or angiotensin II receptor antagonists) can

reduce glomerular perfusion.² The physiological responses to volume depletion and hypotension and the link to prerenal AKI are shown in Fig. 10.1.1.

Renal acute kidney injury

Ischaemic, cytotoxic or inflammatory processes may damage the renal parenchyma. The causes of the damage can be grouped according to the major structures that are damaged: vessels, glomeruli, renal tubules or renal interstitial tissue.

Vascular causes involving the larger vessels include acute thrombosis of the renal artery, embolism of the renal arteries, renal artery dissection and renal vein thrombosis. Microvascular causes include vasculitis, malignant hypertension and thrombotic microangiopathy (TMA).

The glomeruli are the site of injury in acute glomerulonephritis, which can cause proteinuria, haematuria, nephrotic syndrome or nephritic

Table 10.1.1 RIFLE classification of acute renal failure

Stage	Serum creatinine (sCr) concentration	Urine output
Risk	Increase of 1.5 times the baseline	<0.5 mL/kg/h for 6 h
Injury	Increase of 2.0 times the baseline	<0.5 mL/kg/h for 12 h
Failure	Increase of 3.0 times the baseline or sCr is 355 µmol/L or more when there has been an acute rise of greater than 44 µmol/L for 24 h or anuria for 12 h	<0.3 mL/kg/h
Loss	Persistent acute renal failure; complete loss of kidney function for longer than 4 weeks	
End-stage renal disease	End-stage renal disease for longer than 3 months	

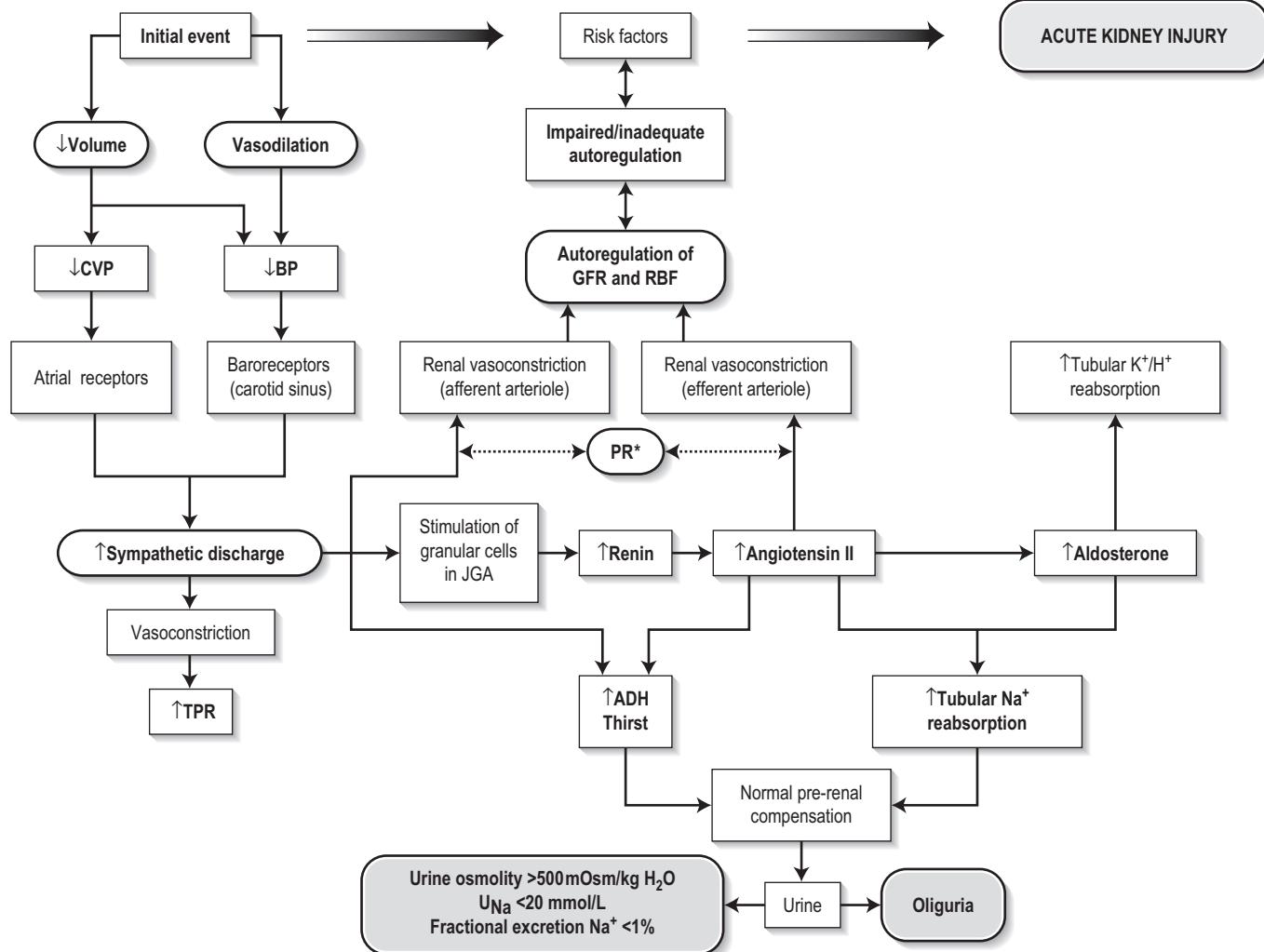


FIG. 10.1.1 Physiological response of the kidney to hypovolaemia or reduced perfusion. The normal response results in a reduced volume of concentrated urine. The presence of risk factors, impaired autoregulation or prolonged hypovolaemia can cause acute kidney injury. ADH, Antidiuretic hormone; BP, blood pressure; CVP, central venous pressure; GFR, glomerular filtration rate; JGA, juxtaglomerular apparatus; PR*, renal prostaglandins; RBF, renal blood flow; TPR, total peripheral resistance.

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syndrome. A number of different forms of glomerulonephritis have been described, generally diagnosed by the histological changes seen on renal biopsy. The distinction between these forms is not of direct concern for the emergency practitioner.

ATN is the most common pathological process causing AKI. Although the terminology suggests that the main cause is tubular damage, the actual pathophysiology is more complex: impaired autoregulation and marked intra-renal vasoconstriction (the main mechanism for the greatly reduced GFR), tubular damage (with cytoskeleton breakdown), increased tubuloglomerular feedback, endothelial cell injury, fibrin deposition in the microcirculation, release of cytokines, activation of inflammation and activation of the immune system.³

ATN is often classified as ischaemic ATN or cytotoxic ATN, but both processes may be present in some patients. Ischaemic ATN represents an advanced form of prerenal AKI, but the distinction between these two entities is based on histopathological changes and is of little use to the clinician. Important causes of cytotoxic ATN are listed in **Box 10.1.1**. Non-steroidal anti-inflammatory drugs (NSAIDs), ACE inhibitors and angiotensin receptor blockers (ARBs) often cause a gradual and asymptomatic decrease in the GFR, but they can also cause AKI. NSAIDs do not impair renal function in healthy persons, but can reduce the GFR in the elderly with atherosclerotic cardiovascular disease, in persons with chronic renal failure, when chronic prerenal hypoperfusion is present (e.g. cardiac failure, cirrhosis) or in persons using diuretics and calcium channel blockers.⁴ AKI may occur after the administration of intravenous or intra-arterial radio-contrast agents. A number of risk factors have been identified for this, the most important being pre-existing renal impairment,

hypovolaemia, a large contrast load and the use of hyperosmolar contrast agents.⁵ Drugs that alter angiotensin levels (ACE inhibitors and ARBs) reduce renal perfusion by their antihypertensive effects or by impairing vasoconstriction of the efferent arteriole when renal perfusion is reduced by renal artery stenosis. The nephrotoxicity of haem pigments (myoglobin and haemoglobin) is enhanced by volume depletion, low urine flow rates and possibly low urine pH.

Abnormalities of renal interstitial structure and function represent only one feature of ATN; in acute tubule-interstitial nephritis (ATIN), however, they constitute the primary abnormality. The damage in ATIN is due to immunological mechanisms, the most important involving cell-mediated immunity. ATIN is usually due to an allergic reaction to a drug, commonly antibiotics (β -lactam antibiotics, sulphonamides, fluoroquinolones), NSAIDs, cyclooxygenase-2 inhibitors, proton pump inhibitors, diuretics, phenytoin, carbamazepine and allopurinol.

Post-renal acute kidney injury

Obstructive uropathy refers to the functional or structural processes in the urinary tract that impede the normal flow of urine; *obstructive nephropathy* is the renal damage caused by the obstruction. *Hydronephrosis* and *hydroureter* refer to dilatation of the renal urinary collecting system and the ureters, respectively. They may occur in the absence of obstruction and, conversely, may be absent in some patients with obstruction.

Casts or crystals within the renal tubular lumen can cause intrarenal obstruction. Extrarenal obstruction can develop in the urethra, bladder, ureter or pelvi-ureteric junction. Obstructive uropathy in adults is commonly caused by prostate disease or retroperitoneal neoplasm (cancer of the cervix, uterus, bladder, ovary or colon). Metastatic cancer, lymphomas or inflammatory processes in the retroperitoneum (appendicitis, diverticulitis, Crohn disease) or a neurogenic bladder can also cause obstructive uropathy. Bilateral renal stones are an uncommon cause of obstructive uropathy.

Obstructive nephropathy usually develops gradually and can cause chronic renal failure if the obstruction involves the urethra, bladder or both ureters. Unilateral ureteric obstruction will cause AKI only if it involves a single functioning kidney.

Epidemiology

Studies of the pathogenesis of community-acquired ARF have produced conflicting results. In one study, the major processes were identified as prerenal in 70% of cases, renal in 11% of cases and post-renal in 17% of cases.⁶ There are geographical differences in the causes of ATN.

In Africa, India, Asia and Latin America, ATN is usually caused by infections (e.g. diarrhoeal illnesses, malaria, leptospirosis), ingestion of plants or medicinal herbs, envenomation, intravascular haemolysis due to glucose-6-phosphate dehydrogenase deficiency or poisoning.

Prevention

Maintaining intravascular volume and renal perfusion

The rate and volume of intravenous fluid given to hypovolaemic persons depends on the nature of the intravascular depletion, the blood pressure and heart rate, the (estimated) volume of fluid lost, cardiac function and ongoing circulatory losses. The response to treatment is evaluated by simple bedside measurements (heart rate, blood pressure, urine output, cardiovascular response to passive leg raise).

Rhabdomyolysis

Most studies on the prevention of ATN after rhabdomyolysis have been in persons with crush injury after earthquakes, where the incidence of AKI is about 50%. In this situation, fluid resuscitation should, if possible, begin before the crush is relieved. These patients may require massive amounts of fluid because of fluid sequestration in the injured muscles. The goal of intravenous fluid treatment is to produce a urine output of 200 to 300 mL/h while myoglobinuria (discoloured urine) persists. There is no evidence to support this rate of fluid replacement in persons who have rhabdomyolysis and AKI without crush injury, although a urine output of 100 mL/h would be reasonable while the urine is discoloured. The intravenous administration of mannitol and sodium bicarbonate to produce an alkaline diuresis as a means of preventing ATN in severe rhabdomyolysis has not been shown to be effective.⁷

Radio-contrast nephropathy

Evidence associating radio-contrast agents with acute nephropathy remains controversial. Numerous studies have been published investigating reduction of the incidence of radio-contrast nephropathy. At present it is unclear whether any specific treatment, including intravascular volume expansion, is effective. Certainly N-acetyl cysteine administration before and after radio-contrast administration does not appear to be effective.⁵

Clinical features

The diagnosis of AKI should be considered when there is a decrease in urine output or an elevated SCr concentration. The clinical features depend on the pre-existing conditions that increase the risk of developing AKI, the initiating factor(s) and the effects of AKI (**Fig. 10.1.2**). The history should

Box 10.1.1 Causes of toxic acute tubular necrosis

Exogenous agents

- Radiocontrast
- Non-steroidal anti-inflammatory drugs
- Antibiotics: aminoglycosides, amphotericin B
- Antiviral drugs: acyclovir, foscarnet
- Immunosuppressive drugs: cyclosporin
- Organic solvents: ethylene glycol
- Poisons: snake venom, paraquat, paracetamol
- Chemotherapeutic drugs: cisplatin
- Herbal remedies
- Heavy metals

Endogenous agents

- Haem pigments: haemoglobin, myoglobin
- Uric acid
- Myeloma proteins

10.1 ACUTE KIDNEY INJURY

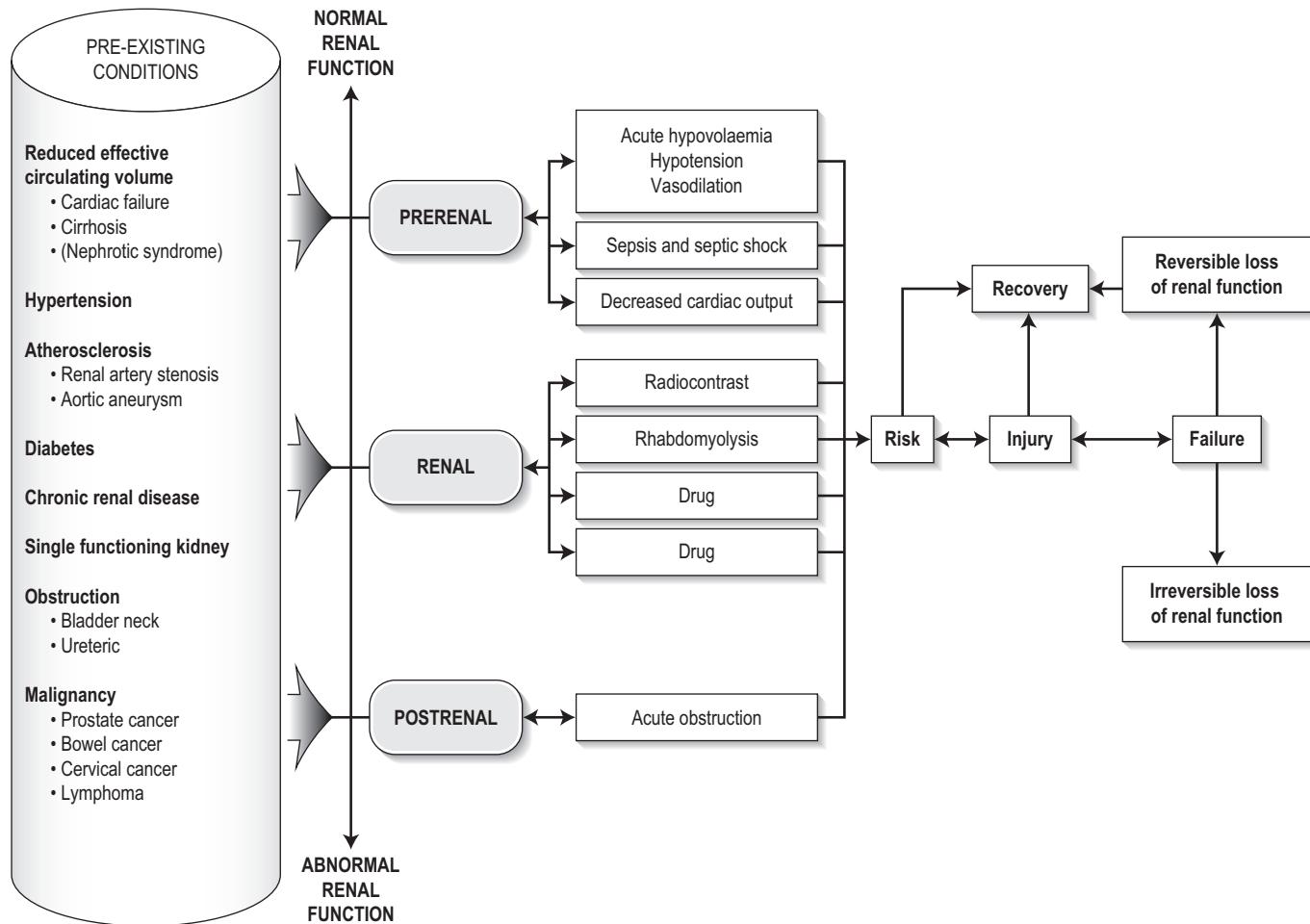


FIG. 10.1.2 The clinical presentation of acute kidney injury (AKI) depends on the presence of any pre-existing conditions, the precipitating event(s) that caused the AKI and the severity of the AKI.

Box 10.1.2 Evaluation of acute kidney injury

Assess the intravascular volume
Look for renovascular disease
Look for symptoms or signs of obstruction to urine flow
Systematic search for presence of infection or sepsis
Evaluate for pre-existing renal disease or chronic renal failure
Obtain a detailed history of medication or drug use
Consider the possibility of glomerulonephritis

include a detailed drug history, enquiry about recent invasive vascular or radiological procedures and any family history of renal disease. This is followed by clinical examination and evaluation of investigations. A number of key issues then need to be resolved (Box 10.1.2).

Evaluation of prerenal (intravascular volume) status

Imprecise terminology, such as 'dry' or 'dehydrated', should be avoided. 'Dehydration' refers to situations where more water than

electrolyte(s) has been lost, shrinking body cells and increasing the serum sodium concentration and osmolality. In other words, 'dehydration' means water depletion. Hypovolaemia is a decrease in the intravascular volume due to loss of blood (haemorrhage, trauma) or loss of sodium and water (e.g. vomiting, diarrhoea, sequestration of fluid in the bowel, etc.).

The (bedside) assessment of the (extracellular) volume status determines the initial resuscitation strategy. This involves evaluation of heart rate and blood pressure, the state of the skin and mucous membranes and the jugular venous pulse. The examination also includes auscultation of the lungs (for pulmonary crackles), abdominal examination (for ascites or masses) and examination of the legs (for peripheral oedema).

The 'typical' features of intravascular volume depletion (tachycardia or hypotension or both in the supine position, or postural hypotension) are not as consistent or reliable as implied by many textbook descriptions. The presence of (supine) tachycardia has low sensitivity as a diagnostic feature of increasing hypovolaemia in healthy persons. An increase in the pulse rate

of 30 beats/min or more between the supine and standing positions is a highly sensitive and specific sign of hypovolaemia after phlebotomy of large volumes (600 to 1100 mL) of blood, but the sensitivity is much less after phlebotomy of smaller volumes. The inability to stand long enough for vital signs to be measured because of severe dizziness is a sensitive and specific feature of acute large blood loss. A systolic blood pressure of 95 mm Hg or less in the supine position has high specificity but low sensitivity for hypovolaemia. Postural hypotension is present in 10% of normovolaemic people younger than 65 years and in up to 30% of normovolaemic people older than 65 years.⁸

The textbook descriptions of the signs of saline depletion in adults (dry mucous membranes, shrivelled tongue, sunken eyes, decreased skin turgor, weakness, confusion) are neither specific nor sensitive compared with laboratory tests for hypovolaemia. The presence of a dry axilla argues somewhat for the presence of saline depletion; the absence of tongue furrows and the presence of moist mucous membranes argue against the presence of saline depletion.

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Evaluation of the renovascular state

Acute renal infarction is caused by dissection of the aorta or renal artery, embolism, renal artery thrombosis, renal vein thrombosis or renal artery aneurysm. Acute arterial occlusion is usually symptomatic, with the development of pain (loin, abdominal or back pain), haematuria, proteinuria, nausea and vomiting. Vascular occlusion of a single functioning kidney produces anuria.

Atheromatous disease of the renal arteries is common in persons older than 50 years with widespread atherosclerosis. Persons with stenosis or occlusion of one or both renal arteries can develop an elevation in SCr concentration after starting treatment with ACE or ARB drugs or they may develop acute or chronic renal failure.

Exclusion of thrombotic microangiopathy

TMA is a syndrome of microangiopathic haemolytic anaemia, thrombocytopenia and varying degrees of organ injury caused by platelet thrombosis in the microcirculation. There are two clinically distinct entities: haemolytic uraemic syndrome (HUS) and thrombotic thrombocytopenic purpura (TTP). HUS affects young children and causes AKI with absent or minimal neurological abnormalities. TTP occurs in adults and causes severe neurological involvement in most cases and variable degrees of renal damage. Both conditions are rare.

Pre-existing renal disease or chronic renal failure

It can be difficult to distinguish between chronic and acute renal impairment. The following features suggest the presence of chronic renal failure: documented renal impairment in the past, family history of renal disease, polyuria or nocturia, uraemic pigmentation, normochromic and normocytic anaemia or small kidneys on ultrasound or computed tomography (CT) scans. Renal size may be normal or increased in chronic renal failure associated with diabetes, polycystic kidney disease or amyloidosis.

Exclusion of urinary obstruction

The symptoms and signs of urinary tract obstruction depend on the site, the cause and the rapidity with which it develops. Pain is more common in acute obstruction and is felt in the lower back, flank or suprapubic region, depending on the level of the obstruction. Chronic obstruction is usually painless. Symptoms of prostatic obstruction include frequency, nocturia, hesitancy, post-void dribbling, poor urinary stream and incontinence. Bladder neck obstruction usually results in an enlarged (and palpable) bladder.

Recognition of rhabdomyolysis

Muscle necrosis releases intracellular contents into the circulation. This causes red-brown urine (which tests positive for haem in the absence of visible red cells on microscopy or tests positive for myoglobin with specific tests), pigmented granular casts in the urine, elevated serum creatine kinase (CK) levels that are five times or more above the upper limit of normal and clear serum (serum is reddish in haemolysis). The severity of the rhabdomyolysis ranges from asymptomatic elevations of muscle enzymes in the serum to AKI and life-threatening electrolyte imbalances.

Urine dipstick findings may be normal because myoglobin is readily cleared from the serum more rapidly than CK; thus myoglobinuria may be absent in patients with renal failure or those who present later in the illness. Muscle pain is absent in about 50% of cases and muscle swelling is an uncommon finding. Muscle weakness occurs in those with severe muscle damage. Fluid sequestration in muscles can cause hypovolaemia. Marked muscle swelling can cause a compartment syndrome.

Other blood test abnormalities include hyperkalaemia, AKI with rapid and marked elevation in SCr (e.g. 220 µmol/L per day), hypocalcaemia (which occurs early and is usually asymptomatic), hyperuricaemia, hyperphosphataemia, metabolic acidosis and disseminated intravascular coagulopathy.⁷

Acute kidney injury and acute renal failure

The early stages of AKI are usually asymptomatic and the diagnosis is based on an elevated SCr concentration. It may take 24 hours or more for an initially normal SCr concentration to show a definite increase and up to 48 hours after the event(s) that caused the AKI to distinguish between the early stages of AKI (risk and injury) and the development of renal failure.

The urine output usually decreases and the patient may be oliguric (urine output <400 mL/day) or anuric (urine output <100 mL/day). Persons with AKI and oliguria have more severe kidney impairment than those without oliguria. Only a few conditions cause complete anuria: total obstruction, vascular lesions, severe ATN or rapidly progressive glomerulonephritis. The clinical features caused by ARF are shown in Box 10.1.3.

Differential diagnosis

The diagnosis of AKI requires synthesis of data from the patient's history, physical examination, laboratory studies and urine output. The category of AKI (Risk, Injury or Failure) may be difficult to determine in the emergency department (ED) if the baseline SCr is unknown. The reversibility

Box 10.1.3 Clinical features of acute renal failure

1. Anorexia, fatigue, confusion, drowsiness, nausea and vomiting, and pruritus
2. Signs of salt and water retention in the intravascular and interstitial spaces: elevated jugular venous pressure, peripheral oedema, pulmonary congestion, acute pulmonary oedema
3. Abnormal plasma electrolyte concentrations, particularly hyperkalaemia
4. Metabolic acidosis
5. Anaemia
6. Uraemic syndrome: ileus, asterixis, psychosis, myoclonus, seizures, pericardial disease (pericarditis, pericardial effusion, tamponade)

of the AKI may be inferred if there is a marked increase in urine output after correction of prerenal problems, but a reduction in SCr (due to an increase in GFR) may not be seen for 12 to 24 hours.

Criteria for diagnosis

Serum biochemistry

The following are measured: serum concentration of electrolytes (sodium, potassium, bicarbonate, chloride, calcium, phosphate), serum urea and SCr concentrations, random blood glucose, liver function tests, coagulation tests and CK concentration.

AKI causes acute elevations in the SCr concentration or serum urea concentrations or both. In prerenal AKI, the low urine flow rate favours urea reabsorption out of proportion to decreases in GFR, resulting in a disproportionate rise of serum urea concentration or blood urea nitrogen (BUN) concentration relative to the SCr concentration. However, serum urea concentrations depend on nitrogen balance, liver function and renal function. Severe liver disease and protein malnutrition reduce urea production, resulting in a low serum urea concentration. Increased dietary protein, gastrointestinal haemorrhage, catabolic states (e.g. infection, trauma) and some medications (corticosteroids) increase both urea production and serum urea concentration without any change in GFR.

The SCr concentration is the best available guide to the GFR. Acute reductions in GFR produce an increase in the SCr concentration. The changes in SCr concentration lag behind the change in GFR and can be affected by the dilutional effect of intravenous fluid. Correct interpretation of the SCr concentration extends beyond just knowing the normal values (Fig. 10.1.3). Creatinine is a metabolic product of creatine and phosphocreatine, which are found almost exclusively in skeletal muscle. The SCr concentration is affected by the muscle mass,

10.1 ACUTE KIDNEY INJURY

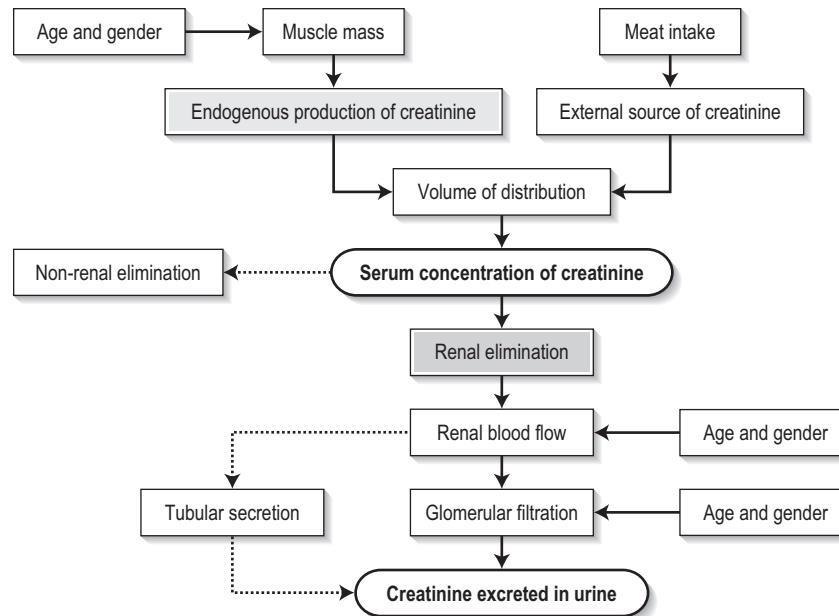


FIG. 10.1.3 Factors that determine the serum creatinine concentration.

$$\text{CCr} = \frac{(140 - \text{age}) \times \text{weight}}{0.814 \times \text{SCr} (\mu\text{mol/L})} \quad \text{in males}$$

$$\text{CCr} = \frac{(140 - \text{age}) \times \text{weight} \times 0.85}{0.814 \times \text{SCr} (\mu\text{mol/L})} \quad \text{in females}$$

Cockcroft–Gault formula

$$\text{GFR} (\text{mL/min}/1.73 \text{ m}^2) = 186 \times \left[\frac{\text{SCr} (\mu\text{mol/L})}{88.4} \right]^{-1.154} \times \text{age}^{-0.203} \times \begin{cases} 0.742 & \text{(if female)} \\ 1.210 & \text{(if black)} \end{cases}$$

MDRD equation

FIG. 10.1.4 Formulae for calculating the creatinine clearance (CCr) or the glomerular filtration rate (GFR) from the serum creatinine concentration (SCr). MDRD, Modified diet renal disease.

meat intake, GFR, tubular secretion (which can vary in the same individual and increases as the GFR decreases) and breakdown of creatinine in the bowel (which increases in chronic renal failure). The GFR decreases by 1% per year after 40 years of age, yet the SCr concentration remains unchanged because the decrease in muscle mass with age reduces the production of creatinine. The GFR (corrected for body surface area) is 10% greater in males than females, but men have a higher muscle mass per kilogram of body weight. The SCr concentration in men is thus greater than that in women.

The creatinine clearance (CCr) or GFR are estimated indirectly using formulae (Cockcroft–Gault formula or the modification of diet in renal disease [MDRD] study equation) based on the SCr concentration (Fig. 10.1.4).⁹ These equations

assume a steady-state SCr concentration and are inaccurate if the GFR is changing rapidly. They will also be less accurate in amputees, very small or very large persons or persons with muscle-wasting diseases.

Knowledge of a patient's baseline SCr concentration is important in assessing the severity and progression of AKI. Small changes when the baseline SCr concentration is low are more important than larger changes when the baseline SCr concentration is high. Major decreases in GFR can occur in the normal range of SCr concentration. If the previous SCr concentration is not known, the MDRD equation can estimate the expected (normal) SCr concentration (using a value for the GFR at the lower range of normal).

Hyperkalaemia is a common complication, with the serum K⁺ usually rising by 0.5 mmol/L

per day in ARF. The serum Ca²⁺ concentration may be normal or reduced in ARF. Both hypocalcaemia and hypercalcaemia may occur at different stages of ARF in rhabdomyolysis. Rhabdomyolysis is characterized by a very high blood CK concentration. Abnormal liver function tests invariably accompany the hepatorenal syndrome associated with hepatic cirrhosis.

Full blood examination

Anaemia develops rapidly in ARF, but its presence or the degree of anaemia does not reliably distinguish between acute and chronic renal failure. Leucocytosis is usually seen if sepsis is the cause of ARF. Eosinophilia is often present in acute interstitial nephritis, polyarteritis nodosa and atheroembolic disease. Anaemia

10.1 ACUTE KIDNEY INJURY

and rouleaux formation suggest a plasma cell dyscrasia. Disseminated intravascular coagulation can complicate ARF due to rhabdomyolysis. A microangiopathic blood film associated with ARF occurs in vasculitis or thrombotic thrombo-cytopenic purpura.

Serological tests

Tests for the detection of antinuclear antibody (ANA), antineutrophil cytoplasmic antibody (ANCA) or measurement of complement concentration are indicated in suspected cases of vasculitis or glomerulonephritis.

Urine tests

The results of urine analysis may be normal in AKI. A positive test for leucocytes, nitrates or both is found in urinary tract infections. A positive test for blood, protein or both suggests a renal inflammatory process. The presence of red cell casts on microscopy is diagnostic of glomerulonephritis.

Measurement of the concentration of electrolytes in the urine and calculation of their fractional excretion is of intellectual interest in understanding the pathophysiological responses of the nephron to different types of AKI. However, the calculations are cumbersome, the results inconsistent and the information obtained does not alter the patient's immediate treatment.

Imaging

A chest x-ray is taken to assess the heart size and the presence of cardiac failure, infection, malignancy or other abnormalities. Ultrasound can define renal size and demonstrate calyceal dilation and hydronephrosis, but the findings depend on the expertise of the operator. Obtaining adequate images is difficult in obese patients, in those with ascites or where there is a large quantity of gas within the bowel. Ultrasound also provides information about bladder size and can detect prostamegaly.

A normal ultrasound examination can occur in the very early stages of obstruction or if ureteric obstruction is due to retroperitoneal fibrosis or to infiltration by tumour. Hydronephrosis not due to obstruction occurs in pregnancy, vesicoureteric reflux or diabetes insipidus.

Doppler scans are useful for detecting the presence and nature of RBF in thromboembolism or renovascular disease; however, because RBF is reduced in prerenal or intrarenal AKI, test findings are of little use in the diagnosis of AKI. CT scans of the urinary tract evaluate renal size and renal position, renal masses, renal calculi, the collecting system and the bladder. Non-contrast CT is the examination of choice in persons with suspected renal calculi and can be used to assess the urinary tract in persons at risk of radiocontrast AKI. Injection of intravenous contrast is used for CT urography, CT angiography and CT

venography, which may be necessary in some circumstances. Radionuclide can be used to assess RBF and tubular function.

Renal biopsy

A renal biopsy provides a tissue diagnosis of the intrarenal cause of AKI and is indicated if the findings will identify a treatable condition. A renal biopsy is also valuable when renal function does not recover after several weeks of ARF and a prognosis is required for long-term management.

Treatment

The basis of emergency management is recognizing that AKI is present, correcting reversible factors, providing haemodynamic support and treating life-threatening complications. This is followed by treatment (if available) of the specific cause of AKI and management of ARF by supportive measures and (if required) renal replacement treatment.

Correction of hypovolaemia

Hypovolaemia not only causes AKI but also worsens all forms of AKI. The clinical diagnosis of hypovolaemia can be difficult if the jugular venous pressure is not easily seen or if there is pre-existing cardiac failure. When there are definite signs of hypovolaemia, the patient is resuscitated with rapid infusion of crystalloid. If hypovolaemia is a possibility or if the person's urine output has decreased markedly, the patient should have 250 to 500 mL of crystalloid infused rapidly (fluid challenge) and the response (urine output, vital signs, jugular venous pressure) evaluated. An increase in urine output or in blood pressure following a fluid challenge suggests that hypovolaemia was present.

Invasive measurement of volume status using central venous and pulmonary artery catheters can increase mortality, lengthen hospital stay and increase the cost of care. There is no evidence to justify the routine use of these invasive measures in patients with AKI. The main indications for central venous cannulation in AKI in the ED are difficulties obtaining intravascular access in the limbs or the need to give drugs that can be given only into a large central vein (e.g. noradrenaline).

Haemodynamic support

AKI impairs the autoregulation of GFR and RBF throughout all ranges of mean arterial pressure. Renal perfusion in ATN is linearly dependent on mean arterial pressure even in the normal range of blood pressure. Episodes of mild or severe decrease in blood pressure lead to recurrent ischaemic injury. Inotrope/vasopressor drugs (noradrenaline or adrenaline) should be commenced if hypotension persists after the correction of hypovolaemia. Dopamine appears to

have no clinical advantage compared with other agents and has, in fact, resulted in increased mortality in some studies.

Monitoring and maintaining urine output

Urinary Catheter

Accurate measurement of urine output requires insertion of a urinary catheter, but this is not needed in the less severe forms of AKI if there is frequent spontaneous voiding. A catheter is required initially in persons with oliguria or (apparent) anuria, shock or obstruction to bladder outflow.

Diuretics

Furosemide is used to produce a diuresis in the treatment of AKI due to hypercalcaemia and in the treatment of severe rhabdomyolysis. A trial of high-dose furosemide (80 to 120 mg intravenously) can be used in persons with AKI who have acute pulmonary oedema if dialysis is not readily available. Persons with less severe forms of AKI (e.g. risk or injury) who have a low urine output (<0.5 mL/kg per hour) that does not increase after correction of hypovolaemia are often given low doses of furosemide (e.g. 20 to 40 mg intravenously). A subsequent increase in urine output is not necessarily associated with a decrease in the SCr concentration. There is no evidence that the use of diuretics to convert the less severe forms of AKI from a (presumed) oliguric to a non-oliguric stage affects outcome.¹⁰

Electrolyte abnormalities

Potassium

The serum potassium concentration may be low, normal or high. AKI due to diarrhoea causes hypokalaemia and metabolic acidosis, whereas AKI due to vomiting or diuretics causes hypokalaemia with metabolic alkalosis. A serum potassium (K^+) below 3.0 mmol/L is treated with oral or intravenous potassium. Diabetic ketoacidosis (DKA) causes renal loss of K^+ , depleting the body of potassium. Persons with AKI due to DKA who have a normal or low serum K^+ need intravenous potassium during treatment with intravenous fluids and insulin.

Hyperkalaemia is due to an imbalance between potassium intake and renal potassium excretion or follows redistribution of potassium from the intracellular to the extracellular space. Hyperkalaemia in AKI can be asymptomatic, produce electrocardiographic (ECG) changes or cause potentially fatal changes in cardiac rhythm.

The initial ECG changes in hyperkalaemia are shortening of the PR and QT intervals, followed by peaked T waves that are most prominent in leads II, III and V₂ through V₄ (Fig. 10.1.5). Marked ST-T segment elevation (pseudo-myocardial infarction pattern) may occur. Bradycardia with

10.1 ACUTE KIDNEY INJURY

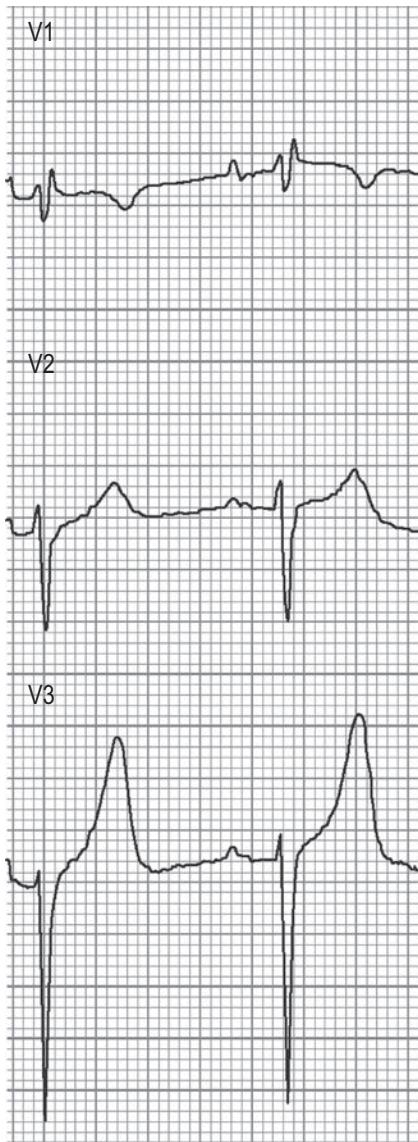


FIG. 10.1.5 The initial electrocardiographic changes in hyperkalaemia. The T waves in leads V₃ to V₅ are very tall and have a 'peaked' tip. The other findings (which may be unrelated to the hyperkalaemia) are the presence of a right bundle branch block pattern and a slightly prolonged PR interval.

sinoatrial (SA) block or atrioventricular block (including complete heart block) can develop and progress to periods of cardiac standstill or asystole. More commonly, the PR interval is prolonged and the QRS complex widened, with the QRS complex having a left- or right-bundle-branch-block configuration (Fig. 10.1.6). At high serum [K⁺] (8 to 9 mmol/L), the SA node may stimulate the ventricles without ECG evidence of atrial activity (sinoventricular rhythm). When the serum [K⁺] is 10 mmol/L or greater, SA conduction no longer occurs and junctional rhythms are seen. The width of the QRS complex continues to increase and, eventually, the QRS complexes

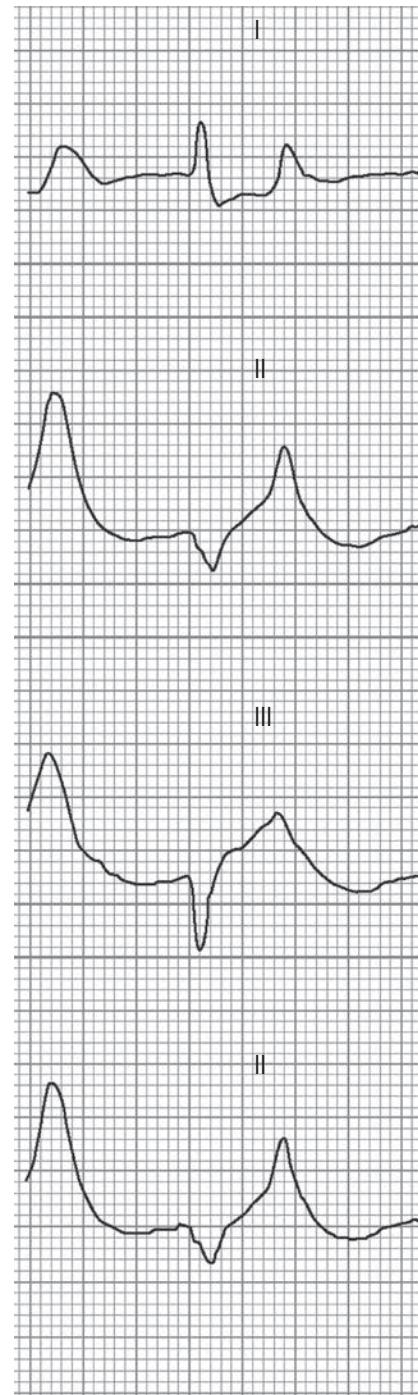


FIG. 10.1.6 Marked electrocardiographic changes in hyperkalaemia. The QRS complexes are widened and have a right bundle branch block type of configuration. Tall T waves are seen in the inferolateral leads. P waves are not visible and a junctional rhythm is present.

and T wave blend, producing a sine-wave ECG. At this stage ventricular fibrillation or asystole is imminent.¹¹

The higher the serum [K⁺] concentration, the more likely become ensuing ECG changes and life-threatening arrhythmias. However, nearly

half of persons with a serum [K⁺] greater than 6.8 mmol/L do not have ECG changes of hyperkalaemia. Physicians predict the presence of hyperkalaemia solely on the basis of ECG changes with a sensitivity of less than 50%.

Drugs, such as oral potassium tablets, ACE inhibitors and aldosterone antagonists, should be ceased in AKI. Hyperkalaemia is treated when the serum [K⁺] is greater than 6.5 mmol/L (even if there are no ECG changes) or when there are ECG changes of hyperkalaemia. The emergency treatment of hyperkalaemia is covered in Chapter 12.2, Electrolyte disturbances.

Sodium

The sodium concentration in AKI may be normal, low (when water excess is present) or high (when water depletion is present). Patients with AKI and symptomatic hyponatraemia should be treated with haemofiltration or dialysis. Hypernatraemia is treated with a slow intravenous infusion of hypotonic saline or 5% dextrose.

Calcium, phosphate, uric acid and magnesium

The serum calcium concentration is normal or slightly reduced in the Risk and Injury stages of AKI and is moderately reduced in later stages. Hypocalcaemia does not require therapy unless tetany is present. Hyperphosphataemia is present in nearly all persons with ARF but does not require treatment in the ED.

Hyperuricaemia is common in AKI but also occurs in chronic renal failure and in persons without AKI. Episodes of acute gout are very uncommon in AKI and the hyperuricaemia does not need treatment. Hypermagnesaemia is common in AKI but is usually asymptomatic. Severe symptomatic hypermagnesaemia can occur if magnesium is administered to persons with AKI.

Acid-base abnormalities

Increased loss of bicarbonate-rich intestinal secretions (due to diarrhoea or an ileal conduit) can cause AKI with a normal anion-gap metabolic acidosis. AKI accompanied by acid loss from the stomach (vomiting or nasogastric suction) or caused by diuretics can result in a hypochloraemic metabolic alkalosis. Persons at the Risk and Injury stages of AKI often have a decrease in the serum bicarbonate concentration. More severe AKI causes a mild to moderate metabolic acidosis with an increased anion gap. This acidosis does not usually require specific treatment. Severe acidosis occurs in rhabdomyolysis and in lactic acidosis. The presence of a very severe metabolic acidosis in AKI is an indication for dialysis.

Fluid overload

The management of AKI in patients with peripheral oedema or pulmonary congestion

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due to cardiac failure is challenging. The clinical diagnosis of hypovolaemia in these patients is difficult and rapid intravenous administration of large volumes of fluid can worsen the pulmonary congestion or heart failure. Hypovolaemia is treated (or excluded) in these cases by assessing the response to small-volume (200 mL) fluid challenges.

Patients with acute pulmonary oedema may have a raised SCr, which can be due to chronic renal failure, AKI or acute-on-chronic renal failure. These patients usually improve following treatment with vasodilators, continuous positive airway pressure (CPAP) ventilation and loop diuretics (frusemide 40 to 80 mg intravenously). Patients with AKI and acute pulmonary oedema who do not respond to these measures need haemofiltration or haemodialysis.

Hypertension

Persons with AKI may have an elevated blood pressure that predated the renal injury, or AKI itself may cause hypertension. A markedly elevated blood pressure reading ($>180/120$ mm Hg) in a person with AKI can be treated with glyceryl trinitrate applied as a skin patch (at a dose of 25 to 50 mg), sublingual nifedipine (5 to 10 mg) or oral hydralazine (20 mg). Intravenous drugs (glyceryl trinitrate or hydralazine) are used if AKI is associated with a hypertensive emergency, such as acute pulmonary oedema, hypertensive retinopathy or hypertensive encephalopathy.

Specific causes of acute kidney injury

Obstruction

Obstruction is relieved by decompression or diversion of the urinary tract. The site of the obstruction determines the technique used: placement of a Foley catheter or insertion of a suprapubic catheter, ureteral catheters (stents) or nephrostomy tubes. Relief of obstruction is often followed by a post-obstructive diuresis. Fluid replacement after relief of obstruction is based on frequent measurements of urine volume and urinary electrolytes.

Other causes

Specific treatments include immunosuppressive agents (for glomerulonephritis or vasculitis),

plasma exchange (for TMA), systemic anticoagulation or revascularization (for renovascular disease).

Management of acute tubular necrosis

Reduction of damage/accelerating recovery

Despite much experimental laboratory work and numerous clinical trials, no therapeutic intervention has hastened the recovery of renal function in established ATN. Therapeutic trials of dopamine, atrial natriuretic peptide and various growth factors have been ineffective. The use of high-dose loop diuretics to convert oliguric ATN to non-oliguric ATN was based on the observation that patients with non-oliguric ATN had a lower mortality and better renal recovery rates than those with oliguric ATN. The use of high-dose loop diuretics does not affect the duration of ATN, the need for dialysis or the outcome.

Supportive treatment

This includes monitoring fluid input and fluid output, measuring serum electrolyte values frequently, preventing sepsis by reducing the number of intravenous lines and removing urinary catheters if possible, culturing periodically and using antibiotics when clinically indicated. The fluid intake is restricted to insensible water loss (about 500 mL/day in the absence of fever) plus all measured fluid losses (urine output, gastrointestinal losses, chest tube drainage). Nephrotoxic agents should be avoided and the dosage of renally excreted drugs reduced. The increase in SCr lags behind the decrease in GFR; therefore drug doses should be calculated based on a GFR of less than 10 mL/min per 1.73 m^2 rather than on the SCr value.

Renal replacement treatment

Renal replacement treatment (RRT) is required in most patients with oliguric ARF and one-third of patients with nonoliguric ARF. The indications for RRT are summarized in **Box 10.1.4**.

Prognosis

The prognosis of ARF is largely dependent on the underlying cause and the presence of

Box 10.1.4 Indications for renal replacement treatment in acute kidney injury

Oliguria (urine output <200 mL/12 h) or anuria (urine output $0-50$ mL/12 h)
Serum urea concentration >35 mmol/L
Serum creatinine concentration >400 $\mu\text{mol}/\text{L}$
Serum potassium concentration >6.5 mmol/L or rapidly rising
Serum sodium concentration <100 mmol/L or >160 mmol/L
Pulmonary oedema not responding to diuretics
Severe (uncompensated) metabolic acidosis with pH <7.1
Uraemic syndrome (asterixis, psychosis, myoclonus, seizures, pericarditis); overdose with a dialyzable toxin

Presence of two or more indications in a patient means that renal replacement will be needed.

co-morbidities. Mortality varies from about 40% in those with no co-morbidity to more than 80% in those who have three or more failed organ systems.

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10.2 THE ACUTE SCROTUM

10.2 The acute scrotum

Gino Toncich

ESSENTIALS

- 1** Torsion is the most time-critical diagnosis in acute scrotal pain.
- 2** Early surgery is mandatory if the diagnosis is strongly suspected. No investigation should delay surgery.
- 3** Colour Doppler ultrasound is helpful and is best used when testicular ischaemia must be excluded in an inflammatory mass or in an older patient.
- 4** Torsion of an appendage can be diagnosed clinically by finding a small blue lump in the scrotal sac (with normal scrotum and non-tender testes) and can be managed non-operatively.
- 5** Epididymo-orchitis is rare in adolescence and torsion should be suspected. Colour Doppler ultrasound may be used to exclude torsion if suspicion remains.
- 6** Masses found on ultrasound should be followed up, as traumatic injury can bring attention to an undiscovered tumour.
- 7** Ultrasound is unreliable in diagnosing testicular rupture.
- 8** Early surgery in scrotal trauma allows diagnosis and treatment of rupture as well as early evacuation of other haematomas with shorter inpatient stays and less pain.

TORSION OF THE SPERMATIC CORD (TESTICLE)

Torsion is a twisting not of the testicle but of the spermatic cord, which then interferes with the vascularity of the testicle, ultimately leading to infarction.

Aetiology

The normal postero-lateral testicular anchoring to the scrotal sac is missing due to an enlarged tunica vaginalis, which surrounds the whole of the testes and epididymis. The testis floats freely like a clapper inside a bell. Contraction of the cremaster causes the testes to be rotated, thereby twisting the cord.¹

Pathology

The twisting of the cord causes obstruction of the lymphatic and venous outflows, leading to venous engorgement; eventually it occludes the arterial inflow. Damage depends on the degree of torsion. Less than one turn (360 degrees) may partially occlude flow, whereas two or more turns (720 degrees) may occlude arterial flow completely, with necrosis occurring in less than 2 hours.^{1,2}

Classical clinical presentation

- There is a sudden onset of severe scrotal or abdominal pain. Between one-third and one-half of patients have had previous episodes of acute scrotal pain.³
- Patient presents with pallor and vomiting.
- The testis is tender and riding high in the scrotum.
- There is loss of the cremasteric reflex; also scrotal oedema, testicular swelling tenderness and retraction.
- There are no irritative voiding symptoms.
- Systemic signs such as fever are usually absent.
- Urinalysis is normal.

Van Glabeke studied over 500 children who had mandatory exploration and found that these clinical signs had false-negative rates of 10% to 40% and false-positive rates of 30% to 70%.⁴

Intermittent torsion of the testis

This is a syndrome of recurrent acute scrotal pain, usually lasting less than 2 hours, which resolves spontaneously.⁵ Some of these cases show evidence of torsion on later exploration.

Differential diagnosis of acute testicular pain

The differential diagnoses to consider in acute testicular pain are listed in **Box 10.2.1**.

Traps in the clinical diagnosis

There are many potential pitfalls in the clinical diagnosis of the acute scrotum⁴:

- Age: The abnormality is present for life, so the torsion could potentially occur at any age. In those under 18 years of age, an acutely painful scrotum should always be considered to be torsion.³ It is most common in adolescence,⁶ with less than 4% of torsions in men over age 30. The increase in sexually transmitted diseases among teenagers may confuse the diagnosis. There is an old surgical aphorism that says, 'When do you diagnose epididymo-orchitis in a teenager? Answer: After you have fixed the torsion'.
- Pain: In 25% of cases pain is *not* sudden in onset, nor is it necessarily severe. However, some patients with epididymo-orchitis (EDO) do have severe pain.^{1,3}
- Localization: Some patients may have no scrotal pain but may have all their pain referred to the lower abdomen or inguinal area. The scrotum must always be examined in males with lower abdominal pain.
- Abnormal position of testis: this is seen only if rotation of 360 degrees or greater occurs.³
- Previous repair: Torsion can occur in a testis that has previously been fixed, especially if absorbable sutures have been used.⁵
- Dysuria: Irritative voiding symptoms rarely occur with torsion and suggests infection.³
- Fever: Temperatures above 102°F have been noted in up to 15% of torsion patients.¹
- Clinical findings remain misleading and none can reliably exclude the diagnosis of torsion.⁷

Box 10.2.1 Differential diagnosis of acute testicular pain

- Epididymo-orchitis
- Strangulated hernia
- Haematocoele
- Hydrocoele
- Testicular tumour
- Henoch-Schönlein purpura in children
- Idiopathic scrotal oedema

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Investigations

Surgical exploration of the scrotum

This is the investigation of choice where the diagnosis of torsion is likely; it also maximizes the chance of saving the testis. Delaying the diagnosis is 'castration by neglect'.^{3,7} Surgical exploration requires only a skin incision and has no major complications.^{4,7}

Low rates of torsion diagnosed at operation have led to interest in other tests to predict torsion preoperatively.

Colour Doppler imaging of the testis

This is useful in diagnosing torsion and also in elucidating other scrotal pathology. Comparison of blood flow to the asymptomatic side is crucial. If there is reduced flow to one side, then some degree of torsion must be suspected. If the testis has untwisted, hyperaemic flow may be noted. The false-negative rate of colour Doppler imaging (CDI) for torsion can be as high as 40%⁴ and is affected by the following:

- Lack of sensitivity in low-flow states
- False flow in early torsion, where hyperaemia and venous engorgement can be seen
- Incomplete torsion or detorted testes
- Inexperience of the operator or inappropriate settings of the ultrasound
- Failure to compare low flow to the normal side²

Role of investigations in suspected testicular torsion

No investigation should delay surgical referral.^{1,3} When there is a high clinical suspicion of torsion, the only investigation is surgical exploration of the scrotum. CDI may be organized on advice from the surgeon.

If torsion is unlikely clinically but must be excluded, CDI can be used provided that it is available on an urgent basis.^{1,3,7}

Treatment

Manual untwisting

This manoeuvre is not universally recommended and should be done only as a temporizing measure or when surgical exploration cannot be performed. The spermatic cord is infiltrated with local anaesthetic and the testis is untwisted. Untwisting is done by turning the left testis anticlockwise (outward) and the right testis clockwise, like opening the pages of a book.⁸

Surgery

An obviously infarcted testis is removed at the initial surgery. A viable testis is sutured into place on the scrotal wall. It is vital that the normal side also be explored and fixed to the scrotal wall, as the abnormality is bilateral in most cases.⁸

Retorsion following orchidopexy has occurred when absorbable sutures were used.^{1,3–6} Testicular fasciotomy has been done to increase the salvage rate.⁴

Prognosis

Viability depends on the number of twists and the time taken to untwist the testis. There is 100% salvage if the testis is untwisted in less than 4 hours, but this falls to 50% within 24 hours. There have been rare case reports of salvage after 30 hours.

Long-term follow-up of salvaged testes shows that 75% have a reduction in volume. Abnormalities are also seen in sperm volume, motility and morphology. These abnormalities are not seen in patients who have had an infarcted testis removed at the initial operation. This suggests some anti-spermatogenesis effect caused by the damaged testicle.^{1,3,5}

Torsion of a testicular appendage

These are embryological remnants found as small (<5 mm) pedunculated structures that may twist on their pedicles. If the appendage can be isolated in the scrotum, a small blue lump may be isolated: 'the blue dot sign'. These do not require surgery and can be treated with analgesia. Late presentations may include scrotal or testicular swelling, in which case they should be treated as torsion until proved otherwise.¹

Acute epididymo-orchitis

Introduction

This is a clinical syndrome resulting from pain and swelling of the epididymis (and testis) of less than 6 weeks' duration. Chronic epididymitis is a long-standing condition of epididymal or testicular pain, usually without swelling.²

Aetiology

A variety of organisms may be responsible for EDO (Box 10.2.2).

The most likely cause depends on the patient's demographic group. For heterosexual males under 35 years of age, the agent is usually gonococcus or chlamydia. These organisms are also responsible for infection in homosexual males under 35 years (where anal sex is practised), but coliforms and even *Haemophilus* can cause infection.

In males older than 35 years, EDO is usually due to obstructive urological disease, so coliforms predominate. EDO may also be part of a systemic disease, for example, mumps.

EDO is usually thought to be an ascending infection from the urethra or prostate, but it

Box 10.2.2 Causative agents in epididymo-orchitis

Bacterial: *Neisseria gonorrhoeae*, *Escherichia coli*, *Pseudomonas aeruginosa*, coliforms, *Klebsiella*, *Mycobacterium tuberculosis*, *Chlamydia trachomatis*

Viral: mumps

Drugs: amiodarone epididymitis

Fungal: cryptococcal

Parasitic: filariasis (usually chronic).

can also be part of a generalized systemic disease. The infection spreads from epididymis to testicle, and eventually may become one large inflammatory mass. Isolated orchitis is rare and usually due to viral causes, which are spread via the bloodstream.^{9–12}

Clinical presentation

The exact features depend on the underlying cause and whether both the epididymis and the testicle are involved. Often the epididymis is painful and tender but, in older men, the whole testicle swells to the size of an Emu egg.

The pain may come on suddenly or slowly. The scrotal swelling and tenderness is relieved by elevating the testis. The spermatic cord is usually tender and swollen. Associated symptoms of urethritis suggest a sexually transmitted infection (STI), whereas bladder symptoms (abdominal pain tenderness) suggest a urinary tract infection (UTI).

In younger males (under 35 years) a history of sexually transmitted disease may be elicited. It is important to take a sexual history and also ask about anal intercourse.

In the older patient there may history of instrumentation, intercurrent UTI or prostatism. Pyuria is common.

Investigations

Urethral swabs

Urethral discharge may not be seen if the patient has just voided, so a urethral swab and smear should be examined for white blood cells (WBCs). If there are more than five WBC per high-powered field, then urethritis is likely. The presence of intracellular diplococci confirms the diagnosis of gonorrhoea; their absence suggests chlamydia.⁹

Urine testing

A standard mid-stream urine (MSU) to look for the presence of WBC or gram negative organisms should be sent for older patients or those with urinary symptoms and abdominal pain as well as EDO.

For those with urethritis or suspected STI, the Australian STI management guidelines

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recommend sending a first-pass urine to the lab for nucleic acid amplification tests (NAATs) looking for chlamydia and gonorrhoea.¹⁰

Differential diagnosis

In the acute non-traumatic setting, the most important differential diagnosis is torsion of the testicle.⁹ Where a large mass is in the scrotum, incarcerated hernias must be considered. Swollen or indurated red scrotal skin in the high-risk patient may indicate Fournier gangrene.

If the clinical features and MSU do not differentiate, then ultrasound may help to exclude other causes of an acute scrotum.

Treatment

Symptomatic treatment consists of bed rest, analgesia and scrotal supports.

If the cause is secondary to a sexually transmitted disease, appropriate antibiotics should be chosen after urethral swabs have been taken—for instance, a single dose of ceftriaxone (250 mg stat) for gonorrhoea and a 14-day course of doxycycline (100 mg) or roxithromycin (300 mg) for chlamydia.^{10,12} The patient's sexual partners should also be investigated and treated. Tests for syphilis, HIV and even hepatitis should be performed.

If the infection is secondary to a UTI, an appropriate antibiotic, such as amoxicillin/clavulanic acid 500/125 bd or trimethoprim 300 mg qd for 14 days, should be used.¹² Antibiotic choice can be adjusted according to the urine culture results. Investigation for underlying urinary tract obstruction should be undertaken according to clinical features.

Complications

These include abscess formation, testicular infarction, chronic pain and infertility.

Necrotizing fascitis of the scrotum

Fournier gangrene is a necrotizing fascitis (mixed aerobic/anaerobic infection) of the perineum that often involves the scrotum.^{13,14}

Risk factors for development are as follows:

- Impaired immunity (e.g. from diabetes or steroid use)
- Trauma to the genitalia
- Spreading of ano-rectal infections

Clinical features

- Prodromal symptoms of fever and lethargy for 2 to 7 days
- Intense genital pain, out of all proportion to the clinical findings
- Tenderness associated with oedema of the overlying skin; pruritus may also be present
- Progressive erythema of the overlying skin
- Dusky appearance of the overlying skin; subcutaneous crepitus
- Obvious gangrene of a portion of the genitalia; purulent drainage from wounds

Computed tomography (CT) a may show air along the fascial planes or deeper tissue involvement. Imaging studies should not delay surgical debridement when there is clinical evidence of progressive soft tissue infection.

Treatment of necrotizing fascitis consists of early aggressive surgical debridement of necrotic tissue, broad-spectrum antibiotic therapy, and hemodynamic support as needed.^{13,14}

Traumatic Injury to the Testicle

Blunt trauma

The mobility of the testicle, cremaster muscle contraction and the tough capsule usually protect the testicle from injury. However, a direct blow that drives the testicle against the symphysis pubis may result in contusion or rupture. Typical mechanisms are a direct kick to the groin or handlebar and straddle injuries.¹⁵

The types of injury include the following:

- Scrotal-wall haematomas
- Tunica vaginalis haematoma (haematocoele)
- Intratesticular (subcapsular) haematoma
- Testicular dislocation

The most serious is testicular rupture, where the tunica is split, allowing blood and seminiferous tubules to extrude into the tunica vaginalis. This occurs in up to 50% of blunt trauma. Complete disruption of the testis may occur.

Ultrasound examination is not 100% sensitive in detecting testicular rupture. Conservative management with analgesia, antibiotics and scrotal support may be considered.¹⁶

Indications for exploratory surgery include the following:

- Uncertainty in diagnosis after appropriate clinical and radiographic evaluations
- Clinical findings consistent with testicular injury
- Disruption of the tunica albuginea on ultrasound

- Absence of blood flow on scrotal ultrasound images with Doppler studies
- Expanding or large haematocoeles (e.g. 5 cm or larger), which should be explored
- Smaller haematocoeles, which are often explored because it has been shown that such practice allows for more optimal pain control and shorter hospital stays

It should be noted that 10% to 15% of testicular tumours present after an episode of trauma; therefore any abnormalities on ultrasound examination should be followed to resolution if surgery is not performed.

Early surgical exploration with evacuation of blood clots in the tunica vaginalis and repair of testicular rupture results in a shortened hospital stay and a faster return to normal activity. Conservative management is complicated by secondary infection of the haematocoele, frank acute necrosis of the testis and delayed atrophy due to pressure effects of haematoma. The orchidectomy rate for early exploration is only 9%, compared with 45% for those managed non-operatively.

Penetrating

- This is due to gunshot wounds, stab wounds, self-mutilation and animal bites. Extensive degloving injuries involve accidents with heavy machinery.
- Up to 75% of injuries are associated with additional injury, so a careful exam should be made of the perineum, rectum and urethra.
- Early surgical referral, wound toilet and antibiotics will be the mainstays of treatment.

CONTROVERSIES AND FUTURE DIRECTIONS

- Should all patients with suspected torsion go straight to surgical exploration, and is there is any role for investigations in older or low-probability patients?
- Should all patients with scrotal and testicular injury have routine surgical exploration regardless of ultrasound findings?
- Should attempts at testicular salvage be abandoned in favour of orchidectomy of the affected side following trauma in order to preserve spermatogenesis of the other side?

Full references are available at <http://expertconsult.inkling.com>

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10.3 Renal colic

Sean Arendse

ESSENTIALS

- 1** The lifetime risk of developing kidney stones is 1 in 10 for men and 1 in 35 for women.
- 2** Approximately 75% of all stones are calcium based.
- 3** Management usually comprises adequate analgesia and hydration.
- 4** Computed tomography or intravenous pyelography establishes the diagnosis and evaluates the possibility of obstruction.
- 5** Most stones (90%) are passed spontaneously within 1 month.
- 6** Obstruction, infection and intractable pain necessitate admission to hospital.
- 7** Urology follow-up is essential to minimize further episodes.

Introduction

The risk of kidney stones is about 1 in 10 for men and 1 in 35 for women. Between 4% and 8% of the Australian population suffer from kidney stones at any given time. The rate is about four to five times higher in 'stone belt' areas.¹ It occurs most frequently between the ages of 20 and 50 years, with a male:female ratio of approximately 3:1. About 50% of patients experience only a single episode, but the remaining 50% have recurrent episodes within 5 years.

Most calculi are believed to originate in the collecting system (renal calyces and pelvis) before passing into the ureter. Supersaturation with stone-forming substances (calcium, phosphate, oxalate, cystine or urate), combined with a decrease in urine volume and lack of chemicals that inhibit stone formation (such as magnesium, citrate and pyrophosphate) result in the production of a calculus. In addition to this, infection with urea-splitting organisms that produce an alkaline urinary pH frequently contribute to the growth of 'struvites' or triple phosphate (calcium, magnesium and ammonium phosphate) stones.

Less commonly, mixed stones occur via nucleation with sodium hydrogen, urate, uric acid and hydroxyapatite crystals, providing a core to which calcium and oxalate ions adhere (heterogeneous nucleation).

Approximately 75% of all stones are calcium based, consisting of calcium oxalate, calcium phosphate or a mixture of the two. Ten percent are uric acid based, 1% are cystine based and the remainder are primarily struvite.

Predisposing factors for stone formation include dehydration and low fluid intake,

hypertension, prolonged immobilization, strong family history of nephrolithiasis, hyperparathyroidism, peptic ulcer disease (hyperexcretion of calcium), small bowel disease such as Crohn disease or ulcerative colitis (hyperoxaluria) and gout (hyperuricaemia). Myeloproliferative disorders, malignancy, glycogen storage disorders, renal tubular acidosis and the use of certain medications (calcium supplements, acetazolamide, vitamins C and D and antacids) may also be conducive to nephrolithiasis.

Persistent obstruction of the ureter leads to hydronephrosis of the urinary tract and may precipitate renal failure. Common sites of obstruction are the ureteropelvic junction, pelvic brim and vesicoureteric junction.

Pathophysiology of pain

The mechanisms implicated in the production of the pain associated with renal colic are an increase in renal pelvic pressure, ureteric spasm, local inflammatory effects at the level of the calculus and increased peristalsis and pressure proximal to the calculus.

Acute obstruction of the upper urinary tract from a calculus results in increased pressure in the renal pelvis, which, in turn, induces the synthesis and secretion of renal prostaglandins, in particular PGE₂, which promotes a diuresis by causing dilatation of the afferent arteriole, thus further elevating renal pelvic pressure. Acute obstruction and renal capsular tension are believed to be the cause of the constant ache in the costovertebral angle.

In experiments utilizing isolated ureteric smooth muscle, prostaglandins have also been

shown to increase phasic and tonic contractile activity, resulting in ureteric spasm and severe, colicky pain.

Presentation

The pain of renal colic has been described as the worst pain a person can endure. The classic textbook description is of severe intermittent flank pain of abrupt onset originating from the area of the costovertebral angle and radiating anteriorly to the lower abdominal and inguinal regions. Testicular or labial pain may be present and may suggest the location of the stone as in a low ureteric position. Urinary frequency or urgency often develops as the stone nears the bladder. Nausea and vomiting frequently accompany the pain and about one-third of patients complain of gross haematuria.

Examination

Examination usually reveals an agitated, pacing patient unable to find a comfortable position. Pulse rate and blood pressure may be elevated secondary to the pain. Fever is unusual and suggests infection. The abdominal examination may reveal only signs of an early ileus with hypoactive bowel sounds and a distended abdomen, but it should not be omitted as it is extremely useful in excluding other intra-abdominal or retroperitoneal causes of the pain (such as pancreatitis, cholecystitis, appendicitis or leaking or rupture of the abdominal aorta).

Investigations

Urinalysis usually shows red blood cells, although the absence of red cells in the urine in the setting of colicky flank loin-to-groin pain does not rule out nephrolithiasis, and between 10% and 30% of patients with documented nephrolithiasis do not have haematuria.² Nitrites, leucocytes or micro-organisms in the urine suggest either the complication of an infection or a diagnosis of acute pyelonephritis. Urine culture is thus indicated. Electrolyte studies may demonstrate obstruction or suggest an underlying metabolic abnormality, such as hypercalcaemia, hyperuricaemia or hypokalaemia. A slightly elevated white blood cell count may occur with renal colic, but a count greater than 15,000/mm³ suggests active infection, as does a fever. Renal tract obstruction with concomitant infection is a urological

Box 10.3.1 Differential diagnosis of renal colic

- Renal carcinoma producing blood clots that temporarily occlude the ureter
- Ectopic pregnancy
- Ovarian torsion
- Abdominal aortic aneurysm
- Acute intestinal obstruction
- Pyelonephritis
- Appendicitis
- Diverticulitis
- Narcotic seekers and Munchausen syndrome

emergency and must be treated immediately and aggressively.

A pregnancy test should be performed in all women of childbearing age, as a positive result needs further investigation to exclude ectopic pregnancy.

Many conditions may have a similar presentation to renal colic; examination and investigations should be directed towards confirming the diagnosis of nephrolithiasis and excluding the other conditions in the differential diagnosis ([Box 10.3.1](#)).

Radiological examination

A variety of imaging modalities are used to evaluate renal colic. Their pros and cons are listed in [Table 10.3.1](#).

Most stones (90%) are radiopaque and theoretically should be visible on plain x-ray; if seen, they are irregularly shaped densities on abdominal radiography. However, a plain x-ray alone is not usually sufficient to make the diagnosis of nephrolithiasis, as its sensitivity, of only around 60%, is poor. Phlebitis in the pelvic veins and calcified mesenteric lymph nodes may add confusion, and many small stones may be obscured by the bony density of the sacrum.

Computed tomography (CT) with or without contrast is the first-line test in most centres and has become the adopted gold standard, with high sensitivity (97%) and specificity (96%) for uretero-lithiasis.³ Nearly all stones are opaque on CT; thus the size of the stone and its position can be accurately measured. Other positive findings include perinephric stranding, dilatation of the kidney (hydronephrosis) or ureter and low density of the kidney, suggesting oedema. Low-dose protocols have allowed a drastic reduction in the effective dose, thus limiting the biological risk due to ionizing radiation. Other strategies to contain the radiation exposure include the dual-split bolus dual-energy CT and the adaptive statistical image reconstruction.

The intravenous pyelogram (IVP) was the standard investigative tool for the evaluation of renal colic until the widespread adoption of CT. It establishes the diagnosis of calculus disease

Table 10.3.1 Pros and cons of imaging modalities in renal colic

	Pros	Cons
Computed tomography (CT)	High sensitivity (97%) High specificity (96%) Nearly all stones are opaque Can accurately measure stone size Can detect obstruction Can diagnose other causes of flank pain Can avoid the use of contrast	Exposes patient to radiation, high cost
Abdominal radiography (KUB)	Readily available, fast	Low sensitivity, exposes patient to radiation
Intravenous urography	Provides information regarding size and location of stone and measurement of renal function	Potential for contrast reaction Exposes patient to radiation More time-consuming than CT Cannot exclude alternative diagnoses
Magnetic resonance imaging	Useful in pregnant patients Does not use ionizing radiation Does not use contrast	Not readily available Time-consuming Accuracy may be less than that of intravenous urography (IVU)
Ultrasound	Non-invasive No exposure to ionizing radiation Modality of choice in pregnant patients	Lower sensitivity than IVU Size of stone cannot be accurately measured May not be readily available, requires a skilled operator

KUB, Kidney, ureter, bladder.

in 96% of cases and determines the severity of obstruction. Classic findings of acute obstruction include a delay in the appearance of one kidney, a dilated ureter and a dilated renal pelvis. The use of IVP has declined more recently, likely due to worse quality than non-contrast CT, lack of bowel preparation, being potentially nephrotoxic from contrast agents, serious allergic and anaphylactic reactions and radiation exposure. There is currently a worldwide shift away from IVP toward using non-contrast CT to evaluate ureteric colic.⁴

Ultrasonography is a useful, safe and a non-invasive alternative when renal function is impaired, risk from radiation is high (e.g. pregnancy) or contrast media are contraindicated. It can identify the stone and its location and demonstrate proximal obstruction—such as hydroureter or a dilated pelvis—as well as the size and configuration of each kidney. Unfortunately, however, it cannot indicate the size of the stone. Ultrasound has significantly lower sensitivity than intravenous urography (IVU) and misses more than 30% of stones. However, point-of-care ultrasound in the hands of appropriately trained emergency physicians in cases of moderate to high pre-test probability of ureteric calculi (as calculated by tools such as the STONE score) can be diagnostic of stone disease.⁵

Magnetic resonance imaging (MRI) can easily depict a dilated ureter and demonstrate the level of obstruction without using ionizing radiation or contrast, but the accuracy of MRI for stones may be lower than that of IVU, as its spatial resolution is often not high enough to detect small stones. When used in combination with ultrasound, it

may have a role in the evaluation of loin pain, especially in the pregnant patient; however, it is expensive, time-consuming and usually not readily available to most emergency departments.

Management

As 90% of stones are passed spontaneously, the most urgent therapeutic step is relief of pain along with the provision of adequate hydration and anti-emetics. Intramuscular non-steroidal anti-inflammatory drugs (NSAIDs) offer the most effective sustained analgesia for renal colic in the emergency department and seem to have fewer side effects than other forms of analgesia.⁶

At 30 minutes, NSAIDs are equivalent to opioids or paracetamol in the relief of acute renal colic pain. There has been less vomiting and fewer requirements for rescue analgesia with NSAIDs compared with opioids. Patients treated with NSAIDs as compared with paracetamol required less rescue analgesia.⁷ Common available alternative options include NSAIDs delivered orally or per rectum. Opiates can be used for breakthrough pain.

Buscopan, an antimuscarinic agent used to treat smooth muscle spasm, has been shown to decrease ureteric activity to some degree in 80% of the subjects studied. However, one study comparing it with an NSAID found that buscopan was less effective and associated with significant side effects, including dry mouth, photophobia, urgency, urinary retention and constipation, thus significantly limiting its use in renal colic.⁸

Box 10.3.2 Indications for hospital admission in renal colic

- Presence of infection
- Deteriorating renal function
- Persistent pain requiring parenteral narcotics
- Stone greater than 5 mm in diameter
- Extravasation of dye (uncommon)

The role of alpha agonists in renal colic continues to be hotly debated. Although there is some evidence that they may reduce time to stone expulsion, particularly in the case of distal ureteric calculi, there is little evidence for their use in the emergency department setting.^{9,10}

Intravenous crystalloid should be administered to ensure a urine volume of 100 to 200 mL/h in those unable to tolerate oral fluids.

The size, shape and site of the stone at initial presentation are factors that determine whether a stone will pass spontaneously or require removal. Stones less than 5 mm in diameter in patients without associated infection or anatomic abnormality pass within 1 month in 90% of cases, stones 4 to 6 mm in diameter pass 50% of the time, but only 5% of stones larger than 7 mm pass; hence these usually require elective surgical removal. The overall passage rate for ureteral stones is as follows:

- Proximal ureteral stones, 25%
- Mid-ureteral stones, 45%
- distal ureteral stones, 70%.

Disposition

Most patients with renal colic can be discharged with oral analgesia (paracetamol and NSAIDs), hydration and a referral for outpatient urology.

Indications for admission to hospital are listed in **Box 10.3.2**.

Further intervention is required if obstruction with hydro-nephrosis is present, the stone is a large stag horn calculus or the patient continues to have pain and no stone is passed within 2 to 3 days. A percutaneous nephrostomy allows drainage of an obstructed kidney until the blockage can be removed, either by ureteroscopic procedures for low stones or by open surgery for large or infected stones. Extracorporeal shockwave lithotripsy is preferred for single or small (<2 cm) stones that are otherwise uncomplicated, as it has minimal complications and morbidity.

Urology follow-up is essential for all patients, for elective removal of stones when complications have not ensued and for the prevention of recurrence. Indications for stone removal include stone diameter greater than 7 mm, stone obstruction associated with infection, single kidneys with obstruction and bilateral obstruction.

Precautions

Renal colic, having minimal findings on examination, is a common presentation offered by those seeking narcotics or with Munchausen syndrome; treating physicians should be aware of this. However, it is essential to give analgesia to patients suffering from renal colic, and it is preferable to give patients analgesia unnecessarily rather than cause unnecessary suffering. Features suggesting narcotic seeking are discussed in [Chapter 21.5](#).

Conclusion

Renal colic is an acutely distressing medical condition that requires a careful evaluation of symptoms and signs to ensure timely analgesia, recognition of other causes of acute abdominal pain and avoidance of inappropriate narcotic usage.

CONTROVERSIES AND FUTURE DIRECTIONS

- Controversies in the management of renal colic relate largely to analgesia. Traditionally it has been taught that parenteral narcotics provide fast and effective pain relief; however, with the advent of injectable NSAIDs, some argue that these should be the first line of care.

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11.1 Diabetes mellitus and hypoglycaemia: an overview

Anthony F.T. Brown

ESSENTIALS

- 1** Type I diabetes is characterized by pancreatic beta cell destruction with an absolute insulin deficiency, usually but not exclusively associated with autoimmune damage.
- 2** Type II diabetes results from a progressive insulin secretory deficiency on the background of insulin resistance.
- 3** Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycaemic state (HHS) are both life-threatening acute complications of diabetes mellitus.
- 4** The aim of excellent long-term blood sugar control is an HbA1c (glycated haemoglobin) level of less than 7.5% without frequent disabling hypoglycaemia for the prevention of microvascular disease, and 6.5% in those at increased risk of arterial disease.
- 5** Oral antidiabetic drug groups include the sulphonylureas, biguanide metformin, alpha-glucosidase inhibitor acarbose, the thiazolidinediones pioglitazone and rosiglitazone, and dipeptidyl peptidase 4 (DDP-4) inhibitors, such as sitagliptin.
- 6** Optimal blood sugar control aids in reducing the incidence of multisystem diabetic complications.
- 7** Hypoglycaemic coma requires immediate treatment with intravenous glucose. Intramuscular glucagon 0.5 to 2.0 mg may be used if liver glycogen stores are adequate, and can be given pre-hospital.

DIABETES MELLITUS

Classification system and diagnostic criteria

The diagnosis and management guidelines for diabetes were revised in 2016 by the American Diabetes Association.¹ The classification of type I and type II diabetes mellitus was retained, with

the recommended criteria for the diagnosis of diabetes as a fasting plasma glucose of 7 mmol/L or greater (fasting is defined as no calorie intake for ≥ 8 hours), a random plasma glucose of over 11 mmol/L associated with polyuria, polydipsia and weight loss, or an HbA1c (glycated haemoglobin) level of $\geq 6.5\%$. The oral glucose tolerance test is no longer routinely recommended.

Aetiology

The exact aetiology of diabetes is unclear. Type I diabetes is characterized by pancreatic beta cell destruction with an absolute insulin deficiency usually, but not exclusively, associated with autoimmune damage from a range of antibodies including islet cells (ICA), glutamic acid decarboxylase, insulin, tyrosine phosphatases and zinc transporter (ZnT8). Genetic and environmental factors are implicated, such as some human leucocyte antigen (HLA) types (most Caucasian patients are HLA-DR3 or DR4 or both), and abnormal immune responses, such as following viral infection. Certain genes are also implicated as co-contributors, particularly sites on chromosomes 6, 7, 11, 12, 14 and 18.

Type II diabetes is far more common, and results from a progressive insulin secretory deficiency on the background of insulin resistance.¹ Genetic factors are implicated by strong familial aggregation of cases, and environmental factors in the context of genetic susceptibility, including obesity and diet. Populations with an increasing predisposition to type II diabetes encompass East Asians including China and the Western Pacific.

Although type I diabetes occurs most frequently among Caucasians throughout the world, diabetes in Australia is three times more common in the Aboriginal community. Other groups with a high prevalence include Pacific Islanders and Native Americans.

Diabetes secondary to other conditions

Diabetes mellitus may be secondary to conditions that damage the exocrine pancreas

11.1 DIABETES MELLITUS AND HYPOGLYCAEMIA: AN OVERVIEW

Table 11.1.1 Pharmacokinetic characteristics of currently available human insulins

Insulin	Onset of action	Peak of action	Duration of action
Lispro	5–15 min	1–2 h	4–5 h
Regular	30–60 min	2–4 h	6–8 h
NPH	1–2 h	5–7 h	13–18 h
Glargine	1–3 h	4–8 h	13–20 h
Detemir	2–4 h	8–10 h	18–30 h

including chronic pancreatitis, carcinoma of the pancreas and pancreatectomy, haemochromatosis, cystic fibrosis, pregnancy (gestational) and endocrinopathies, such as Cushing syndrome, acromegaly, phaeochromocytoma and glucagonoma.²

Drug-induced diabetic state

Certain drugs can impair glucose tolerance or cause overt diabetes mellitus. These include glucocorticoids, the oral contraceptive pill, thiazide diuretics at higher doses, clozapine, tacrolimus, sirolimus and ciclosporin, pentamidine (which may also cause severe hypoglycaemia) and HIV protease inhibitors.

Emergency presentations of a high blood sugar

Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycaemic state (HHS) are both life-threatening acute complications of diabetes mellitus. Although important differences do exist, the pathophysiology and treatment are similar. DKA is usually seen in type I diabetes and HHS in patients with type II, but both complications can occur in type I and type II diabetes. See Chapter 11.2 for the diagnosis and management of DKA and HHS.

General management of diabetes mellitus

Aims of long-term blood sugar control

The aim of optimal long-term blood sugar control is an HbA1c (glycated haemoglobin) level of less than 7.5% without frequent disabling hypoglycaemia for the prevention of microvascular disease, and 6.5% in those at increased risk of arterial disease.³ This should be represented by a pre-prandial blood glucose level of 4.0 to 7.0 mmol/L and a post-prandial blood glucose level of less than 9.0 mmol/L.

Insulins

Insulin was first administered to humans in 1922. Animal insulins (bovine, porcine) have been used

for many years but, in the 1980s, human insulins became commercially available. Today, with the widespread availability of human insulins, animal insulins are of historical interest only.

Types of insulins

Table 11.1.1 lists the different types of insulins and the important parameters of each type. Mixtures of short- and intermediate-acting insulins are also available: Humulin 30/70 (30% regular/70% NPH) and Humalog Mix50 (50% lispro protamine/50% insulin lispro).

Antidiabetic drugs

Two major groups of oral hypoglycaemic agents used in the management of type II diabetes are the sulphonylureas and the biguanides. The sulphonylurea group of drugs acts by stimulating the pancreatic secretion of insulin, and the biguanide metformin acts by suppressing hepatic glucose production and enhancing the peripheral use of glucose. It is the first-choice medication, particularly in the overweight patient.

Other oral agents now available for the treatment of diabetes include the alpha-glucosidase inhibitor acarbose, which acts on the gastrointestinal tract to interfere with carbohydrate digestion, but flatulence and diarrhoea may be troublesome. The thiazolidinediones, such as pioglitazone and rosiglitazone, act primarily by reducing insulin resistance, thereby enhancing the effect of circulating insulin. Rosiglitazone increases the risk of myocardial infarction and cardiovascular deaths, and thus should be avoided in ischaemic heart disease.⁴ All thiazolidinediones must be avoided in people with moderate or severe heart failure. Finally, the dipeptidyl peptidase 4 (DDP-4) inhibitors, such as sitagliptin, inhibit DDP-4 to prolong the action of the incretin hormones.

Other non-diabetic drugs

Angiotensin-converting enzyme inhibitors delay the onset of diabetic nephropathy even in normotensive patients with diabetes. Statins are important in the strict treatment of dyslipidaemia in diabetic patients.

Box 11.1.1 Causes of hypoglycaemia

Diabetic patients

- Medication change or error, particularly with insulin or oral hypoglycaemic sulphonylurea (very rarely metformin)
- Inadequate dietary intake
- Excessive calorie use, such as exercise

Any patient

- Insulin, sulphonylurea, salicylates, β-blockers, quinine, chloroquine, valproic acid, pentamidine (note ingestion of any these may be accidental, deliberate or malicious)
- Ethanol
- Liver disease
- Sepsis, other critical illness
- Malnourishment, including anorexia nervosa
- Post-gastrointestinal surgery 'dumping syndrome'
- Adrenal insufficiency
- Hypopituitarism
- Islet cell tumour/extrapancreatic tumour
- Tumour-related, such as mesenchymal, epithelial or endothelial tumours
- Artefact 'Munchausen syndrome'

DIABETIC HYPOGLYCAEMIA

Hypoglycaemia is more common in type I diabetes. The critical plasma level at which hypoglycaemia manifests varies between different individuals, but symptoms are likely below a plasma glucose of 3.5 mmol/L. Precipitants include exercise, a late meal, inadequate carbohydrate intake, errors of insulin dosage and ethanol ingestion.

Hypoglycaemia may also occur in the non-diabetic patient, precipitated by a variety of conditions (Box 11.1.1).⁵

Clinical features

Hypoglycaemia produces neurological and mental dysfunction from tremor, sweating and anxiety to cognitive impairment, seizures and coma. Less commonly, it can present with hypothermia, behavioural changes and transient neurological deficits. In some instances, hypoglycaemia is relatively asymptomatic.

Management of hypoglycaemic coma

- The ABC approach is important in the patient with coma.
- Give 50 mL of 50% glucose intravenously initially after taking a blood sugar level.

Further glucose administration is often necessary, such as an infusion of 10% dextrose.

- Alternatively give 0.5 to 2 mg of glucagon intramuscularly when venous access has not been established or has failed. Glucagon is unhelpful in the patient with liver disease and depleted glycogen reserves.

CONTROVERSIES

- Non-parenteral insulin delivery, such as nasal, oral or intra-pulmonary.
- The combination use and risk–benefit profile of newer antidiabetic drugs, such as the thiazolidinediones and DDP-4 inhibitors.

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11.2 Diabetic ketoacidosis and hyperosmolar, hyperglycaemic state

Anthony F.T. Brown

ESSENTIALS

1 Diabetic ketoacidosis (DKA) consists of the triad of ketonaemia, hyperglycaemia and acidaemia—a high anion-gap metabolic acidosis.

2 DKA is caused by insulin omission or error, intercurrent illness (including infection) or is a presenting feature of new diabetes.

3 Key management components of DKA include:

- fluids (0.9% normal saline) to replace deficits of sodium of 7 to 10 mmol/kg and water 100 mL/kg
- soluble insulin infusion at 0.1 unit/kg/h to a maximum of 6 units/h to suppress ketogenesis, reduce blood sugar and help correct the electrolyte abnormalities
- potassium replacement, providing the serum (potassium) is less than 5.5 mmol/L and there is urine output (note anuria is rare in DKA)
- education—all patients on insulin need to know the ‘sick day rules’, plus be familiar with regular home testing for capillary blood sugar.

4 Meticulous monitoring and documentation of treatment in DKA are essential.

5 Hyperosmolar hyperglycaemic state (HHS) is characterized by hypovolaemia, marked hyperglycaemia (>30 mmol/L) without ketonaemia or acidosis, and a raised osmolality usually >320 mOsmol/kg.

6 Mortality and morbidity of HHS are greater than with DKA, usually related to the older age of patients, co-morbidities and complications, such as stroke.

7 Treatment of HHS is similar to DKA except:

- lower dose insulin infusion rate is used at 0.05 unit/kg/h
- this infusion rate is titrated against the serum osmolarity rather than ketoacids
- 0.9% normal saline is used and *only* changed to half normal (0.45%) saline if the osmolality and glucose are not declining
- low-molecular-weight heparin (LMWH) thromboprophylaxis is indicated.

Introduction

Diabetic ketoacidosis (DKA) is an acute, potentially life-threatening complication in an insulin-independent diabetic and in some type II diabetics. It consists of the triad of ketonaemia, hyperglycaemia and acidaemia—a high anion-gap metabolic acidosis. Although DKA is preventable, its prevalence and suboptimal management may highlight shortfalls in the quality of care for patients with diabetes. The mortality rate in developed countries has dropped to <1%.

Hyperosmolar hyperglycaemic state (HHS) is characterized by hypovolaemia, marked hyperglycaemia (>30 mmol/L) *without* ketonaemia or acidosis, and a raised osmolality usually >320 mOsmol/kg. It comes on more insidiously and has a worse prognosis with an increased mortality of around 15% to 20% and greater morbidity, in part related to underlying chronic medical disorders, and often occurring in an older population.

Epidemiology and aetiology

An annual incidence of DKA of approximately 1:170 patients with type I diabetes is reported, or 2 episodes per 100 patient years of diabetes, for a prevalence of 4.6 to 8 episodes per 1000 patients with diabetes.^{1,2} The mortality rate in developed countries is under 1% most commonly due to cerebral oedema particularly in children/young adults, severe hypokalaemia, adult respiratory distress syndrome (ARDS) and co-morbid conditions such as sepsis or acute myocardial infarction (MI).

DKA may be the presenting feature of new diabetes mellitus (3% to 25% DKA), but it more

11.2 DIABETIC KETOACIDOSIS AND HYPEROSMOLAR, HYPERGLYCAEMIC STATE

usually follows intercurrent illness in a patient with known autoimmune type I diabetes (35% DKA); when there has been an insulin error with poor compliance or inadequate insulin (30% DKA); and/or for instance an insulin infusion pump blockage. A variant of type II diabetes is also ‘ketosis-prone (type II) diabetes’, usually in the obese with a strong family history. This was originally described in Africans and African Americans, but is now noted worldwide.

Pathogenesis

DKA arises from an absolute or relative lack of insulin accompanied by an increase in counter-regulatory hormones, such as glucagon, cortisol and growth hormone.^{1,3} Insulin absence leads to increased hepatic gluconeogenesis and glycogenolysis, with an incomplete lack of insulin related to greater hyperosmolarity (in HHS). Lack of insulin and excess counter-regulatory hormones increase lipolysis and free fatty acid production as an alternate energy source. This leads to subsequent ketone body formation produced from acetyl coenzyme A, mainly in hepatic mitochondria, including acetone, beta-hydroxybutyrate and acetoacetate, and a reduced ability to prevent ketonaemia.

HHS is the other end of the hyperglycaemia spectrum from DKA, occurring with a relative rather than an absolute deficiency of insulin leading to a greater level of hyperglycaemia, therefore higher hyperosmolarity than is seen in DKA. The degree of dehydration is greater (typically 10% to 15% body weight), but significant ketosis does not occur. HHS is more insidious in onset than DKA and patients with HHS are typically older with pre-existing type II diabetes. However, HHS is seen in young adults and even teenagers.

Clinical features

Malaise and fatigue on a background of polyuria, polydipsia, weakness and fatigability are common, but gastrointestinal symptoms, such as nausea, vomiting and abdominal pain, may predominate.³ Lack of a history of diabetes does not rule out the diagnosis of DKA, as it may be a first presentation, often presaged by recent, unexplained rapid weight loss.

Laboured, sighing respirations with an increased rate and depth, known as Kussmaul breathing, are characteristic of DKA in association with dehydration causing decreased tissue turgor, a dry mouth and sweet foetor of pear drops (ketotic), which is not always noticed. The conscious level may be reduced, but coma is rare.

Look carefully for signs of an underlying precipitating cause. This can include chest, urine or skin infection, such as boils, as well as meningitis or an acute abdomen, although non-surgical

upper abdominal pain is common in DKA. A silent MI is another potential cause. In those with HHS, look out for the complications of acute MI, stroke or arterial thrombosis.^{4,5}

The urine output should be measured regularly, which does not always require urinary catheterization. Likewise, invasive haemodynamic monitoring should not be instituted as a ‘routine’ for patients with DKA or HHS. It should be reserved for severe cases and those who fail to respond, or in the elderly who are at risk of fluid overload. In addition, venous blood gases are sufficient to monitor progress in DKA, rather than repeated arterial sampling.

Diagnostic criteria

Diabetic ketoacidosis

- Metabolic acidosis with pH <7.3 or serum bicarbonate <15 mmol/L.
- Ketonaemia >3.0 mmol/L, or marked ketonuria >2+ on dipstick (note urinalysis may miss 3-beta hydroxybutyrate early).
- Hyperglycaemia with blood glucose >11 mmol/L.

Hyperosmolar hyperglycaemic state

Note that there is no precise definition of HHS, but it is characterized by⁵:

- Hyperglycaemia. Serum glucose >30 mmol/L.
- Hyperosmolarity. Serum osmolality >320 mOsmol/kg. (If unable to measure regularly, use an approximation of the osmolarity = [2 × Na + glucose + urea].)
- Significant dehydration with hypovolaemia.
- Minimal ketonaemia (<3.0 mmol/L) with no more than 1+ ketonuria on urinalysis.
- pH >7.30, bicarbonate >15 mmol/L.

Typical deficits per body weight

Diabetic ketoacidosis

- Water 100 mL/kg
- Sodium 7 to 10 mmol/kg
- Potassium 3 to 5 mmol/kg.

Hyperosmolar hyperglycaemic state

- Water 100 to 220 mL/kg
- Sodium 5 to 13 mmol/kg
- Potassium 4 to 6 mmol/kg.

Investigations

Blood testing

Measure both glucose and ketones in capillary blood hourly until they are near to the normal range. Or measure serum urea and electrolytes (U&Es), glucose and pH initially hourly, then 2-hourly once the serum glucose and capillary glucose are in agreement. Venous blood

sampling is acceptable rather than repeated arterial punctures, but an intra-arterial line may be sited for repeat blood sampling (although it is not essential).

Send blood cultures if there is evidence of an underlying septic process, but remember that a mild leucocytosis is common in DKA, and should not be interpreted as signifying infection.

Urinalysis

DKA is highly likely in the presence of glycosuria and ketonuria in an unwell patient. Send the urine for microscopy and culture to rule out a urinary tract infection. Check a beta-HCG.

Electrocardiograph

Perform an early electrocardiograph to look for T-wave changes as a first indicator of hyperkalaemia (tall and peaked) or hypokalaemia (flat or inverted), or a clinically silent MI as a precipitant of HHS or DKA.

Point-of-care testing

Point-of-care testing for blood glucose and ketones, such as beta-hydroxybutyrate, is helpful at triage and to monitor the response to treatment.

Differential diagnosis of diabetic ketoacidosis

Other causes of high anion-gap (>16) metabolic acidosis include:

- alcoholic or fasting ketoacidosis
- lactic acidosis (multiple causes)
- uraemia
- methanol, ethylene glycol (note ethanol predominantly leads to a lactic acidosis)
- salicylate, iron, isoniazid ingestion.

Other causes of hyperglycaemia include:

- HHS
- drugs, such as corticosteroids, octreotide, thiazide diuretics, ritonavir, diazoxide and atypical antipsychotics (clozapine, olanzapine, risperidone, quetiapine – these may actually precipitate DKA soon after commencement, even in the absence of weight gain)⁶
- critical illness
- endocrine, such as Cushing syndrome, acromegaly, phaeochromocytoma, glucagonoma, VIPoma.

Management

Diabetic ketoacidosis

The treatment of DKA is rigorous and requires careful monitoring of the patient, both clinically and biochemically. Ideally, all observations and results are entered onto a purpose-designed record sheet, such as an integrated care pathway that includes data recording and guidance.⁷

11.2 DIABETIC KETOACIDOSIS AND HYPEROSMOLAR, HYPERGLYCAEMIC STATE

Table 11.2.1 Replacement normal saline fluid regimen in a well 70 kg patient^a with diabetic ketoacidosis, who is not haemodynamically compromised/in shock

Litre	Time (hours from starting treatment)
First at 1000 mL/h	0–1
Second at 500 mL/h+K	1–3
Third at 500 mL/h+K	3–5
Fourth at 250 mL/h+K	5–9
Fifth at 250 mL/h+K	9–13
Reassess cardiovascular status after 12 h and adjust rate accordingly	
Sixth at 166 mL/h+K	13–19

^aIn a small (<70 kg), young adult (18 to 25 years) adopt a slower rate initially, with total volume replacement over 24 to 48 hours to reduce the risk of cerebral oedema.

K, Potassium.

Severe diabetic ketoacidosis

Severe DKA necessitating intensive management includes a venous or arterial pH <7.1, ketonaemia >6 mmol/L, bicarbonate <5 mmol/L, hypokalaemia on admission (<3.5 mmol/L), Glasgow coma scale (GCS) <12, systolic blood pressure (BP) <90 mmHg and SaO₂ <92% on room air.

Fluid regimen

Intravenous fluids should be started within 30 min of the patient's arrival in the emergency department (ED). A shocked patient should receive a fluid bolus on arrival to restore perfusion, although care is needed in patients with co-morbidities, such as the elderly with heart or renal impairment, to avoid fluid overload.

Fluid rate

Give patients who are not shocked 1 L 0.9% normal saline over 1 hour, then at a rate of 500 mL/h for 4 hours with added potassium, then 250 mL/h for the next 8 hours, again with added potassium.¹ A suggested fluid regimen is shown in Table 11.2.1 that delivers 5 L of IV fluid over the first 13 hours of treatment.

Most intravenous fluid regimens recommend replacing the total volume deficit (often 10% of body weight) by 24 hours. However, in a patient with significant co-morbidities, it is prudent (although unproven) to aim to correct half the fluid deficit in the first 24 hours and the remainder in the next 24 hours. Likewise, adopt a slower rate initially in a child/young adult aged 18 to 25 years with the total volume replaced over 24 to 48 hours to reduce the risk of cerebral oedema (see Table 11.2.1).¹

Cerebral oedema

The incidence of cerebral oedema is greatest in children under 12 years, and becomes rare over the age of 20 years. It may relate to a lower pH/PaCO₂ and a higher potassium and urea at

presentation, and smaller increases in serum sodium. The aetiology remains unclear and may also relate to cerebral hypoperfusion followed by reperfusion, with an increased risk associated with early (in first hour) insulin administration (odds ratio [OR] 12.7) and large volumes of fluid in the first 4 hours (OR 6.55).⁸ Headache is the earliest feature, followed by lethargy and a decreased conscious level.

Choice of fluid

There are no data from randomized controlled trials to support the choice of one crystalloid over another in the treatment of DKA. The risk of hyperchloraemic acidosis from the use of large volumes of normal saline with renal vasoconstriction and slowing of resolution of acidosis is not clinically significant. In addition, colloids are a less physiological replacement for electrolyte losses and are not recommended.

Addition of 10% dextrose

If serum (glucose) falls to <15 mmol/L, add 10% dextrose at 125 mL/h alongside the 0.9% saline infusion, with continuance of the insulin infusion until the electrolyte and volume losses have been replaced and the ketoacidosis/ketonaemia has been cleared.

Insulin

An intravenous insulin infusion should be started within 60 minutes of the patient's arrival in the ED.

Insulin infusion regimen

A standard regimen is an infusion of soluble insulin, made up by adding 50 units of soluble insulin to a total of 50 mL in 0.9% saline to produce a solution containing 1 unit/mL. Do not start this insulin infusion until the serum (potassium; K) has been checked to make sure it is not below the lower limit of the reference range; that is, it

should be greater than 3.4 mmol/L. If it is below this, begin the IV fluids with potassium first, prior to commencing the insulin infusion.

Run the infusion at an initial rate of 0.1 units/kg/h (to a maximum of 6 units/h). Adjust the rate to reduce the serum (glucose) by around 3 mmol/L/h, with a rise in the serum (bicarbonate) of at least 3 mmol/L/h, and/or a fall in (ketones) of at least 0.5 mmol/L/h.

When the serum (glucose) is less than 15 mmol/L, halve the insulin infusion rate and then adjust it to maintain the serum (glucose) between 9 and 14 mmol/L⁷, as well as adding 10% dextrose at 125 mL/h to the normal saline IV until the ketonaemia is cleared (discussed earlier).

Remember when prescribing insulin always to write 'units' in full rather than as 'u', as the latter is too easily confused with a 0 (zero) and a 10-fold dose increase can be given in error.

Initial hypokalaemia

Severe hypokalaemia is associated with arrhythmias and sudden death in DKA. Replace the potassium prior to commencing any insulin if below 3.4 mmol/L (discussed earlier).

Switching to intermittent insulin

Switching from an insulin infusion to intermittent insulin is unlikely to occur until the patient is on the medical ward. If ED staff do supervise cessation of an insulin infusion, ensure the first subcutaneous insulin dose is given at least 1 h before the infusion is stopped in association with a meal, providing all the following criteria have been met before ceasing the insulin infusion:

- serum (glucose) <11 mmol/L
- pH >7.30
- serum ketones <0.6 mmol/L
- serum bicarbonate >15 mmol/L
- patient is eating and drinking normally, with a normal conscious level.

Potassium replacement

Initial hyperkalaemia followed by hypokalaemia are the most common life-threatening electrolyte problems seen in DKA. Therefore the serum (K) must be monitored closely and treatment planned to treat either condition rapidly, particularly the risk of hypokalaemia. A typical total body deficit of potassium in DKA is 3 to 5 mmol/kg.^{1,2}

Hyperkalaemia from intracellular shift from the acidosis and lack of insulin seen in the early phase of DKA may cause life-threatening dysrhythmias. This hyperkalaemia rapidly resolves soon after fluid and insulin commencement.

Conversely, add potassium to intravenous fluids once the serum (K) is below 5.5 mmol/L and the patient is passing urine. However, do not add potassium to the first fluid bolus infused rapidly for volume resuscitation.

11.2 DIABETIC KETOACIDOSIS AND HYPEROSMOLAR, HYPERGLYCAEMIC STATE

Infusion rate

Replacing potassium at 10 to 20 mmol/h is usually sufficient, with the rate adjusted to the serum (K) measurement, with the aim of maintaining serum (K) in the range 4 to 5 mmol/L. Use pre-mixed intravenous potassium in fluid bags with an intravenous fluid infuser to avoid dosing or infusion rate errors.

Education and prevention

Arguably, every episode of DKA represents a failure of patient education, except for those patients in whom DKA is the first presentation of diabetes mellitus. All patients treated with insulin must understand 'sick day rules' to increase their normal insulin dose by 4 units or more when they have an intercurrent illness, even if they are not eating, as their insulin requirements will rise. Stopping insulin because a person is 'not eating properly' is all too common and an entirely avoidable precipitant of DKA.

Hyperosmolar, hyperglycaemic state

The management of HHS is similar to that of DKA, although patients are older, the water deficit is considerably greater, the sodium and potassium deficits greater and the overall mortality and morbidity higher. Focal or global neurological changes may occur, including an altered conscious level, coma, seizures and stroke (cause or effect).

Give 0.9% normal saline for initial volume resuscitation, with insulin by intravenous infusion and potassium supplementation to maintain serum (K) between 4 and 5 mmol/L, similar to DKA. In addition, the fall in serum osmolality is monitored as a marker of response to treatment.

Severe hyperosmolar hyperglycaemic state

Severe HHS necessitating intensive management includes an osmolality >350 mOsmol/kg, sodium >160 mmol/L, creatinine >200 µmol/L or urine output <0.5 mL/kg/h, hypokalaemia on admission (<3.5 mmol/L), GCS <12, systolic BP <90 mm Hg, Sa_O₂ <92% on room air and a venous or arterial pH <7.1. (Look for other causes, such as a concomitant lactic acidosis.)

Management differences in hyperosmolar hyperglycaemic state (to diabetic ketoacidosis)

Insulin infusion

Start fluid replacement first, before commencing an insulin infusion at 0.05 units/kg/h to a

maximum of 3 units, as a patient with HHS may be more sensitive to insulin, plus the replacement of fluid alone will lead to a fall in serum glucose. Aim for a rate of decline in serum osmolarity of less than 3 mOsmol/kg/h and in blood glucose of not more than 5 mmol/L/h.

Reduce the insulin infusion rate when the serum (glucose) drops to 15 to 18 mmol/L, to maintain serum (glucose) in the range 10 to 15 mmol/L until the serum osmolarity is less than 315 mOsmol/kg. Complete normalization of osmolarity and electrolytes may take up to 72 hours.

Fluid choice

Use 0.9% normal saline as the principal fluid to restore circulation volume.⁵ An initial rise in serum sodium may occur due to a shift of water intracellularly from a lowering of the blood glucose, which is not an indication to use a more hypotonic solution (normal saline is already relatively hypotonic compared to serum in HHS).

Only change to 0.45% half-normal saline if the serum osmolality and blood sugar are not reducing. Avoid a rapid fall in serum sodium, which should not exceed 10 mmol/L/24 h.⁵

Other considerations

- Shock may be partly cardiogenic rather than due to volume depletion. Thus invasive monitoring, central venous access and the use of vasoactive drugs rather than fluid alone will be required in this circumstance.
- Give LMWH for thromboprophylaxis as there is a higher risk of developing venous thromboembolism including during the 3 months post-hospital discharge.⁹

Miscellaneous issues

There are no data to support the use of phosphate or magnesium in the treatment of DKA or HHS, despite there often being hypophosphataemia and hypomagnesaemia.

Heparin thromboprophylaxis is not used routinely in DKA, nor are antibiotics in the absence of a focus of infection or sepsis, even though it is common for the white cell count to be mildly elevated.

Sodium bicarbonate should never be used in DKA if the pH is greater than 7.0 and even below that level its value is unproven. Significant disadvantages of giving IV bicarbonate are a rapid fall in serum (K), worsened intracellular acidosis, reduced tissue oxygen delivery, a delay in clearing ketones and a possible association with cerebral oedema.

CONTROVERSIES

- Choice and rate of intravenous fluid replacement and its impact on the unexpected but devastating development of cerebral oedema (usually seen in children).
- Titrating insulin use against β-hydroxybutyrate rather than serum glucose.
- Point-of-care measurement of beta-hydroxybutyrate is becoming more widespread, although its precise role in the care of patients with DKA is yet to be determined (discussed earlier).
- Use of ultrafast-acting insulin analogues subcutaneously in the treatment of DKA in children.

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11.3 Thyroid and adrenal emergencies

Andrew Maclean

ESSENTIALS

- 1** The thyroid and adrenal emergencies that pose an acute threat to life are thyroid storm, myxoedema coma and acute adrenal insufficiency. Diagnosis of these conditions requires a high index of suspicion and treatment frequently must be initiated on clinical rather than laboratory diagnosis.
- 2** Common features of thyroid storm are fever, alteration in mental state, cardiovascular complications, such as tachyarrhythmias and cardiac failure, and signs of hyperthyroidism. Treatment is with β -blockers, drugs that block thyroid hormone synthesis and release, and corticosteroids.
- 3** Common clinical signs of myxoedema coma are an alteration in conscious state, hypothermia and features of hypothyroidism. Treatment is with intravenous tri-iodothyronine and corticosteroids.
- 4** The most important clinical feature of acute adrenal insufficiency is hypotension unresponsive to fluid therapy. Although hyponatraemia and hyperkalaemia are usual in acute adrenal insufficiency, serum electrolytes may be normal. Treatment is with intravenous corticosteroid replacement on suspicion of the diagnosis.
- 5** General supportive measures and treatment of the precipitating event must parallel the specific treatment regimen in all of these conditions.

Thyroiditis may be acute (rare), subacute or chronic. Inflammation of the thyroid is associated with damage to follicles with the release of thyroid hormone. Subacute thyroiditis (de Quervain syndrome, also known as subacute granulomatous) may follow a viral infection and is typically painful, with localized tenderness and neck pain, sometimes with odynophagia.

Multinodular goitre occurs in areas of both iodine deficiency and sufficiency, indicating that a multiplicity of genetic and environmental factors is at play. Fibrosis, hypercellularity and colloid cysts are the main pathological findings.

Epidemiology

Graves disease accounts for at least 80% of cases of thyrotoxicosis.¹ The prevalence increases in areas with high iodine intake. Graves disease has a strong female predominance, affecting up to 2% of all women.¹ Thyrotoxicosis due to Graves disease usually occurs in the second to fourth decades of life, whereas the prevalence of a toxic nodular goitre increases with age.

Clinical features

The signs and symptoms of hyperthyroidism are secondary to the effects of excess thyroid hormone in the circulation. The severity of the signs and symptoms is related to the duration of the illness, the magnitude of the hormone excess and the age of the patient. These symptoms and signs are summarized in Box 11.3.1, which illustrates the wide spectrum of possible clinical features.

A comprehensive history and physical examination should be performed, with particular attention to weight, blood pressure, pulse rate

Introduction

Four conditions are covered in this chapter: thyrotoxicosis, hypothyroidism, hypoadrenal states and hyper adrenal states. Patients with the first three present relatively infrequently to emergency departments (EDs), but all four conditions are potentially fatal if they go unrecognized and untreated. The most common cause of Cushing syndrome is exogenous steroid administration. An inability to produce endogenous steroids in times of physiological stress and therefore the potential for adrenal insufficiency occurring with insufficient replacement therapy must be considered in such patients.

suppress TRH and TSH production, and act at a cellular level, binding with nuclear receptors to enable gene expression and protein synthesis. Thyroid hormone may also have an effect on modulating cellular metabolism.

There are a number of pathological causes of thyrotoxicosis (Table 11.3.1). Graves disease is an autoimmune condition related to a combination of genetic and environmental factors, including iodine intake, stress and smoking. The thyrotoxicosis of Graves disease is caused by autoantibodies, which stimulate the thyroid resulting in excess thyroid hormone production.

THYROTOXICOSIS

Aetiology, genetics, pathogenesis and pathology

Normal secretion of thyroid hormone relies on an intact feedback loop involving the hypothalamus, pituitary gland and thyroid gland. Thyrotropin-releasing hormone (TRH) released from the hypothalamus stimulates thyroid-stimulating hormone (TSH) production in the anterior pituitary, which stimulates thyroid hormone release from thyroid follicular cells. Thyroid hormones

Table 11.3.1 Causes of thyrotoxicosis

Primary hyperthyroidism	Graves disease Toxic multinodular goitre Toxic adenoma
Thyroiditis	de Quervain syndrome (subacute) Postpartum Radiation
Central hyperthyroidism	Pituitary adenoma Ectopic thyroid tissue Metastatic thyroid tissue
Drug-induced	Lithium Iodine (including radiographic contrast) Amiodarone Excess thyroid hormone ingestion ('factitious thyrotoxicosis')

11.3 THYROID AND ADRENAL EMERGENCIES

Box 11.3.1 Clinical features of thyrotoxicosis

- Nervousness, irritability
- Heat intolerance and increased sweating
- Tremor
- Weight loss and alteration in appetite
- Palpitations and tachycardia, particularly atrial fibrillation
- Widened pulse pressure
- Exertional intolerance and dyspnoea
- Frequent bowel movements
- Fatigue and muscle weakness
- Thyroid enlargement (depending on cause)
- Pretibial myxoedema (with Graves disease)
- Menstrual disturbance and impaired fertility
- Mental changes
- Sleep disturbances
- Changes in vision, photophobia, eye irritation, diplopia, lid lag or exophthalmos
- Dependent lower extremity oedema
- Sudden paralysis, with or without hypokalaemia

and rhythm, looking specifically for cardiac failure, palpation and auscultation of the thyroid to determine thyroid size, nodularity and vascularity, neuromuscular examination and an eye examination for evidence of exophthalmos or ophthalmoplegia.

Clinical investigations and criteria for diagnosis^{1–3}

The TSH level is the single best screening test for hyperthyroidism. Hyperthyroidism of any cause (except excess TSH production from the anterior pituitary) results in a lower than normal TSH. The reference range is 0.4 to 5.0 mIU/L depending on the method.

Other laboratory and isotope tests may include:

- Free thyroxine (T4) or free tri-iodothyronine (T3) assay, when there is strong clinical suspicion of hyperthyroidism but the TSH is high or high normal.
- Thyroid autoantibodies, including TSH receptor antibody. These are not routine but may be helpful in selected cases.
- Radioactive iodine uptake and/or thyroid scan. These tests are helpful in establishing the cause of the hyperthyroidism, but are not part of the ED assessment.

Treatment

Mild hyperthyroidism does not require any treatment in the ED and the patient may simply be referred to an appropriate outpatient clinic. Any features of thyroid storm (discussed later) mandate admission, as does any significant intercurrent illness. Atrial arrhythmias should be controlled by the use of β-blockers, aiming to achieve a rate of less than 100 beats/min.

Ensure that all bloods have been collected first if thyroid-blocking drugs are to be commenced in the ED. High doses of thyroid-blocking drugs are often required to gain an initial response, after which the dose can be tapered.

Commence carbimazole 10 to 45 mg daily or propylthiouracil 200 to 600 mg daily in two or three divided doses initially, using the larger doses for more severe cases.³ Ideally, discuss the initiation of these agents with the physician who will continue managing the patient after his or her discharge from the ED.

Thyroid storm

Aetiology

Thyroid storm occurs in about 1% of patients with hyperthyroidism. It usually occurs as an acute deterioration in a patient with poorly controlled or undiagnosed hyperthyroidism, precipitated by factors such as surgery, trauma, infection, radioiodine treatment, use of iodinated contrast, exogenous thyroxine ingestion or any other significant stressor.

The diagnosis is entirely clinical, as there is no test to differentiate a thyroid storm from thyrotoxicosis. The mortality rate, if untreated or if the diagnosis is missed, is over 90%. Death is usually due to cardiovascular collapse.

Clinical features of a thyroid storm

The symptoms and signs of thyrotoxicosis are present and significantly exaggerated, with the abrupt onset of a combination of the following:

- fever >37.6°C up to 41°C
- cardiovascular complications:
 - tachycardia with pulse rates up to 200 to 300/min, including rapid atrial fibrillation
 - wide pulse pressure
 - high output cardiac failure
- alteration in mental state, varying from agitation and restlessness to delirium, coma and seizures
- abdominal pain with vomiting and diarrhoea.

Differential diagnosis

The following differential diagnoses of a thyroid storm need to be considered:

- sepsis
- heat stroke
- malignant hyperthermia
- neuroleptic syndrome
- sympathomimetic ingestion
- drug withdrawal (including alcohol)
- phaeochromocytoma crisis.

Treatment

The treatment of thyroid storm is directed to blocking thyroid hormone synthesis and release, the peripheral effects of the thyroid hormones, and corticosteroids.

β-Blockers

β-Blockade is the most important factor in decreasing morbidity and mortality. Many of the peripheral manifestations of hyperthyroidism, in particular the cardiovascular effects, are reduced by the use of propranolol. Propranolol also inhibits the peripheral conversion of T4 to T3 as well as antagonizing the effects of thyroid hormones and the hypersensitivity to catecholamines.

Give intravenous increments of 0.5 mg initially up to 10 mg total with continuous cardiovascular monitoring. Subsequent doses of 40 to 120 mg 6-hourly orally can be given.

β-Blockers should treat the cardiac failure secondary to the tachyarrhythmia or high cardiac output, but may cause complications in patients with pre-existing heart disease or asthma.

In this situation, use the short-acting β-blocker esmolol, as any adverse effects will be of brief duration. Give a 250 to 500 µg/kg bolus followed by an infusion starting at 50 to 100 µg/kg/min titrated to effect. Another option is to use the combination of a β-blocker and digoxin.

Thyroid-blocking drugs

Give propylthiouracil 900 to 1200 mg loading dose orally or via a nasogastric tube if necessary. This is followed by 200 to 300 mg 4- to 6-hourly. Propylthiouracil acts by preventing hormone synthesis by blocking the iodination of tyrosine and also inhibits the peripheral conversion of T4 to T3.

Iodine in large doses inhibits the synthesis and release of thyroid hormones and may be given either orally as Lugol's iodine, 30 to 60 drops daily in divided doses, or intravenously as sodium iodide 1 g 12-hourly. Iodine should not be given until at least 1 hour after anti-thyroid medication has been commenced as otherwise it will provide substrate for the production of more thyroid hormone. Lithium carbonate may be used in patients allergic to iodine or be added when there is difficulty with control.³

Cholestyramine also can be considered, which acts by binding with thyroxine after biliary excretion and hence increases elimination.

Corticosteroids

Corticosteroids are given to inhibit the peripheral conversion of T4 to T3 and as a relative deficiency may also be present. Hydrocortisone 100 mg IV 6-hourly or dexamethasone 4 mg IV 12-hourly are used.

General supportive measures

Dehydration and electrolyte disturbances need correction. Aggressive treatment of hyperthermia with cooling measures and paracetamol are necessary, but induction of shivering should be avoided. Salicylates are contraindicated as they displace T4 from binding proteins. In addition, it

is essential to look for and treat any precipitating cause, which will improve the prognosis.

Prognosis

Mortality rates are high, at 10% to 30%, despite treatment.

Apathetic hyperthyroidism

Patients with this condition are generally older, although it has been recorded in all age groups. The clinical picture is of a depressed mental state with cardiac complications, in particular cardiac failure. Weight loss is usually not significant and eye signs are rare. Most of the usual hyperkinetic manifestations of hyperthyroidism are absent. Treatment is as for standard hyperthyroidism.

HYPOTHYROIDISM

Aetiology, genetics, pathogenesis and pathology

Hypothyroidism results from the undersecretion of thyroid hormone from the thyroid gland. Causes of primary hypothyroidism include iodine deficiency, chronic autoimmune thyroiditis (Hashimoto thyroiditis), congenital, surgical removal of the thyroid gland, post-radioactive iodine, thyroid gland ablation and external irradiation. A significant number of cases are idiopathic. Secondary causes of hypothyroidism include pituitary and hypothalamic disease.

Epidemiology

Iodine deficiency is the most common cause worldwide, whereas in areas of iodine sufficiency, autoimmune disease and hypothyroidism secondary to treatment of hyperthyroid disease are more common. The prevalence of hyperthyroidism in adults is around 2% in women and 0.2% in men.¹ Congenital hypothyroidism is rare, occurring in about 1:4000 births.

Clinical features

The symptoms of hypothyroidism are related to the duration and severity of hypothyroidism, the rapidity with which hypothyroidism occurs and the psychological characteristics of the patient. These are summarized in Box 11.3.2.

A complete evaluation, including a comprehensive history, physical examination and appropriate laboratory evaluation should be performed in every patient with a goitre. Patients with chronic thyroiditis have a higher incidence of other associated autoimmune disorders, such as vitiligo, rheumatoid arthritis, Addison disease, diabetes mellitus and pernicious anaemia.

Box 11.3.2 Clinical features of hypothyroidism

- Dry skin and cold intolerance
- Coarse facial features
- Enlarged tongue
- Coarse brittle hair or loss of hair, loss of outer third of eyebrows
- Periorbital oedema
- Fatigue
- Constipation
- Weight gain/obesity
- Memory and mental impairment, decreased concentration
- Depression, personality changes
- Yellow skin (carotenaemia)
- Swelling of ankles
- Irregular or heavy menses and infertility
- Hoarseness
- Myalgias
- Goitre
- Hyperlipidaemia
- Delayed relaxation phase of tendon reflexes, ataxia
- Sinus bradycardia (atrioventricular block, rare)
- Cardiac failure, pericardial effusion (rare)
- Hypothermia (uncommon)

Clinical investigations and criteria for diagnosis

Laboratory evaluation

Perform a TSH assay as the primary test to establish the diagnosis of hypothyroidism if raised. The reference range is 0.4 to 5.0 mIU/L depending on the method. Additional tests may include free thyroxine assay and thyroid autoantibodies. A combination of an elevated TSH and low free thyroxine is diagnostic.³⁻⁵ A patient may be hypothyroid with a TSH greater than twice the reference interval, but with a free thyroxine within the normal range. Subnormal thyroxine with a normal TSH can occur in secondary hypothyroidism.

Thyroid autoantibodies are positive in 95% of patients with autoimmune thyroiditis (Hashimoto thyroiditis). The high titres are of value in making this specific diagnosis.

Other investigations

A thyroid scan and/or an ultrasound are useful if structural thyroid abnormalities are suspected.

Thyroid nodules are not uncommon with chronic thyroiditis and carry a small risk of thyroid cancer.

Treatment

Start thyroxine at 50 to 100 µg orally daily in adults under 60 years of age without evidence of ischaemic heart disease. Too rapid commencement of full thyroid hormone replacement may cause myocardial ischaemia from

increased myocardial oxygen consumption without a corresponding increase in cardiac output. The initial daily replacement dose is therefore 25 µg thyroxine in the elderly and where there is suspicion of heart disease. This dose should remain unchanged for 3 to 4 weeks to allow a steady state to be reached. It is appropriate to start this in the ED, when a firm diagnosis has been made and appropriate follow-up arranged.

The dose of thyroxine is then increased in 25 to 50 µg increments at not less than 4-weekly intervals, until the optimum dose is reached as determined by clinical response and TSH level. Consider admission for any patient with coexistent unstable angina to monitor cardiac function. Any features of myxoedema coma (discussed later) also mandate admission.

Myxoedema coma

The clinical syndrome of altered mental state, features of hypothyroidism and hypothermia is referred to as myxoedema coma, or sometimes as myxoedema crisis. There is usually a precipitating event, such as infection, stroke, trauma, myocardial infarction or administration of drugs, particularly phenothiazines, phenytoin, amiodarone, propranolol or lithium, that initiates this terminal decompensation phase of hypothyroidism.

The mortality for myxoedema coma remains up to 50% despite aggressive treatment.

Clinical features

- Altered mental state, usually coma due to cerebral oedema, hypoxia and hypercarbia.
- Seizures may precede coma in 25% of patients.
- Hypothermia with temperature usually less than 32.2°C. Notably, patients do not shiver.
- Hypoventilation resulting in hypoxia and hypercarbia.
- Cardiovascular complications, including hypotension and bradycardia, with heart rate inappropriate for the hypotension. Pericardial effusion, rarely with cardiac tamponade.
- Hypoglycaemia (common).
- Hyponatraemia.
- Paralytic ileus, megacolon, and urinary retention.
- Usual clinical features of hypothyroidism (see Box 11.3.2).

Treatment

Treatment should commence on clinical suspicion.

Administration of thyroid hormones

Tri-iodothyronine Intravenous T₃ may give a faster clinical response in myxoedema coma, as

11.3 THYROID AND ADRENAL EMERGENCIES

it is the active form of the hormone, although there is no consensus as to whether T₃ or T₄ replacement is preferable.⁴ Give T₃ as an initial IV bolus of 25 to 50 µg followed by 10 to 20 µg 8-hourly to a maximum of 60 µg/day. Alternatively, commence an infusion with a lower total dose of 20 µg/day, as large initial doses appear unnecessary for recovery and may, in fact, be harmful. Oral or nasogastric replacement of T₃ is not recommended in the initial phase of management because of unreliable gastrointestinal absorption.

Thyroxine The use of T₄ is supported as the gradual delivery of T₃ through the peripheral conversion of T₄ is better tolerated and as the onset of action is more predictable. Give a 400 to 500 µg IV bolus (300 µg/m²), followed by 50 µg IV daily until oral therapy is tolerated. Combined approaches are now also described.

Corticosteroids

Corticosteroids are given as there is impaired response to stress and the potential for coexistent adrenal insufficiency. Give hydrocortisone 100 mg IV 6-hourly. If an adrenocorticotrophic hormone (ACTH) stimulation test is being considered, give dexamethasone 4 mg until results are known.

General supportive measures

Requires correction of ventilatory, circulatory, temperature and metabolic abnormalities, and includes the use of warm humidified oxygen. Look for and treat any precipitating cause. Finally, avoid sedative drugs and watch out for water overload.

HYPoadrenal states

Aetiology, genetics, pathogenesis and pathology

Glucocorticoids act to produce multiple effects on metabolism, including gluconeogenesis, mobilization of fatty acids and amino acids, inhibiting the effects of insulin and ketogenesis. Glucocorticoids have anti-inflammatory effects related to the inhibition of production and the reduction of the effects of cytokines and the reduction of cell-mediated immunity. They also maintain the normal response of the vascular system to vasoconstrictors. In addition, glucocorticoids affect the regulation of body water by increasing free water excretion. This occurs by an increase in the glomerular filtration rate as well as inhibition of migration of water into cells. Aldosterone acts primarily to cause the reabsorption of sodium and the excretion of potassium and hydrogen ions.

Table 11.3.2 Causes of adrenal insufficiency

Primary (Addison disease)	Autoimmune surgical removal
	Infection (tuberculosis, viral, fungal)
	Haemorrhage, including Waterhouse–Friedrichsen syndrome
	Congenital
Secondary	Exogenous steroid suppression (single most common cause of adrenal insufficiency)
	Endogenous steroid (from tumour)
	Pituitary failure (hypopituitarism)

The adrenals normally respond within minutes by elevating corticosteroid levels in response to any physiological or pathological stress. When glucocorticoid insufficiency is present such stressors may result in hypotension, shock and ultimately death if left untreated.

Primary adrenal insufficiency (Addison disease)

Primary adrenal insufficiency (Addison disease) is due to the inability of the adrenal cortex to produce adequate levels of adrenal hormones. Hyponatraemia, hyperkalaemia, acidosis and elevated serum creatinine occur mainly due to aldosterone deficiency, whereas hypoglycaemia is related to cortisol deficiency. Hypercalcaemia occurs as a result of reduction in the glomerular filtration rate as well as increased proximal tubular reabsorption of calcium. Also, there may be some increased mobilization of calcium from bone in patients with adrenal insufficiency.

Secondary adrenal insufficiency

Secondary adrenal insufficiency is due to failure of adequate ACTH from the pituitary gland (Table 11.3.2). Hyponatraemia still occurs in secondary adrenal insufficiency, but is due to cortisol deficiency.^{6,7}

The majority of presentations of acute adrenal insufficiency occur as an exacerbation of a chronic disease process where there is a malfunctioning adrenal system. Acute precipitating factors include sepsis, major trauma, surgery and a myocardial infarct.

Causes of primary or secondary adrenal insufficiency

The cause of 80% of primary adrenal insufficiency is autoimmune. Other causes of acute adrenal gland insufficiency include primary or secondary malignancy, infection (e.g. tuberculosis), adrenal infarction or haemorrhage (Waterhouse–Friedrichsen syndrome) seen in meningococcaemia or severe sepsis, and drugs.

Primary adrenal insufficiency also occurs in up to 20% of patients with AIDS. Up to 60% of patients with sepsis have a low baseline cortisol level, although fewer meet criteria for insufficiency on suppression testing.^{5,8}

The most common cause of secondary adrenal insufficiency is suppression of the adrenopituitary axis by long-term corticosteroid therapy, although other causes include pituitary failure, such as panhypopituitarism or isolated ACTH production failure.

Clinical features

Suspect adrenocortical failure in any hypotensive patient when no apparent cause is found, particularly anyone who is unresponsive to fluid therapy. Orthostatic postural hypotension is almost always present. Other common features include abdominal pain, which may be severe, with vomiting.

Less obvious findings are weakness, anorexia, diarrhoea, postural syncope, mucocutaneous pigmentation/vitiligo (only with primary adrenal disease) and a dulled mental state.

Hypercalcaemia and/or hyperkalaemia can be the first sign of adrenal insufficiency in the critically ill patient. The other features of adrenal insufficiency may be masked by coexisting illness, but the possibility of adrenal insufficiency should always be considered.

Differential diagnosis

The diagnosis of adrenal insufficiency in the early stages is difficult as weakness, lethargy and gastrointestinal symptoms are common and non-specific. Consider adrenal insufficiency in any patient presenting with these symptoms when more common causes have been excluded.

Clinical investigations

Laboratory findings

The classical laboratory findings are hyponatraemia (due to sodium depletion and the intracellular movement of sodium), hypochloraemia and

hyperkalaemia (due to acidosis and aldosterone deficiency). Mild hypercalcaemia (in 10% to 20% of cases) and a non-anion-gap metabolic acidosis may be seen. Hypoglycaemia, if present, is usually mild. However, all basic laboratory investigations can be within normal limits, even in the presence of an addisonian crisis.

Anti-adrenal antibodies are positive in 70% of patients with autoimmune adrenalitis.

Criteria for diagnosis

Baseline cortisol and ACTH levels should be taken prior to treatment. The normal reference range for cortisol is 200 to 650 nmol/L. An ACTH level should be <50 ng/L, although interpretation needs to take into account the time of day when the sample is taken. ACTH should be high in primary adrenal disease and low in pituitary disease.

The Synacthen stimulation test is the definitive investigation and may be required if the initial test results are not diagnostic. It is usually performed during a hospital stay, when Synacthen 250 µg is administered intramuscularly and cortisol levels are taken at baseline, 30 and 60 minutes. A baseline or post-Synacthen cortisol level of >550 nmol/L is considered normal.

Treatment

Corticosteroid replacement

Do not delay treatment awaiting confirmatory results if acute adrenal insufficiency is suspected.

Give immediate corticosteroid replacement with either intravenous hydrocortisone or dexamethasone. Dexamethasone is recommended when the diagnosis has not been confirmed by laboratory investigations, as it does not interfere with the cortisol assay. Give 10 mg dexamethasone IV stat followed by 4 mg IV 8-hourly. Alternatively, give hydrocortisone at a dose of 250 mg stat followed by 100 mg IV 6-hourly.

Fluid replacement therapy

Give normal saline 1 L stat, then titrated to response, although the total volume deficit is rarely greater than 10% body weight. Intravenous dextrose should be given at the same time, either separately or as 5% dextrose in normal saline to avoid hypoglycaemia.

General supportive measures

These include treatment of hypoglycaemia and other electrolyte replacement abnormalities, although most will be corrected with saline rehydration alone. Mineralocorticoid replacement is usually not necessary in the acute crisis, if salt and water replacement are adequate.

Once the crisis has been successfully treated, it is important to investigate and manage the cause, and to develop a maintenance regimen.

Prognosis

The patient with acute adrenal insufficiency may die if the diagnosis is not made promptly. When the diagnosis is suspected and treatment is early, the outcome is favourable depending on the nature of any precipitating illness.

Response to severe illness

The normal response to severe illness should see cortisol levels rising to at least 500 nmol/L. States of 'relative adrenal insufficiency' are described where glucocorticoid administration diminishes or even eliminates the requirements for vasoressor agents, even though measured cortisol levels are normal or close to normal.⁵ There is no consensus on what constitutes 'normal' cortisol levels in severe illness.

Up to 60% of patients with severe sepsis may have some degree of adrenal insufficiency depending upon the threshold cortisol level used.⁸ Moreover, it appears that it is the delta cortisol rather than the basal cortisol level that is associated with clinical outcome.⁹ Repeat adrenal function testing is indicated in patients with severe illness who remain unstable or who fail to improve with aggressive supportive therapy.

The use of hydrocortisone has been recommended in septic shock after an abnormal 250 µg Synacthen stimulation test.⁶ This should continue for a week if adrenal insufficiency is confirmed.

HYPERADRENAL STATES

Aetiology, pathogenesis and epidemiology

Cushing disease usually refers to hyperadrenalinism due to a pituitary adenoma. Cushing syndrome occurs as a result of hyperadrenalinism from exposure to excess glucocorticoids over a prolonged period. Endogenous causes of Cushing syndrome are related to primary adrenal disorders, such as adrenal adenoma, carcinoma or hyperplasia, or are secondary to ACTH or corticotropin-releasing hormone stimulation and ectopic ACTH production from bronchogenic carcinoma or carcinoid tumours in particular. However, by far the most common cause of Cushing syndrome is from the exogenous (iatrogenic) administration of steroids.

The incidence of Cushing syndrome ranges from 0.7 to 2.4 per million population per year, but the reported prevalence in obese patients with type II diabetes may be between 2% and 5%.⁷

Clinical features

The classical clinical features of Cushing syndrome are increased body weight with central obesity, rounded face, hypertension, fatigue, weakness and proximal myopathy, hirsutism, striae, bruising, decreased libido, amenorrhoea, depression and/or personality changes, osteopaenia or fracture. Proximal weakness or myopathy is useful to differentiate simple obesity (strong limbs) from possible Cushing syndrome (relative weakness for the patient's size).

Clinical investigations and criteria for diagnosis

Laboratory tests

Full blood examination may reveal polycythaemia, neutrophilia and eosinophilia. Electrolytes may show hyperglycaemia, hypokalaemia and metabolic alkalosis.

24-h urinary cortisol level

A measured 24-hour urinary cortisol level with a value more than four times the upper normal range is rare except in Cushing syndrome (normal range 100 to 300 nmol/24 hour).

Overnight dexamethasone suppression test

This is an outpatient screening test for Cushing syndrome²:

- Day 1, 09:00 hours: 5 mL blood taken for baseline cortisol
- Day 1, 23:00 hours: 1 mg dexamethasone taken orally
- Day 2, 5 mL blood for cortisol.

The baseline reference range for cortisol is 200 to 650 nmol/L. The day 2 cortisol level should drop to lower than 50% of the baseline level, indicating normal suppression and excluding Cushing syndrome.

Long dexamethasone suppression test

The long dexamethasone suppression test is performed as an inpatient, using increasing doses of dexamethasone to determine at what level suppression occurs, with testing of both cortisol and ACTH levels. Cushing syndrome only suppresses at high doses.

Other tests

A chest x-ray is important if bronchogenic carcinoma of the lung is suspected. Magnetic resonance imaging of the adrenals and/or head is used for the identification of tumours.

Treatment

Treatment will depend on the cause. When a pituitary or adrenal adenoma is identified,

11.3 THYROID AND ADRENAL EMERGENCIES

optimal treatment is removal of the tumour.^{3,7} Glucocorticoid replacement is then required for up to 2 years following surgery to allow full recovery of the normal pituitary–adrenal axis.

Pharmacological blockade of adrenal corticosteroid production may be required in some circumstances. Ketoconazole, amino-glutethimide, Metapirone and mitotane may be used for this purpose.

CONTROVERSIES

- What constitutes ‘normal’ cortisol levels in severe illness.
- Whether T₃ or T₄ replacement therapy is preferable in myxoedema coma.
- Differentiating simple obesity with hypertension from Cushing syndrome.

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SECTION 12

METABOLIC EMERGENCIES

Edited by *Mark Little*

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12.1 Acid–base disorders

Alan Gault

ESSENTIALS

- 1 Acid–base homeostasis is one of the most tightly regulated systems within the body. It is maintained by buffering, respiratory and renal mechanisms.
- 2 Most acid–base disturbances are complex and require a systematic approach to determine underlying processes.
- 3 High-anion-gap metabolic acidosis and respiratory acidosis are both common in emergency medicine and should direct the clinician to determine and treat the aetiology.
- 4 Administration of NaHCO_3 is not routine; however, it is indicated in severe hyperkalaemia, sodium channel blockade and other selected poisonings.
- 5 Lactate levels greater than 4 mmol/L are associated with raised mortality and should highlight the need for resuscitation and immediate assessment of precipitating pathology.

These mechanisms include buffering, respiratory manipulation of CO_2 and renal handling of bicarbonate. Buffering with plasma proteins, haemoglobin and the carbonic-acid–bicarbonate systems provide the most immediate mechanism. This is followed by respiratory compensation, which occurs within minutes and is achieved by alterations in alveolar ventilation. Renal compensation usually takes hours to days to take effect.

Acidaemia

Systemic acidaemia is defined as the presence of an increased concentration of hydrogen ions ($[\text{H}^+]$) in the blood. An acidaemia can result from respiratory acidosis, metabolic acidosis or both in combination. The physiological effects of acidaemia are a decrease in the affinity of haemoglobin for oxygen and an increase in serum K^+ of approximately 0.4 to 0.6 mmol/L for each decrease in pH of 0.1.¹ Although the presence of acidaemia is often associated with a poor prognosis, the presence of acidaemia per se usually has few clinically significant effects. It is the nature and severity of the underlying illness that principally determines the outcome.

Metabolic acidosis

Metabolic acidosis is defined as an increase in the $[\text{H}^+]$ of the blood as a result of increased acid production or bicarbonate wasting from the gastrointestinal (GI) or renal tract. The cause is often multifactorial and can be further classified into ‘anion-gap’ and ‘non-anion-gap’ (or hyperchloraemic) metabolic acidosis.

Introduction

Acid–base disorders are commonly encountered in the emergency department (ED) and their recognition is important for the diagnosis, assessment of severity and monitoring of many disease processes. Although these disorders are usually classified according to the major metabolic abnormality present (acidosis or alkalosis) and its origin (metabolic or respiratory), it is important to realize that acid–base disorders of a mixed type commonly occur, and that the recognition and assessment of these are more complex.

Carbon dioxide (CO_2) produces acid when in solution and altering PaCO_2 through changes in ventilation can produce or remove acid from the body. The terms respiratory acidosis/alkalosis refer to the pH shifts resulting from

alterations in PaCO_2 from changes in ventilation. Bicarbonate (HCO_3^-) acts as a base in solution with bicarbonate accumulation resulting in a more alkaline state and its wasting or consumption indicating a more acidic state. The terms metabolic acidosis/alkalosis refer to pH shifts characterized by alterations in bicarbonate levels. By convention, the overall pH abnormality as defined by the blood gas assessment is termed alkalaemia (for pH >7.44) or acidaemia (pH <7.34).

Acid–base homeostasis

Acid–base status is one of the most tightly regulated systems in the body. The term compensation is used to describe the processes by which shifts in plasma pH are attenuated.

12.1 ACID-BASE DISORDERS

Table 12.1.1 Causes of high-anion-gap metabolic acidosis

Acid	Cause
Lactic acid	Numerous causes—see Box 12.1.1
Ketoacids	Diabetic ketoacidosis Alcoholic ketoacidosis Starvation ketoacidosis
Phosphate and sulphate	Renal failure Uraemia
Other	Ethylene glycol—oxalic, glycolic, glyoxylic acid Methanol—formic acid Salicylate—salicylic, salicyruic, gentisic acid Toluene—benzoic, hippuric acid Paraldehyde—acetic acid Ethanol—acetic, lactic acid Uraemia

High-anion-gap metabolic acidosis (Table 12.1.1)

As electro-neutrality must exist in all solutions, the anion gap represents the concentration of anions that are not commonly measured. The most commonly used formula for the calculation of the anion gap is:

$$AG = [\text{Na}^+] - ([\text{Cl}^-] + [\text{HCO}_3^-])$$

The normal value for the anion gap depends on the type of biochemical analyser used and, while the upper limit of normal has been commonly quoted as 14, the mean range with some modern analysers is only 5 to 12.² In the normal resting state, the serum ionic proteins account for most of the anion gap, with a lesser contribution from other ‘unmeasured’ anions, such as phosphate (PO_4^{3-}) and sulphate (SO_4^{2-}). In pathological conditions where there is an increase in the concentration of unmeasured anions, high-anion-gap metabolic acidosis (HAGMA) results. The anions responsible for the increase in the anion gap depends on the cause of the acidosis. Lactic acid is the predominant anion in hypoxia and shock, PO_4^{3-} and SO_4^{2-} in renal failure, keto-acids in diabetic, alcoholic and starvation keto-acidosis, glycolic, glyoxylic and oxalic acid in ethylene glycol poisoning and formic acid in methanol poisoning.

Of the causes of a HAGMA, lactic acidosis is the most commonly encountered in the ED and is defined as a serum lactate of $>2.5 \text{ mmol/L}$ (Box 12.1.1). The presence of lactic acidosis is determined by the balance between lactate production and metabolism. In the seriously ill patient, it is common for increased production and decreased metabolism to be present simultaneously.

It is important to realize that in many conditions, a variety of factors may produce the

Box 12.1.1 Causes of hyperlactataemia

Type A: imbalance between oxygen demand and supply	Type B: metabolic derangements
Carbon monoxide poisoning	Beta ₂ -agonists
Cyanide poisoning	Cancer
Iron poisoning	Ethanol
Isoniazid poisoning	Hepatic failure
Excessive oxygen demand	Inborn errors of metabolism
<ul style="list-style-type: none"> • Seizure • Hyperpyrexia • Shivering • Exercise 	Ketoacidosis
Shock	Metformin/Phenformin
Severe anaemia	Sepsis
Hypoxia	Vitamin deficiency (thiamine, biotin)
	Paracetamol poisoning
	Salicylate poisoning

Box 12.1.2 Causes of non-anion-gap metabolic acidosis

GIT Bicarbonate Loss	Renal bicarbonate loss
Diarrhoea	Ureteroenterostomy
Small bowel fistula	Renal tubular acidosis
Pancreatic fistula	Adrenal insufficiency
Drugs	Excess chloride administration
Carbonic anhydrase inhibitors	
<ul style="list-style-type: none"> • Acetazolamide • Topiramate 	
Acidifying agents	
<ul style="list-style-type: none"> • Ammonium chloride Cholestyramine 	

GIT, Gastrointestinal tract.

acidosis and that multiple anions may be involved in the production of anion-gap acidosis. In a patient with HAGMA, non-anion-gap metabolic acidosis may also co-exist.

Non-anion-gap metabolic acidosis (Box 12.1.2)

Non-anion-gap metabolic acidosis results from the loss of HCO_3^- from the body, rather than from increased acid production. To maintain electro-neutrality, chloride is usually retained by the renal tubules when HCO_3^- is lost and the hallmark of non-anion-gap acidosis is an elevation of the serum chloride. The causes of non-anion-gap metabolic acidosis are further classified according to the site of HCO_3^- loss. GI losses can occur with lower GI tract (GIT) fluid losses that are rich in HCO_3^- or with cholestyramine ingestion due to binding of HCO_3^- in the gut. Renal losses can occur with renal tubular acidosis (RTA), carbonic anhydrase inhibitor therapy or adrenocortical insufficiency. Occasionally, direct chloride excess drives the renal bicarbonate loss (again due to electro-neutrality)—which can be observed with large volumes of chloride-rich crystalloid administration (chiefly normal saline).

Renal tubular acidosis (Table 12.1.2) RTA is a group of conditions where there is an inability to acidify the urine. It occurs either from impaired secretion of H^+ in the distal convoluted tubule or failure to reabsorb HCO_3^- in the proximal convoluted tubule. This may result in a chronic metabolic acidosis, with hypokalaemia, nephrocalcinosis, rickets or osteomalacia. There are three subtypes of RTA and many different causes. In the ED it is most commonly due to the abuse of ibuprofen.

Low-anion-gap metabolic acidosis (Box 12.1.3) This is uncommon in the ED. It can occur in disease states that result in an increase in unmeasured cations or falsely measured high chlorine concentrations.

Treatment of metabolic acidosis

The treatment of acidosis should usually be directed primarily towards the correction of the underlying cause. Intravenous HCO_3^- is of use in the presence of severe acidosis and hyperkalaemia, sodium channel blockade (e.g. tricyclic antidepressant), salicylate and methanol poisoning. The use of HCO_3^- in patients with diabetic ketoacidosis and lactic acidosis associated with sepsis or severe cardiorespiratory disease does not appear to improve outcome.³⁻⁵ The potential hazards of HCO_3^- therapy include fluid overload, hypernatremia, hypokalaemia, alkalemia, decreased ionized serum calcium, tissue injury from extravasation and worsening of intracellular acidosis.

Respiratory acidosis (Box 12.1.4)

Respiratory acidosis may be acute or chronic and is defined as an elevation of the arterial partial pressure of carbon dioxide (PCO_2). It is due to alveolar hypoventilation. This can result from central depression in respiratory drive, neuromuscular weakness, mechanical factors, lung parenchymal disorders and ventilation/perfusion mismatch. With significant elevations in CO_2 , sweating, tachycardia, confusion and mydriasis occur. When the PCO_2 is greater than 80 mm Hg, the level of consciousness is usually depressed, known as CO_2 narcosis.

Treatment

The treatment of respiratory acidosis is directed towards reversal of the causative factors while supporting and promoting ventilation. Indications for and methods of therapy are clinically determined.

Alkalaemia

Alkalaemia is defined as a decrease in $[\text{H}^+]$ in the blood. Extreme alkalaemia may cause altered mental status, tetany and seizures. These are

12.1 ACID-BASE DISORDERS

Table 12.1.2 Types and causes of renal tubular acidosis

Type	Anatomical location	Pathophysiology	Causes
Type 1	Distal—collecting tubules	Failure to secrete H ⁺	Hereditary Autoimmune • Sjogren syndrome • Systemic Lupus Erythematosus (SLE) • Rheumatoid arthritis Nephrocalcinosis Sickle cell anaemia Toxins • Lithium • Toluene • Amphotericin B • Ifosfamide Liver cirrhosis
Type 2	Proximal tubules	Failure to reabsorb HCO ₃ ⁻	Hereditary Amyloidosis Multiple myeloma Paroxysmal nocturnal haemoglobinuria Toxins • HAART • Ifosfamide • Lead • Cadmium
Type 3	Combined type 1 + 2		
Type 4	Adrenal gland	Hypoaldosteronism	Aldosterone deficiency • Primary hypoaldosteronism • Hyporeninaemic hypoaldosteronism Aldosterone resistance • NSAIDs • ACE inhibitors • Spironolactone • Trimethoprim • Pseudohypoaldosteronism

ACE, Angiotensin-converting enzyme; HAART, highly active antiretroviral therapy; NSAIDs, non-steroidal anti-inflammatory drugs.

Box 12.1.3 Causes of low-anion-gap metabolic acidosis

Increased unmeasured cations	Artefactual
Hypercalcaemia	Bromism
Hypermagnesaemia	Iodism
Lithium	Hypoalbuminaemia
Multiple myeloma and other gammopathies	Hypertriglyceridaemia
Dilution	

predominantly related to a reduction in the concentration of ionized calcium, which is more commonly present in respiratory alkalosis due to anxiety, than from other causes. Like acidaemia, there are metabolic and respiratory processes by which it occurs.

Metabolic alkalosis (Box 12.1.5)

Metabolic alkalosis most commonly results from loss of acid from the GIT; however, renal acid losses or the accumulation of bicarbonate from exogenous sources can also contribute.

Box 12.1.5 Causes of metabolic alkalosis

Chloride responsive (Urinary chloride <10 mmol/L)	Chloride unresponsive (Urinary chloride >20 mmol/L)
Gastrointestinal losses	Bartter syndrome
• Vomiting	Liddle syndrome
• Nasogastric suctioning	Gitelman syndrome
• Bulimia nervosa	Liquorice excess (glycyrrhizic acid)
• Pyloric stenosis	Conn syndrome (primary hyperaldosteronism)
• Tetrahydrocannabinol (THC)-induced cyclical vomiting	Excess bicarbonate administration
Diuretics	• Antacids
Chloride losing enteropathy	• Dialysis
Chloride losing nephropathy	• Milk-alkali syndrome

Diagnostically and therapeutically, metabolic alkalosis can be divided into two distinct aetiological groups—chloride-responsive and chloride-unresponsive metabolic alkalosis.

Chloride-responsive metabolic alkalosis arises from conditions that result in both chloride and volume loss. Reduction in extracellular volume leads to increased mineralocorticoid activity causing the reabsorption of sodium and the excretion of hydrogen with bicarbonate retention. The urine is usually alkaline with higher concentrations of bicarbonate; thus minimal chloride is excreted to maintain electro-neutrality. Hence a urinary chloride <10 mmol/L is a common finding in these conditions. The commonest causes seen in the ED are as a result of severe and prolonged vomiting and diuretic use.

Chloride-unresponsive metabolic alkalosis is typically due to disease states that either result in mineralocorticoid excess in the absence of hypovolaemia and chloride wasting, or congenital disorders with defects in the various ionic transport channels within the kidney. As extracellular volume is either normal or increased, urinary chloride is typically >20 mmol/L. These conditions are seen in the ED infrequently.

Treatment should be directed primarily towards correction of the underlying cause.

Respiratory alkalosis (Box 12.1.6)

Respiratory alkalosis can also be acute or chronic, of which the acute form is most commonly encountered in the ED.

Respiratory alkalosis may physiologically occur in the general population secondary to exercise, altitude-related hypoxia and stimulation of the medullary respiratory centre by progesterones during pregnancy. Disease states that

Box 12.1.4 Causes of respiratory acidosis

Acute respiratory acidosis	Chronic respiratory acidosis
Airway obstruction	Pulmonary disease
Aspiration	• e.g. emphysema, pulmonary fibrosis
Bronchospasm	Neuromuscular disorders
Drug-induced CNS depression	• e.g. muscular dystrophy
Hypoventilation of Central Nervous System (CNS) origin	Obesity
• e.g. cerebral tumour	Severe kyphoscoliosis
Hypoventilation of Peripheral Nervous System (PNS) origin	
• e.g. Guillain-Barré Syndrome (GBS) or Organophosphate (OP) poisoning	
Pulmonary disease	

12.1 ACID-BASE DISORDERS

Box 12.1.6 Causes of respiratory alkalosis

Central nervous system-mediated hyperventilation	Pulmonary-mediated hyperventilation
Psychogenic	Congestive cardiac failure
Raised intracranial pressure	Mechanical hyperventilation
Cerebrovascular accidents	Pulmonary emboli
	Pneumonia
Hypoxia-mediated hyperventilation	Toxin-induced hyperventilation
Altitude	Salicylates
Anaemia	Nicotine
V/Q mismatch	Xanthines
Sepsis	Caffeine
	Sympathomimetics

give rise to respiratory alkalosis are more likely to be seen in the ED. Treatment is again directed towards correcting the underlying cause.

Systematic acid-base interpretation

A systematic stepwise approach to acid–base interpretation is beneficial in the evaluation of disturbances as they are often multiple. What follows is an example of a conventional methodology as outlined by Whittier and Ruteckiⁱ⁶:

Step 1: what is the pH (primary acid–base disturbance)?

- Acidaemia exists if pH <7.40
- Alkaemia exists if pH >7.44.

Step 2: determine whether the primary process is respiratory, metabolic or both

- Respiratory acidosis exists if PaCO₂ >44 mm Hg
- Respiratory alkalosis exists if PaCO₂ <40 mm Hg

- Metabolic acidosis exists if HCO₃⁻ <25 mEq/L
- Metabolic alkalosis exists if HCO₃⁻ >25 mEq/L

Step 3: calculate the anion gap

$$AG = [\text{Na}^+] - ([\text{Cl}^-] + [\text{HCO}_3^-])$$

Step 4: check for the degree of compensation

- Metabolic acidosis: For every 1 mEq/L decrease in HCO₃⁻, PaCO₂ should decrease by 1.3 mm Hg.
 - Expected CO₂ = 1.5 × [HCO₃⁻] + 8 (+/-2)
- Metabolic alkalosis: For every 1 mEq/L increase in HCO₃⁻, PaCO₂ should increase by 0.6 mm Hg
 - Expected CO₂ = 0.7 × [HCO₃⁻] + 20 (+/-5)
- Respiratory acidosis: For every 10 mm Hg increase in PaCO₂, HCO₃⁻ should increase by 1 mEq/L (acute) or 4 mEq/L (chronic)
- Respiratory alkalosis: For every 10 mm Hg decrease in PaCO₂, HCO₃⁻ should decrease by 2 mEq/L (acute) or 5 mEq/L (chronic).

Step 5: determine if there is a 1:1 relationship between the anions in the blood (presence of a delta gap)

In HAGMA, this step determines whether there is a concurrent non-anion-gap metabolic acidosis or metabolic alkalosis. There should be a 1:1 relationship between the rise in the anion gap over normal and the decrease in the bicarbonate. If the bicarbonate is higher than predicted, then a metabolic alkalosis is also present. If the bicarbonate is lower than predicted, then a non-anion-gap acidosis is also present.

Lactate gap

Lactate gap is the difference in lactate concentrations measured by laboratory analysis and point-of-care analysis. Some point-of-care analysers are unable to distinguish between lactate and glycolate—the major metabolite in ethylene glycol poisoning—and give a falsely elevated lactate result. The presence of a lactate gap helps refine the risk assessment in the setting of a suspected ethylene glycol intoxication.

CONTROVERSIES

- Whether the Stewart approach is advantageous in teaching and characterizing acid–base abnormalities compared to traditional approaches.

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12.2 Electrolyte disturbances

John Pasco

ESSENTIALS

- 1** Sodium disorders are relatively common in hospitalized patients and elderly people.
- 2** The brain is most at risk from acute hyponatraemia because the osmotically expanded intracellular volume may induce increased intracranial pressure (hyponatraemic encephalopathy).
- 3** Treatment of hyponatraemia needs to be carefully individualized because of the risk of osmotic myelinolysis.
- 4** Hypernatraemia has a high in-hospital mortality rate, which often reflects severe associated medical conditions.
- 5** Although usually benign, hypokalaemia may cause cardiac arrhythmias and rhabdomyolysis. Oral replacement is usually sufficient, except where there is severe myopathy or cardiac arrhythmias.
- 6** Electrocardiogram changes in the presence of hyperkalaemia require urgent potassium-lowering measures and myocardial protection with calcium.
- 7** Management of severe hypercalcaemia includes enhancement of renal excretion of calcium, inhibition of osteoclast activity and treatment of the underlying condition.
- 8** Acute symptomatic hypocalcaemia should be treated with intravenous calcium.
- 9** Hypomagnesaemia is difficult to diagnose because its symptoms are non-specific and the serum level often does not reflect the true magnesium status of the patient. It usually exists as a 'deficiency triad' with hypokalaemia and hypocalcaemia.
- 10** Hypermagnesaemia is often iatrogenic, particularly in elderly patients or patients with renal impairment and/or chronic bowel conditions receiving magnesium therapy.

HYPONATRAEMIA

Introduction

Hyponatraemia, defined as serum sodium concentration of less than 130 mmol/L, is a common condition. The prevalence is estimated at 2.5% in hospitalized patients, two-thirds of whom develop the condition while in hospital.

Pathophysiology

Hyponatraemia is almost always associated with extracellular hypotonicity, with an excess of total body water relative to sodium (hypotonic hyponatraemia). The exceptions are:

- Normotonic hyponatraemia (pseudohyponatraemia): an artefactually low, and rarely seen, sodium measurement seen in hyperlipidaemia and hyperproteinaemia.

- Hypertonic hyponatraemia: a dilutional lowering of the measured serum sodium concentration in the presence of osmotically active substances, such as glucose, mannitol, glycerol and sorbitol. In the presence of hyperglycaemia, the true serum sodium can be estimated by adjusting the measured serum sodium upwards by 1 mmol/L for each 3 mmol/L rise in glucose above normal.

Hyponatraemia causes cellular swelling as water moves down an osmotic gradient into the intracellular fluid. Most of the symptomatology of hyponatraemia is produced in the central nervous system (CNS) by the swelling of brain cells within the rigid calvarium, causing raised intracranial pressure (hyponatraemic encephalopathy). As intracranial pressure rises, adaptive responses come into play, returning brain volume towards normal and restoring cellular function.

For this reason, chronic hyponatraemia is generally better tolerated than acute hyponatraemia. Patients can become encephalopathic when hyponatraemia develops rapidly and the adaptive responses have not had time to develop or fail.

Hyponatraemic encephalopathy carries a high mortality (50%) if left untreated.

Aetiology and classification

Hypotonic hyponatraemia may be classified according to the volume status of the patient (hypovolaemic, euvoalaemic or hypervolaemic).

Hypovolaemic hyponatraemia

These patients have deficits in both total body sodium and total body water, but the sodium deficit exceeds the water deficit. Causes are listed in [Box 12.2.1](#). Determination of the urinary sodium concentration can differentiate renal or extra renal losses. Extrarenal losses are usually associated with low urinary sodium concentrations (<20 mmol/L) and hyperosmolar urine. The exception is with severe vomiting and metabolic alkalosis, where bicarbonaturia obligates renal sodium loss and urinary sodium is high (>20 mmol/L), despite volume depletion. However, urinary chloride, a better indicator of extracellular fluid (ECF) volume, is low.

Euvolaemic hyponatraemia

Total body water is increased with only minimal change in total body sodium. Volume expansion is mild and usually not clinically detectable. Causes are listed in [Box 12.2.2](#).

Box 12.2.1 Causes of hypovolaemic hyponatraemia

- Renal losses (urinary [Na] >20 mmol/L)**
- Diuretics
- Mineralocorticoid deficiency—Addison disease
- Salt-losing nephropathy
- Ketonuria
- Osmotic diuresis—glucose, mannitol, urea
- Bicarbonaturia with metabolic alkalosis

Extrarenal losses (urinary [Na] <20 mmol/L)

- Vomiting—self-induced, gastroenteritis, pyloric obstruction
- Diarrhoea
- Excessive sweating
- Blood loss
- Third-space fluid loss—burns, pancreatitis, trauma

12.2 ELECTROLYTE DISTURBANCES

Box 12.2.2 Causes of euvolaeemic hyponatraemia

- Psychogenic polydipsia
- Iatrogenic water intoxication
 - Absorption of hypotonic irrigation fluids during TURP
 - Inappropriate intravenous fluid administration
- Postoperative hyponatraemia (elevated ADH levels)
- Non-osmotic ADH secretion
 - Glucocorticoid deficiency
 - Severe hypothyroidism
 - Thiazide diuretics
- Drugs (ADH analogues, potentiation of ADH release, unknown mechanisms)
- Psychoactive agents: phenothiazines, SSRIs, TCAs, MAOIs, 'ecstasy'
- Oxytocin
- Anticancer agents: cyclophosphamide, vincristine, vinblastine
- NSAIDs
- Carbamazepine
- Chlorpropamide
- SIADH

ADH, Antidiuretic hormone; *MAOI*, monoamine oxidase inhibitor; *NSAIDs*, non-steroidal anti-inflammatory drugs; *SIADH*, syndrome of inappropriate antidiuretic hormone; *SSRI*, selective serotonin reuptake inhibitor; *TCA*, tricyclic antidepressant; *TURP*, transurethral resection of prostate.

Hypervolaemic hyponatraemia

Total body water is increased in excess of total body sodium. Causes include congestive cardiac failure, hepatic cirrhosis with ascites, nephrotic syndrome and chronic renal failure.

Clinical features

In addition to the features of the underlying medical condition and alteration in extracellular volume, clinical manifestations of hyponatraemia per se usually develop when serum sodium is less than 130 mmol/L. The severity of symptoms depends partly on the absolute serum sodium concentration and partly on its rate of fall. At sodium concentrations from 125 to 130 mmol/L, the symptoms are principally gastrointestinal, whereas at concentrations below 125 mmol/L, the symptoms are predominantly neuropsychiatric. The principal signs and symptoms of hyponatraemia are listed in [Box 12.2.3](#).

Population groups particularly prone to acute hyponatraemic encephalopathy have been identified ([Box 12.2.4](#)).

Premenopausal women appear at risk because oestrogen and progesterone are thought to inhibit the brain Na-K-ATPase and increase circulating levels of antidiuretic hormone (ADH).

Psychogenic polydipsia occurs primarily in patients with schizophrenia or bipolar disorder. These patients develop hyponatraemia with a far lower fluid intake than is usually necessary

Box 12.2.3 Clinical manifestations of hyponatraemia

- Anorexia
- Nausea
- Vomiting
- Lethargy
- Muscle cramps
- Muscle weakness
- Headache
- Confusion/agitation
- Altered conscious state
- Seizures
- Coma

Box 12.2.5 Diagnostic criteria for syndrome of inappropriate antidiuretic hormone

- Hypotonic hyponatraemia
- Urine osmolality >100 mmol/kg (i.e. inappropriately concentrated)
- Urine sodium >20 mmol/mL while on a normal salt and water intake
- Absence of extracellular volume depletion
- Normal thyroid and adrenal function
- Normal cardiac, hepatic and renal function
- No diuretic use

Box 12.2.6 Conditions associated with syndrome of inappropriate antidiuretic hormone

- Neoplasms (ectopic ADH production)
 - Bronchogenic carcinoma
 - Pancreatic carcinoma
 - Lymphoma
 - Mesothelioma
 - Thymoma
 - Carcinoma of the bladder
 - Pulmonary disease
 - Pneumonia
 - Tuberculosis
 - Aspergillosis
 - Cystic fibrosis
 - Chronic obstructive airways disease
 - Positive-pressure ventilation
- CNS disease
 - Encephalitis
 - Acute psychosis
 - Head trauma
 - Brain abscess
 - Meningitis
 - Hydrocephalus
 - Brain tumour
 - Delirium tremens
 - Guillain–Barré syndrome
 - Stroke
 - Subdural or subarachnoid bleed
 - HIV infection
 - Pneumocystis carinii* pneumonia

ADH, Antidiuretic hormone; *CNS*, central nervous system.

Clinical investigations

Measurement of serum and urine sodium concentrations and osmolalities, in addition to clinical assessment of volume status, are essential for the assessment of hyponatraemia ([Fig. 12.2.1](#)).

Treatment

There is ongoing controversy over the treatment of hyponatraemia because of the risk of osmotic demyelination, which is discussed below.

Treatment of the underlying cause is obviously essential; it should be carefully individualized and depends on the presence of symptoms, the

Syndrome of inappropriate antidiuretic hormone secretion

This is a diagnosis of exclusion and is characterized by inappropriately concentrated urine in the setting of hypotonicity. It accounts for approximately 50% of all cases of hyponatraemia. These patients have elevated serum ADH levels without an obvious volume or osmotic stimulus. The diagnostic criteria for SIADH secretion are shown in [Box 12.2.5](#) and conditions associated with the syndrome are listed in [Box 12.2.6](#).

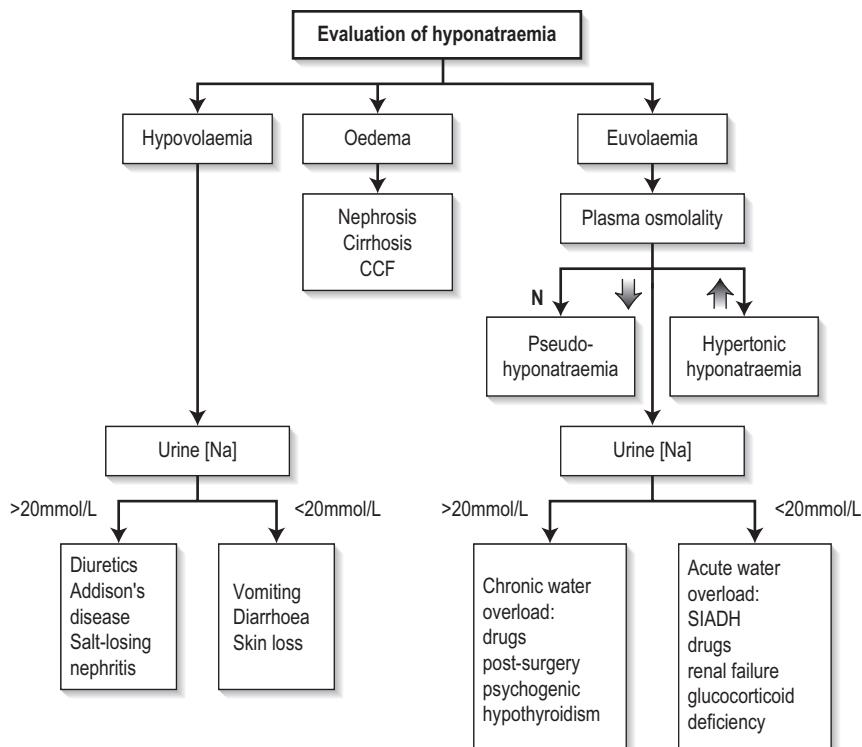


FIG. 12.2.1 Assessment of hyponatraemia. CCF, Congestive cardiac failure; SIADH, syndrome of inappropriate antidiuretic hormone. (Modified with permission from Walmsley R, Cuerin M. *Disorders of Fluid and Electrolyte Balance*. Bristol: John Wright & Sons; 1984.)

duration of the hyponatraemia and the absolute value of sodium. Ideally, correction of the serum sodium should be of a sufficient pace and magnitude to reverse the manifestations of hypotonicity but not be so rapid and large as to pose a risk of the development of osmotic demyelination.

Acute (<48 hours onset) symptomatic hyponatraemia (hyponatraemic encephalopathy)

Acute symptomatic hyponatraemia is a medical emergency requiring prompt and aggressive treatment, aiming to achieve a serum sodium level of at least 125 mEq/L. An immediate increase in serum sodium concentration by 8 mEq/L over 4 to 6 hours is recommended. This can be achieved by infusing hypertonic saline (3% NaCl) at a rate of 1 to 2 mL/kg/h, which should raise the serum sodium by 1 to 2 mmol/L/h. Where neurological symptoms are severe, hypertonic saline can be infused at 4 to 6 mL/kg/h. Serum sodium concentrations should be monitored closely. Other measures to reduce intracranial pressure, such as intubation and intermittent positive pressure ventilation, may also be required.

Chronic (>48 hours onset or unknown) symptomatic hyponatraemia

Chronic hyponatraemia presents the greatest dilemma. Care must be taken with correction of

sodium as these patients are at the greatest risk of developing osmotic demyelination, yet the presence of encephalopathy mandates urgent treatment. In these patients, hypertonic saline can be infused so that a correction rate of no more than 1 to 1.5 mmol/L/h is maintained. Therapy with hypertonic saline should be discontinued when (1) the patient becomes asymptomatic, (2) the serum sodium has risen by 20 mmol/L, or (3) the serum sodium reaches 120 to 125 mmol/L. Thereafter, slower correction with water restriction should follow. The serum sodium should never be acutely elevated to hypernatraemic or normonatraemic levels and should not be elevated by more than 25 mmol/L during the first 48 hours of therapy.

Chronic (>48 hours onset or unknown) asymptomatic hyponatraemia

In this situation, saline infusion is usually not required and patients can be managed by treating the underlying disorder, discontinuing diuretic therapy or restricting fluids. Fluid restriction is inexpensive and effective but is often limited by patient non-compliance. Other treatment options include pharmacological inhibition of ADH with demeclocycline, which is limited by its neuro- and nephrotoxic side effects, or increasing solute with the use of furosemide or urea.

Osmotic myelinolysis

This is an iatrogenic disorder which develops progressively over 3 to 5 days following the correction of hyponatraemia. It classically produces symmetrical lesions centred on the midline of the pons and was originally described as 'central pontine myelinolysis'. However, about 10% of cases involve extrapontine lesions. It is reported as occurring in 25% of severely hyponatraemic patients following correction of serum sodium. Clinically, the disorder is initially manifested by dysarthria, mutism, lethargy and affective changes, which may be mistaken for psychiatric illness. Classically, pseudobulbar palsy and spastic quadripareisis are observed. Recovery is usually gradual and incomplete, although both fatalities and complete recovery are reported. Demyelination in the central pons and extrapontine sites can be demonstrated on magnetic resonance imaging (MRI) scan or at autopsy.

It appears that the risk of developing osmotic myelinolysis is associated with severity and chronicity of hyponatraemia. It rarely occurs if the serum sodium is >120 mmol/L or where hyponatraemia has been present for <48 hours. Alcoholics, malnourished patients, hypokalaemic patients, burn victims and elderly patients on thiazides seem to be most at risk of developing osmotic demyelination.

Both the rate and the magnitude of sodium correction appear important in the development of osmotic myelinolysis. To date, although there is no agreed rate of correction regarded as completely safe, most authorities suggest that the serum sodium concentration should not rise by more than 10 to 14 mmol/L during any 24-hour period.

HYPERNATRAEMIA

Introduction

Hypernatraemia (Na >150 mEq/L) is much less common than hyponatraemia.

It is important to recognize hypernatraemia because it is usually associated with severe underlying medical illness. It is a condition of hospitalized patients, the elderly and dependent people. The incidence of hypernatraemia in hospitalized patients ranges from 0.3% to 1%, with from 60% to 80% of these developing hypernatraemia after admission. In-hospital mortality is high (40% to 55%).

Pathophysiology

Hypernatraemia is a relative deficiency of total body water compared to total body sodium, thus rendering the body fluids hypertonic. The normal compensatory response

12.2 ELECTROLYTE DISTURBANCES

Box 12.2.7 Causes of hypernatraemia

Altered perception of thirst

Osmoreceptor damage/destruction

Exogenous: trauma

Endogenous: vasculitis, carcinoma, granuloma

Idiopathic: psychogenic, head injury

Drugs

Normal perception of thirst

Poor intake

Confusion

Coma

Depression

Dysphagia

Odynophagia

Increased water loss and decreased intake

Diuresis

Renal loss

Diabetes insipidus

Chronic renal failure

Diuretic excess

GIT loss: fistulae, diarrhoea

Exogenous increase in salt intake

GIT, Gastrointestinal tract.

includes stimulated thirst—the most important response—and renal water conservation through ADH secretion. In the absence of ADH, water intake can match urinary losses because of increased thirst, but where the thirst mechanism is absent or defective, patients become hypernatraemic even in the presence of maximal ADH stimulation. Therefore hypernatraemia is usually seen where water intake is inadequate, that is, in patients too young, too old or too sick to drink, with no access to water or with a defective thirst mechanism.

Extracellular hypertonicity causes a shift of water from the intracellular space until there is osmotic equilibrium. The resultant cellular contraction may explain some of the clinical features of hypernatraemia. The brain is especially at risk from shrinkage because of its vascular attachments to the calvarium. Haemorrhage may occur if these vascular attachments tear.

As with hyponatraemia, the rate and magnitude of the rise in sodium determine the severity of the symptoms, which is a reflection of the brain's capacity to adapt to the deranged osmotic conditions.

Aetiology and classification

The clinical causes of hypernatraemia are listed in [Box 12.2.7](#). Population groups at particular risk of developing hypernatraemia are listed in [Box 12.2.8](#).

Hypernatraemia is classified into three categories based on extracellular volume status:

Box 12.2.8 Groups at particular risk for hypernatraemia

Elderly or disabled, unable to obtain oral fluids independently

Infants

Inpatients receiving: hypertonic infusions tube feedings osmotic diuretics lactulose mechanical ventilation

Altered mental status

Uncontrolled diabetes mellitus

Underlying polyuric disorders

Hypovolaemic hypernatraemia

This occurs where there is loss of both total body water and sodium, but with a greater loss of water. Renal causes include osmotic diuresis and diuretic excess. Urinary sodium is usually >20 mmol/L. Extrarenal losses include profuse diarrhoea, sweating, burns and fistulae. Urinary sodium is usually <20 mmol/L.

Euvolaemic hypernatraemia

This is the most common form of hypernatraemia. Patients have pure water losses, with intracellular dehydration as water shifts according to the osmotic gradient. Hypernatraemia in these patients occurs only when there is no accompanying water intake, that is, restricted access to water or a defect in thirst sensation.

Extrarenal losses are usually seen in skin losses in burns patients and via the respiratory system in respiratory infections and at high altitude. Renal water loss is usually due to diabetes insipidus—a failure of ADH production or secretion (central diabetes insipidus) or a failure of the collecting duct of the kidney to respond to ADH (nephrogenic diabetes insipidus).

Hypervolaemic hypernatraemia

This is not very common. These patients are typically extracellular volume expanded but intracellular volume depleted. It is seen following resuscitation with sodium bicarbonate, with the use of hypertonic saline solutions, with excess salt intake, in primary hyperaldosteronism and in Cushing syndrome.

Clinical features

In addition to the features of the underlying medical condition and alteration in extracellular volume, the clinical features of hypernatraemia per se are primarily CNS. Early symptoms are anorexia, nausea and vomiting; lethargy, hyperreflexia, confusion, seizures and coma occur later.

Treatment

The speed at which hypernatraemia is corrected should take into account the rate of development

and severity of symptoms. Too rapid correction, especially in chronic hypernatraemia, can cause cerebral oedema or isotonic water intoxication. The rate of correction of chronic hypernatraemia should not exceed 0.5 to 0.7 mmol/L/h.

Treatment is based on clinical assessment of the patient's volume status.

Hypovolaemic hypernatraemia

These patients require restoration of the volume deficit with isotonic saline, colloid or blood in the first instance, to prevent peripheral vascular collapse and treatment of the underlying cause. Following this, the water deficit is corrected with 0.45% saline, 5% dextrose or oral water.

The water deficit is calculated as follows:

$$\text{Water deficit} = \text{total body water} \\ \times (1 - \frac{\text{Na}_2}{\text{Na}_1})$$

where Na_2 = desired sodium, Na_1 = actual sodium and total body water is usually 60% of the body weight. The calculated normal daily maintenance fluids should be added to the above volumes.

Euvolaemic hypernatraemia

Calculate the water deficit as above and replace the deficit and ongoing losses with 5% dextrose, 0.45% saline or oral water. To avoid cerebral oedema, particularly in chronic hypernatraemia, 50% of the water deficit should be replaced over the first 6 to 12 hours and the rest given slowly over 1 to 2 days. Serum sodium estimations should be repeated at regular intervals.

Hypervolaemic hypernatraemia

Removal of sodium is required with the use of diuretics, such as furosemide, and discontinuation of causative agents. Furosemide causes excretion of more water than sodium, so a hypotonic fluid, such as 5% dextrose, may need to be infused. In severe cases or in renal failure, dialysis may be required.

HYPOKALAEMIA

Introduction

Hypokalaemia may be defined as a serum potassium concentration of less than 3.5 mmol/L. It is usually considered to be severe when this is less than 2.4 mmol/L.

Pathophysiology

Hypokalaemia may develop as a consequence of potassium depletion or a shift of potassium into cells. In either case, there is an increase in the ratio of intracellular to extracellular potassium

Box 12.2.9 Causes of hypokalaemia

- Inadequate dietary intake
- Abnormal losses
 - Gastrointestinal
 - Vomiting, nasogastric aspiration
 - Diarrhoea, fistula loss
 - Villous adenoma of the colon
 - Laxative abuse
- Renal
 - Mineralocorticoid excess
 - Conn's syndrome
 - Barter syndrome
 - Ectopic ACTH syndrome
 - Small cell carcinoma of the lung
 - Pancreatic carcinoma
 - Carcinoma of the thymus
 - Renal tubular acidosis
 - Magnesium deficiency
- Drugs
 - Diuretics
 - Corticosteroids
 - Gentamicin, amphotericin B
 - Cisplatin
- Compartmental shift
 - Alkalosis insulin
 - Na-K-ATPase stimulation
 - Sympathomimetic agents with β_2 effect
 - Methylxanthines
 - Barium poisoning
 - Hypothermia
 - Toluene intoxication
 - Hypokalaemic periodic paralysis

ACTH, Adrenocorticotrophic hormone.

concentrations. This, in turn, produces hyperpolarization across excitable membranes and is responsible for the effects of hypokalaemia on striated muscle and the cardiac conducting system.

Aetiology

The causes of hypokalaemia are listed in [Box 12.2.9](#).

Clinical presentation

Hypokalaemia commonly produces no symptoms in otherwise healthy subjects.

Clinical features may include weakness, constipation, ileus and ventilatory failure. Myopathy may develop, with weakness of the extremities, which characteristically worsens with exercise. If the hypokalaemia is severe and untreated, rhabdomyolysis may occur. Polyuria and polydipsia may result from the effect of hypokalaemia on the distal renal tubule (nephrogenic diabetes insipidus of hypokalaemia). Cardiac effects include ventricular tachycardias and atrial tachycardias, with or without block. Characteristic electrocardiogram (ECG) changes include PR

prolongation, T-wave flattening and inversion and prominent U waves

Treatment

Oral replacement is safe for asymptomatic patients and 40 to 60 mmol of potassium every 1 to 4 hours is usually well tolerated.

Intravenous administration of potassium is recommended when hypokalaemia is associated with cardiac arrhythmias, familial periodic paralysis or severe myopathy. Usual infusion rates are 10 to 20 mmol/h. Rates greater than 40 mmol/h are not recommended. Potassium is a sclerosant and should, therefore, be given via a large peripheral or central vein. Serum potassium estimations every 1 to 4 hours and continuous cardiac monitoring are mandatory.

HYPERKALAEMIA**Introduction**

Hyperkalaemia, defined as a serum potassium concentration greater than 5.5 mmol/L, is less common than hypokalaemia. Moderate (6.1 to 6.9 mmol/L) and severe (>7 mmol/L) hyperkalaemia can have grave consequences, particularly if acute.

Pathophysiology

Two homeostatic mechanisms are responsible for maintaining potassium balance. The renal system maintains external potassium balance by excreting 90% to 95% of the average daily potassium load (100 mmol/day); the gut excretes the remainder. This is a relatively slow process: only half the administered load of potassium will have been excreted in the urine after 3 to 6 hours. The extrarenal system involves hormonal and acid-base mechanisms that rapidly translocate potassium intracellularly. This system is critical in the management of acute hyperkalaemia.

Aetiology

The causes of hyperkalaemia are listed in [Box 12.2.10](#).

Clinical features

The clinical features of hyperkalaemia are often non-specific. Diagnosis depends on clinical suspicion, measurement of potassium concentration in the plasma and the characteristic changes on the ECG.

Generalized muscle weakness, flaccid paralysis and paraesthesia of the hands and feet are common, but there is poor correlation between the

Box 12.2.10 Causes of hyperkalaemia

- Pseudohyperkalaemia
 - Delay in separating red cells
 - Specimen haemolysis during or after venesection
 - Severe leucocytosis/thrombocytosis
- Excessive intake
 - Exogenous: IV or oral KCl, massive blood transfusion
 - Endogenous: tissue damage
 - Burns
 - Trauma
 - Rhabdomyolysis
 - Tumour lysis
- Decrease in renal excretion
 - Drugs
 - Spironolactone, triamterene, amiloride
 - Indomethacin
 - Captopril, enalapril
 - Renal failure
 - Addison disease
 - Hyporeninaemic hypoaldosteronism
 - Compartmental shift
 - Acidosis
 - Insulin deficiency
 - Digoxin overdose
 - Succinylcholine
 - Fluoride poisoning
 - Hyperkalaemic periodic paralysis

IV, Intravenous.

degree of muscle weakness and serum potassium concentration.

The ECG changes ([Table 12.2.1](#)) are characteristic, but are an insensitive method of evaluating hyperkalaemia.

Serum biochemistry in almost all patients with hyperkalaemia shows some degree of renal impairment and metabolic acidosis. In dialysis patients, hyperkalaemia may develop without concomitant metabolic acidosis.

Treatment

Pseudohyperkalaemia is common due to release of potassium during or after venipuncture, so if hyperkalaemia is an unexpected finding, the serum potassium should be remeasured.

Hyperkalaemia with ECG changes requires urgent management. The priorities are as follows:

1. Antagonize potassium cardiac toxicity:
 - IV calcium chloride 10%, 5 to 10 mL or
 - IV calcium gluconate 10%, 15 to 30 mL.

The effects of calcium should be evident within minutes and last for 30 to 60 minutes. A calcium infusion may be required. Calcium antagonizes the myocardial membrane excitability induced by hyperkalaemia. It does not lower serum potassium levels.

12.2 ELECTROLYTE DISTURBANCES

Table 12.2.1 Electrocardiogram changes of hyperkalaemia

Plasma potassium (mmol/L)	Electrocardiogram characteristics
6–7	Tall peaked T waves (>5 mm)
7–8	QRS widening, small-amplitude P waves
8–9	Fusion of QRS complex with T wave producing sine wave
>9	AV dissociation, ventricular tachycardia, ventricular fibrillation

AV, Atrioventricular.

2. Shift potassium into cells:

- IV soluble insulin, 20 U with dextrose 50 g and/or
- salbutamol nebulized (10 to 20 mg) or IV (0.5 mg diluted in 100 mL over 10 to 15 min) and or
- IV sodium bicarbonate, 50 to 200 mmol

3. Enhance potassium excretion:

- oral and/or rectal resonium A 50 g. This is a cation exchange resin; as the resin passes through the gastrointestinal tract, Na and K are exchanged and the cationically modified resin is then excreted in the faeces. This takes hours to have an effect.
- furosemide diuresis
- haemodialysis. This is usually reserved for cases of acute renal failure or end-stage renal disease. It is the most effective treatment for acutely lowering serum potassium, but there is usually a time delay in instituting dialysis and the temporizing measures outlined above must be employed in the interim.

The use of insulin and glucose is well supported in the literature. A response is usually seen within 20 to 30 min, with lowering of plasma potassium by up to 1 mmol/L and reversal of ECG changes. Transient hypoglycaemia may be observed within 15 minutes of insulin administration. In some patients, particularly those with end-stage renal failure, late hypoglycaemia may develop. For this reason, a 10% dextrose infusion at 50 L/hr is recommended and the blood glucose should be monitored closely. The exact mechanism by which insulin translocates potassium is not known; it is thought to be stimulation of Na-K-ATPase independent of cAMP.

β_2 -Agonists significantly lower plasma potassium when given intravenously or via a nebulizer. Potassium levels are reduced by up to 1.00 mmol/L within 30 minutes following 10 to 20 mg of nebulized salbutamol. The effect is sustained for up to 2 hours. Adverse effects of

Box 12.2.11 Causes of hypocalcaemia

Factitious EDTA contamination
Hypoalbuminaemia
Decreased PTH activity
Hypoparathyroidism
Pseudohypoparathyroidism
Hypomagnesaemia
Decreased vitamin D activity
Acute pancreatitis
Hyperphosphataemia
Renal failure
Phosphate supplements
'Hungry bone' syndrome
Drugs
Mithramycin
Diuretics: furosemide, ethacrynic acid

EDTA, Ethylenediaminetetraacetic acid; PTH, Parathyroid hormone.

salbutamol administration include tachyarrhythmias and precipitation of angina in patients with coronary artery disease. Patients on non-selective β -blockers and with end-stage renal disease may not respond. Greater decreases in potassium have been observed when salbutamol treatment is combined with insulin and glucose. The additive effect is thought to be due to stimulation of Na-K-ATPase via different pathways.

HYPOCALCAEMIA

Introduction

A reduction in serum calcium concentration manifests principally as abnormal neuromuscular function.

Pathophysiology

Calcium is involved in smooth and skeletal muscle contraction and relaxation, platelet aggregation, neurotransmission, hepatic and adipose glycogenolysis, thermogenesis and neutrophil function. In addition, most endocrine and exocrine gland function is calcium dependent.

Aetiology

The major cause of severe hypocalcaemia is hypoparathyroidism, as a result of surgery for thyroid disease, autoimmune destruction or from developmental abnormalities of the parathyroid glands. Other causes are listed in Box 12.2.11.

Clinical features

Patients with acute hypocalcaemia are more likely to be symptomatic than those with chronic hypocalcaemia. Symptomatic hypocalcaemia is characterized by abnormal neuromuscular excitability and neurological

sensations. Early signs are perioral numbness and paraesthesia of distal extremities. Hyperreflexia, muscle cramps and carpopedal spasm follow. Chvostek sign (ipsilateral contraction of the facial muscles elicited by tapping the facial nerve just anterior to the ear) and Trouseau sign (carmopedal spasm with inflation of a blood pressure cuff for 3 to 5 minutes) are signs of neuromuscular irritability. If muscle contractions become uncontrollable, tetany results and this can prove fatal if laryngospasm occurs. Seizures may occur when there is CNS instability. Cardiovascular manifestations include hypotension, bradycardia, impaired cardiac contractility and arrhythmias. ECG evidence of hypocalcaemia includes prolonged QT interval and possibly ST prolongation and T-wave abnormalities.

Treatment

Acute symptomatic hypocalcaemia

In the emergency situation where seizures, tetany, life-threatening hypotension or arrhythmias are present, IV calcium is the treatment of choice. Infusion of 15 mg/kg of elemental calcium over 4 to 6 hours increases the total serum calcium by 0.5 to 0.75 mmol/L.

Administration of 10 to 20 mL of 10% calcium gluconate (89 mg elemental calcium per 10 mL) IV over 5 to 10 minutes is recommended. This should be followed by a continuous infusion because the effects of a single IV dose last only about 2 hours. The infusion rate should be adjusted according to serial calcium measurements obtained every 2 to 4 hours. Over-rapid infusion may cause facial flushing, headache and arrhythmias.

Calcium chloride 10% may also be used. This contains more calcium per ampoule (272 mg in 10 mL), resulting in a more rapid rise in serum calcium, but is more irritant to veins and can cause thrombophlebitis with extravasation.

Where hypocalcaemia and metabolic acidosis are present (usually in sepsis or renal failure), correction of the acidosis with bicarbonate may result in a rapid fall in ionized calcium as the number of calcium-binding sites is increased. Therefore hypocalcaemia must be corrected before the acidosis. Bicarbonate or phosphate should not be infused with calcium because of possible precipitation of calcium salts.

Cardiac monitoring is recommended during rapid calcium administration.

Chronic asymptomatic hypocalcaemia

These patients are usually managed with oral calcium supplements taken between meals. Calcitriol, the active hormonal form of vitamin D, 0.5 to 1.5 mg daily, can also be given.

HYPERCALCAEMIA

Introduction

Hypercalcaemia is a relatively common condition with a frequency estimated at 1:1000 to 1:10,000. The most frequent are malignancy and hyperparathyroidism.

Pathophysiology

Total serum calcium is made up of protein-bound calcium (40%, mostly albumin and not filterable by the kidneys), ion-bound complexes (13%, bound to anions such as bicarbonate, lactate, citrate and phosphate) and the unbound, ionized fraction (47%). The ionized fraction is the biologically active component of calcium and is closely regulated by parathyroid hormone (PTH). Total serum calcium is affected by albumin and does not necessarily reflect the level of plasma ionized calcium. Normal ionized calcium levels are 1.14 to 1.30 mmol/L. Protein binding, in turn, is influenced by ECF pH and alterations in serum albumin. Acidemia decreases protein binding and increases the level of ionized calcium. To correct for pH: ionized calcium rises 0.05 mmol/L for each 0.1 decrease in pH.

To correct for serum albumin:

$$\text{Corrected } [\text{Ca}^+] = \text{measured } [\text{Ca}^+] + (40 - \text{albumin g/L}) \times 0.02 \text{ mmol/L}$$

Corrected calcium is used for all treatment decisions except where direct measurement of ionized calcium using an ion-specific electrode is available.

Three pathophysiological mechanisms may produce hypercalcaemia:

- Accelerated osteoclastic bone resorption. This is the most common cause of severe hypercalcaemia. Osteoclasts are activated by PTH and various humoral tumour products, the most common being parathyroid hormone-related protein (PTHrP).
- Increased gastrointestinal absorption (rarely important).
- Decreased renal excretion of calcium. PTH and PTHrP stimulate renal tubular reabsorption of calcium. Hypercalcaemia per se causes polyuria by interfering with renal mechanisms for the reabsorption of water and sodium. If there is inadequate fluid intake to compensate, extracellular volume depletion occurs, reducing glomerular filtration and exacerbating the hypercalcaemia.

Aetiology

The majority of cases of hypercalcaemia requiring urgent treatment are due to malignancy or,

Box 12.2.12 Causes of hypercalcaemia

Factitious
Haemoconcentration
Postprandial
Malignancy:
Lung and breast cancer, squamous cell carcinoma of the head and neck and cholangiocarcinoma and the haematological malignancies, multiple myeloma and lymphoma
Primary hyperparathyroidism
Drugs
Thiazides
Vitamin D
Lithium
Vitamin A
Hormonal
Thyrotoxicosis
Acromegaly
Hypoadrenalinism
Phaeochromocytoma
Granulomas
Tuberculosis
Sarcoidosis
Renal failure
Milk alkali syndrome
Immobilization

less commonly, primary hyperparathyroidism (parathyroid crisis). (Box 12.2.12).

Clinical features

Hypercalcaemia causes disturbances of the gastrointestinal, cardiovascular and renal systems, and CNS.

Gastrointestinal manifestations include anorexia, nausea, vomiting and constipation. Cardiovascular manifestations include hypertension and a shortened QT interval on the ECG. Renal manifestations include polyuria, polydipsia and nephrocalcinosis (rare). CNS symptoms include psychotic behaviour, seizures, apathy, cognitive difficulties, obtundation and coma. Renal elimination of digoxin is also impaired.

Moderately elevated total serum calcium (3.00 to 3.50 mmol/L) is usually associated with symptoms. Markedly elevated total serum calcium (>3.5 mmol/L) mandates urgent treatment regardless of symptoms.

Treatment

Irrespective of the cause, the management of hypercalcaemic crisis is the same. There are three primary treatment goals:

- hydration of the patient ± enhancement of renal excretion of calcium
- inhibition of accelerated bone resorption
- treatment of the underlying problem.

Hydration and diuresis

Since hypercalcaemia invariably causes dehydration, volume expansion with intravenous fluids dilutes calcium and increases calcium clearance. Infusion rates of 200 to 300 mL/h of 0.9% saline, depending on the degree of hypovolaemia and the ability of the patient to tolerate fluid, may be required and, once adequate rehydration has been achieved, the infusion rate can be adjusted to maintain a urine output of 100 to 150 mL/h.

This treatment, although effective, results in a relatively modest reduction in serum calcium and patients with severe hypercalcaemia usually require additional treatment with bisphosphonates.

The routine use of loop diuretics is no longer recommended.

Enhancement of renal excretion

Haemodialysis is the treatment of choice to decrease rapidly serum calcium in patients with heart failure or renal insufficiency.

Inhibition of bone resorption

Pharmacological inhibition of osteoclastic bone resorption is the most effective treatment for hypercalcaemia, particularly hypercalcaemia of malignancy. Bisphosphonates, analogues of pyrophosphate, are the principal agents used. They inhibit osteoclast function and hydroxyapatite crystal dissolution. Unfortunately, normalization of calcium levels may take 3 to 6 days, which is too slow in critically ill patients.

Disodium pamidronate is currently one of the bisphosphonates of choice. The dose is 60 mg IV (in 500 mL 0.9% saline over 4 hours) if serum calcium is <3.5 mmol/L, and 80 mg IV if serum calcium is >3.5 mmol/L. Calcium levels normalize in up to 80% of patients within 7 days and this effect can persist for up to a month. Common adverse reactions include a mild transient elevation in temperature, local infusion site reactions, mild gastrointestinal symptoms and mild hypophosphataemia, hypokalaemia and hypomagnesaemia.

An alternative treatment to pamidronate is zoledronic acid 4 mg/100 mL (N saline or 5% dextrose) IV over 15 minutes. It is more potent and effective than pamidronate.

Glucocorticoids, after rehydration, are the treatment of choice in selected patient populations where there is inappropriately high production of 1,25-dihydroxyvitamin D as the mechanism for causing hypercalcaemia. Such conditions include vitamin D toxicity, sarcoidosis, other granulomatous diseases and haematological malignancies. The usual dose is 200 to 300 mg hydrocortisone IV for

12.2 ELECTROLYTE DISTURBANCES

3 to 5 days. However, the maximal calcium-lowering effect does not occur for several days and glucocorticoids should only be regarded as adjunctive therapy in hypercalcaemic crises.

Treat the underlying disorder

The definitive treatment for hypercalcaemia is to treat the underlying disease: surgery for hyperparathyroidism and tumour-specific therapy for hypercalcaemia of malignancy.

HYPOMAGNESEAEMIA

Introduction

The diagnosis of magnesium deficiency is difficult and often overlooked largely because the symptoms are non-specific and do not usually appear until the patient is severely deficient.

Serum magnesium concentration (normal range: 0.76 to 0.96 mmol/L) is not a sensitive indicator of magnesium deficiency as it may not truly reflect total body stores. However, it is commonly used in the absence of other reliable methods to estimate the 'true' magnesium status. A low serum magnesium concentration is usually present in symptomatic magnesium deficiency, but it is important to remember that it may be normal in the presence of significant intracellular depletion.

Pathophysiology

Magnesium plays a critical role in metabolism: as an enzyme co-factor, in the maintenance of cell membranes and in electrolyte balance. It is the fourth most common cation in the body and is predominantly an intracellular ion with the majority found in bone (>50%) and soft tissue. Only 0.3% of total body magnesium is located extracellularly, of which 33% is protein bound, 12% is complexed to anions, such as citrate, bicarbonate and phosphate, and 55% is found in the free ionized form.

Hypokalaemia is present in 40% to 60% of cases of magnesium deficiency, due to renal wasting of potassium. The hypokalaemia is resistant to potassium replacement alone, as a result of a combination of factors, including impaired cellular cation pump activity and increased cellular permeability to potassium.

Hypocalcaemia is usually present at serum magnesium concentrations below 0.49 mmol/L. This may be due to impaired PTH synthesis or secretion or to PTH resistance as a result of magnesium deficiency.

Box 12.2.13 Causes of magnesium deficiency

Gastrointestinal losses

Acute and chronic diarrhoea
Acute pancreatitis
Severe malnutrition
Intestinal fistulae
Extensive bowel resection
Prolonged nasogastric suction

Renal losses

Osmotic diuresis—diabetes, urea, mannitol
Hypercalcaemia and hypercalciuria
Volume expanded states
Chronic parenteral fluid therapy

Drugs

ACE inhibitors
Alcohol
Aminoglycosides
Amphotericin B
Cisplatin
Ciclosporin

Diuretics—thiazide or loop

Other
Phosphate depletion

ACE, Angiotensin-converting enzyme.

(From Weisinger JR, Bellorin-Font E. Magnesium and phosphorus-electrolyte quintet. *Lancet*. 1998;352:391–396.)

Aetiology

From an emergency medicine perspective, hypomagnesaemia is most frequently encountered in the context of acute and chronic diarrhoea, acute pancreatitis, diuretic use, in alcoholics (in 30% of those admitted to hospital) and in diabetic ketoacidosis, secondary to glycosuria and osmotic diuresis (Box 12.2.13).

Clinical features

The clinical manifestations of severe magnesium deficiency include metabolic, neurological and cardiac effects (Box 12.2.14).

The presenting symptoms are non-specific and can be attributed to associated metabolic abnormalities, such as hypocalcaemia, hypokalaemia and metabolic alkalosis. In particular, patients may present with symptoms of hypocalcaemia: neuromuscular hyperexcitability, carpopedal spasm and positive Chvostek and Trousseau signs.

Early ECG changes of magnesium deficiency include prolongation of the PR and QT intervals, with progressive QRS widening and U-wave appearance as severity progresses. Changes in cardiac automaticity and conduction, atrial and ventricular arrhythmias, including torsades des pointes, can occur. Administration of a magnesium bolus can abolish torsades des pointes, even in the presence of normal serum magnesium levels. Magnesium is a co-factor in the

Box 12.2.14 Clinical manifestations of severe magnesium deficiency

Cardiac effects	Metabolic effects	Neurological effects
Atrial fibrillation	Hypokalaemia	Grand mal seizures
Atrial flutter	Hypocalcaemia	Focal seizures
Supraventricular tachycardia	Hyponatraemia	Paraesthesiae
Ventricular tachycardia	Hypophosphataemia	Dizziness
Torsades des pointes	Metabolic alkalosis	Vertigo
Coronary artery spasm	Hyperglycaemia	Ataxia
Hypertension	Hyperlipidaemia	Nystagmus
ECG changes		Tremor
Atherosclerosis		Myopathy
		Dysphagia
		Oesophageal spasm
		Delirium, personality changes
		Depression
		Coma

ECG, Electrocardiogram.

(From Fawcett WJ, Haxby EJ, Male DA. Magnesium: physiology and pharmacology. *Br J Anaesth*. 1999;83:302–320.)

Box 12.2.15 Magnesium doses (in mmol magnesium)

Emergency—IV route
8–16 mmol <i>statim</i>
40 mmol over next 5 h
Severely ill—IM route
48 mmol on day 1
17–25 mmol on days 2–5
Asymptomatic—oral route
15 mmol/day

IM, Intramuscularly; IV, intravenously.

Na-K-ATPase system, so magnesium deficiency enhances myocardial sensitivity to digitalis and may precipitate digitalis toxicity. Digitalis-toxic arrhythmias, in turn, can be terminated with intravenous magnesium.

Treatment

Oral replacement is the preferred option in asymptomatic patients, although this route takes longer.

Symptomatic moderate-to-severe magnesium deficiency should be treated with parenteral magnesium salts. The patient should be closely monitored and therapy discontinued if deep tendon reflexes disappear or if serum magnesium exceeds 2.5 mmol/L. Suggested dosing regimens are outlined in Box 12.2.15.

HYPERMAGNESEAEMIA

Hypermagnesaemia (serum magnesium above 0.95 mmol/L) is rare and usually iatrogenic.

The elderly and patients with renal impairment or chronic bowel disorders are particularly at risk, especially when IV magnesium or magnesium-containing cathartics or antacids are used.

Clinical manifestations include mental obtundation progressing to coma, cardiac arrhythmias, loss of deep tendon reflexes, refractory hypotension and respiratory arrest, nausea and vomiting, muscle paralysis and flushing.

Magnesium administration should be immediately discontinued. Further management is largely supportive. Maintain urine output at greater than 60 mL/h with fluid administration to enhance renal excretion. Furosemide (40 to 80 mg IV) may also be given once the patient is adequately hydrated. Haemodialysis may be of benefit in severe cases, particularly if there is impaired renal function.

CONTROVERSIES

- The safest and most effective ways of correcting hyponatraemia remain controversial because of the risk of inducing osmotic myelinolysis.
- The usefulness of bicarbonate for the acute therapy of hyperkalaemia has been questioned. A number of studies have shown that bicarbonate fails to lower potassium levels sufficiently in the acute, life-threatening situation to justify its use as first-line treatment. However, it is still recommended when hyperkalaemia is associated with severe metabolic acidosis ($\text{pH} < 7.20$).

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SECTION 13

HAEMATOLOGY EMERGENCIES

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13.1 Anaemia

Mark Little

ESSENTIALS

- 1** Anaemia is a condition in which the absolute number of red cells in the circulation is abnormally low.
- 2** Anaemia is not a diagnosis: it is a finding, which should prompt a search for an underlying cause.
- 3** The anaemic patient is doing at least one of three things: not producing enough red cells, destroying them too quickly or bleeding.
- 4** Bleeding is the most common cause of life-threatening anaemia encountered in the emergency department (ED).

Introduction

Anaemia is a condition in which the absolute number of red cells in the circulation is abnormally low. The diagnosis is usually made on the basis of the full blood count (FBC). This, together with the blood film, offers qualitative as well as quantitative data on the blood components; a set of normal values is shown in [Box 13.1.1](#).

The average life span of a normal red blood cell in the circulation is from 100 to 120 days. Aged red cells are removed by the reticuloendothelial system but, under normal conditions, are replaced by the marrow, such that a dynamic equilibrium is maintained. Anaemia develops when red cell loss exceeds red cell production. It follows that the anaemic patient is doing at least one of three things: not producing enough red cells, destroying them too quickly or bleeding.

The overriding functional importance of the red cell resides in its ability to transport oxygen, bound to the haemoglobin (Hb) molecule, from the lungs to the tissues. Functionally, anaemia may be regarded as an impairment in the supply of oxygen to the tissues, and the adverse effects of anaemia, from whatever cause, are a consequence of the resultant tissue hypoxia.

Anaemia is not a diagnosis: rather, it is a clinical or a laboratory finding that should prompt a search for an underlying cause ([Box 13.1.2](#)).

ANAEMIA SECONDARY TO HAEMORRHAGE

Aetiology

By far the most common cause of severe anaemia encountered in the ED is haemorrhage.

Therefore assessment of the anaemic patient is often chiefly concerned with a search for a site of blood loss. The most common causes of haemorrhage are outlined in [Box 13.1.3](#). However, the emergency physician must remain alert to the possibility that the patient who is not bleeding is manifesting a rarer pathological condition.

Box 13.1.1 Full blood count: normal parameters

Haemoglobin (Hb)	
Males	135–180 g/L
Females	115–165 g/L
Red blood cell count	
Males	4500–6500 × 10 ⁹ /L
Females	3900–5600 × 10 ⁹ /L
Haematocrit	
Males	42%–54%
Females	37%–47%
Other values	
MCH	27–32 pg
MCHC	32–36 g/dL
MCV	76–98 fL
Reticulocytes	0.2%–2%
White blood cells	4–11 × 10 ⁹ /L
Neutrophils	1.8–8 × 10 ⁹ /L
Eosinophils	0–0.6 × 10 ⁹ /L
Basophils	0–0.2 × 10 ⁹ /L
Lymphocytes	1–5 × 10 ⁹ /L
Monocytes	0–0.8 × 10 ⁹ /L
Platelets	150–400 × 10 ⁹ /L

MCH, Hb divided by RBC; MCHC, Hb divided by HCT; MCV, HCT divided by RBC. Most automated counting machines now give the red cell distribution width, a measure of degree of variation of cell size.

Box 13.1.2 Causes of anaemia**Haemorrhage**

Traumatic
Non-traumatic
 Acute
 Chronic
Megaloblastic anaemia
Vitamin B₁₂ deficiency
Folate deficiency
Aplastic anaemia
Pure red cell aplasia
Myelodysplastic syndromes
Invasive marrow diseases
Chronic renal failure

Decreased RBC survival (haemolytic anaemia)

Congenital
Spherocytosis
Elliptocytosis
Glucose-6-phosphate-dehydrogenase deficiency
Pyruvate kinase deficiency
Haemoglobinopathies: sickle cell diseases
Acquired autoimmune haemolytic anaemia, warm
Acquired autoimmune haemolytic anaemia, cold
Microangiopathic haemolytic anaemias
RBC mechanical trauma
Infections
Paroxysmal nocturnal haemoglobinuria

RBC, Red blood cell.

Box 13.1.3 Common causes of haemorrhage in the emergency department**Trauma**

Blunt trauma to mediastinum
Pulmonary contusions/haemopneumothorax
Intraperitoneal injury
Retroperitoneal injury
Pelvic disruption
Long bone injury
Open wounds: inadequate first aid

Non-trauma

Gastrointestinal haemorrhage
Oesophageal varices
Peptic ulcer
Gastritis/Mallory-Weiss
Colonic/rectal bleeding

Obstetric/gynaecological bleeding

Ruptured ectopic pregnancy
Menorrhagia
Threatened miscarriage
Antepartum haemorrhage
Postpartum haemorrhage

Other

Epistaxis
Postoperative
Secondary to bleeding diathesis

Clinical features

Although it may be obvious on history and examination that a patient is bleeding, occasionally the source of blood loss is occult and the extent of the loss underestimated.

In the context of trauma, the history often gives clear pointers to both the sites and extent of blood loss. Consideration of the mechanism of injury may allow anticipation of occult pelvic, intraperitoneal or retroperitoneal bleeding. Intracranial bleeding is never an explanation for hypovolaemic shock in an adult.

In the absence of trauma, it is essential to obtain an obstetric and gynaecological history especially in women of childbearing age. The past medical history may point to a known haematological abnormality or a chronic disease process. A drug history is always relevant, as many drugs cause marrow suppression, haemolytic anaemia and bleeding. The family history may point to hereditary disease, and the social history may alert the clinician to an unusual occupational exposure in the patient's past or to recreational activities liable to exacerbate an ongoing disease process. The systems review is particularly relevant to the consultation with middle-aged or elderly male patients, who must be asked about symptoms of altered bowel habit and weight loss.

The symptomatology of anaemia proceeds from vague complaints of tiredness, lethargy and impaired performance through to more sharply defined entities such as shortness of breath on exertion, giddiness, restlessness, apprehension, confusion and collapse. Co-morbid conditions may be exacerbated (the dyspnoea of chronic obstructive airway disease) and occult pathologies unmasked (exertional angina in ischaemic heart disease).

Anaemia of insidious onset is generally better tolerated than that of rapid onset because of cardiovascular and other compensatory mechanisms. Acute loss of 40% of the blood volume may result in collapse, whereas—in some developing countries—it is not rare for patients with Hb concentrations only 10% of normal to be ambulant. Trauma superimposed on an already established anaemia can lead to rapid decompensation.

The cardinal sign of anaemia is pallor. This can be seen in the skin, lips, mucous membranes and conjunctival reflections. Yet not all anaemic patients are pallid and not all patients with a pale complexion are anaemic. Patients who have suffered an acute haemorrhage may show evidence of hypovolaemia: tachycardia, hypotension, cold peripheries and sluggish capillary refill. The detection of postural hypotension is an important pointer toward occult blood loss. Conversely, patients with anaemia of insidious

onset are not hypovolaemic and may manifest high-output cardiac failure as a physiological response to hypoxia.

Other features of the physical examination may provide clues to the aetiology of anaemia. The glossitis, angular stomatitis, koilonychia and oesophageal web of iron deficiency anaemia are uncommon findings. Bone tenderness, lymphadenopathy, hepatomegaly and splenomegaly may point to an underlying haematological abnormality. The rectal and gynaecological examinations can sometimes be diagnostic.

Clinical investigations

The FBC often reveals an anaemia that has not been clinically suspected and that must be interpreted in the light of the history and examination. If the anaemia is mild, it may be a chance finding with little relevance to the patient's presenting complaint, but such a finding should never be ignored. At the very least a follow-up blood count should be arranged.

Anaemic patients have a low red cell count, a low haematocrit and a low Hb, but some caveats must be borne in mind:

- Patients who are bleeding acutely may initially have a normal FBC.
- Normal or high haematocrits may reflect haemoconcentration.
- Mixed pictures can be difficult to interpret (e.g. that of a polycythaemic patient who is bleeding).

Red cell morphology, particularly the mean corpuscular volume (MCV), can help to elucidate the cause of anaemia. The finding of a pancytopenia suggests a problem in haematopoiesis rather than haemolysis or blood loss. In women of childbearing age, assay of blood or urine β-HCG is important.

Treatment

The principles of management of haemorrhage are as follows:

- Maintain the circulation.
- Identify the site of bleeding.
- Control the bleeding.
- Identify the underlying pathological process.
- Arrange for definitive treatment.
- Restore the blood volume.

The indications for red cell transfusion are discussed in Chapter 13.5. The faster the onset of the anaemia, the greater the need for urgent replacement. Patients who are tolerating their anaemia may require no more than an appropriate diet with or without the addition of haematinics. Elderly patients with severe bleeding often need red cells urgently. Excessive administration of colloid and/or crystalloid precipitates left ventricular failure, and it can then be difficult to administer red cells.

13.1 ANAEMIA

Chronic haemorrhage

The finding of a hypochromic microcytic anaemia on blood film is usually indicative of iron deficiency and, in the absence of an overt history of bleeding, should prompt a search for occult blood loss. Iron deficiency anaemia may be due to malnutrition, but inadequate dietary intake of iron is not usually the sole cause of anaemia in developed countries: much more commonly it is the result of chronic blood loss from the gastrointestinal (GI) tract, the uterus or the renal tract. More unusual causes are haemoptysis and recurrent epistaxis.

Patients present with insidious and rather vague symptoms. They may be unaware that they are bleeding and will probably show none of the trophic skin, nail and mucosal changes of iron deficiency. The automated cell count, in addition to showing a hypochromic, microcytic picture, may also show a raised red cell distribution width, which reflects anisocytosis on the blood film.

Iron studies may confirm the diagnosis of iron deficiency without pointing to the underlying cause. Serum iron and ferritin are low and total iron-binding capacity is high.

Disposition

If the source of blood loss is obvious—for example heavy menstrual bleeding—appropriate referral may be all that is indicated. If the source is not obvious, particularly in older patients, sequential investigation of the GI and renal tracts may be indicated. Decisions to admit or discharge these patients depend on the red cell reserves, the patient's cardiorespiratory status, his or her home circumstances and the likelihood of compliance with follow-up.

The anaemia itself can be corrected with oral or injectable iron supplementation. Intravenous ferric carboxymaltose over 20 minutes for the treatment of iron deficiency anaemia is now being used in EDs.

ANAEMIA SECONDARY TO DECREASED RED CELL PRODUCTION

Megaloblastic anaemia

The finding of a raised MCV is common in the presence or absence of anaemia. Alcohol abuse is a frequent underlying cause; other causes are listed in **Box 13.1.4**. MCVs greater than 115 fL are usually due to megaloblastic anaemia which, in turn, is usually due to either vitamin B12 or folate deficiency. Vitamin B12 and folate are essential to

Box 13.1.4 Some causes of a raised mass cell volume

- Alcohol
- Drugs
- Hypothyroidism
- Liver disease
- Megaloblastic anaemias (B12 and folate deficiency)
- Myelodysplasia
- Pregnancy
- Reticulocytosis

DNA synthesis in all cells. Deficiencies manifest principally in red cell production because of the sheer number of red cells that are produced. B12 deficiency is usually the result of a malabsorption syndrome, whereas folate deficiency is of dietary origin. Tetrahydrofolate is a co-factor in DNA synthesis; in turn, the formation of tetrahydrofolate from its methylated precursor is B12-dependent. Unabated cytoplasmic production of RNA in the context of impaired DNA synthesis appears to produce the enlarged nucleus and abundant cytoplasm of the megaloblast. When these cells are released to the periphery, they have poor function and poor survival.

B12 deficiency due to pernicious anaemia is an autoimmune disorder in which autoantibodies to gastric parietal cells and the B12 transport factor (intrinsic factor) interfere with B12 absorption in the terminal ileum. Patients have achlorhydria, mucosal atrophy (a painful smooth tongue) and, sometimes, evidence of other autoimmune disorders, such as vitiligo, thyroid disease and Addison disease.

A rare but important manifestation of this disease is 'subacute combined degeneration of the spinal cord'. Demyelination of the posterior and lateral columns of the spinal cord manifests as a peripheral neuropathy and an abnormal gait. The central nervous system abnormalities worsen and become irreversible in the absence of B12 supplementation. Treatment of B12-deficient patients with folate alone may accelerate the onset of this condition.

Undiagnosed untreated pernicious anaemia is not a common finding in the ED, but the laboratory finding of anaemia and megaloblastosis should prompt haematological consultation. The investigative workup—which includes B12 and red cell folate levels, autoantibodies to parietal cells and intrinsic factor, a marrow aspirate, and Schilling's test of B12 absorption—may well necessitate hospital admission.

The workup for folate deficiency is similar to that for B12. Occasionally patients require investigation for a malabsorption syndrome (tropical sprue, coeliac disease), which includes jejunal biopsy. Folate deficiency is common in pregnancy because of the large folate requirements of

the growing foetus. It can be difficult to diagnose because of the maternal physiological expansion of plasma volume and also of red cell mass, but diagnosis and treatment with oral folate supplements are important because of the risk of associated neural tube defects.

Both B12 and folate deficiency are usually manifestations of chronic disease processes. Rarely, an acute megaloblastic anaemia and pancytopenia can develop over the course of days and nitrous oxide therapy has been identified as a principal cause of this condition.

Anaemia of chronic disorders

Patients with chronic infective, malignant or connective tissue disorders can develop a mild to moderate normochromic normocytic anaemia. Evidence of bleeding or haemolysis is absent and there is no response to haematinic therapy. The pathophysiology of this anaemia is complex and probably involves both decreased red cell production and red cell survival. Possible underlying mechanisms include reticuloendothelial overactivity in chronic inflammation and defects in iron metabolism mediated by a variety of acute-phase reactants and cytokines, such as interleukin-1, tumour necrosis factor and interferon γ , which impair renal erythropoietin production and function.

Anaemia of chronic disorders (ACD) is generally not so severe as to warrant emergency therapy. The importance of ACD in the ED lies in its recognition as a pointer toward an underlying chronic process. Difficulties can arise in distinguishing ACD from iron deficiency, and the two conditions may coexist—in rheumatoid arthritis, for example. Iron studies generally elucidate the nature of the anaemia. In iron deficiency, iron and ferritin are low and total iron binding is high, whereas in ACD iron and total iron binding are low and ferritin is normal or high.

Other causes of decreased red cell production

Bone marrow failure is rarely encountered in emergency medicine practice. The physician must be alert to the unusual, insidious or sinister presentation and be particularly attuned to the triad of decreased tissue oxygenation, immunocompromise and a bleeding diathesis that may herald a pancytopenia. An FBC may dictate the need for haematological consultation, hospital admission and further investigation.

Among the entities to be considered are the aplastic anaemias, characterized by a pancytopenia secondary to failure of pluripotent myeloid stem cells. Half of such cases are idiopathic, but important aetiologies are infections (e.g. non-A, non-B hepatitis), inherited diseases

Box 13.1.5 Classification of the myelodysplastic syndromes

- Refractory anaemia
- Refractory anaemia with ringed sideroblasts
- Refractory anaemia with excess of blasts
- Chronic myelomonocytic leukaemia

(e.g. Fanconi anaemia), irradiation therapeutic or otherwise and, most important in the emergency setting, drugs. Drugs that have been implicated in the development of aplastic anaemia include—in addition to antimetabolites and alkylating agents—chloramphenicol, chlorpromazine and streptomycin.

Characteristic of patients with a primary marrow failure is the absence of splenomegaly and of a reticulocyte response. There is a correlation between prognosis and the severity of the pancytopenia. Platelet counts less than $20 \times 10^9/L$ and neutrophil counts less than $500/\mu L$ equate to severe disease. Depending on the severity of the accompanying anaemia, patients may require red cell and sometimes platelet transfusion in the ED as well as broad-spectrum antibiotic cover. It is imperative to stop all medications that might be causing the marrow failure. Other forms of marrow failure include pure red cell aplasia, where marrow red cell precursors are absent or diminished. This can be a complication of haemolytic states in which a viral insult leads to an aplastic crisis (see The haemolytic anaemias, further on).

The myelodysplastic syndromes are a group of disorders primarily affecting the elderly. In these states there is no reduction in marrow cellularity but the mature red cells, granulocytes and platelets generated from an abnormal clone of stem cells are disordered and dysfunctional. There is peripheral pancytopenia. These disorders are classified according to observed cellular morphology (Box 13.1.5). These conditions were once termed 'preleukaemia' and one-third of patients progress to acute myeloid leukaemia.

Two more causes of failure of erythropoiesis might be mentioned. One is invasion of the marrow and disruption of its architecture by extraneous tissue, the most common cause being metastatic cancer. Finally, but not at all uncommon, is the anaemia of chronic renal failure, where deficient erythropoiesis is attributed to decreased production of erythropoietin. Most patients with chronic renal failure on dialysis treatment tolerate a moderate degree of anaemia but occasionally require either transfusion or treatment with erythropoietin. Emergency physicians should recognize anaemia as a predictable entity in patients with chronic renal failure, which usually does not require any action.

ANAEMIA SECONDARY TO DECREASED RED CELL SURVIVAL: THE HAEMOLYTIC ANAEMIAS

Patients whose main problem is haemolysis are rarely encountered in the ED. The most fulminant haemolytic emergency imaginable is that following transfusion of ABO-incompatible blood (discussed in Chapter 13.5), a vanishingly rare event where proper procedures are followed. Haemolysis and haemolytic anaemia are occasionally encountered in decompensating patients with multisystem problems. Rarely, first presentations of unusual hematologic conditions occur.

Some of the haemolytic anaemias are hereditary conditions in which the inherited disorder is an abnormality intrinsic to the red cell, its membrane, its metabolic pathways or the structure of the Hb contained in the cells. Such red cells are liable to be dysfunctional and to have increased fragility and a shortened life span. Lysis in the circulation may lead to clinical jaundice as bilirubin is formed from the breakdown of Hb. Lysis in the reticuloendothelial system generally does not cause jaundice but may produce splenomegaly. The anaemia tends to be normochromic normocytic; sometimes a mildly raised MCV is due to an appropriate reticulocyte response from a normally functioning marrow. Serum bilirubin may be raised even in the absence of jaundice. Urinary urobilinogen and faecal stercobilinogen are detectable and serum haptoglobin is depleted. The antiglobulin (Coombs) test is important in the elucidation of some haemolytic anaemias. In this test, red cells coated in vivo (direct test) or in vitro (indirect test) with IgG antibodies are washed to remove unbound antibodies; they are then incubated with an anti-human globulin reagent. The resultant agglutination indicates a positive test.

Any chronic haemolytic process may be complicated by an 'aplastic crisis'. This is usually a transient marrow suppression brought on by a viral infection, which can result in a severe and life-threatening anaemia. Red cell transfusion in these circumstances may be lifesaving.

Hereditary spherocytosis

A deficiency of spectrin, the red cell wall protein, leads to loss of deformability and increased red cell fragility. These cells are destroyed prematurely in the spleen. The condition may present at any age with anaemia, intermittent jaundice and cholelithiasis. Patients are Coombs-negative and show normal red cell osmotic fragility. Splenectomy radically improves general health. Hereditary elliptocytosis is a similar disease with usually a milder course.

Glucose-6-phosphate dehydrogenase deficiency

Glucose-6-phosphate dehydrogenase (G6PD) generates reduced glutathione, which protects the red cell from oxidant stress. G6PD deficiency is an X-linked disorder present in heterozygous males and homozygous females. The disorder is commonly seen in West Africa, southern Europe, the Middle East and Southeast Asia. Oxidant stress leads to severe haemolytic anaemia. Precipitants include fava beans, antimalarial and analgesic drugs and infections. The enzyme deficiency can be demonstrated by direct assay and treatment is supportive.

Sickle cell anaemia

Whereas in the thalassaemias there is a deficiency in a given globin chain within the Hb molecule, in the haemoglobinopathies a given globin chain is present but structurally abnormal. HbS differs from normal HbA by one amino acid residue: valine replaces glutamic acid at the sixth amino acid from the N-terminus of the β -globin chain. Red cells containing HbS tend to 'sickle' at states of low oxygen tension. The deformed sickle-shaped red cell has increased rigidity, which causes it to lodge in the microcirculation and sequester in the reticuloendothelial system—thus causing a haemolytic anaemia.

Sickle cell disease is encountered in Afro-Caribbean people. The higher incidence in tropical areas is attributed to the survival value of the β -S gene against *falciparum* malaria. Heterozygous individuals have 'sickle trait' and are usually asymptomatic. Homozygous (HbSS) individuals manifest the disease in varying degrees. The haemolytic anaemia is usually in the range of 60 to 100 g/L and can be well tolerated because HbS offloads oxygen to the tissues more efficiently than HbA.

A patient with sickle cell disease may occasionally develop a rapidly worsening anaemia. This may be due to

- a production defect—reduced marrow erythropoiesis may be secondary to folate deficiency or to a parvovirus infection. This is an aplastic crisis.
- a survival defect—increased haemolysis is usually secondary to infection.
- splenic sequestration.

In any of these circumstances, transfusion may be lifesaving. However, these events are unusual. More commonly encountered is the vaso-occlusive crisis. A stressor—for example, infection, dehydration, or cold—causes sickle cells to lodge in the microcirculation. Bone marrow infarction is one well-recognized complication of the phenomenon, but virtually any body system can be affected. Common presenting

13.1 ANAEMIA

Box 13.1.6 Indications for exchange transfusion in sickle cell crisis

Neurological presentations: TIAs, stroke, seizures
Lung involvement ($\text{PaO}_2 < 65 \text{ mm Hg}$ with $\text{FiO}_2 60\%$)
Sequestration syndromes
Priapism

TIA, Transient ischaemic attack

complaints include acute spinal pain, abdominal pain (the mesenteric occlusion of 'girdle sequestration'), chest pain (pulmonary vascular occlusion), joint pain, fever (secondary to tissue necrosis), neurological involvement (transient ischaemic attacks, strokes, seizures, obtundation, coma), respiratory embarrassment and hypoxia, priapism, 'hand-foot syndrome' (dactylitis of infancy), haematuria (nephrotic syndrome, papillary necrosis), skin ulcers of the lower limbs, retinopathies, glaucoma and gallstones.

Most patients presenting with a vaso-occlusive crisis know they have the disease, but otherwise the differential diagnosis is difficult. Sickle cells may be seen on the blood film and can also be induced by deoxygenating the sample. Hb electrophoresis can establish the type of Hb present. Other investigations are dictated by the presentation and may include blood cultures, urinalysis and culture, chest x-ray, arterial blood gases and electrocardiography.

Pain relief should commence early. A morphine infusion may be required for patients with severe ongoing pain. Other supportive measures are dictated by the presentation. Intravenous fluids are particularly important for patients with renal involvement. Aim to establish a urine output in excess of 100 mL/h in adults. Antibiotic cover may be required in the case of febrile patients with lung involvement. It may be impossible to differentiate between pulmonary vaso-occlusion and pneumonia. Many patients with sickle cell disease are effectively splenectomized owing to chronic splenic sequestration with infarction and are prone to infection from encapsulated bacteria. The choice of antibiotic depends on the clinical presentation. Indications for exchange transfusion are shown in Box 13.1.6. The efficacy of exchange transfusion in painful crises remains unproven.

Haemoglobin S-C disease

Sickle cell trait or Hb S-C disease occurs in up to 10% of the African American population. The clinical presentation resembles that of sickle cell disease but is usually less severe.

Haemoglobin C disease

In HbC, lysine replaces glutamic acid in the sixth position from the N terminus of the β chain. Red cells containing HbC tend to be abnormally rigid, but the cells do not sickle. Homozygotes manifest

a normocytic anaemia, but there is no specific treatment and transfusion is seldom required.

Thalassaemias

There is a high incidence of β -thalassaemia trait among people of Mediterranean origin; the region of high frequency extends in a broad band eastward to Southeast Asia.

Thalassaemias are disorders of Hb synthesis. In the Hb molecule, four haem molecules are attached to four long polypeptide globin chains. Four globin chain types (each with their own minor variations in amino acid order) are designated α , β , γ and δ . Hb A comprises two α and two β chains; 97% of adult Hb is HbA. In thalassaemia, there is diminished or absent production of either the α chain (α thalassaemia) or the β chain (β thalassaemia). Most patients are heterozygous and have a mild asymptomatic anaemia, although the red cells are small. In fact, the finding of a marked microcytosis in conjunction with a mild anaemia suggests the diagnosis.

There are 4 genes on paired chromosomes 16 coding for α -globin and 2 genes on paired chromosomes 11 coding for β -globin. α -Thalassaemias are associated with patterns of gene deletion as follows: $(-/-)$ is Hb-Barts hydrops syndrome, incompatible with life, and $(/-)$ is HbH disease.

Patients who are heterozygous for β thalassaemia have β thalassaemia minor or thalassaemia trait. They are usually symptomless. Homozygous patients have β thalassaemia major.

Diagnosis of the major clinical syndromes is usually possible through consideration of the presenting features in conjunction with an FBC, blood film and Hb electrophoresis.

Patients with HbH disease present with moderate haemolytic anaemia and splenomegaly. The HbH molecule is detectable on electrophoresis and comprises unstable β tetramers. α Trait occurs with the deletion of one or two genes. Hb, MCV and mean corpuscular Hb (MCH) are low but the patient is often asymptomatic.

β Thalassaemia major becomes apparent in the first 6 months of life with the decline of foetal Hb. There is a severe haemolytic anaemia, ineffective erythropoiesis, hepatosplenomegaly and failure to thrive. With improved care, many of these patients survive to adulthood and may possibly present to the ED, where transfusion can be lifesaving. Patients with β thalassaemia trait may be encountered in the ED relatively frequently. They are generally asymptomatic, with a mild hypochromic microcytic anaemia. It is important not to work up these patients for iron deficiency repeatedly and not to subject them to inappropriate haematinic therapy.

Box 13.1.7 Causes of microangiopathic haemolytic anaemia

Disseminated intravascular coagulation
Haemolytic uraemic syndrome
HELLP
Malignancy
Malignant hypertension
Snake envenoming
Thrombotic thrombocytopaenic purpura
Vasculitis

HELLP, Haemolysis, elevated liver enzymes and a low platelet count

Acquired haemolytic anaemias

Many of the acquired haemolytic anaemias are autoimmune in nature, a manifestation of a type II (cytotoxic) hypersensitivity reaction. Here, normal red cells are attacked by aberrant autoantibodies targeting antigens on the red cell membrane. These reactions may occur more readily at 37°C (warm autoimmune haemolytic anaemia, or AIHA), or at 4°C (cold AIHA). Warm AIHA is more common. Red cells are coated with IgG, complement or both. The cells are destroyed in the reticuloendothelial system. Fifty percent of cases are idiopathic, but other recognized causes include lymphoproliferative disorders, neoplasms, connective tissue disorders, infections and drugs (notably methyldopa and penicillin). Patients have haemolytic anaemia, splenomegaly and a positive Coombs test. In the ED setting, it is important to stop any potentially offending drugs and search for the underlying disease. The idiopathic group may respond to steroids, other immunosuppressive or cytotoxic drugs or splenectomy.

In cold AIHA, IgM attaches to the red cell antigen in the cooler peripheries. Primary cold antibody AIHA is known as cold haemagglutinin disease. Other causes include lymphoproliferative disorders, infections such as those due to *Mycoplasma* and paroxysmal cold haemoglobinuria. Patients sometimes manifest Reynaud disease and other signs of circulatory obstruction. Symptoms worsen in winter. Red cell lysis leads to haemoglobinuria.

Microangiopathic haemolytic anaemia

In this important group of conditions, intravascular haemolysis occurs in conjunction with a disorder of microcirculation. Important causes are shown in Box 13.1.7.

Haemolytic uraemic syndrome and thrombotic thrombocytopaenic purpura

These are probably manifestations of the same pathological entity, with haemolytic uraemic syndrome occurring in children and thrombotic

thrombocytopaenic purpura most commonly in the fourth decade of life, especially in women. The primary lesion is likely to be in the vascular endothelium. Fibrin and platelet microthrombi are laid down in arterioles and capillaries, possibly as an autoimmune reaction. The clotting system is not activated. Haemolytic anaemia, thrombocytopaenia and acute renal failure are sometimes accompanied by fever and neurological deficits.

In adults, the presentation is usually one of a neurological disturbance (headache, confusion, obtundation, seizures or focal signs). The blood film reveals anaemia, thrombocytopaenia, reticulocytosis and schistocytes. The Coombs test is negative.

Patients require hospital admission. Adults with this condition may require aggressive therapy with prednisone, antiplatelet therapy, further immunosuppressive therapy and plasma exchange transfusions.

HELLP syndrome

HELLP stands for haemolysis, elevated liver enzymes and a low platelet count; it is seen in pregnant women in the context of pre-eclampsia. Treatment is as for pre-eclampsia, early delivery of the baby being of paramount importance.

Disseminated intravascular coagulation

The introduction of procoagulants into the circulation resulting in the overwhelming of anticoagulant control systems may occur as a consequence of a substantial number of pathophysiological insults—obstetric, infective, malignant and traumatic. Disseminated intravascular coagulation has an intimate association with shock of any cause. The widespread production of thrombin leads to deposition of microthrombi, bleeding secondary to thrombocytopaenia and a consumption coagulopathy as well as red cell damage within abnormal vasculature, leading to a haemolytic anaemia.

Recognition of this condition prompts intensive care admission and aggressive therapy. Principles of treatment include definitive management of the underlying cause and, from the haematological point of view, replacement therapy; this may involve the transfusion of red cells, platelets, fresh frozen plasma (FFP) and cryoprecipitate. There may be a role for heparin and other anticoagulant treatments if specific tissue and organ survival is threatened by thrombus.

Paroxysmal nocturnal haemoglobinuria

This entity is unusual in that an intrinsic red cell defect is seen in the context of an acquired haemolytic anaemia. A somatic stem cell mutation results in a clonal disorder. A family of membrane proteins (CD55, CD59 and C8 binding protein) is deficient and renders cells prone to complement-mediated lysis. The same proteins are deficient in white cells and platelets; therefore, in addition to being anaemic, patients are prone to infections and haemostatic abnormalities. They may go on to develop aplastic anaemia or leukaemia. Treatment is supportive. Marrow transplant can be curative.

Other causes of haemolysis

Haemolysis may be due to mechanical trauma, as in 'march haemoglobinuria'. Artificial heart valves can potentially traumatize red cells. Historically valves of the ball-and-cage type have been most likely to cause haemolysis, whereas disc valves are more thrombogenic. Improvements in design have made cardiac haemolytic anaemia very rare. Haemolysis is sometimes seen in association with a number of infectious diseases, notably malaria. Other infections that have been implicated are listed in **Box 13.1.8**. Certain drugs and toxins are associated with haemolytic anaemia (**Box 13.1.9**). The haemolytic anaemia that is commonly seen in patients with severe burns is attributed to direct damage to the red cells by heat.

Box 13.1.8 Infections associated with haemolysis

Babesiosis
<i>Bartonella</i>
Clostridia
Cytomegalovirus
Coxsackievirus
Epstein-Barr virus
<i>Haemophilus</i>
Herpes simplex
HIV
Malaria, especially <i>Plasmodium falciparum</i> (Black-water fever)
Measles
<i>Mycoplasma</i>
Varicella

Box 13.1.9 Drugs and toxins associated with haemolysis

Antimalarials
Arsine (arsenic hydride)
Bites: bees, wasps, spiders, snakes
Copper
Dapsone
Lead (plumbism)
Local anaesthetics: lidocaine, benzocaine
Nitrates, nitrites
Sulphonamides

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13.2 Neutropaenia

Mark Little

ESSENTIALS

- 1** The risk of infection increases significantly as the absolute neutrophil count drops below $1.0 \times 10^9/L$.
- 2** Life-threatening neutropaenia is most likely due to impaired haematopoiesis.
- 3** A detailed medication history is vital to the 'workup' of neutropaenia.
- 4** Fever in the presence of severe neutropaenia constitutes a true emergency that mandates rapid assessment and aggressive management to prevent progression to overwhelming sepsis.
- 5** Strategies of early empiric broad-spectrum antibiotic administration have significantly reduced the overall mortality of febrile neutropaenia.

Introduction

Neutropaenia is defined as a decrease in the number of circulating neutrophils. The neutrophil count varies with age, sex and racial grouping. The severity of neutropaenia is usually graded as follows:

- Mild: neutrophil count 1.0 to $1.5 \times 10^9/L$
- Moderate: neutrophil count 0.5 to $1.0 \times 10^9/L$
- Severe: neutrophil count $<0.5 \times 10^9/L$.

The risk of infection rises as the neutrophil count falls; it becomes significant once the neutrophil count drops below $1.0 \times 10^9/L$. Australian guidelines have defined febrile neutropaenia as existing in a patient with a temperature above 38.4°C (or above 38°C on two occasions) with a neutrophil count less than $0.5 \times 10^9/L$ or less than $1.0 \times 10^9/L$ and likely to fall to less than $0.5 \times 10^9/L$. These patients must be examined for signs of systemic compromise (Box 13.2.1).

Box 13.2.1 Features of systemic compromise

- Systolic BP ≤ 90 mm Hg or ≥ 30 mm Hg below patients usual BP or inotropic support
- Room air arterial $\text{pO}_2 \leq 60$ mm Hg, $\text{SpO}_2 < 90\%$ or need for mechanical ventilation
- Confusion or altered mental state
- Disseminated intravascular coagulation or abnormal PT/aPTT
- Cardiac failure or arrhythmia, renal failure, liver failure or any major organ failure (only if new or deteriorating and not atrial fibrillation or congestive heart failure)

(Reproduced with permission from Tam CS, O'Reilly M, Andersen D, et al. Use of empiric antimicrobial therapy in neutropenic fever. Australian Consensus Guidelines 2011 Steering Committee. *Intern Med J.* 2011;41:90–101.)

Neutropaenic patients are at greater risk of overwhelming infection if the onset of the neutropaenia is acute rather than chronic and, in the case of patients receiving cancer chemotherapy, if the absolute neutrophil count is in the process of falling rather than rising.

Signs or symptoms of infection in the presence of severe neutropaenia, especially with features of systemic compromise, constitute a true emergency that mandates rapid assessment and aggressive management to prevent progression to overwhelming sepsis. In the emergency department (ED) setting, this is most commonly encountered when a patient presents with fever in the context of chemotherapy for cancer.

Pathophysiology and aetiology

Polymorphonuclear neutrophils are formed in marrow from the myelogenous cell series. Pluripotent haematopoietic stem cells are committed to a particular cell lineage through the formation of colony forming units, which further differentiate to form given white cell precursors. The mature neutrophil has a multi-lobed nucleus and granules in the cytoplasm. The cells are termed 'neutrophilic' because of the lilac colour of the granules caused by the uptake of both acidic and basic dyes.

The neutrophils leave the marrow and enter the circulation, where they have a life span of only 6 to 10 hours before entering the tissues. Here they migrate by chemotaxis to sites of infection and injury, where they phagocytose and destroy foreign material. In health, about half of the available mature neutrophils are in the circulation. 'Marginal' cells are adherent to

vascular endothelium or in the tissues and are not measured by the full blood count. Some individuals have fixed increased marginal neutrophil pools and decreased circulating pools; they are said to have benign idiopathic neutropaenia.

For a previously normal individual to become neutropaenic, there must be decreased production of neutrophils in the marrow, decreased survival of mature neutrophils or a redistribution of neutrophils from the circulating pool. The important causes are shown in Box 13.2.2.

It is a defect in neutrophil production that is most likely to prove life threatening. Consumption of neutrophils in the periphery, as occurs early in infectious processes, is likely to be rapidly compensated for by a functioning marrow. Fortunately, most of the primary diseases of haematopoiesis are rare and, in practice, many of the acquired neutropaenias are drug induced. Processes interfering with haematopoiesis, often involving autoimmune mechanisms, may affect neutrophils both in the marrow and in the periphery. Some drugs cause neutropaenia universally, but many more reactions are idiosyncratic, be they dose-related or independent of dose. Some commonly implicated drugs are listed in Box 13.2.3. Cancer chemotherapy drugs are now recognized as the commonest cause of neutropaenia.

Box 13.2.2 Important causes of neutropaenia

Decreased production

- Aplastic anaemia
- Leukaemias
- Lymphomas
- Metastatic cancer
- Drug-induced agranulocytosis
- Megaloblastic anaemias
- Vitamin B12 deficiency
- Folate deficiency
- CD8 and large granular lymphocytosis
- Myelodysplastic syndromes

Decreased survival

- Idiopathic immune related
- Systemic lupus erythematosus
- Felty syndrome
- Drugs

Redistribution

- Sequestration (hypersplenism)
- Increased utilization (overwhelming sepsis)
- Viraemia

Box 13.2.3 Drugs commonly associated with neutropaenia

Antibiotics: chloramphenicol, sulphonamides, isoniazid, rifampicin, β lactams, carbencilllin
Antidysrhythmic agents: quinidine, procainamide
Antiepileptics: phenytoin, carbamazepine
Antihypertensives: thiazides, ethacrynic acid, captopril, methyldopa, hydralazine
Antithyroid agents
Chemotherapeutic agents: especially methotrexate, cytosine arabinoside, 5-azacytidine, azathioprine, doxorubicin, daunorubicin, hydroxyurea, alkylating agents
Connective tissue disorderagents: phenylbutazone, penicillamine, gold
 H_2 -receptor antagonists
Phenothiazines, especially chlorpromazine
Miscellaneous: imipramine, allopurinol, clozapine, ticlopidine, tolbutamide

of indwelling venous access devices should be noted and insertion sites inspected for evidence of inflammation or infection.

Clinical investigations

Investigation in the ED is first aimed at confirming and quantifying the severity of neutropaenia, identifying the cause and then identifying the focus and severity of infection. An urgent full blood count and blood film should be ordered for any patient who is suspected of suffering febrile neutropaenia. A coagulation profile and full biochemistry are indicated once severe neutropaenia is confirmed. Anaemic patients may require a group-and-hold or cross-match.

Microbiological cultures aimed at isolating a causative organism should be taken, but antibiotics should not be unreasonably delayed in the presence of fever and confirmed significant neutropaenia. Blood cultures should be taken at the time of cannulation and, if possible, prior to the instigation of antibiotic therapy. Swabs of skin lesions; throat, nose and indwelling venous access device sites; sputum; urinalysis and urine culture; as well as stool cultures (including *Clostridium difficile* toxin) may be indicated depending on the clinical picture. Computed tomography scanning may be required to find an occult infection. Patients with apparent central nervous system infections might require a lumbar puncture provided that there are no contraindications.

Treatment

Management of the patient with confirmed febrile neutropaenia in the ED involves early recognition with a high-acuity triage, treatment of bacterial infection and institution of supportive care. Evolving or established haemodynamic instability requires immediate aggressive resuscitation.

For any patient with fever and suspected or confirmed significant neutropaenia, empiric broad-spectrum antibiotic therapy should be started in the ED after blood has been drawn for culture. Most protocols aim for antibiotic administration within 60 minutes of presentation or 30 minutes if there are signs of sepsis/septic shock. This strategy has played a pivotal role in reducing mortality rates in individuals with febrile neutropaenia. Australian consensus-based clinical recommendations for the management of neutropaenic fever in adults reinforce the need for the early administration of antibiotics. In general, antibiotics should provide good cover for both gram positive and gram negative organisms. With the increased use of indwelling venous access devices for cancer chemotherapy, there has been an increase in the incidence of sepsis due to gram-positive organisms, such as coagulase-negative staphylococci,

Staphylococcus aureus and methicillin-resistant *S. aureus* (MRSA). Although it occurs infrequently, bacteraemia due to *Pseudomonas aeruginosa* is associated with a high morbidity and mortality; therefore it should also be covered.

Recent evidence suggests that antibiotic monotherapy is as efficacious as combined therapy. Therefore, for clinically stable patients, Australian consensus guidelines recommend a β -lactam monotherapy (such as pipperacilllin-tazobactam 4.5 g q6h, cefepime 2 g q8h or ceftazidime 2 g q8h). These antibiotics should be administered within 1 hour of presentation and after at least one set of blood cultures has been ordered.

For patients with systemic compromise, the Australian consensus guidelines recommend the previously mentioned β -lactam antibiotics plus gentamicin (5–7 mg/kg daily) given within 30 minutes of presentation. If the clinicians believe that the shocked patient was colonized with gram positive organisms (e.g. MRSA, or if he or she has clinical evidence of a catheter-related infection in a unit with a high incidence of MRSA) and the patient has normal renal function), vancomycin (1.5 g q12h) should be added. Empiric antifungal therapy is not generally required unless there is persistent fever in a high-risk patient beyond 96 hours of antibacterial therapy.

Disposition

The presence of significant neutropaenia with fever generally mandates admission to hospital. Patients with severe acute neutropaenia without an established aetiology will also generally require admission regardless of the presence or absence of fever. Both the haematological abnormality and the likely presence of infection require investigation. Sometimes the aetiology of the neutropaenia will be evident; in other cases marrow aspiration and biopsy will be required.

There is emerging evidence that a subset of febrile neutropaenic patients can be identified who are at low risk of life-threatening complications and in whom the duration of hospitalization and intensity of treatment may be safely reduced. Strategies that involve outpatient treatment of low-risk patients with oral antibiotics have also been evaluated. Such regimens rely on the accurate prediction of risk as well as the availability of structured programmes and resources.

Prognosis

The prognosis of the neutropaenic patient is largely dependent on the underlying aetiology of the condition. Improvements in therapy, such as rapid treatment with empiric broad-spectrum antibiotics, have significantly reduced mortality rates from this condition. Overall mortality rates for patients with febrile neutropaenia have declined from more than 20% to less than 4% in recent datasets.

Clinical features

Neutropaenia is frequently anticipated based on the clinical presentation, such as fever developing in the context of cancer chemotherapy; this is by far the most common scenario in which severe neutropaenia is seen in the ED. Alternatively, it may be identified in the course of investigation for a likely infective illness, or it might be an incidental finding during investigation for an unrelated condition.

Chronic neutropaenia may be asymptomatic unless secondary or recurrent infections develop. Acute severe neutropaenia may present with fever, sore throat and mucosal ulceration or inflammation. Symptoms or signs of an associated disease process may also be present, such as pallor from anaemia or bleeding from thrombocytopaenia, as might occur in conditions causing pancytopenia.

The history of the mode of onset and duration of the illness is important. Systems enquiry may reveal localizing infective symptoms. The past history may reveal a known haematological illness or previous evidence of immunosuppression, such as frequent and recurrent infections. A detailed drug history is vital. Most neutropaenic drug reactions occur within the first 3 months of taking a given drug.

In the ED, all observations should be performed at initial assessment and monitored regularly until disposition. Attention should be paid to identifying early signs of severe sepsis and the progression to septic shock.

Physical examination may reveal necrotizing mucosal lesions, pallor, petechial rashes, lymphadenopathy, bone tenderness, abnormal tonsillar or respiratory findings, spleno- or other organomegaly. Careful examination of the skin of the back, the lower limbs and the perineum for evidence of infection is important. The presence

13.3 THROMBOCYTOPAENIA

CONTROVERSIES

- The prophylactic use of granulocyte colony-stimulating factors, such as filgrastim and pegfilgrastim, to reduce the incidence of febrile neutropaenia during cancer chemotherapy
- The indications for and efficacy of granulocyte transfusions in the management of febrile neutropaenia
- The development and validation of clinical decision rules to risk stratify patients with febrile neutropaenia and the use of these rules to determine suitability for oral antibiotic and/or outpatient therapy

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13.3 Thrombocytopaenia

Mark Little

ESSENTIALS

- A low platelet count detected on automated blood count should always be confirmed by examination of the blood film prior to further investigation or treatment.
- The cause of isolated thrombocytopaenia can often be determined by a careful history and physical examination in addition to assessment of the full blood count (FBC) and blood film.
- Platelet transfusion is unnecessary in the management of the thrombocytopaenic patient unless the platelet count is extremely low or there is ongoing bleeding.
- In the absence of other clotting disorders or abnormal platelet function, bleeding in the thrombocytopaenic patient is often amenable to local measures of haemostasis.

Introduction

Thrombocytopaenia is defined as a reduction in the number of circulating platelets, the normal circulating platelet count being 150 to $400 \times 10^9/L$. It is the most common cause of abnormal bleeding. Like anaemia, thrombocytopaenia itself is not a diagnosis but rather a manifestation of another underlying disease process.

In the emergency department setting, thrombocytopaenia may present as an incidental finding on a routine blood count or may be diagnosed in the context of abnormal bleeding. In most cases the underlying aetiology can be determined by a careful history and physical examination combined with interpretation of the blood count.

Aetiology

The clinically important causes of thrombocytopaenia are outlined in Box 13.3.1. Diagnoses are classified by pathological process. It should be noted that more than one pathological process may be present. The causes can be divided into three different groups: pseudothrombocytopaenia, increased destruction of platelets and reduced production of platelets.

Pseudothrombocytopaenia

Pseudothrombocytopaenia results from an underestimation of the platelet count as measured by an automated particle counter. The most common mechanism is platelet clumping. Clumping is most often due to the anticoagulant

ethylenediaminetetraacetic acid (EDTA) but may also result from autoantibodies, such as cold agglutinins. The presence of giant platelets and platelet satellitism may also yield falsely low automated platelet counts.

Any case of thrombocytopaenia found on an automated blood count should be confirmed by examination of the peripheral smear prior to further investigation or treatment.

Thrombocytopaenia due to increased platelet destruction

Immune-related thrombocytopaenia

Immune thrombocytopaenia

Immune thrombocytopaenia (ITP) is defined as an isolated thrombocytopaenia (low platelet count with an otherwise normal FBC and peripheral blood smear) in a patient with no clinically apparent associated conditions that can cause thrombocytopaenia. It is a common cause of a low platelet count and abnormal bleeding in both children and adults. ITP is thought to be caused by the development of autoantibodies to platelet membrane antigens.

In addition to the primary idiopathic form, ITP may also accompany autoimmune disorders, such as Graves disease and systemic lupus erythematosus. It is the main mechanism of the thrombocytopaenia related to HIV infection.

Drug-related thrombocytopaenia

A large number of drugs have been reported to cause immune-related thrombocytopaenia. By far the most commonly implicated are quinine,

Box 13.3.1 Causes of thrombocytopenia

Pseudothrombocytopenia

Platelet clumping
Collection into anticoagulant (ethylenediaminetetraacetic acid)
Platelet agglutinins
Giant platelets

Increased platelet destruction

Immune

Primary
Idiopathic thrombocytopenic purpura
Secondary
Autoimmune thrombocytopenia associated with other disorders
Graves disease, Hashimoto thyroiditis, systemic lupus erythematosus
HIV-related thrombocytopenia
Drug-induced thrombocytopenia
Heparin, gold salts, quinine/quinidine, sulphonamides, rifampicin, H2 blockers, indomethacin, carbamazepine, valproic acid, ticlopidine, clopidogrel, monoclonal antibodies (infliximab, efalizumab, rituximab)
Post-transfusion purpura

Non-immune

Thrombotic thrombocytopenic purpura—haemolytic uraemic syndrome
Pregnancy
Gestational benign thrombocytopenia
Pre-eclampsia/haemolysis, elevated liver enzymes, low platelets
Disseminated intravascular coagulation

Decreased platelet production

Congenital

Thrombocytopenia with absent radius, Wiskott-Aldrich syndrome

Fanconi anaemia

Acquired

Viral infection
Epstein-Barr virus, rubella, dengue fever
Marrow aplasia
Malignant bone marrow infiltrates
Chemotherapeutic agents
Radiation therapy
Abnormal distribution and dilution
Splenic sequestration (hypersplenism)
Splenic enlargement
Hypothermia
Massive blood transfusion

are also associated with an acute, severe, but usually self-limited thrombocytopenia.

In most cases of drug-related thrombocytopenia, recovery occurs rapidly after withdrawal of the offending agent. The exception is patients with gold sensitivity, who may remain thrombocytopenic for months due to the slow clearance of this drug.

Post-transfusion purpura

Post-transfusion purpura is clinically distinct from thrombocytopenia due to dilution of platelets following massive transfusion. It is an acute, severe thrombocytopenia occurring about 1 week after blood transfusion and is associated with a high titre of platelet-specific alloantibodies. It is most commonly reported in multiparous women following their first blood transfusion. The mechanism for alloantibody formation is unclear. Spontaneous recovery occurs within weeks, although fatalities from severe haemorrhage have been reported.

Non-immune platelet destruction

Thrombotic thrombocytopenic purpura

TTP is considered to be the adult form of the haemolytic uraemic syndrome (HUS). Essentially a thrombotic microangiopathy, the classic pentad of clinical findings is (1) fever, (2) thrombocytopenia, (3) microangiopathic haemolytic anaemia, (4) neurological abnormalities and (5) renal involvement.

TTP can occur sporadically as an idiopathic disorder or may be associated with pregnancy, epidemics of verotoxin-producing *Escherichia coli* and *Shigella dysenteriae*, malignancy, chemotherapy, marrow transplantation and drug-dependent antibodies. Treatment with plasma exchange has dramatically influenced the outcome of TTP. Mortality has fallen from more than 90% prior to introduction of plasma exchange to less than 20% with this treatment.

Thrombocytopenia in pregnancy

Gestational thrombocytopenia develops during an otherwise normal pregnancy and is clinically distinct from autoimmune thrombocytopenias such as ITP. It is thought to be due to decreased platelet survival consequent to activation of the coagulation system. Thrombocytopenia is usually mild and there is no corresponding thrombocytopenia in the infant. The platelet count returns to normal after delivery, although thrombocytopenia may recur in subsequent pregnancies.

Autoimmune thrombocytopenias, on the other hand, are often associated with more severe reductions in the platelet count. Antiplatelet antibodies are capable of crossing the placenta and may result in significant thrombocytopenia in the foetus and newborn. This can lead to complications, such as intracranial haemorrhage, during the delivery. Treatment of the mother with

autoimmune thrombocytopenia is similar in principle to the treatment of non-pregnant cases.

In the context of pregnancy, thrombocytopenia may also be seen as part of the HELLP (haemolysis, elevated liver enzymes, low platelets) and pre-eclampsia syndromes. The two syndromes are thought to be related. Common to both is a process of microvascular endothelial damage and intravascular platelet activation. This leads to the release of thromboxane A and serotonin, which provoke vasospasm, platelet aggregation and further endothelial damage. In both syndromes, the process is terminated by delivery.

Disseminated intravascular coagulation

Thrombocytopenia is one manifestation of the syndrome of disseminated intravascular coagulation (DIC). DIC is an acquired syndrome of diffuse intravascular coagulation up to the level of fibrin formation, accompanied by secondary fibrinolysis or inhibited fibrinolysis. It occurs in the course of severe systemic diseases or may be provoked by toxins, such as snake venoms.

Thrombocytopenia due to impaired platelet production

Congenital disorders of impaired platelet production usually present in childhood and are not discussed here.

Of the acquired disorders of impaired platelet production, the most commonly seen in the emergency setting is the incidental finding of reduced platelet count in patients suffering viral illnesses. Causative viruses include Epstein-Barr virus, rubella and dengue fever. Thrombocytopenia in these cases is reversible and requires no specific therapy other than monitoring of the platelet count to ensure normalization.

Disorders of bone marrow dysfunction, such as malignant infiltration and bone marrow suppression, cause thrombocytopenia accompanied by reductions in numbers of other blood components. Examination of the FBC and blood film usually distinguishes these from other causes of isolated thrombocytopenia. Further investigation is best referred to a haematologist.

Massive blood transfusion and thrombocytopenia

Massive blood transfusion is defined as the transfusion of a volume equivalent to the patient's normal blood volume within a 24-hour period. Thrombocytopenia results from dilution of the patient's remaining platelets and, where whole blood is used, decreased survival of platelets in stored blood. It is possibly the most important factor contributing to the haemostatic abnormality seen in massively transfused patients. Platelet transfusion should be reserved for cases where the platelet count falls below $50 \times 10^9/L$.

quinidine and heparin. Heparin is associated with a syndrome of thrombosis due to diffuse platelet activation accompanied by a consumptive thrombocytopenia. Some platelet inhibitors, particularly ticlopidine and, less commonly, clopidogrel, are associated with severe thrombocytopenia and other signs and symptoms of thrombotic thrombocytopenic purpura (TTP). Recently developed monoclonal antibodies, such as infliximab (anti-tumour necrosis factor- α antibody), efalizumab (anti-CD11a antibody) and rituximab (anti-CD20 antibody)

13.3 THROMBOCYTOPAENIA

Hypersplenism

Hypersplenism refers to the thrombocytopenia due to pooling in patients with splenic enlargement. It is the primary cause of thrombocytopenia in hepatic cirrhosis, portal venous hypertension and congestive splenomegaly. In these cases, thrombocytopenia is rarely severe and not usually of clinical importance.

Transient thrombocytopenia has been described in patients suffering severe hypothermia and is due to splenic sequestration. Platelet counts usually return to normal within days of rewarming.

Clinical features

There are distinct differences in the patterns of abnormal bleeding associated with disorders of platelet deficiency and disorders of impaired coagulation.

Spontaneous bleeding related to thrombocytopenia typically manifests as cutaneous petechiae and/or purpura, most commonly in dependent areas such as the legs and buttocks. Other spontaneous manifestations include multiple small retinal haemorrhages, epistaxis and gingival/gastrointestinal bleeding. Bleeding following trauma or surgery in thrombocytopenic patients is often immediate and may respond to local methods of haemostasis. In distinction to this, the bleeding associated with coagulation disorders is most commonly in the form of large haematomas or haemarthroses that occur spontaneously or develop hours to days following trauma.

In addition to the haemorrhagic manifestations of platelet insufficiency, patients with thrombocytopenia may present with the clinical features of the underlying causative disorder. Splenic enlargement may be present in cases where thrombocytopenia is due to hypersplenism, but it is not a feature of immune-related thrombocytopenia.

The level of platelets associated with clinically significant abnormal bleeding is not precisely defined. It varies depending on the platelets' functional integrity and with the presence or absence of other risk factors, such as coagulation disorder, trauma, and surgery. There is evidence that platelet counts above $5 \times 10^9/L$ are sufficient to prevent bleeding when the platelets are functionally normal and there are no other risk factors. Severe haemorrhage is uncommon at platelet counts above $20 \times 10^9/L$; in the setting of surgery, the risk of abnormal haemorrhage is reduced at counts above $50 \times 10^9/L$.

Clinical investigation

The FBC and examination of the blood film are diagnostic of thrombocytopenia. *Isolated thrombocytopenia* refers to a low platelet count in the presence of an otherwise normal FBC and blood film. In these cases, FBC combined with a

careful clinical history and examination is often sufficient to lead to a final diagnosis. Co-existent anaemia and/or leucopaenia suggest bone marrow dysfunction as the primary aetiological process.

Other useful investigations may include coagulation studies and D-dimer (DIC, pre-eclampsia), electrolytes, urea and creatinine (TTP), liver function tests (HELLP and liver disease) and thyroid function tests (autoimmune thyroid disorders). Platelet antibody titres are indicated in the workup of pregnancy-related thrombocytopenia, and bone marrow aspirate may be indicated in the investigation of thrombocytopenia due to bone marrow dysfunction. However, neither of these tests is useful in the emergency department setting.

Treatment

Treatment is aimed at modulating the immune response and reducing the rate of platelet destruction and is indicated in all patients who have counts less than $20 \times 10^9/L$ as well as those with counts less than $50 \times 10^9/L$ accompanied by significant mucous membrane bleeding. First-phase treatment includes parenteral glucocorticoids (e.g. prednisolone 1 mg/kg/day for 4–6 weeks in tapered doses) and/or intravenous IgG. Splenectomy is usually reserved for patients who do not respond to medical therapy and have ongoing bleeding symptoms. There are a number of studies demonstrating benefit using rituximab, a humanized monoclonal antibody against the CD20 antigen on B lymphocytes.

Bleeding in the face of a low platelet count may be responsive to local methods of haemostasis if the remaining platelets are functionally normal and there is no other disorder of coagulation.

The threshold for prophylactic transfusion in these patients is controversial.

Platelet transfusions may cause temporary increases in platelet count and may be used in cases of life-threatening haemorrhage but are otherwise not usually indicated.

Platelet transfusion is rarely indicated in immune-related thrombocytopenias, as the transfused platelets are rapidly destroyed. Transfusion of platelets may aggravate TTP. In DIC, platelet transfusion has not been proven to be effective but may be indicated in bleeding patients. In cases of massive blood transfusion, platelets are not routinely indicated unless there is ongoing bleeding and the platelet count is below $50 \times 10^9/L$.

Raising the platelet count to 20 to $50 \times 10^9/L$ is sufficient to prevent serious bleeding. In patients undergoing surgery or other invasive procedures, counts up to 60 to $100 \times 10^9/L$ may be required. A useful rule of thumb is that in a 70-kg adult, transfusion of one unit of platelets will increase the platelet count by $11 \times 10^9/L$.

At present, platelet preparations for transfusion are stored in liquid at 22°C . Problems include the continued risk of febrile non-haemolytic reactions, transmission of infectious agents and graft-versus-host disease. Alternatives to conventional liquid storage include frozen storage, cold liquid storage, photochemical treatment and lyophilized platelets. None of these methods is currently widely available. Several platelet substitutes (fibrinogen-coated albumin microcapsules and liposome-based haemostatic agents) have been developed but remain untested in the clinical setting.

Disposition

Disposition will depend on the presence and extent of abnormal bleeding, the degree of thrombocytopenia and the underlying aetiology. In general, patients who present with abnormal bleeding and a low platelet count should be admitted for further evaluation and treatment. In the absence of bleeding, patients who have isolated thrombocytopenia with counts above $20 \times 10^9/L$ may be investigated on an outpatient basis.

CONTROVERSIES

- The platelet count at which prophylactic platelet transfusion is indicated
- The development and clinical testing of alternative methods of platelet preparation and platelet substitutes
- Whether splenectomy is still the second-line therapy for adults with chronic ITP

Further reading

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13.4 Haemophilia

Sean Arendse

ESSENTIALS

- 1** Haemophilia is a disorder that should be managed by the emergency physician in consultation with the nearest haemophilia centre.
- 2** Patients should carry their treatment regimen cards with them. If they do not, they should be encouraged to do so.

Introduction

Haemophilia is a group of congenital disorders of blood coagulation that arise as a result of a deficiency of clotting factor proteins, which are essential to the normal intrinsic coagulation pathway. The classic form, haemophilia A, is attributable to deficiency of factor VIII, whereas haemophilia B (also known as Christmas disease) is attributable to deficiency of factor IX. Both these diseases have a classic X-linked pattern of inheritance and thus affect males, although female carriers may also have mild deficiency of the appropriate coagulation factor.

Haemophilia A is the commoner disease (80%), with an incidence of 1 in 8000 to 10,000 live male births, compared with an incidence of 1 in 25,000 to 30,000 for haemophilia B (20%).

Pathophysiology

The normal clotting system is activated in the presence of vascular injury to produce (1) vascular spasm, (2) platelet plug formation and (3) coagulation—factor activation and the production of fibrin. Normal coagulation of blood is dependent on the generation of adequate thrombin via the clotting cascade. Deficiency of factor VIII or IX reduces the amplification of the clotting cascade, thus causing haemophilia. The severity of the bleeding disorder is inversely related to the level of functional factor present and is categorized into mild, moderate and severe disease, as follows:

- Mild disease (6%–30% of normal factor level)—manifests with persistent bleeding after surgery, dental extractions and trauma. Spontaneous bleeds do not occur in this group of patients.
- Moderate disease (1%–5% of normal factor level)—manifests with bleeding into joints and muscles after minor trauma and excessive bleeding after surgery and dental extractions.

- Severe disease (<1% of normal factor level)—manifests with spontaneous joint and muscle bleeding and excessive bleeding following minor trauma, surgery or dental extractions.

Clinical features

Haemophilia A and B are clinically indistinguishable, and symptoms vary according to the severity of the inherited disorder. Mild disease may not present until adulthood, whereas moderate to severe disease usually presents in infancy or early childhood.

Bleeding in haemophilia tends to occur spontaneously or following minor trauma; it is typically delayed and persistent. This is because, although initial platelet 'plugging' function is normal, the subsequent coagulation 'cascade' response is abnormal. This delay is usually hours and occasionally days. Once bleeding occurs, it may persist for days or even weeks. Patients who are severely affected may present with bleeding episodes on a weekly basis.

The most common manifestations of haemophilia are as follows:

- Bleeding into joints (knees, elbows, ankles, shoulders, hips, wrists—in descending order of frequency)
- Bleeding into soft tissues and muscles (the iliopsoas muscle around the hip, calf, forearm, upper arm, Achilles tendon, buttocks)
- Bleeding in the mouth from a cut, bitten tongue or loss of a tooth
- Haematuria
- Superficial bruising
- Haemarthroses—bleeding from a synovial membrane appendicular structure with inflammation of the synovium, leading to degenerative arthritis, joint destruction and loss of joint mobility and function
- Bleeding into tissue planes—tense flexor haematomas in limbs, potentially causing compartment syndromes; haemorrhage into muscles, possibly leading to atrophy and contracture

- Bleeding into the neck (may cause airway compromise)
- Central nervous system bleeding
- Retroperitoneal bleeding

Patients may also present with a complication of therapy. Most haemophiliac patients treated before 1985 have been exposed to pathogenic viruses, of which the most important are hepatitis C, hepatitis B and HIV. Of those who received plasma prior to the mid-1980s, 90% are hepatitis B-positive, 85% to 100% are hepatitis C-positive and 60% to 90% are HIV-positive.

Clinical investigations

Investigations are tailored to the individual presentation. A full blood count, blood film and coagulation profiles are useful in the evaluation of first presentations or major bleed but unlikely to be helpful in patients with an established diagnosis. It is important to note that in an acute presentation, investigations and awaiting their results should not delay treatment with factor. The most important role for us in the emergency department (ED) is to administer factor as soon as is possible; blood results are not used to guide our use of factor in this group of patients. Generally we administer factor if we have any suspicion of a bleeding, regardless of how small we may think that bleed is.

Plain radiography of affected joints and computed tomography (CT) scanning of the head, chest, abdomen and pelvis may be essential to establish the presence or absence of bleeding complications.

The prothrombin time measures primarily factors II, VII, V and X; thus patients with either haemophilia A or B have a normal prothrombin time and a normal thrombin clotting time. The partial thromboplastin time measures activation of all factors other than factor VIII and is prolonged in haemophilia (although it can be normal if factor activity exceeds 30%). Specific factor assays are required to distinguish between haemophilias A and B.

Treatment

Treatment of haemophilia has evolved dramatically in the past 40 years with the discovery in the 1960s that coagulation factor VIII was concentrated in cryoprecipitate. More recently, highly purified concentrates of factor VIII and factor IX have been developed.

13.4 HAEMOPHILIA

Box 13.4.1 RICES

- R = rest (in position of comfort)
- I = ice (cold pack to reduce bleeding and pain)
- C = gentle compression bandage
- E = elevation
- S = splint (severe/recurrent bleeds)

Products currently available for the treatment of haemophilia include the following:

- Recombinate (recombinant factor VIII)
- BeneFix (recombinant factor IX)
- Biostate (plasma-derived factor VIII, which includes von Willebrand factor [vWF])
- Monofix (plasma-derived factor IX)
- DDAVP (desmopressin)

Treatment of acute bleeding episodes primarily involves administration of factor replacement therapy. Complications of bleeding may require specific intervention. Adjunctive therapies include pain relief, rest and immobilization. Specific treatment is influenced by

- the type of haemophilia.
- the severity of haemophilia.
- the severity of the bleed.

Haemophilia patients presenting with suspected bleeds should be triaged to be seen within 30 minutes and receive prompt assessment by a senior doctor. For muscle and joint bleeds RICES (Box 13.4.1) should be initiated on arrival in order to limit bleeding and reduce pain, as should adequate analgesics.

Options for adequate analgesia include

- paracetamol
- inhaled nitrous oxide
- tramadol
- intravenous morphine
- possibly also patient-controlled analgesia (PCA)/opioid infusion

Avoid non-steroidal anti-inflammatory drugs (NSAIDs) and intramuscular (IM) injections

In the context of pain relief, aspirin (or other platelet-modifying drugs) should be avoided and NSAIDs used with caution. IM injections should never be administered. In major bleeds, there may be a requirement for red cell transfusion. Developing limb compartment syndromes may require surgical decompression, and intracranial bleeds may require neurosurgical intervention. In all of these cases, factor replacement must commence as quickly as possible. Management of complex presentations requires a multidisciplinary approach and early consultation with the relevant state haemophilia centre, especially if the presentation is a major bleed or the patient has inhibitors.

Intravenous cannulation is best performed by a skilled practitioner to help ensure vein preservation. Invasive procedures, such as

arterial puncture and lumbar puncture, must be performed only after the replacement of clotting factor.

Some patients with factor VIII levels higher than 10% may be successfully treated with 1-amino-8-D-arginine vasopressin (desmopressin, DDAVP), which acts by releasing vWF stored in the lining of the blood vessels. vWF is a protein that transports factor VIII in the bloodstream and, as such, plays an important role in blood clotting. Desmopressin appears to mobilize available factor VIII stores and may raise factor VIII activity by a factor of three. If the patient has previously had a documented good response to desmopressin, this can be used as first-line therapy for minor bleeding, such as haemarthroses.

Desmopressin can be administered intravenously, subcutaneously or by nasal spray. The intravenous dose is 0.3 µg/kg in 100 mL saline over no less than 45 minutes. A response should be evident within the first hour. More rapid administration can be associated with blood pressure changes. Side effects, including facial flushing and headache, are usually well tolerated. Tachyphylaxis tends to develop after three or four doses. The antidiuretic properties of desmopressin (which can last up to 24 hours after a dose) can produce fluid retention and hyponatraemia (leading to seizures), and the serum sodium levels should be measured before further doses are given. Desmopressin is useful in treating mild and very rarely moderate haemophilia A. It is not of value in severe haemophilia A or with any type of haemophilia B. In serious bleeds or major surgery, desmopressin alone will not control bleeding. In such a case, most patients should also receive factor VIII concentrate, recombinant factor VIII replacement and recombinant factor IX replacement.

Most haemophiliac patients are usually well known to their state haemophilia centres, which often have specialized treatment protocols for difficult or complex patients. Patients should have their treatment regimen cards with them. If not they should be encouraged to do so.

One unit of factor VIII concentrate provides the amount of factor VIII activity in 1 mL of normal plasma. Given that a 70-kg adult has a plasma volume of 3500 mL, we can expect that an infusion of 3500 units of factor VIII will produce 100% factor VIII activity in a haemophiliac individual with negligible activity prior to treatment. The half-life of factor VIII is approximately 12 hours. Accordingly, a further dose of 1750 units in 12 hours' time will again restore 100% activity.

It is not always necessary to provide 100% factor VIII activity in order to ensure haemostasis: levels of 30% to 50% may be sufficient in the context of haemarthrosis or dental extraction. Larger infusions should be reserved for life-threatening situations.

Treatment of bleeding

MINOR/MODERATE BLEED – Including, haemarthrosis, minor trauma, epistaxis and suturing:

- Factor VIII (Advate®, Xyntha®)
- 30 IU/kg for the 1st dose, then 20 IU/kg at 12/12 and 24/24 post 1st dose
- DDAVP (Desmopressin)
- 0.3 microgram/kg in 100ml sodium chloride 0.9% over 45 mins
- Factor IX (BeneFIX)
- 60 IU/kg 1st dose, then 30 IU/kg at 24/24.
- Some injuries will require ongoing Factor treatment.

MAJOR BLEED – Intra cerebral, GIT, hip, throat, major muscle, e.g. Psoas or limb muscle bleeds with risk of compartment syndrome and fractures:

- Factor VIII (Advate, Xyntha)
- 45 IU/kg stat. Commence continuous Factor VIII infusion within 4 hours to maintain factor level >70%. Continuous infusion is initiated by HTH.
- Factor IX (BeneFIX)
- 90 IU/kg. Commence continuous Factor IX infusion within 4 hours to maintain factor level > 70%. Continuous infusion is initiated by HTH.
- If Blood Bank unable to prepare infusion overnight, seek advice from haematology registrar rebusol regime

Many patients can administer factor VIII concentrate at home 'on demand'. Indeed, the availability of factor VIII and the ease of administration have revolutionized the care of haemophiliac patients in the community. However, the following are indications for hospital admission:

- Suspected intracranial haemorrhage
- A large bleed
- Ongoing bleed
- Suspected bleeding into the head, neck or throat
- Need for ongoing therapy, especially infusions
- Suspected compartment syndrome (especially of forearm and calf)
- Bleeding into hip or inguinal area, suspected iliopsoas haemorrhage
- Undiagnosed abdominal pain
- Persistent haematuria
- Ongoing analgesia requirements
- Inadequate social circumstances

Antifibrinolytic agents, such as tranexamic acid (Cyclokapron) and aminocaproic acid (Amicar), have been used as adjunctive therapy in episodes of gastrointestinal and mucosal bleeding—for example, following dental extraction. Fibrin tissue adhesives containing fibrinogen, thrombin and factor XIII have also been successfully placed in tooth sockets and similar surgical sites.

Tranexamic acid and aminocaproic acid are useful in treating both haemophilia A and B. These drugs help to hold a clot in place once it has formed. They act by stopping the activity of

plasmin, which dissolves blood clots. They do not actually help to form a clot, which means that they cannot be used instead of desmopressin or factor VIII or IX concentrate but can be used to hold a clot in place on mucous membranes, including in the oral cavity, nasal cavity, intestinal and uterine walls. Tranexamic acid and aminocaproic acid are associated with minor side effects including nausea, lethargy, vertigo, diarrhoea and abdominal pain.

Oral/dental bleeds

First-line therapy should be topical tranexamic acid mouthwash (5%). Patients hold 10 mL of the solution in the mouth near the site of bleeding (without gargling) for 2 minutes repeated five times a day for a week.

Haematuria

Factor replacement and antifibrinolytic therapy is not usually recommended in these cases due to the risk of clot retention and renal tract obstruction.

Head injury

Haemophiliac patients with even apparently minor head trauma need hospital assessment and CT head scanning. Beware of subtle signs of a developing subdural haematoma. If an intracranial bleed is suspected, replacement therapy should be initiated prior to radiological investigation.

Compartment syndrome

Compartment syndromes are relatively common in patients with hereditary and acquired bleeding disorders. As compartment syndrome is a clinical diagnosis, measuring compartment pressure is generally not needed to make the diagnosis.

Four of the classic signs of compartment syndrome—pallor, pulselessness, paraesthesia and paralysis—are all (very) late signs.

Pain is the earliest sign and has the following characteristics:

- Pain out of proportion to the expected
- Associated with a hard/tense compartment on clinical examination
- Severe pain on gentle passive stretch of that compartment (e.g. plantarflexion of ankle/toes, thus stretching the anterior compartment)
- Unremitting/increasing pain with increasing requirement of pain medications

The treatment for this condition is urgent fasciotomy.

Patients who present to the ED with bleeding disorders and suspected compartment syndrome should have the usual management for these conditions plus immediate referral to the orthopaedic unit and haematology unit.

Surgical decision making and indications for fasciotomy are the same as for patients without bleeding disorders and factor replacement

dosage and frequency for these patients is the same as for any major surgery.

Antibodies to Factor VIII

Some patients develop antibodies to factor VIII, known as 'inhibitors'. Treatment has to be modified according to the titre of inhibitor present (measured by the Bethesda inhibitor assay). Patients are classified as high responders if their baseline inhibitor titre exceeds 10 Bethesda units (BU) or if the titre rises above 10 BU on exposure to factor VIII. Different management strategies are employed according to the severity of the bleed. These include increasing the dose of factor VIII or alternative therapies, such as activated prothrombin complex, porcine factor VIII or recombinant factor VIIa.

Most patients who develop inhibitors do so early in life and are known to have severe hereditary haemophilia, but inhibitors can also arise in previously normal individuals to produce an acquired haemophilia. The incidence of this phenomenon is from 0.2 to 1 per 1 million per year. Patients tend to be elderly and some have autoimmune disease, but there is also an association with pregnancy as well as with some drugs, notably penicillin. Patients haemorrhage into muscle and soft tissues and may present with haematemesis or with unusual postoperative bleeding. In the laboratory, the patient's blood shows a prolonged activated partial prothrombin time (APPT) that is not corrected by 'mixing'—that is, by the addition of normal plasma. Factor VIII levels are low. Management is directed towards control of the bleeding episode, replacement therapy and the prevention of further reactions using a variety of immunosuppressive remedies.

Disposition

- Patients with 'minor' bleeds and no other complicating issues may be discharged after treatment in the ED, but management should ideally be discussed first with the treating haemophilia unit and early review arranged.
- Patients with 'moderate' bleeds may need admission, preferably at the state treatment centre. These cases must be discussed with the treating unit before discharge from the ED.
- All patients with 'major' bleeds *must* be admitted and management discussed on an urgent basis with the treating haemophilia unit prior to transferring care.

von Willebrand disease

Factor VIII has an intimate association with vWF. This is an adhesive glycoprotein, secreted by

endothelium and megakaryocytes, which is required for the normal instigation of platelet plug formation and for stabilization and transport of factor VIII within the circulation. Thus von Willebrand disease (vWD) is a result of dysfunction, reduction or a complete lack of the vWF and is often associated with low factor VIII activity. It is the most common inherited bleeding disorder, affecting 0.1% to 1% of the population and males and females equally.

Three types of vWD are recognized:

- Type I (common): reduced levels of vWF—clinically associated with mild bleeding
- Type II (uncommon): abnormally functioning vWF—clinically associated with a variable bleeding pattern
- Type III (rare): a near absence of vWF—clinical presentation is similar to that of moderate to severe haemophilia

Common symptoms of vWD include the following:

- Frequent nose bleeds
- Easy bruising
- Bleeding from gums following tooth extractions
- Menorrhagia
- Gastrointestinal bleeding

Treatment

If the patient has previously had a documented good response to DDAVP, this can be used as first-line treatment in type I vWD. It is occasionally also effective in type II vWD but never in type III vWD. The dose is the same as used in haemophilia (0.3 µg/kg). Antifibrinolytic agents, such as tranexamic acid, are often helpful for mucosal bleeding, epistaxis and menorrhagia. 'Biostate' (plasma-derived factor VIII, includes vWF) may be required in type I vWD if bleeding is severe or unresponsive to DDAVP; it can also be used to treat bleeding in patients with type II and type III vWD.

Contacts

For a list of useful contacts, see the online appendix.

Further reading

- Bell BA, Birch K, Glazer S. Experience with recombinant factor VIIA in an infant with haemophiliac with inhibitors to FVIII:C undergoing emergency central line placement. A case report. *Am J Pediatr Hematol Oncol.* 1993;15:77–79.
 Bush MT, Roy N. Hemophilia emergencies. *J Emerg Nurs.* 1995;21:531–538.
 De Behnke DJ, Angelos MG. Intracranial hemorrhage and hemophilia: case report and management guidelines. *J Emerg Med.* 1990;8:423–427.
 Pfaff JA, Geninatti M. Hemophilia. *Emerg Med Clin North Am.* 1993;11:337–363.
 Warrier I, Ewenstein BM, Koerner MA, et al. Factor IX inhibitors and anaphylaxis in hemophilia B. *J Pediatr Hematol Oncol.* 1997;19:23–27.

13.4 HAEMOPHILIA

Useful contacts

Websites

- Australian Haemophilia Centre Directors' Organisation: www.ahcdo.org.au
 Haemophilia Foundation Australia: www.haemophilia.org.au
 Canadian Hemophilia Society: www.hemophilia.ca
 Hemophilia Federation of America: www.hemophilafed.org
 Haemophilia Foundation Australia: www.haemophilia.org.au
 Haemophilia Foundation of New Zealand: www.haemophilia.org.nz
 Haemophilia Society (UK): www.haemophilia.org.uk
 World Federation of Hemophilia: www.wfh.org

Contact numbers for advice/referrals

ACT

Canberra Hospital, Haemophilia Treatment Centre, Canberra Region Cancer Centre, Room 401, 4th Floor, Building 19, Yamba Drive, Garran, ACT 2605
 T 0481 013 323
 Drop-in Clinic Days: Tuesday, Thursday & Friday
 Other days by prior arrangement: Monday & Wednesday

Canberra hospital contacts

Main Switchboard: T (02) 6244 2222
 Accident & Emergency: T (02) 6244 2611
 Hours: 24 hours a day, 7 days a week

NSW

Calvary Mater Newcastle, Haemophilia Centre, Edith Street, Waratah, NSW 2298
 T 02 4014 3032
 Emergency 02 4921 1211 (switchboard)
 Fax 02 4960 2136

Royal Prince Alfred Hospital, Haemophilia Centre
 Building 77, Level 5 Missenden Road, Camperdown, NSW 2050
 T 02 9515 7013
 Emergency 02 9515 6111
 Fax 02 9515 8946

The Children's Hospital at Westmead, Cnr Hawkesbury Rd & Hainsworth St, Westmead, NSW 2145
 T 02 9845 1138

Emergency 02 9845 0000 & page Haematologist on call
 Fax 02 9845 2041

Sydney Children's Hospital, Centre for Children's Cancer & Blood Disorders, High St Randwick, NSW 2031
 Doctor 02 9382 1690
 Nurse 02 9382 1240
 After Hours 02 9382 1111 & ask for Haematologist on call

Prince of Wales Hospital, SEALS, Barker St, Randwick, NSW 2031
 T 02 9382 9013
 Fax 02 9382 9116

NT

Royal Darwin Hospital, Rocklands Drive, Tiwi, NT 0810
 T 08 8944 8346 (Monday, Tuesday)
 Emergency 08 8922 8888 (Hospital switchboard)
 Fax 08 8922 8843

Royal Brisbane & Women's Hospital, Queensland Haemophilia Centre, Level 4, Joyce Tweddell Building, Butterfield Street, Herston, QLD 4029
 T 07 3646 5727
 Emergency 07 3646 8111 and page Haematologist on call
 Fax 07 3646 4221

Lady Cilento Children's Hospital (LCCH), Queensland Haemophilia Centre, Haemophilia/Haematology Dept., 501 Stanley St, South Brisbane, QLD 4101
 T 07 3068 2389
 Doctor Haematology Fellow/Registrar 07 3068 4403

Nurse 0438 792 063
 After Hours Switchboard 07 3068 1111 and ask for the Haematologist on call
 Fax 07 3068 4139

Royal Adelaide Hospital, 3E Day Treatment, Port Road, Adelaide, SA 5000
 T 08 7074 2385
 Emergency 08 7074 0000 & ask for Haematologist on call
 Fax 08 7074 6209

Women's and Children's Hospital, The Michael Rice Centre for Haematology/Oncology, 72 King William Road, North Adelaide, SA 5006
 Emergency 08 8222 8222 & ask for haematologist on call
 Fax 08 9341 9842

T 08 8161 7411

Emergency 08 8161 7000 (switchboard)
 After Hours 08 8161 7225
 Fax 08 8161 6567

Royal Hobart Hospital, Tasmanian Haemophilia Treatment Centre, Paediatric Oncology—Haematology, Liverpool Street, Hobart, TAS 7000
 T 03 6166 8045
 Emergency 03 6166 8308 & page haematologist on call
 Fax 03 6222 6767

VIC

The Alfred, Ronald Sawers Haemophilia Centre, 1st Floor, South Block Commercial Road, Melbourne, VIC 3004
 T 03 9076 2178
 Emergency 03 9076 2000 (switchboard)
 Fax 03 9076 3021

Royal Children's Hospital—The Henry Ekert Haemophilia Treatment Centre, Flemington Road Parkville, VIC 3052
 T 03 9345 5099
 Emergency 03 9345 5522 and ask for Haematologist on call
 Fax 03 9349 1819

WA

The Haemophilia and Haemostasis Centre, Level 1 Cancer Centre, Fiona Stanley Hospital 102-118 Murdoch Drive, Murdoch, WA 6150
 T (Centre) 08 6152 4137 | (CNC) 08 6152 6527
 Emergency 08 6152 2222
 Fax 08 6152 4138

Princess Margaret Hospital for Children, Oncology & Haematology Ward 3B, Roberts Road, Subiaco, WA 6008
 T 08 9340 8682 / 8234
 Emergency 08 9340 8222 & ask for haematologist on call
 Fax 08 9341 9842

Hollywood Haemophilia Treatment Centre, Hollywood Hospital, Monash Ave., Nedlands, WA 6009
 T 0429 445 121 Nurses Hotline 8 a.m.–4 p.m. Mon–Fri
 After Hours 08 9364 6000—After Hours Manager will contact Haematologist
 Fax 08 9389 8470

13.5 Blood and blood products

Sean Arendse • Biswadev Mitra

ESSENTIALS

- 1** The decision to transfuse packed red cells should ultimately be based on the knowledge that the patient's oxygen carrying capacity has dropped to an unacceptably low level.
- 2** The administration of blood products carries substantial risk. The emergency physician should always ensure that potential benefits outweigh potential risks and communicate these risks and benefits in order to obtain informed consent where possible.
- 3** Rigorous risk management of administrative and clinical processes minimizes the risk of serious adverse reaction from the transfusion of blood products.

Introduction

Blood is living tissue composed of blood cells suspended in plasma; it transports nutrients and oxygen and facilitates temperature control. An average 70-kg male has a blood volume of about 5 L. The cellular elements comprise red blood cells, white blood cells and platelets and make up about 45% of the volume of whole blood. Plasma, which is 92% water, makes up the remaining 55%.

Early attempts at blood transfusion were thwarted by adverse reactions. In 1900, Karl Landsteiner demonstrated the ABO blood group system and explained many of the observed severe incompatibility reactions (**Table 13.5.1**). He won the Nobel Prize for medicine in 1930 and went on to discover the rhesus factor in 1940. The next major advance in transfusion medicine occurred with the development of long-term anticoagulants, such as sodium citrate, which allowed extended preservation of blood. The development of refrigeration procedures enabled the storage of anticoagulated blood. The addition of a citrate-glucose solution extended the viability of collected blood to several days. The ability to

preserve blood for longer than a few hours paved the way for the establishment of the first blood bank in a Leningrad hospital in 1932.

Transfusion of blood and blood products is now routine and vital to the practice of emergency medicine. As with any prescribed treatment, these products are associated with potential hazards as well as advantages. The hazards are more likely to be encountered with blood products used during emergencies. The blood products available in most Australian emergency departments (EDs) are packed red blood cells, platelets, fresh frozen plasma (FFP), cryoprecipitate, activated factor VII, prothrombin complex concentrates, and other factor concentrates.

In the Australian urban hospital setting, 50% of packed red cells are used for the treatment of anaemia, 22% pre- or perioperatively and 13% for abnormal, excessive or continued bleeding. Medical oncology uses 78% of all platelets. Approximately 41% of all FFP is used to correct coagulopathy associated with surgery, 27% to correct coagulopathy in bleeding, 16% to reverse haemostatic disorders in patients having massive blood transfusion, 11.5% for reversal of warfarin effect and the remaining 4.5% for a number of miscellaneous conditions, including liver disease and disseminated intravascular coagulation (DIC).

In the ED setting, blood products are most often administered to patients with acute rather than chronic blood loss. In trauma centres, severely injured patients are the major consumers of blood products; in non-trauma centres, patients with gastrointestinal haemorrhage account for the majority of transfusions. In these settings of acute blood loss, transfusion may be required rapidly and in large quantities.

However, as short-stay units are developed, non-time critical transfusions of blood products for other medical indications are increasingly the responsibility of ED staff.

Packed red blood cells

Packed red blood cells are produced from whole blood collections by removing most of the plasma by centrifugation and then resuspending the red cells in citrate-based anticoagulant/preservative solution to prolong storage time. Each unit of packed cells contains approximately 200 mL of red cells. Transfusion of one unit can be expected to raise the haematocrit by 3% and the haemoglobin by 10 g/L provided that there is no ongoing blood loss.

Packed red cells are the blood product most commonly prescribed in the ED, the usual indication being the replacement of acute blood loss. Transfusion of packed red cells is indicated where the patient's oxygen-carrying capacity is so impaired that control of bleeding alone, if indeed it can be readily achieved, is regarded as insufficient to prevent tissue hypoxia. In patients with primary haematological conditions, failure of erythropoiesis or a haemolysis, the indication for transfusion is usually the same as for haemorrhage: a severe reduction in oxygen-carrying capacity. In patients with associated complex multi-system failure, such as DIC or septic shock, red cell transfusion may be lifesaving by improving the oxygen debt in tissues (**Box 13.5.1**).

The indication for transfusion in haemorrhagic shock has been traditionally defined as persistent haemodynamic instability despite a small volume fluid challenge. However, two further patient factors must be considered. First is the concept of hypotensive resuscitation, which states that prior to definitive cessation of bleeding, relative hypotension may stabilize clots and reduce

Box 13.5.1 Potential indications for red cell transfusion

- Haemorrhage
- Dilutional anaemia following severe burns
- Iron deficiency anaemia
- Megaloblastic anaemia
- Anaemia of chronic disorders
- Chronic renal failure
- Failure of erythropoiesis
- Sickle cell disease
- Septic shock
- Disseminated intravascular coagulopathy

Table 13.5.1 The ABO group system

ABO blood group	Antigens on red cells	Antibody in serum
O	None	Anti-A, anti-B
A	A	Anti-B
B	B	Anti-A
AB	A, B	None

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further bleeding. Clinician must therefore alter their thresholds of haemodynamic instability. Patient factors must be borne in mind, including the cardiovascular co-morbidities and the presence of head injuries. Second, both high-volume crystalloid and blood transfusion have been associated with adverse outcomes. This suggests that both should be limited rather than focusing resuscitation efforts on the management of coagulopathy and early surgical management of haemorrhage.

Transfusion is not indicated when alternative haematinic therapy is deemed safe and appropriate. A moderately anaemic patient who is asymptomatic and not bleeding, with some reserve oxygen-carrying capacity, does not require blood transfusion. A haemoglobin of 7 g/dL is sometimes taken as the failsafe point in the decision regarding whether to transfuse, although of course the patient's unique circumstances must be taken into account: in other words, treat the patient, not the number. It should be also considered that, in an acutely bleeding patient, the initial haemoglobin result, measured at a time of volume contraction, may be an inaccurate representation of circulating oxygen-carrying capacity. The National Health and Medical Research Council together with the Australasian Society of Blood Transfusion have published transfusion guidelines for red blood cells and other products (Table 13.5.2).

Prior to any blood product transfusion, informed consent should be sought, obtained and documented except in emergent cases, where the delays may result in substantial adverse effects. The following sections discuss the risks of red cell transfusion.

Effect of storage on red blood cells

Although it makes intuitive sense that blood loss should be replaced by blood products, there is evidence that the immediate observed benefit is from volume replacement rather than improved oxygen carriage. Red blood cells may not be fully functional until 2 to 6 hours after transfusion, because storage affects the oxygen-carrying capacity of blood. This is probably due to decreased intracellular 2,3-diphosphoglycerate (2,3-DPG), loss of red cell viability, decreased red cell deformability, relative acidosis and potassium leakage.

Storage reduces 2,3-DPG levels, leading to a leftward shift of the oxyhaemoglobin dissociation curve and increased affinity of oxygen binding. The transfused red cell does regenerate 2,3-DPG to normal levels, but this can take 6 to 24 hours post-transfusion. With increasing age of stored red cells, levels of 2,3-DPG progressively fall, such that by 5 to 6 weeks the level is only 10% of normal. It is still uncertain whether this abnormality is physiologically important, even in

Table 13.5.2 Guidelines for transfusion of blood components

Indications	Considerations
Red blood cells	
Hb	
<70 g/L	Lower thresholds may be acceptable in patients without symptoms and/or where specific therapy is available.
70–100 g/L	Likely to be appropriate during surgery associated with major blood loss or if there are signs or symptoms of impaired oxygen transport.
>80 g/L	May be appropriate to control anaemia-related symptoms in a patient on a chronic transfusion regimen or during marrow suppressive therapy.
>100 g/L	Not likely to be appropriate unless there are specific indications.
Platelets	
Bone marrow failure	At a platelet count of $<10 \times 10^9/\text{L}$ in the absence of risk factors and $<20 \times 10^9/\text{L}$ in the presence of risk factors (e.g. fever, antibiotics, evidence of systemic haemostatic failure).
Surgery/invasive procedure	To maintain platelet count at $>50 \times 10^9/\text{L}$. For surgical procedures with high risk of bleeding (e.g. ocular or neurosurgery), it may be appropriate to maintain at $100 \times 10^9/\text{L}$.
Platelet function disorders	May be appropriate in inherited or acquired disorders, depending on clinical features and setting. In this situation, platelet count is not a reliable indicator.
Bleeding	May be appropriate in any patient in whom thrombocytopenia is considered a major contributory factor.
Massive haemorrhage/ transfusion	Use should be confined to patients with thrombocytopenia and/or functional abnormalities who have significant bleeding from this cause. May be appropriate when the platelet count is $<50 \times 10^9/\text{L}$ ($<100 \times 10^9/\text{L}$ in the presence of diffuse microvascular bleeding).
Fresh frozen plasma	
Single factor deficiencies Warfarin effect	Use specific factors if available. Use in the presence of life-threatening bleeding. Use in addition to vitamin K-dependent concentrates.
Acute DIC	Indicated where there is bleeding and abnormal coagulation; not indicated for chronic DIC.
TTP	Accepted treatment.
Coagulation inhibitor deficiencies	May be appropriate in patients undergoing high-risk procedures.
Following massive transfusion or cardiac bypass	Use specific factors if available May be appropriate in the presence of bleeding and abnormal coagulation.
Liver disease	May be appropriate in the presence of bleeding and abnormal coagulation
Cryoprecipitate	
Fibrinogen deficiency	May be appropriate where there is clinical bleeding, an invasive procedure, trauma or DIC.

DIC, Disseminated intravascular coagulation; TTP, thrombocytopenia purpura.

(Modified from the National Health and Medical Research Council and Australasian Society Clinical Practice Guidelines on appropriate use of blood components. https://transfusion.com.au/transfusion_practice/patient_blood_management_guidelines.)

critically ill patients. In addition, hypocalcaemia, cell lysis, release of free haemoglobin, changes in nitric oxide levels, alterations in pH and increases in lipids, complement and cytokines are other effects of red cell storage. These changes are accompanied by increased membrane fragility, which can compromise microcirculatory flow and lead to increased red cell–endothelial cell interaction and inflammatory cytokine release. Such changes may explain recent findings associating the age of red blood cells with adverse outcomes

and may be particularly disadvantageous to critically ill patients with a higher mortality risk.

When red cells are transfused, some of the cells are removed from the circulation within a few hours, with the rest surviving normally; as the storage time increases to 42 days, more cells are removed immediately after transfusion. This loss of viability is highly dependent on the anticoagulant/preservative solution used.

Potassium gradually leaks out of stored red cells, and this raises the plasma potassium by

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approximately 1 mEq/L/day. Citrate toxicity results when the citrate in the transfused blood begins to bind calcium in the patient's body, resulting in hypocalcaemia. Clinically significant hypocalcaemia does not usually occur unless the rate of transfusion exceeds 1 unit every 5 minutes or so. Citrate metabolism is primarily hepatic; therefore hepatic disease or dysfunction can cause this effect to be more pronounced.

Choice of red cell product

The choice of red cell product is determined by time and safety considerations. O-negative red cells, the universal donor group, are readily available in most major hospitals. Supplies of O-negative blood are limited, and the product should be used with care. O-negative blood is generally reserved for transfusion immediately during patient reception and the initial stages of resuscitation, with a switch to cross-matched blood as soon as it is available. It is preferable that blood be collected prior to transfusion so as to characterize the recipient's blood group serology. Premenopausal female patients should be given group O Rh-negative, Kell-negative blood in an emergency situation in order to avoid sensitization and the possibility of haemolytic disease of the newborn in subsequent pregnancies. Male patients, however, can be transfused with either Rh-positive or negative blood. The incidence of adverse reaction using this type of blood is approximately 3%. By contrast, the provision of group-specific blood requires matching a blood sample to the major (ABO) and Rh-D compatibility groups only. Group-specific blood can be available for transfusion within 35 minutes, depending on the logistic support and staffing levels within the haematology laboratory. It has an incidence of adverse reactions similar to O-negative blood. As O-negative blood is usually in short supply, it is preferable, where possible, to infuse group-specific blood. A more comprehensive cross-match where there are no atypical antibodies identified in the initial screening can take 30 minutes or more and the incidence of adverse transfusion reaction is then reduced to 0.01%.

Precautions when cross-matching and transfusing blood

Although most patients do not require transfusion in the ED, it is often appropriate to 'group and hold' or cross-match the patient while in the department. Many hospitals have written protocols detailing the anticipated requirements for a given surgical procedure. Documentation should be meticulous. It should be mandated that the person drawing the blood for cross-matching should also fill in and sign the laboratory request form. Most severe incompatibility reactions to blood transfusion result not from exposure to

Table 13.5.3 Adverse effects of blood transfusion

<i>Immunological transfusion reactions</i>	<i>Transmission of infection</i>
Immediate	Bacterial
Febrile non-haemolytic reactions	<i>Brucella</i>
Acute haemolytic transfusion reactions	<i>Pseudomonas</i>
Allergic reactions and anaphylaxis	<i>Salmonella</i>
Transfusion-related acute lung injury	<i>Treponema pallidum</i>
Delayed	Parasites
Delayed haemolytic transfusion reactions	<i>Babesia</i>
Alloimmunization	<i>Plasmodium</i>
Transfusion-associated graft-versus-host disease	<i>Toxoplasma</i>
Hypothermia	<i>Trypanosoma</i>
Dilutional coagulopathy	Viruses
Volume overload	Cytomegalovirus
	Hepatitis B and delta agent
	Hepatitis A
	Hepatitis C
	Other hepatitis, 'non-A, non-B'
	HIV-1 and HIV-2
	HTLV-1 and HTLV-2
	Parvovirus

HIV, Human immunodeficiency virus; HTLV, human T-cell lymphotropic virus.

unusual antigens but from administrative errors. Any systematic change in documentation protocols—for example, the adoption of an electronic record—must be accompanied by obsessive risk-management strategies.

The checking of the compatibility details of blood to be transfused must be meticulous. Blood products should not be left lying around workbenches. Universal precautions must be observed by staff setting up transfusions. Rapid or large transfusions should be given via a blood warmer. Blood should be transfused intravenously through sterile giving sets containing 170-μm filters. Alternative routes (arterial, intraperitoneal or intraosseous) should be used in exceptional circumstances. Lines for transfusion should be dedicated lines; drugs and other additives should be administered at separate sites. Normal saline is compatible with all blood components.

Pulse, blood pressure and temperature are measured at regular intervals and particular attention is paid to the patient during the first 25 minutes of the transfusion. The transfusion is started slowly. The rate at which it continues depends on clinical urgency. As a general rule, the faster the anaemia has developed, the more rapidly it must be corrected. Rapid infusion

techniques may be indicated in patients who appear to be exsanguinating, but an overly rapid infusion may precipitate cardiac failure in the elderly. Hypothermia may be a problem if a blood warmer is not used.

Adverse reactions to transfusion

The principal adverse reactions to blood transfusion are listed in Table 13.5.3. Serious adverse reactions are relatively rare (Table 13.5.4), although some are more likely to occur when blood is administered urgently.

Immunological transfusion reactions

Immunological transfusion reactions may be immediate or delayed in onset.

Immediate

Febrile non-haemolytic reactions The most common transfusion reaction is a febrile, non-haemolytic transfusion reaction (FNHTR), which is defined as an increase in temperature of 1°C or more over baseline during a transfusion. It manifests as fever and occasionally shortness of breath 1 to 6 hours after transfusion. FNHTRs are benign, but their presentation is very similar to that of an acute

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Table 13.5.4 Incidence of adverse transfusion reactions (per unit packed red cells transfused)

Adverse transfusion reaction	Incidence	Mortality
Bacterial sepsis	1 in 40,000–500,000	1 in 4–8 million
Acute haemolytic reaction	1 in 12,000–38,000	1 in 600,000–1.5 million
Delayed haemolytic reaction	1 in 1,000–12,000	1 in 2.5 million
Anaphylaxis	1 in 20,000–50,000	
Transfusion-related acute lung injury	1 in 5,000–100,000	1 in 5 million
Fluid overload	1 in 100–700	
Transfusion-associated graft-versus-host disease	Rare	90% fatality

(Modified from Australian Red Cross website: https://transfusion.com.au/adverse_events_overview. Accessed February 2017.)

Table 13.5.5 ABO and rhesus compatibility between donors and recipients

Donors	O+	A+	B+	AB+	O-	A-	B-	AB-
Recipients								
O+	C				C			
A+	C	C			C	C		
B+	C		C		C		C	
AB+	C	C	C	C	C	C	C	C
O-					C			
A-					C	C		
B-					C		C	
AB-					C	C	C	C

C, Compatible.

haemolytic transfusion reaction and infection, which have a higher rate of mortality and morbidity, mandating early clinical review to exclude more serious complications.

Acute haemolytic reactions Acute haemolytic transfusion reactions (AHTRs) result from the rapid destruction of donor red cells by preformed recipient antibodies and are medical emergencies. They are usually due to ABO incompatibility and most often the result of clerical or procedural errors. ABO and Rh compatibility between donors and recipients is presented in Table 13.5.5. Some acquired alloantibodies, such as anti-Rh or anti-Jka, are occasionally implicated, but AHTRs more typically occur when a group O recipient is transfused with non-group O red cells. This may lead to DIC, shock and acute tubular necrosis, precipitating acute renal failure. These reactions usually manifest with fever and rigors, lumbar pain, crushing chest pain, tachycardia, hypotension and haemoglobinuria, with subsequent haemoglobinuria. The symptoms usually develop within the first 30 minutes of transfusion.

Anaphylactoid transfusion reactions Anaphylactoid reactions usually begin within 1 to 45 minutes of the start of transfusion of blood products, but less severe reactions can be delayed up to 2 to 3 hours. Generally a shorter time between commencement of the transfusion and onset of symptoms is associated with a more severe reaction. These reactions are manifested by the rapid onset of shock, hypotension, angio-oedema and respiratory distress. They are almost always due to the presence of class-specific immunoglobulin (Ig) G, anti-IgA antibodies in patients who are IgA-deficient. Selective IgA deficiency is not uncommon, occurring in about 1 in 300 to 500 people. The incidence of anaphylactic transfusion reactions can be reduced by the use of washed products (e.g. washed red cells) and by premedicating the patient with antipyretics and antihistamines.

Treatment of an anaphylactoid transfusion reaction consists of immediate cessation of transfusion and standard treatment of anaphylaxis, including oxygen fluids and adrenaline (see Chapter 2.8).

Transfusion-related acute lung injury Transfusion-related acute lung injury (TRALI) is a

syndrome characterized by acute respiratory distress following transfusion. All plasma-containing blood products have been implicated including rare reports involving intravenous immunoglobulin (IVIG) and cryoprecipitate. It is a rare complication of allogeneic blood transfusion, but the incidence has not been well established due to difficulty in defining the syndrome and variable reporting mechanisms worldwide. Symptoms of TRALI typically develop during the transfusion or within 6 hours. Patients present with a rapid onset of dyspnoea and tachypnoea. There may be associated fever, cyanosis and hypotension. Clinical exam reveals respiratory distress, and pulmonary crackles may be present with no signs of congestive heart failure or volume overload. Chest x-ray (CXR) shows evidence of bilateral pulmonary oedema unassociated with heart failure (non-cardiogenic pulmonary oedema) with bilateral patchy infiltrates, which may rapidly progress to complete 'white out' indistinguishable from acute respiratory distress syndrome. The central venous pressure is normal, which helps to distinguish the condition from transfusion-associated circulatory overload. Treatment is supportive. There is no role for diuretics or corticosteroids. The blood bank must be notified, as reporting of TRALI allows better understanding of the true incidence of this reaction in addition to its clinical course and associated mortality.

Delayed

Delayed haemolytic transfusion reaction These reactions occur in patients who have developed antibodies from previous transfusions or pregnancy; however, at the time of pretransfusion testing, the antibody in question is too weak to be detected by standard procedures. Subsequent transfusion with red cells having the corresponding antigen results in an anamnestic antibody response and the haemolysis of transfused red cells. These delayed reactions are seen generally within 2 to 10 days after transfusion. Haemolysis is usually extravascular, gradual and less severe than with acute reactions, but rapid haemolysis can occur. A falling haematocrit, slight fever, mild increase in serum unconjugated bilirubin and spherocytosis on the blood smear may be noted.

Treatment of a delayed haemolytic transfusion reaction is usually not required unless anaemia is severe enough to require treatment. However, future transfusions containing the implicated red-cell antigen must be avoided. Alternatives to transfusion should be explored whenever possible.

Red-cell alloimmunization When antibodies are formed against foreign antigens from an individual's own species, the process is termed *alloimmunization* and the antibodies

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are called *alloantibodies* (as opposed to forming autoantibodies to an individual's own antigens or forming *xenoantibodies* to antigens from a foreign species). Transfused (non-leucocyte depleted) red cells and platelets contain leucocytes to which antibodies can be made. This may cause patients to become resistant to subsequent platelet transfusions. Approximately 50% of patients undergoing multiple blood transfusions become alloimmunized and are refractory to further platelet transfusions. Refractory patients require platelets matched to their specific platelet/human leucocyte antigen (HLA) type. Patients receiving leucocyte-reduced blood products are at a much lower risk for refractoriness to platelet transfusion than are recipients of non-leucocyte reduced blood products. Although debate exists about its merits, for selected high-risk patients with transfusion-dependent diseases (e.g. sickle cell anaemia, thalassaemia), some transfusion services phenotype patients and provide phenotypically matched donor red blood cells (RBCs), even to those patients without alloantibodies (i.e. to prevent the formation of antibodies). There is general agreement that this is useful for Rh and Kell blood-group antigens in these groups of patients, but debate exists about its merits for more extensive phenotyping.

Transfusion-associated graft-versus-host disease Transfusion-associated graft-versus-host disease (TA-GVHD) results from the transfusion of viable T lymphocytes that proliferate and damage the recipient's tissue, particularly skin, gastrointestinal tract, liver, spleen and bone marrow. This is a rare and almost always fatal complication of transfusion. Clinical manifestations typically develop 10 to 14 days following transfusion and consist of fever, erythematous skin rash, pancytopenia, diarrhoea and abnormal liver function. High-risk patients for this complication include bone marrow transplant recipients, patients receiving granulocyte transfusions, transfusions from a biologically related donor (directed donation), the fetus (intrauterine transfusion), exchange transfusion, patients with Hodgkin lymphoma and those with congenital cellular immune deficiency.

The investigation begins with the confirmation of the presence of GVHD. This is a pathological diagnosis requiring a skin or intestinal biopsy. Currently, the only method of preventing TA-GVHD is to γ -irradiate cellular components at risk of causing TA-GVHD or destined for at-risk recipients. Current techniques to leuco-reduce cellular blood components are not adequate to prevent TA-GVHD.

Transmission of infection

In Australia, blood is tested for ABO and Rh (D) blood groups, red-cell antibodies and the following infections:

- human immunodeficiency virus 1 and 2
- hepatitis B and C
- human T-cell lymphotropic virus I and II
- syphilis

In terms of viral safety, Australia has one of the safest blood supplies in the world (Table 13.5.6).

Hypothermia

Red blood cells are stored at 4°C. Rapid infusion of large volumes of stored blood can contribute to hypothermia. Blood warmers should be used during massive blood transfusion. In addition, other intravenous fluids should be warmed and other measures instituted to maintain the patient's body temperature (see Chapter 24.2).

Dilutional coagulopathies

Clinically significant depletion of coagulation proteins and platelets is a complication of massive transfusion, secondary to dilution and the consumptive coagulopathy of trauma. Stored red cells are deficient in platelets and clotting factors and the transfusion of large amounts can complicate bleeding when it is not accompanied by the assessment and correction of coagulation disturbances. Coagulation parameters including the prothrombin time (PT), activated partial thromboplastin time (APTT), platelet count and fibrinogen level should be monitored and corrected if deficiencies occur in the presence of abnormal bleeding. In actively bleeding patients, however, these parameters may not provide an accurate estimate of clot strength and results are often delayed by 30 to 60 minutes. Thromboelastography has the advantage of providing real-time assessment of clot strength and should be utilized where available.

Volume overload

This complication occurs when an excessive volume of fluid is administered. Pulmonary oedema is a particular risk in the elderly, infants and patients with chronic severe anaemia where the red-cell mass is decreased but the blood volume is normal. Abdominal compartment syndrome may result in bowel ischaemia and should be watched for.

Management of transfusion reactions

The first action to be taken in the management of any suspected transfusion reaction is to stop the transfusion immediately and assess the patient. The bag containing the transfused cells, along with all attached labels, should not be discarded

Table 13.5.6 Risks of transfusion-transmitted infection (per unit tested blood transfused)

Infection	Residual risk
CMV	1 in 127,000
Hepatitis B	Approximately 1 in 660,000
Syphilis	Considerably <1 in a million
Hepatitis C	<1 in 10 million
HIV	<1 in 10 million
HTLV I and II	<1 in 10 million
Variant CJD	Possible and cannot be excluded

CJD, Creutzfeldt-Jakob disease; *CMV*, cytomegalovirus; *HIV*, human immunodeficiency virus; *HTLV*, human T-cell lymphotropic virus. (Modified from Australian Red Cross. http://www.transfusion.com.au/adverse_events. Accessed February 2017.)

so as to allow repeat typing and cross-matching of this unit by the blood bank. Management then proceeds as follows:

- Maintain the patient's airway, blood pressure and heart rate.
- From a different limb to the one transfused, obtain a sample for a direct antiglobulin test, plasma-free haemoglobin and repeat blood group and cross-match. Save a urine sample for haemoglobin testing.
- Culture the patient's blood.
- Commence broad-spectrum antibiotics to cover gram positive skin organisms and gram negative organisms.

The laboratory that tested and issued the blood should be alerted immediately and a search for any clerical error instituted. Every hospital has a protocol for evaluating transfusion reactions, which should be rigorously followed. The haematology unit should notify the local blood bank, which has a haematologist on call at all times and is responsible for the recall of any other implicated components from the same donor in the case of suspected infection or TRALI. If there is any suggestion (e.g. clerical mistake, hypotension, pink plasma or urine) that an AHTR is possible, oxygen should be applied to the patient and fluid resuscitation with saline to maintain a urine output of 2 to 3 mL/kg/h in an attempt to prevent acute oliguric renal failure. A vasopressor such as adrenaline may be required. If massive intravascular haemolysis has already occurred, hyperkalaemia is likely and cardiac monitoring and acute haemodialysis may be required.

Platelets

Platelets are among the main cellular components of blood and are central to haemostasis. Platelet products commonly available for transfusion are obtained by apheresis from a single donor or from donated blood using buff-coat or platelet-rich

13.5 BLOOD AND BLOOD PRODUCTS

plasma techniques. Modifications to reduce the risk of viral transmission and prevent GVHD include leucocyte reduction, irradiation, plasma depletion and the use of platelet additive solutions.

Platelets are transfused to prevent or treat haemorrhage in patients with thrombocytopenia or defects in platelet function. Specific indications for platelet transfusion are shown in **Table 13.5.2**. The use of platelets is not generally considered appropriate in the treatment of immune-mediated platelet destruction, thrombotic thrombocytopenic purpura, haemolytic uraemic syndrome or drug-induced or cardiac bypass thrombocytopenia without haemorrhage.

In general one platelet unit will raise the platelet count about $5 \text{ to } 10 \times 10^9/\text{L}$ in an average adult. Depending on the method of manufacture, the volume of each unit of platelets varies from 100 to 160 mL, with a storage life of about 5 days at 20 to 24°C.

Compatibility testing is not necessary in routine platelet transfusion, although platelet components should preferably be compatible with the recipient's ABO and Rh type. ABO-incompatible platelets may be used if ABO-compatible platelets are not available. The usual dose in an adult patient is 4 units, which is equivalent to 1 unit of apheresis platelets or 1 unit of pooled platelets.

Fresh frozen plasma

FFP is prepared from anticoagulated blood by separating the plasma from the blood cells through centrifugation of whole blood or apheresis. It is stored frozen until used. It contains all coagulation factors including small amounts of factor V and approximately 200 units of factor VIII. FFP can be stored at below 25°C for up to 12 months. Indications for use of FFP are shown in **Table 13.5.2**.

The appropriate dose depends on the clinical indication, patient size and results of laboratory tests. A general guide is 10 to 15 mL/kg per dose, but in some situations dosages greater than this may be required (e.g. dilutional coagulopathy in the context of massive transfusion). On average 1 mL of FFP/kg patient weight will raise most coagulation factors by 1%; therefore a dose of 10 to 15 mL/kg would be expected to increase levels by 10% to 15%. Compatibility testing is not required; however, ABO-compatible plasma should be used wherever possible. Group AB plasma can be used for all patients in an emergency.

Cryoprecipitate

Cryoprecipitate is prepared by thawing FFP to between 1°C and 6°C and recovering the precipitable protein fraction. It contains most of the factor VIII, fibrinogen, factor XIII, von Willebrand factor and fibronectin from the FFP. It may be stored for up to 12 months at 25°C or below. Once thawed, it must be used immediately or stored at 2°C to 6°C for up to 24 hours. Cryoprecipitate is indicated in

fibrinogen deficiency with clinical bleeding or prior to an invasive procedure and in DIC. Cryoprecipitate is transfused to keep fibrinogen levels above 1.0 g/L in the acutely bleeding patient. Compatibility tests before transfusion are not necessary. It is preferable to use an ABO group compatible with the recipient's red cells; however, ABO-incompatible blood can be used with caution. Up to 4 units/10 kg body weight may be required to raise the fibrinogen concentration by approximately 0.5 g/L in the absence of continued haemorrhage.

The use of cryoprecipitate is not generally considered appropriate in the treatment of haemophilia, von Willebrand disease or deficiencies of factor XIII or fibronectin unless alternative therapies are unavailable.

Refusal of blood and blood product transfusion

Patients with certain religious beliefs may refuse blood and blood product transfusion (e.g. Jehovah's witnesses). Healthy volunteers can tolerate Hb levels of 50 g/L without evidence of end-organ hypoxia. However, it is estimated that the median Hb concentration associated with mortality is about 25 g/L. The patient's wishes must be rigorously protected and blood products avoided. Several strategies may be used to manage the anaemia. Sedation should be instituted to minimize metabolic demand. A ventilation cycle of 2 hours of 90% FiO₂, followed by 2 hours of 90% SpO₂ and then 20 hours of 95% SpO₂ may be employed to maximize oxygen delivery while minimizing shunt from absorption atelectasis and to promote erythropoiesis. Recombinant erythropoietin (36,000 units/day), folic acid (5 mg qd), vitamin B12 (1 mg qd) and iron infusions are options to maximize haematopoiesis. In female patients, where applicable, menses should be inhibited with progesterone. Blood testing should be rationalized and performed using paediatric-size samples.

A few case studies on the use of synthetic haemoglobin have been published. HBOC-201 is the commonest product used and is a modified lactated Ringer solution containing 130 g/L of polymerized Hb of bovine origin. It is compatible with all blood types, stable for 3 years when stored at 2°C to 30°C and stable for 2 years when stored at 40°C. When fully saturated, HBOC-201 has the same oxygen-carrying capacity as whole blood, with the same Hb concentration. The partial pressure of oxygen at which HBOC-201 is 50% saturated (40 mm Hg) is higher than that for cellular Hb (27 mm Hg), which facilitates oxygen delivery to tissues. The half-life of HBOC-201 is approximately 20 hours. Polymerization of the Hb reduces its glomerular diffusion and nephrotoxicity. The use of synthetic haemoglobin remains experimental at this stage and further trials are needed to determine the efficacy and safety profile of such products.

CONTROVERSIES

- Although the changes observed during red-cell storage affect overall red-cell viability and function, there are no randomized controlled studies examining the effect of storage duration on recipient morbidity and mortality.
- Acute coagulopathy has been observed in up to 40% of cases of massive acute haemorrhage associated with tissue injury and shock. Best practice guidelines for the use of platelets, cryoprecipitate or FFP in the shocked patient are determined primarily from observational studies and expert opinion. Prospective randomized controlled trials are required to determine optimal management strategies in the acutely haemorrhaging and coagulopathic patient.
- The potential for prions, thought to be the infective molecules in the variant form of Creutzfeldt-Jakob disease, to be transmitted by blood transfusion has become a subject of intense scrutiny in transfusion medicine.

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SECTION 14

RHEUMATOLOGY AND MUSCULOSKELETAL EMERGENCIES

Edited by *Conor Deasy*

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14.1 Rheumatological emergencies

Michelle C. Papandoni • Michael J. Gingold • Flavia M. Cicuttini

ESSENTIALS

1 Rheumatological emergencies relate to the disease, extra-articular manifestations of the disease or toxicity from treatment.

2 Infection must be considered and promptly treated in patients on antirheumatic and immunosuppressive medication, including those on biological therapies.

biological and non-biological DMARDs prevents joint destruction and disease progression, such agents are used increasingly more frequently in rheumatology patients.

ARTICULAR MANIFESTATIONS OF RHEUMATOID ARTHRITIS

Introduction

Rheumatological conditions are common and encompass (1) inflammatory diseases, such as rheumatoid arthritis (RA); (2) connective tissue diseases, such as systemic lupus erythematosus (SLE); and (3) mechanical/musculoskeletal conditions. Life-threatening emergencies are rare and relate to either the underlying condition or a complication from its treatment. The most common rheumatological emergency seen in the emergency department (ED) is acute monoarthritis (see [Chapter 14.2](#)). This chapter discusses the important general emergencies associated with rheumatological conditions.

Many of these conditions are autoimmune; thus immunosuppression is usually central to their management, making infection a frequent complication. More targeted, so-called biological therapies, which inhibit proinflammatory cytokines including tumour necrosis factor- α (TNF- α) and interleukin-6 (IL-6), as well as B- and T-cell activity, have been developed. They carry their own set of potential complications, again including infection.

RHEUMATOID ARTHRITIS

RA affects 1% to 2% of the population across most ethnic subgroups and is two to three times more common in females than males. RA is a systemic inflammatory condition of unknown aetiology characterized by widespread synovitis, resulting in joint erosions and destruction. It may also produce extra-articular manifestations, including vasculitis and visceral involvement.

Management typically involves symptom relief with non-steroidal anti-inflammatory drugs (NSAIDs) and/or corticosteroids and early initiation of conventional disease-modifying antirheumatic drugs (DMARDs). These include methotrexate, leflunomide, sulfasalazine and hydroxychloroquine, and if these agents fail to control disease progression, biological agents are commenced. The latter act by inhibiting TNF- α (infliximab, etanercept, adalimumab, golimumab, certolizumab pegol), IL-6 (tocilizumab), T-cell co-stimulation (abatacept), janus kinase 1 (JAK1) (tofacitinib) or by depleting B cells (rituximab). With increasing medical evidence suggesting that early and aggressive use of

Acute monoarthritis

Although a patient with established RA may present with an acutely painful, hot, swollen joint that is due to the underlying condition, consideration of septic arthritis is important. Patients with RA are two to three times more susceptible to septic arthritis than matched controls.¹ The risk is approximately twofold higher again in RA patients on TNF- α inhibitors compared with RA patients on conventional DMARDs.² Septic arthritis must be considered in a patient with RA who has acute monoarthritis out of keeping with their disease activity.

Cervical spine involvement

Cervical spine involvement in RA is common with a prevalence of up to 80%.³ Cervical spine involvement may manifest as atlanto-axial subluxation (most commonly anterior movement on the axis) or subluxation of lower cervical vertebrae.⁴ Either of these can result in cervical myelopathy.

Cervical spine subluxation is often asymptomatic.³ The most common symptom is neck pain that may radiate towards the occiput. Other

14.1 RHEUMATOLOGICAL EMERGENCIES

Box 14.1.1 Symptoms and signs of cervical myelopathy

Symptoms

Pain
Weakness
Peripheral paraesthesia
Gait disturbance
Sphincter dysfunction
Changes in consciousness
Respiratory dysfunction
Lhermitte phenomenon

Signs

Spasticity
Weakness
Hyperreflexia of deep tendon reflexes
Extensor plantar response
Gait ataxia
Respiratory irregularity

suggestive symptoms include sensory loss in hands or feet, paraesthesia or weakness in the distribution of cervical nerve roots, and slowly progressive spastic quadripareis.

Important 'red flags' suggesting cervical myelopathy are listed in [Box 14.1.1](#).

Imaging

Plain x-rays of the cervical spine (lateral view) may demonstrate an increase in separation between the odontoid and arch of C1. Prior to taking flexion-extension films, perform plain 'peg' x-rays to exclude odontoid fracture or severe atlanto-axial subluxation. Computed tomography (CT) can provide additional useful information; magnetic resonance imaging (MRI) is more sensitive for myelopathy.

Management

An important consideration with RA of the cervical spine in the ED is avoiding excessive manipulation when endotracheal intubation is required.

Patients with subluxation and signs of spinal cord compression represent a neurosurgical emergency.

EXTRA-ARTICULAR MANIFESTATIONS OF RHEUMATOID ARTHRITIS

Rheumatoid vasculitis

Vasculitis in RA can occur in both small- and medium-sized vessels. Patients typically have long-standing, aggressive joint disease. This presentation, although important, is becoming less frequent due to the development of effective RA treatment.

Clinical features

Rheumatoid vasculitis presentations are varied and non-specific. Patients frequently have constitutional symptoms and fatigue. One of the most common manifestation of medium vessel RA vasculitis includes deep skin ulcers on the lower limbs,⁵ digital ischaemia and gangrene. Palpable purpura is a manifestation of small vessel RA vasculitis. Mononeuritis multiplex is another frequent presentation resulting from vasculitic infarction of the vasa nervorum, which typically has an acute onset.

Medium vessel rheumatoid vasculitis may also cause organ infarction and necrosis and mimics polyarteritis nodosa (PAN) with vasculitis of the renal arteries and, less commonly, the mesenteric circulation. Pericarditis may accompany rheumatoid vasculitis, but coronary vasculitis is rare. Ocular manifestations include episcleritis and peripheral ulcerative keratitis. Central nervous system (CNS) involvement is rare.

Investigations and diagnosis

Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are elevated in rheumatoid vasculitis. Rheumatoid factor titre is typically elevated in rheumatoid vasculitis, although this is a non-specific finding. Rheumatoid vasculitis in the absence of rheumatoid factor is rare. Anti-citrullinated protein antibody (anti-CCP) may be positive in rheumatoid vasculitis, but once again, is a non-specific finding. Check a full blood count, urea and electrolytes, and a midstream urine specimen for active urinary sediment, including abnormal red cells or casts, proteinuria, as well as infection. In the work-up of vasculitis, it is also important to exclude infections that may mimic vasculitis. These include hepatitis B and C, human immunodeficiency virus (HIV) and syphilis, as well as a basic infection screen.

Further investigations are directed at the relevant organ system involved usually after specialist consultation:

- skin biopsy for cutaneous involvement
- nerve conduction studies/electromyography (EMG) for mononeuritis multiplex
- sural nerve biopsy for mononeuritis multiplex
- renal biopsy for deranged renal function or active urinary sediment

Angiography findings are non-specific and not always diagnostic.

Management

Systemic rheumatoid vasculitis has a poor prognosis without immune-suppressive therapy. Urgent rheumatology consultation is required, as treatment usually consists of high-dose

corticosteroids as well as cyclophosphamide or, a DMARD, often necessitating hospital admission.

Other extra-articular manifestations of rheumatoid arthritis

Pulmonary disease

Pulmonary manifestations include pleural-based disease, such as pleurisy or pleural effusions, or parenchymal disease, such as interstitial lung disease (the most common manifestation), organizing pneumonia and rheumatoid nodules. Caplan's syndrome occurs when RA is associated with pneumoconiosis. Important differential diagnoses include infection due to immune suppression, treatment-related toxicity, such as methotrexate-induced pneumonitis, and other medical co-morbidities, including chronic obstructive pulmonary disease.

Parenchymal disease documented on chest x-ray or high-resolution CT requires specialist treatment.

Cardiac disease

Pericarditis occurs in 30% of RA patients based on electrocardiogram and/or echocardiography, but less than 10% have clinical features. It generally presents when there is active joint and other extra-articular disease, and management consists of NSAIDs or prednisolone.

Myocarditis is a rare manifestation of RA. It may be granulomatous and, depending on its location, can produce valvular (especially mitral) incompetence or conduction defects. It is investigated with troponin, cardiac MRI and/or cardiac biopsy.

Sjögren syndrome

Sjögren syndrome may present in a primary form as a systemic disease, but can also occur secondary to RA and other connective tissue disorders. The classic symptoms are dry gritty eyes, dry mouth or both. Treatment is usually symptomatic in patients with no other features.

Felty syndrome

Felty syndrome is characterized by seropositive RA, splenomegaly and neutropaenia. There may be other cytopaenias, as well as leg ulcers, and infection is a risk.

Renal disease

Renal involvement with RA is rare and includes vasculitis and glomerulonephritis. Secondary amyloidosis can occur in patients with long-standing active disease. However, many medications used in RA are nephrotoxic, in particular NSAIDs and cyclosporin. Medication induced nephrotoxicity should not cause an active sediment.

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Neurological disease

Vasculitis may produce mononeuritis multiplex, otherwise CNS involvement is rare.

Ischaemic heart disease in rheumatoid arthritis and other connective tissue diseases

Patients with RA and other connective tissue diseases, such as SLE, have an increased risk of ischaemic heart disease (IHD), independent of traditional cardiac risk factors.⁶ The higher incidence of IHD appears related to disease factors, such as widespread inflammation, extra-articular disease⁷ and medications, such as NSAIDs (including selective COX-2 inhibitors) and corticosteroids, may also play a role.

SYSTEMIC LUPUS ERYTHEMATOSUS

SLE is a multisystem, autoimmune disease. It is the prototype disease of immune complex deposition resulting in tissue damage across a wide range of organ systems and one of the most common autoimmune conditions in women of childbearing age.

Clinical features

Common presenting features of SLE include general constitutional symptoms, such as fatigue, malaise and weight loss. There are a variety of skin manifestations in SLE that are lupus-specific (malar rash, discoid lupus, subacute cutaneous lupus erythematosus) or non-specific (pannici-litis, alopecia, oral ulceration). Arthralgia or an acute non-erosive arthritis are the most common presenting symptoms of SLE.

Another common manifestation is serositis, causing pleurisy, pericarditis or peritonitis. SLE also causes renal and CNS disease (discussed later) and, rarely, can involve the lung (pneumonitis, pulmonary hypertension) and heart (myocarditis, endocarditis). Myositis may also occur.

Investigations

FBC often reveals cytopaenias, in particular leukopenia and thrombocytopenia, which are a common feature of active SLE. Biochemistry may indicate renal impairment. ESR and CRP may be raised in acute disease.

Clotting abnormalities can include a prolonged activated partial thromboplastin time due to the lupus anticoagulant (LA), one of the antiphospholipid antibodies, along with anticardiolipin antibody (aCL) and others. Paradoxically, there is an associated predisposition to both venous and arterial blood clots when these are positive.

Serological abnormalities

The antinuclear antibody (ANA) is present in 95% of patients with SLE, but may also occur in other connective tissue and inflammatory diseases, as well as at low levels in healthy adults. The anti-Smith (Sm) and anti-dsDNA (double-stranded DNA) antibodies are more specific but less sensitive for SLE. Anti-Sm is obtained as part of a panel of antibody tests for extractable nuclear antigens (anti-ENA). Serological abnormalities also include decreased levels of complement components C3 and C4, in particular when SLE is active.

Other tests are directed towards the organ system involved, for example, midstream urine specimen looking for proteinuria or glomerular haematuria (>70% dysmorphic red blood cells or red-cell casts) and chest x-ray in the patient with serositis.

Assessing systemic lupus erythematosus disease activity

Useful symptoms of disease activity include mouth ulcers, alopecia and constitutional symptoms, as well as organ-specific symptoms, such as arthralgia or pleuritic chest pain.

Investigations used to assess disease activity include complement levels (low C3 and C4 in active SLE), CRP and ESR (elevated), as well as anti-dsDNA titre (rising in active SLE). These are not diagnostic and many people with quiescent SLE may also have hypocomplementaemia or elevated anti-dsDNA titres.

A midstream urine for urinary sediment or proteinuria is an essential marker of renal involvement.

Management

Management of SLE is directed by the organ system involved and includes topical therapies for cutaneous lupus and NSAIDs for arthralgias and mild serositis. Most patients with SLE will be on an antimalarial, such as hydroxychloroquine, helpful for skin and musculoskeletal manifestations as well as organ involvement. Many patients will also be on corticosteroids. Those with major organ involvement will also be taking other immunosuppressants, such as methotrexate, cyclophosphamide or azathioprine. Mycophenolate mofetil is frequently now used as an alternative to cyclophosphamide for lupus nephritis. Rituximab may also be used for severe SLE, including cerebral and gastrointestinal manifestations.

Lupus nephritis

Early diagnosis of lupus nephritis is essential to prompt management and prevent progression

of renal damage. Patients may be asymptomatic or present with nocturia, haematuria or proteinuria. Other presentations include hypertension, rapidly progressive glomerulonephritis and the nephrotic syndrome.

Urinalysis is the most useful investigation in detecting lupus nephritis, and proteinuria is the most common abnormality detected. The fresh urine specimen should be sent for phase contrast microscopy in order to detect the presence of dysmorphic erythrocytes (>70% indicates glomerular disease) or cellular casts.

Urinalysis can expedite the investigation and further management of this potentially organ-threatening condition. Prompt referral for consideration of renal biopsy and further management is indicated.

Neuropsychiatric systemic lupus erythematosus

There is a myriad of neuropsychiatric manifestations of neuropsychiatric SLE. Neurological presentations include:

- stroke (due to vasculitis, emboli, atherosclerosis or antiphospholipid antibodies)
 - seizure
 - migraine
 - aseptic meningitis
- Psychiatric presentations include:
- headache and mood disturbance, including anxiety
 - cognitive dysfunction 'lupus fog'
 - dementia
 - psychosis

These presentations are non-specific and have a broad differential diagnosis; the role of the ED is first to exclude the more common non-SLE presentations, such as meningitis or intracranial haemorrhage.

Investigations

Brain imaging studies are needed as well as tests for SLE activity (discussed previously).

Cerebrospinal fluid (CSF) analysis is essential to exclude infection, but may be normal in SLE. Changes, such as elevated protein, low glucose or even a positive ANA, are non-specific and do not always reflect active SLE.

GIANT CELL (TEMPORAL) ARTERITIS AND OTHER VASCULITIDES

Giant cell (temporal) arteritis

Giant cell arteritis (GCA) is the most frequent vasculitis and most commonly affects Caucasians. It is a large and medium vessel vasculitis of unknown aetiology, which predominantly

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affects the cranial branches of arteries originating from the aortic arch and, commonly though not exclusively, the temporal artery.

Polymyalgia rheumatica (PMR) is a syndrome of inflammatory pain and stiffness in the neck, shoulder and pelvic girdles, worse in the morning or after exercise, that occurs alone or frequently in association with GCA.

Epidemiology

GCA and PMR rarely occur before the age of 50 years,⁸ with a mean age at diagnosis of approximately 72 years. The incidence of GCA is roughly 1 in 500 of people over the age of 50 years, although the incidence and prevalence of PMR are less well studied.

Clinical features

The most common symptom of GCA is new headache, usually localizing to the temporal region, although it can be more diffuse. The area is often tender and associated with scalp sensitivity, worsened by brushing the hair. Most patients complain of constitutional symptoms, such as malaise, fatigue, anorexia and weight loss. Jaw claudication (pain after a period of chewing) is the most specific symptom for GCA, although not sensitive, as it is present in only 34%.⁸ On examination, the temporal arteries may be thickened, 'ropey' and tender with a reduced or absent pulse.

The most serious complication of GCA is anterior ischaemic optic neuropathy (AION) resulting in sudden painless loss of vision which can be bilateral, particularly if untreated. Less commonly, other branches of the aorta may be involved resulting in hemiparesis, arm claudication, aortic dissection or myocardial infarction.

Polymyalgia rheumatica

The relationship between onset of symptoms of GCA and PMR is highly variable. PMR symptoms may occur before, after or with GCA symptoms. Five percent to 15% of patients with PMR will have a diagnosis of GCA, and about 50% of patients with GCA have symptoms of PMR.

Differential diagnosis of giant cell arteritis and polymyalgia rheumatica

GCA can mimic any of the other vasculitides. Non-arteritic AION can also mimic GCA. The differential diagnosis of PMR includes late-onset RA, polymyositis and other myopathies, fibromyalgia, malignancy and hypothyroidism.

Investigations

The classic non-specific laboratory finding in GCA and/or PMR is a markedly elevated ESR (often >100 mm/h). CRP is also usually elevated, and a full blood count often shows a mild normochromic normocytic anaemia.

A temporal artery biopsy confirms the diagnosis of GCA and is particularly useful when the diagnosis is doubtful or the presentation atypical. However, as GCA can cause isolated foci of arteritis ('skip lesions'), there is a false negative rate of 10% to 30%. As such, a negative biopsy does not exclude GCA.

Criteria for diagnosis

The ACR classification criteria for GCA are helpful in differentiating GCA from other forms of vasculitis.⁹ They include:

- age at onset >50 years
- a new headache
- temporal artery tenderness or decreased pulsation
- ESR >50

An abnormal artery biopsy showing vasculitis with mononuclear infiltrate or granulomatous inflammation with multinucleated giant cells also confirms the diagnosis.

Although various classification criteria for PMR have been published, having excluded other diagnoses (except GCA), the presence of all three of the following clinical and laboratory criteria defines the diagnosis⁹:

- age ≥50 at onset of symptoms
- bilateral aching and stiffness for over 30 minutes after waking, in two of the following three areas; neck and torso, shoulder girdle, hips/pelvic girdle
- ESR >40

In practice, rapid response to prednisolone ≤20 mg daily is also used as an additional criterion with 50% to 70% improvement within 72 hours.

Management

Corticosteroids are essential for GCA and should not be withheld to perform a biopsy. The initial dose for GCA is unclear, but prednisone 40 to 60 mg daily (or 1 mg/kg/day) is generally recommended for uncomplicated disease. A new onset of clinical manifestations suggesting an unstable blood supply to the eyes or the CNS (e.g. arteritic optic neuropathy) is typically managed with intravenous pulse therapy (e.g. 1000 mg of methylprednisolone per day for 3 consecutive days).¹⁰

The dose of prednisone for PMR uncomplicated by GCA is lower at 10 to 20 mg/day; 15 mg is generally agreed as an appropriate standard dose.¹⁰ Most GCA patients do not require hospital admission, provided a temporal artery biopsy can be organized within 2 weeks. After 2 weeks, corticosteroid treatment may affect diagnostic yield of a temporal artery biopsy. Patients with visual loss at diagnosis require urgent treatment often with pulsed parenteral corticosteroids and inpatient admission. Patients with GCA should also be commenced on aspirin.

Approach to the other systemic vasculitides

The systemic vasculitides are a group of disorders characterized by an inflammatory infiltrate in the walls of blood vessels resulting in damage to the vessel wall. Table 14.1.1 classifies vasculitic syndromes according to vessel size. (There is much overlap.)

Clinical features

An underlying vasculitis should be considered in patients who present with one or more of the following:

- unexplained systemic illness—fatigue, fevers, night sweats, malaise
- unexplained ischaemia of an organ or limb
- rash with palpable purpura
- chronic inflammatory sinusitis and chronic discharge or bleeding from the nose or ears
- mononeuritis multiplex
- pulmonary infiltrates
- microscopic haematuria, especially if dysmorphic glomerular erythrocytes
- any of the above in the setting of atopy and peripheral blood eosinophilia

Investigations and diagnosis

Baseline investigations include Full Blood Count (FBC), Urea and Electrolytes (U&E), Liver Function Tests (LFTs) and clotting studies, as well as CRP and ESR. A panel of autoimmune serological tests is carried out, including ANA, ENA, dsDNA rheumatoid factor, anticyclic citrullinated peptides (anti-CCP), complement levels (C3, C4), anti-neutrophil cytoplasmic antibodies (ANCA) and cryoglobulins. PAN is associated with hepatitis B and cryoglobulinaemic vasculitis with hepatitis C infection. HIV infection should also be excluded.

Collection of a midstream urine specimen to look for glomerular haematuria and proteinuria is mandatory when vasculitis is suspected. Imaging is indicated, such as chest x-ray, CT scan of the chest or sinuses or other areas, depending

Table 14.1.1 Classification of systemic vasculitis according to vessel size

Vessel size	Vasculitis
Large	Takayasu arteritis Temporal (giant cell) arteritis
Medium	Polyarteritis nodosa Kawasaki disease
Small	Wegener granulomatosis (ANCA+) Microscopic polyangiitis (ANCA+/-) Churg–Strauss syndrome (ANCA+/-) Henoch–Schönlein purpura Cryoglobulinaemic vasculitis Leucocytoclastic cutaneous vasculitis

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on the suspected organ involved. The definitive diagnosis of vasculitis requires biopsy of affected tissue or angiography.

Differential diagnosis of systemic vasculitis

Other conditions that may mimic systemic vasculitis include:

- infections, such as infective endocarditis, meningococcaemia, gonococcaemia, hepatitis B, hepatitis C, HIV and syphilis
- disorders of haemostasis and thrombosis, such as thrombotic thrombocytopaenic purpura (TTP), antiphospholipid syndrome
- malignancy, such as lymphoma, myxoma
- sarcoidosis.

Management of systemic vasculitis

Treatment is usually with high-dose corticosteroids and, depending on the condition, additional immunosuppression, such as cyclophosphamide or rituximab. Urgent specialist referral is essential.

ANKYLOSING SPONDYLITIS

Ankylosing spondylitis (AS) is an inflammatory arthritis of the axial skeleton, which can result in progressive spinal fusion. It affects <1% of the general population, and its prevalence is linked to the prevalence of HLA-B27.

The hallmark pathological feature of AS is new bone formation and spinal fusion, which makes spinal injury a particular risk. Reduced mobility and muscle atrophy lead to a higher falls risk.

Spinal fractures are up to four times more common in AS patients than in the general population, and the risk of spinal cord injury is even higher. Fractures can occur at any point in the spine and do not have the classical appearance of wedge or endplate compression. There is also a higher rate of atlanto-axial subluxation, with similar precautions required, as in those with RA. Patients with advanced fusion may also develop cauda equina syndrome in the absence of a fracture.

Fractures in AS can be missed by plain x-ray, and the onset of new spinal pain or a change in spinal pain necessitates further imaging with either CT or MRI.

Systemic sclerosis

Systemic sclerosis, or scleroderma, is a chronic connective tissue disorder. The hallmark of this disease is thickening or hardening of the skin. Scleroderma can cause serious damage to internal organs, including the lungs, heart, kidneys, oesophagus and gastrointestinal tract.

Classification

Scleroderma can be classified as localized or systemic. Localized scleroderma presents with purely dermatological manifestations, including morphea and linear scleroderma. There is no internal organ involvement associated with localized scleroderma. Systemic scleroderma can be classified into limited and diffuse. There is often overlap between the manifestations of limited and diffuse scleroderma. Some of the manifestations include:

- Skin thickening of the fingers of both hands, extending above the elbow in diffuse disease
- Sclerodactyly
- Telangiectasia
- Raynaud phenomenon
- Digital tip ulcers
- Pulmonary arterial hypertension
- Interstitial lung disease
- Scleroderma renal crisis

Investigations

Inflammatory markers (CRP and ESR) may not be elevated in scleroderma. A full blood examination may reveal microcytic anaemia, due to slow GI bleeding from telangiectasia. Biochemistry may indicate renal impairment, as a result of current or past scleroderma renal crisis. Anti Scl-70 antibodies (also called anti-topoisomerase I, which constitutes part of the ENA panel) may be positive in diffuse scleroderma. Anti-centromere antibodies may be positive in limited scleroderma. Anti-RNA polymerase III antibodies are useful for the diagnosis and risk stratification of severe manifestations, such as renal crisis and severe skin sclerosis.

Scleroderma renal crisis

Severe and life-threatening renal disease develops in approximately 10% to 15% of patients. Scleroderma renal crisis is characterized by:

- Acute onset renal failure
- Abrupt onset of moderate to marked hypertension (some patients may remain normotensive)
- A urinary sediment that is normal or has mild proteinuria

Scleroderma renal crisis requires prompt clinical identification and management. Renal biopsy does not definitively establish the diagnosis, as indistinguishable changes can occur in other conditions such as transplantation rejection and haemolytic-uraemic syndrome.

The cornerstone of treatment for scleroderma renal crisis is blood pressure control with angiotensin-converting enzyme (ACE) inhibitors. This is one of the few cases in rheumatology where corticosteroids are not used, as they may potentiate hypertension and renal crisis.

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Non-steroidal anti-inflammatory drugs

NSAIDs are commonly used for relief of arthralgia in both inflammatory and non-inflammatory conditions. They are of equal efficacy, although those with shorter half-lives appear to have less gastrointestinal toxicity.¹¹ NSAIDs should be used in the lowest possible dose for the shortest duration and combinations of NSAIDs (except aspirin) should be avoided.¹¹ The COX-2 selective inhibitors, such as celecoxib, have a reduced incidence of peptic ulcer disease, but a similar incidence of other adverse effects including hypertension, peripheral oedema and cardiac failure. There is an increased risk of cardiovascular deaths with prolonged courses and higher doses.

Corticosteroids

Corticosteroids are the mainstay of treatment for most inflammatory rheumatological conditions. At high doses, they provide rapid control of inflammatory disease and are often required for long-term management at low doses. Long-term use is associated with numerous adverse effects.

Although there is concern about infection among patients on DMARDs, prednisolone contributes considerably (possibly more) to the immune-suppressed patient's overall infection risk.

Immunosuppressants/disease-modifying antirheumatic drugs

This heterogeneous group of medications is used to prevent joint destruction in the inflammatory arthritides and as steroid-sparing therapy in many connective tissue diseases. They include methotrexate, leflunomide, hydroxychloroquine, sulphasalazine, ciclosporin, azathioprine and cyclophosphamide. Each drug has its own range of adverse effects, but common adverse effects include cytopaenias, rashes including Stevens–Johnson syndrome, abnormal liver function tests, GI toxicity and heightened susceptibility to infections (Table 14.1.2).

Biological disease-modifying antirheumatic drugs

The so-called biological DMARDs are a newer and expanding collection of therapies directed against molecules and cells that mediate joint destruction and help drive the inflammatory process. These therapies are being increasingly used for those who fail conventional DMARD therapy for RA. Some of the biological DMARDs

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Table 14.1.2 Adverse effects of disease-modifying antirheumatic drugs

DMARD	Adverse effects
Methotrexate	Nausea and other GI upset, mouth ulcers, abnormal liver function (transaminases), bone marrow suppression, rash, alopecia, pneumonitis Increased bone marrow toxicity in renal impairment— withhold in acute renal failure Teratogenic
Leflunomide	Abnormal liver function (transaminases), diarrhoea, rash, alopecia, hypertension, peripheral neuropathy Teratogenic
Hydroxychloroquine	Nausea, rash, dizziness ('cinchonism'), retinal toxicity at higher doses (all uncommon)
Sulphasalazine	GI upset, uncommonly abnormal liver function and bone marrow suppression, rashes (rarely, Stevens–Johnson syndrome)
Ciclosporin	Renal impairment, hypertension, electrolyte disturbance, hyperuricaemia and gout, gingival hyperplasia, hirsutism
Cyclophosphamide	Bone marrow suppression especially neutropaenia, GI upset, bladder toxicity, including haemorrhagic cystitis (acute) and bladder cancer (chronic), opportunistic infections Teratogenic
Azathioprine	GI upset, rash, systemic symptoms, abnormal liver function, bone marrow suppression, skin cancers, infections

DMARDs, Disease-modifying antirheumatic drugs; GI, gastrointestinal.

are also used for treatment-resistant psoriatic arthritis and ankylosing spondylitis, as well as other non-rheumatological conditions.

Adverse effects associated with biological DMARDs include an increased risk of infections, particularly soft-tissue and joint infections, as well as reactivation of tuberculosis (in particular, with TNF inhibitor treatment) and varicella (in particular, with JAK1 inhibitor treatment). Other opportunistic infections appear more common, such as listeriosis. Patients may also develop local injection site reactions and infusion-related reactions, which can be delayed in nature. Less common adverse effects include a form of drug-induced lupus and demyelination.

Presentations of treatment-related emergencies

Infections

As treatment of rheumatological conditions is directed at immunosuppression, infections are a common and expected adverse effect of therapy. Although most of the larger studies have focused on TNF inhibitors, which have been available the longest, there is an increased risk of serious infections compared with the general RA population. This risk may be highest in the first 6 months of therapy.¹²

Patients on biological therapy who develop an infection are advised temporarily to cease their treatment and to commence antibiotics. If in doubt, they should be admitted to hospital to receive parenteral antibiotics. There is also an increased risk of reactivation of tuberculosis and

infections such as *Varicella*, *Listeria* and *Salmonella*.¹² Rigorous tuberculosis screening prior to commencement of anti-TNF therapy should now be universal.

Special mention must be made of the biological agent tocilizumab directed against IL-6. Tocilizumab causes marked suppression of acute phase reactants, particularly CRP, and even in the presence of active infection, a patient on this medication may have a normal CRP. Thus if there is a clinical suspicion of infection, appropriate antibiotic therapy must be instituted.

Bone marrow suppression

Anaemia, leucopaenia and thrombocytopaenia all may occur in patients taking DMARDs, such as methotrexate, cyclophosphamide, sulphasalazine and azathioprine, with neutropaenic sepsis presenting a particular danger.

Cytopaenia in a patient taking methotrexate is uncommon, but those at increased risk include the elderly and those with renal impairment, related to the drug's mechanism of action as an inhibitor of dihydrofolate reductase. Management includes temporary cessation of treatment and administration of folic acid, the active form of folic acid.

The most common adverse effect of cyclophosphamide is myelosuppression, particularly leucopaenia. The white cell nadir occurs at 2 weeks post-infusion following intravenous therapy. Patients on oral therapy may experience a gradual decrease in white cell count, which is typically less predictable than on intravenous therapy.

Bone marrow suppression may also occur as a side effect of azathioprine treatment, especially if given in combination with allopurinol, which inhibits its metabolism, thus potentiating bone marrow toxicity. Cytopaenias are also more common in patients with deficient thiopurine methyltransferase enzyme, which should be checked prior to the commencement of azathioprine. Sulphasalazine therapy is uncommonly complicated by bone marrow suppression.

Disease-modifying antirheumatic drug-related pneumonitis

Methotrexate and leflunomide may both result in lung toxicity. The most frequent is a hypersensitivity pneumonitis, but other forms of lung injury may occur. Clinical features are non-specific and include constitutional symptoms, cough and progressive dyspnoea. Subacute presentations are more common.

Imaging reveals interstitial opacities and patchy consolidation. High-resolution CT scanning typically shows a ground-glass appearance. The main differential diagnosis is of a respiratory infection which may be due to typical pathogens or opportunistic infections, such as *Pneumocystis jirovecii*.

Management is supportive, with empiric antibiotic therapy in case of infection. Corticosteroids are also used. Patients may become seriously ill and require intensive care, but mortality is still low (1%).

Leflunomide may also cause lung injury, typically in the first few months of therapy and usually when given in combination with methotrexate.

Allopurinol hypersensitivity syndrome

Minor hypersensitivity reactions to allopurinol occur in about 2% of patients and usually consist of a mild rash. Rarely, a severe hypersensitivity syndrome may present in an unwell patient with fever, rash, abnormalities of liver function, peripheral blood eosinophilia and acute renal failure due to interstitial nephritis. It is more common in those with renal impairment who do not have an appropriate dose reduction. Treatment is supportive.

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14.2 Monoarthritis

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ESSENTIALS

- 1 Presenting features alone, including absence of fever, do not reliably exclude a septic arthritis, especially in older people and those who are immunosuppressed.
- 2 Synovial aspirate in appropriate pathology transport media should be performed prior to commencing antibiotics when septic arthritis is being considered.
- 3 Acute monoarthritis affecting a prosthetic joint or the hip should *not* be aspirated in the emergency department. It requires urgent orthopaedic assessment.

SEPTIC ARTHRITIS

The assessment of a patient with acute monoarthritis is focused on excluding a septic arthritis. Septic arthritis can cause rapid joint destruction, morbidity and mortality.¹

Pathogenesis and pathology

Non-gonococcal bacterial arthritis occurs when bacteria enter the synovial lining of a joint via the haematogenous route, local spread from nearby soft-tissue infections or following penetrating trauma or injury to a joint. Bacteria reach the synovium, cause swelling and destruction of articular cartilage, which may extend to subchondral bone, and produce irreversible damage within days. The commonest causative organisms are staphylococci and streptococci.

Epidemiology and risk factors

The prevalence of septic arthritis ranges between 4 and 10 per 100,000 patients per year and appears to be rising. It is also almost seven times more common in Indigenous Australians.²

Risk factors for septic arthritis include inflammatory arthritis (especially rheumatoid arthritis), diabetes mellitus and systemic factors, such as age greater than 80 years, as well as local factors, such as recent joint surgery, joint prosthesis and overlying skin infection. These individual risk factors increase the risk of septic arthritis by two- to threefold.³ Skin infection overlying a prosthetic joint increases the risk of infection by 15-fold.³ Immunosuppressants heighten susceptibility to septic arthritis. The risk of septic arthritis depends on the potency of immunosuppression that is used.

Clinical features

Septic arthritis presents with joint pain and swelling in more than 80% of cases, which may be associated with systemic symptoms, such as sweats and rigors.³ The hip and knee joints are the most commonly involved joints.

The patient may be febrile and the affected joint is usually swollen, warm, erythematous and tender. Classically there is reduced ability to actively move the joint and marked pain on passive movement. Unfortunately, the symptoms and signs are not sensitive, and a patient with septic arthritis may

present with only some of these features. Thus septic arthritis cannot be excluded with confidence on the history and examination alone, and so must be considered in any presentation of monoarthritis.

Differential diagnosis

The differential diagnosis of acute monoarthritis is shown in Table 14.2.1. Risk factors include a history of rheumatoid arthritis, connective tissue disease, gout or other inflammatory arthritis, as well as risk factors for infection, such as immunosuppression (which patients may neglect to mention), diabetes and corticosteroids. Recent trauma or history of a bleeding diathesis or anticoagulation are also relevant. Recent sexually transmitted infections, including gonococcal infection or non-specific urethritis, or any systemic features including uveitis and/or gastrointestinal infection, may point toward a reactive arthritis.

Clinical investigations

Blood tests

Perform a full blood count (FBC), C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). ESR and CRP are non-specific and not sensitive

Table 14.2.1 Common presentations with acute monoarthritis to an emergency department

Gout
Reactive arthritis such as post-viral
Acute exacerbation of pre-existing inflammatory arthritis
Rheumatoid arthritis
Septic arthritis

Note: Orthopaedic-related joint problems, such as trauma and/or haemarthrosis, plus osteoarthritis (OA) were not included in this series.⁴

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for septic arthritis, but may help in the differential diagnosis. Blood cultures should be taken prior to antibiotic administration. Serum urate may be elevated, but can be normal in acute gout and should not be used to diagnose acute gout.

Imaging

X-ray may be normal in septic arthritis, as it takes at least 1 week for destructive changes to appear on plain x-ray. Magnetic Resonance Imaging (MRI) is helpful to determine if the pathology is in the joint or juxta-articular bone.

Joint aspiration

The single most important investigation is synovial fluid aspiration and analysis. Send the aspirate in a sterile container for Gram stain and culture, as well as for polarizing light microscopy to look for the presence of urate (strongly negative birefringent) crystals or calcium pyrophosphate crystals (weakly positive birefringent crystals). Using blood culture bottles does not appear to increase the yield of a positive culture.

Place some of the aspirate in an Ethylenediaminetetraacetic Acid (EDTA) tube for a cell count to be performed. The likelihood of septic arthritis increases from 2.9% with a synovial white cell count above 25,000/ μL up to 28% with a synovial white cell count of greater than 100,000/ μL . Synovial glucose and protein levels are unhelpful.

Criteria for diagnosis of septic arthritis

There is no 'gold standard' test for the diagnosis of septic arthritis. Synovial fluid Gram stain has a sensitivity of up to 50% only, while culture has a sensitivity up to 85%.³ Combined with an appropriate clinical presentation, the presence of microorganisms in synovial fluid on Gram stain and/or a positive synovial fluid culture with high synovial white cell count are diagnostic. New molecular techniques for diagnosis of infection in synovial fluid are promising but not yet readily available (e.g. 16S rRNA polymerase chain reaction [PCR]).

Treatment

Treatment of septic arthritis requires an urgent referral to orthopaedics for surgical drainage with admission to hospital. Antibiotic use should follow local guidelines and be discussed with the orthopaedic and infectious disease units. Empirical antibiotic therapy pending microbiology results should cover against *Staphylococcus*; administer dicloxacillin or flucloxacillin 2 g IV 6 hourly or cephazolin 2 g IV 6 hourly if the patient is allergic to penicillin. The patient with suspected hip or prosthetic joint sepsis must be referred to orthopaedics urgently without attempting joint aspiration.

GOUT

Gout is an intra-articular inflammatory response to monosodium urate crystal deposition usually related to hyperuricaemia. It is more common in males than females, but is extremely rare in the premenopausal female.

Aetiology and pathogenesis

Uric acid is derived from purine metabolism. Hyperuricaemia is the strongest predictor for gout and relates to either overproduction or under excretion of uric acid. Hyperuricaemia may also cause radiolucent renal calculi.

Overproduction of uric acid is due to dietary factors or endogenous factors associated with high cell turnover, such as a haematological malignancy. Reduced excretion is related to chronic kidney disease, hypovolaemia, metabolic acidosis and medications, such as diuretics, cyclosporin, pyrazinamide and ethambutol. There is also frequently a family history of gout.

Epidemiology

The peak incidence of acute gout occurs in men between the ages of 30 and 60 years and in women between 55 and 70 years. The presentation of gout in younger patients should prompt a search for a secondary cause (including lifestyle factors). Gout is more common in Maori and Polynesian populations.

Clinical features

The classic presentation is of acute onset of a hot, swollen and painful first metatarsophalangeal joint (75% of cases) known as podagra. Other commonly affected joints include joints in the foot, the ankle, knee and small joints of the hand.

Common triggers of an acute attack are binges of alcohol or purine-rich foods, dehydration, severe illness such as sepsis, acute renal failure, trauma and surgery. Sudden cessation or the introduction (especially in an acute attack) of hypouricaemic agents, such as allopurinol or febuxostat, may also precipitate gouty arthritis, as can the introduction or a dose change of a diuretic.

Untreated, the symptoms will abate over the course of several days to 2 weeks. Occasionally, the patient may appear systemically unwell during an acute attack with malaise and systemic inflammatory response features. The patient may also be febrile, however, should not have rigors. Examination reveals a tender, warm and erythematous joint with severely restricted range of movement. Presentations of acute gout may also be polyarticular (see Chapter 14.3).

Recurrent untreated acute gout and hyperuricaemia results in chronic tophaceous gout, where the patient is no longer pain-free between attacks. Examination reveals tophus formation on the first metacarpophalangeal joint, ears, around the elbows and in the fingers with marked joint deformity.

Investigations and diagnosis

Synovial fluid aspiration

Synovial fluid aspirate to identify monosodium urate crystals is diagnostic of acute gout. The crystals may be phagocytosed (intracellular) and the synovial fluid will have a high white cell count. A delay in crystal analysis in the laboratory, as well as concurrent use of local anaesthetic with joint aspiration, may result in the crystals being dissolved and a negative aspirate. Send fluid for Gram stain and culture to rule out septic arthritis, which may coexist with gout. Podagra with a typical clinical scenario has a sensitivity of 96% and specificity of 95% for acute gout, so aspiration is not indicated.⁴

Blood tests

Hyperuricaemia on blood testing is not diagnostic of gout; although up to 5% of adults may have a raised serum uric acid at some point, only one-fifth (1% overall) will ever have an attack of gout. Conversely, in about one-third of patients with gout, the serum uric acid level is normal during an acute attack. Other blood tests, such as FBE, ESR, and CRP, are sent and may be abnormally elevated. Check renal function to identify a potential aetiology and help guide treatment, such as avoidance or reduced doses of non-steroidal anti-inflammatory drugs (NSAIDs) or colchicine.

Imaging

Plain x-ray is performed to exclude injury, but should be normal in the acute attack other than soft-tissue swelling. Punched-out periarticular erosions are seen in chronic gouty arthritis, which, when associated with calcium deposition, deforming arthritis and soft-tissue swelling, are characteristic of chronic tophaceous gout.

Management

Treat acute pain and then prevent chronic relapse with hypouricaemic drugs. Educate all patients to correct lifestyle factors where appropriate.

Acute attack

Colchicine

When NSAIDs are contraindicated, colchicine may be used. A loading dose of 1 mg of colchicine, followed by 0.5 mg 6 hours later and 0.5 mg once or twice daily 12 hours later, is recommended until the gout attack resolves.^{4,5} Higher doses are no longer recommended, due to increased toxicity

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with nausea, vomiting, diarrhoea and the risk of renal impairment. Colchicine doses should be lowered in patients with renal impairment and/or patients on statins; this combination may increase the risk of neuromyopathy, myopathy and rhabdomyolysis.

Non-steroidal anti-inflammatory drugs

After excluding infection, give either an NSAID, corticosteroid and/or colchicine in the absence of contraindications. Corticosteroids, such as prednisolone 30 to 35 mg daily for 3 days, then tapered over 1 to 2 weeks,⁴ are used in gout refractory to NSAIDs. An alternative approach is intra-articular corticosteroid for monoarticular gout, provided sepsis has been excluded.

Recurrent attacks

Urate lowering therapy

A second attack of gout usually requires urate lowering therapy, although this is not commenced in the emergency setting, as treatment should be delayed until the acute flare has settled; commencing treatment during an acute attack may prolong and worsen the severity of the acute episode. Allopurinol, a xanthine oxidase inhibitor, prevents the production of uric acid from xanthine. It is introduced at a low dose (100 mg daily) once the acute attack has settled and gradually titrated up to 300 mg daily.⁴ Typically the patient will remain on a low-dose NSAID (or prednisolone/low-dose colchicine) as prophylaxis against precipitating further acute attacks. For patients with gouty tophi, a target uric acid level of <0.36 mmol/L is recommended; continue flare prophylaxis for 3 months after the target uric acid level is achieved, then cease.

Febuxostat is a new orally administered selective xanthine oxidase inhibitor that may be used to reduce urate levels, particularly in patients with poor kidney function or intolerant of allopurinol; a Phase III trial is currently being conducted to evaluate the cardiovascular safety.

An alternative uricosuric agent to allopurinol is probenecid. However, it should be avoided in renal impairment (eGFR <30), as it is ineffective.

ACUTE PSEUDOGOUT

Acute pseudogout causes an acute monoarthritis and is one of the several potential presentations of calcium pyrophosphate dihydrate (CPPD) deposition disease. It is more common in females and patients over 65 years old.

Aetiology and pathogenesis

Calcium pyrophosphate disease is characterized by deposition of CPPD crystals in cartilage

causing chondrocalcinosis. When released, there may be uptake in other synovial structures and an inflammatory response producing acute synovitis, tenosynovitis or bursitis.

Advanced age is the strongest risk factor. Other associations are a family history, metabolic diseases such as haemochromatosis, Wilson disease, hyperparathyroidism, hypophosphataemia or hypomagnesaemia and mechanical factors, such as previous injury or osteoarthritis (OA).

Clinical features

CPPD deposition disease presents in a variety of ways. The two most common are acute pseudogout and chronic pyrophosphate arthropathy, which may mimic OA. Other presentations include tenosynovitis, bursitis or as an incidental radiographic finding of chondrocalcinosis. CPPD deposition disease may also mimic rheumatoid arthritis or ankylosing spondylitis, as well as the neuropathic joint.

Acute pseudogout typically presents in older patients, and the knee is the most commonly affected joint. Other common sites include the wrist, shoulder, elbow and ankle. Occasionally, there may be an oligo-articular presentation. Presentation is with a hot, red and swollen joint. There may be systemic inflammatory response features and the patient may be febrile. Once again, the patient should not have rigors. Triggers include trauma, surgery or illness, but most cases are spontaneous.

Investigations and clinical diagnosis

Joint aspiration

Diagnosis of pseudogout depends on the demonstration of CPPD crystals in synovial fluid, which is frequently blood stained. Polarizing light microscopy demonstrates weakly positive birefringent rhomboid-shaped crystals.

Laboratory studies and imaging

Younger patients presenting with polyarticular chondrocalcinosis should be screened for an underlying metabolic cause, checking serum calcium, magnesium, phosphate, alkaline phosphatase, parathyroid hormone, thyroid function and iron studies.

Plain x-rays of the joint may reveal chondrocalcinosis seen in fibrocartilage, such as the knee menisci, triangular cartilage of the wrist and pubic symphysis. Other characteristic findings are of marked degenerative change in joints that are not usually affected by OA.

Management

Symptoms of acute pseudogout frequently improve once the joint has been aspirated. Intra-articular injection of corticosteroid is also appropriate for acute monoarthritis, once infection has

been excluded. In addition, rest and splintage for 48 to 72 hours is beneficial.

Give oral analgesics and NSAIDs similar to acute gout, particularly for polyarticular pseudogout, as performing multiple joint injections is impractical and painful.

In many patients, NSAIDs are contraindicated due to comorbidities such as renal impairment and cardiovascular disease, so an intra-articular or a tapering course of oral corticosteroids is needed (1/2 mg/kg).

HAEMARTHROSIS

Haemarthrosis is bleeding into a joint which may be traumatic and related to intra-articular injury or non-traumatic related to an underlying bleeding diathesis.

Aetiology

The causes of haemarthrosis are listed in Table 14.2.2.

Clinical features

A haemarthrosis causes a painful swollen, often warm, joint with a reduced range of movement. Ask about a history of trauma and, if minimal or absent, consider a bleeding disorder, such as haemophilia or anticoagulant use. Also ask about troublesome bleeding during a previous operation or following dental instrumentation, and about a family history.

Investigations

Perform plain radiography to exclude a fracture. Consider a computed tomography scan if there is a high index of clinical suspicion for a fracture but normal plain imaging. Send a FBC and a coagulation screen if there is no history of significant trauma.

Haemarthrosis is diagnosed on aspiration of synovial fluid. An intra-articular fracture is indicated by observing fat globules floating on the surface of the blood.

Table 14.2.2 Causes of haemarthrosis

Traumatic

- Fracture
- Ligamentous (e.g. anterior cruciate or peripheral meniscal tear in the knee)

Non-traumatic

- Bleeding diathesis, e.g. haemophilia, von Willebrand disease
- Anticoagulation
- Neuropathic joint
- Acute pseudogout
- Septic arthritis
- Pigmented villonodular synovitis
- Vascular abnormalities, such as arteriovenous malformation, haemangioma

14.3 POLYARTHRITIS

Management

Management includes rest, immobilization, ice and compression as well as analgesia. Aspiration frequently provides pain relief if performed within 24 hours of onset. NSAIDs should be avoided in patients with a bleeding diathesis.

Haemophilia or other bleeding diathesis

Haemarthrosis due to haemophilia or other disorders of clotting factor deficiency requires immediate factor replacement therapy to a level of 40% to 50% of normal. This should be performed as soon as possible after the presentation, in consultation with a haematology specialist.

Often the patient will be able to advise on his or her normal treatment (and usually knows what factor he or she is deficient in), his or her usual basal level and how much replacement is necessary in an acute bleed).

Vitamin K and administration of fresh frozen plasma may be required in patients with elevated International Normalised Ratio (INR) related to warfarin toxicity. Obtain advice from the haematology specialist for patients that are on novel oral anticoagulants (NOACs).

SPONDYLOARTHRITIS

Monoarthritis is occasionally a presentation of a spondyloarthritis, such as reactive arthritis,

psoriatic arthritis or inflammatory bowel disease-associated arthritis.

Clinical features suggesting a reactive arthritis include a recent history of infective diarrhoea, uveitis or sexually transmitted infection, such as urethritis. The patient may appear ill and be febrile with a tachycardia. The patient should be asked about a history of psoriasis or inflammatory bowel disease in the past.

Check for sites of enthesitis with inflammation at a tendon insertion points, such as the Achilles tendon or plantar fascia around the heel, or dactylitis causing 'sausage-shaped' digits.

GUIDELINE APPROACH TO THE MANAGEMENT OF ACUTE MONOARTHRITIS

The British Society for Rheumatology guidelines⁶ regarding the approach to the hot swollen joint include the following:

- The hot, swollen and tender joint should be considered as septic arthritis until proven otherwise. This may occur in the absence of fever.
- Synovial fluid must be obtained and sent for appropriate investigations prior to commencement of antibiotics. In situations of high clinical suspicion, a negative Gram stain or culture does not exclude septic arthritis.
- Other investigations should include blood cultures, CRP, ESR and FBC.

- X-ray of the affected joint should be performed as a baseline.
- Septic joints require aspiration to dryness in addition to parenteral antibiotics.
- Prosthetic joints and suspected hip sepsis require an urgent orthopaedic opinion.
- The presentation of a hot and swollen first metatarso-phalangeal joint is almost always gout, and is diagnosed clinically.

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14.3 Polyarthritis

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ESSENTIALS

- 1** Polyarthritis is a common adult rheumatological presentation with a wide differential diagnosis.
- 2** Recording articular and extra-articular involvement facilitates decision making, particularly with regards to patient admission.
- 3** Joint aspiration is paramount for both diagnosis and excluding a septic arthritis.
- 4** Early rheumatological consultation is essential to ensure appropriate and timely diagnosis and treatment for inflammatory arthritis to prevent joint damage and maintain joint function.
- 5** Early rheumatological consultation or admission is essential in the presence of extra-articular or systemic inflammatory response features.
- 6** Emergency management is with anti-inflammatory medication that may include systemic or intra-articular corticosteroids.

Introduction

Polyarthritis is a frequent rheumatological presentation to the emergency department in adults. This chapter focuses on the initial assessment, management and most appropriate follow-up of the more common conditions encountered. These include rheumatoid arthritis (RA), seronegative spondyloarthritis including psoriatic arthritis, reactive arthritis with reference to arthritides occurring in association with enteric and urogenital infections, and infectious arthritis including viral arthritis and rheumatic fever. Management principles include establishing the diagnosis, treating the acute problem and arranging appropriate follow-up.

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Box 14.3.1 Differential diagnosis of polyarthritis syndromes

Inflammatory

- Rheumatoid arthritis
- Inflammatory osteoarthritis
- Systemic connective tissue disease, including SLE, vasculitis, Behçet disease, relapsing polychondritis
- Seronegative spondyloarthropathies, commonly psoriatic arthropathy
- Gout
- Pseudogout (calcium pyrophosphate arthropathy)
- Drug induced, including lupus syndromes
- Infectious arthritis—bacterial including mycobacteria, endocarditis, protozoal, viral
- Reactive or post-infectious arthritis including rheumatic fever

Non-inflammatory

- Neoplastic/paraneoplastic disease, including hypertrophic pulmonary osteoarthropathy
- Sarcoidosis
- Endocrine disease, such as haemochromatosis, acromegaly
- Haematological disease, such as haemophilia, leukaemia

SLE, Systemic lupus erythematosus.

ACUTE POLYARTHRITIS

Polyarthritis syndromes may be difficult to diagnose accurately due to the wide range of differential diagnoses, as seen in [Box 14.3.1](#). Important principles include:

1. Exclude infection.
2. Consider relevant differential diagnosis, such as early presentation of inflammatory arthritis.
3. Document extra-articular involvement.

Clinical features and diagnosis

History

Take a focused history to include the following:

Mode of onset

- Acute (less than 6 weeks): gonococcal, viral including human immunodeficiency virus (HIV), reactive arthritis, rheumatic fever, crystal arthritis (gout or pseudogout)
- Chronic (longer than 6 weeks): RA, psoriatic arthropathy, systemic lupus erythematosus (SLE), systemic sclerosis, dermatomyositis, other autoimmune diseases, crystal arthritis (gout or pseudogout)

Distribution

- Symmetric or asymmetric
- Large or small joint involvement

Course

- Progressive, intermittent or migratory

Constitutional symptoms

- Fever, night sweats, fatigue, significant weight loss >10%

Rheumatological systems review

- Symptoms suggestive of an inflammatory arthritis: early morning stiffness, joint swelling, uveitis, scleritis, urethritis, cervicitis, chronic bowel symptoms
- Symptoms suggestive of a connective tissue disorder: Raynaud phenomenon, sclerodactyly, sicca syndrome, oral, nasal, digital or genital ulcers, rash, alopecia, and serositis with pleuritis or pericarditis
- Symptoms suggestive of vasculitis: haemoptysis, haematuria, hypertension, symptomatic peripheral neuropathy
- Many of these symptoms may overlap in rheumatological conditions.

Extra-articular organ involvement

- Cough, dyspnoea, hypertension, haematuria, symptomatic peripheral neuropathy

Other history

History of recent sore throat, febrile illness, new sexual contact, features of a sexually transmitted disease, diarrhoea, rash or uveitis, suggesting reactive arthritis

Past medical history of psoriasis, gout, rheumatic fever, inflammatory bowel disease (IBD), malignancy and juvenile polyarthritis

Family history of gout, psoriasis, IBD, uveitis or chronic back pain suggesting ankylosing spondylitis (AS) and other seronegative arthritis

Examination

Perform a detailed physical examination¹ and document:

- vital signs
- painful joints and soft-tissue swelling and their distribution
- cutaneous stigmata of underlying diseases, such as nail changes (psoriatic), rash and subcutaneous nodules, oral, genital or digital ulceration
- features of organ involvement, such as a pleural or pericardial rub, cardiac murmur or pulmonary crackles
- lumbosacral spine and pelvis including sacroiliac joints

Investigations

Laboratory studies

Send blood for full blood count (FBC), urea, electrolytes and liver function tests (ELFTs) and inflammatory markers, including erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP).

Exclude infection by sending blood cultures, urine microscopy and chest x-ray.

Send serum antibody or antigen tests as indicated by the history for infectious exposure, such as hepatitis B and C serology, HIV serology, syphilis serology, chlamydia and gonorrhoea urine polymerase chain reaction (PCR), streptococcal antigen test (ASO titre) and an autoantibody panel including anti-nuclear antibody (ANA), extractable nuclear antigen antibodies (ENA), double stranded DNA, rheumatoid factor (RF) and antibodies against citrullinated peptides (ACPA), usually ordered as anticyclic citrullinated peptide (anti-CCP). Antibody tests in particular should be interpreted with caution and in the context of each individual patient, due to their varying sensitivity and specificity.

Joint aspiration

Joint aspiration and analysis of synovial fluid are essential to diagnose septic arthritis and crystal arthropathy (see [Chapter 14.2](#)).

Imaging studies

Imaging studies, such as plain x-rays, may demonstrate diagnostic features in erosive arthropathy, but these do not occur for some time after the acute onset. They may also demonstrate chondrocalcinosis, which may suggest a diagnosis of pseudogout.

RHEUMATOID ARTHRITIS

RA is a chronic systemic inflammatory disorder characterized by symmetric synovitis, erosive polyarthritis and numerous extra-articular manifestations. The onset is often indolent and may lack the characteristic symmetrical joint involvement. Joint destruction may begin within a few weeks of symptom onset and is irreversible. A window of opportunity exists to initiate early treatment that will alter the course of the disease; early referral to rheumatology is important.

Diagnosis

The diagnosis in adults is guided by the American College of Rheumatology/European League Against Rheumatism Criteria. These criteria were revised in 2010² to identify features predictive of erosive disease earlier in the illness. Constitutional features, such as malaise and fatigue, are common.

'Definite RA' is based on the confirmed presence of:

- synovitis in at least one joint
- absence of an alternative diagnosis that better explains the synovitis

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- a total score of 6 or greater (of a possible 10) from individual scores in four domains: number and site of involved joints (score range 0 to 5); serological abnormality (score range 0 to 3); elevated acute-phase response (score range 0 to 1) and symptom duration (2 levels; range 0 to 1) (Box 14.3.2)

Morning stiffness, symmetric involvement and radiographic erosions are no longer included in the diagnostic criteria; however, they are also suggestive of RA.

Clinical features

Characteristic presentations in RA include the following:

Cervical spine

Degeneration of the transverse ligament of the C1 vertebra produces C1 to C2 instability in patients and can result in cervical cord compression or vertebral artery insufficiency. In addition, decreased motion and myelopathy may result from long-standing joint involvement (see Chapter 14.1).

Upper limb

The wrist, metacarpophalangeal and proximal interphalangeal joints are typically affected, with sparing of the distal interphalangeal joints.

Box 14.3.2 Classification criteria for rheumatoid arthritis

A. Joint involvement

- 1 large joint—0 pts
- 2–10 large joints—1 pt
- 1–3 small joints (with or without involvement of large joints)—2 pts
- 4–10 small joints (with or without involvement of large joints)—3 pts
- >10 joints (at least 1 small joint)—5 pts

B. Serology (at least 1 test result is needed for classification)

- Negative RF and negative ACPA—0 pts
- Low-positive (<3 × ULN) RF or low-positive ACPA—2 pts
- High-positive ($\geq 3 \times$ ULN) RF or high-positive ACPA—3 pts

C. Acute-phase reactants (at least 1 test result is needed for classification)

- Normal CRP and normal ESR—0 pts
- Abnormal CRP or abnormal ESR—1 pt

D. Duration of symptoms

- <6 weeks—0 pts
- ≥6 weeks—1 pt
- Add score of categories A–D: a score of >6/10 classifies a patient as having definite RA

ACPA, Antibodies against citrullinated peptides; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; RA, rheumatoid arthritis; RF, rheumatoid factor; ULN, upper limit normal.
(Adapted from Kay J, Upchurch KS. ACR/EULAR 2010 rheumatoid arthritis classification criteria. *Rheumatology (Oxford)*. 2012;51(6):vi5–vi9.)

Swan-necking and boutonnière deformities are common, together with ulnar deviation at the metacarpophalangeal joints. Fixed flexion deformities may result in entrapment neuropathies, in particular, carpal tunnel syndrome with median nerve involvement. Tenosynovitis may lead to tendon rupture, particularly of the extensor pollicis longus, or degenerative changes in the long extensors of the middle, ring and the little fingers with rupture of these tendons.

Lower limb

The hip and knee are frequently involved. Metatarsophalangeal joint subluxation may occur. Talo-navicular joint inflammation causes pronation and eversion deformity, with overlying muscle spasm. A Baker cyst due to posterior herniation of the joint capsule of the knee joint may occur and require differentiation from a deep vein thrombosis by Doppler ultrasound. Entrapment of the posterior tibial nerve causes burning paraesthesiae on the sole of the foot.

Extra-articular manifestations

The extra-articular manifestations of RA are protean and may involve any organ system due to local inflammation causing functional or neurological deficits, rheumatoid vasculitis or distant inflammation (see Chapter 14.1). Patients may also present with the side effects of the treatment, including sepsis related to immunosuppression. Sepsis with encapsulated organisms is of particular concern in patients with the Felty syndrome of RA with splenomegaly and neutropenia.

Investigations

Laboratory studies

Send blood for FBC, UEC and LFTs and non-specific markers of inflammation, such as ESR, and CRP, with assays for serum RF and anti-CCP. Anti-CCP is as sensitive but more specific than RF for RA and is more frequently positive early in the disease process. It is also thought to identify individuals at higher risk of erosive disease.³ Some patients with RA may be classified as 'seronegative', meaning that RF and anti-CCP are negative despite their clinical presentation being consistent with RA. Send blood cultures as well as midstream urine for suspected sepsis.

Joint aspiration

Joint aspiration is essential to exclude coexistent or primary sepsis in any sudden hot, swollen joint.

Imaging

Initial plain imaging of affected joints at first presentation does not usually demonstrate erosive changes, but is useful in patients with long-standing disease. However, always request x-rays of the cervical spine in any patient with

cervical or neurological features to look for an atlanto-dens interval of greater than 2.5 mm, which is diagnostic of instability. Include a chest x-ray if there is a fever and/or any respiratory features. Request an ultrasound examination to differentiate deep vein thrombosis from a Baker cyst.

Emergency management

Emergency therapy aims to exclude infection and relieve acute pain. Rheumatology referral enables early and appropriate intervention with disease-modifying antirheumatic drugs (DMARDs), reducing joint damage and disability. Admit patients if there is evidence of multisystem involvement, severe symptoms requiring nursing or allied health management, or if they are unable to tolerate oral therapy.

Medication falls broadly under the categories of non-steroidal anti-inflammatory drugs (NSAIDs) and DMARD therapy, including biological DMARDs. Readers are referred to Chapter 14.1 for a brief overview of these medications and common adverse effects. If arthritis is not well controlled on DMARDs such as Methotrexate and Sulfasalazine, patients are quickly escalated to biological DMARDs in order to achieve the two primary management goals: (1) prevent joint damage, and (2) maintain joint function. In addition to medication, important principles include education and exercise. Other long-term measures include orthopaedic and orthotic intervention. Surgery involving joint fusion, synovectomy, total joint arthroplasty and reconstruction may be required.

Prognosis

The spontaneous remission rate in RA is approximately 13%.⁴ High titres of anti-CCP or RF, which are present in up to 75% of patients with RA, the presence of nodules and human leucocyte antigen (HLA)-DR4 haplotype are markers of severity. A patient's life expectancy is shortened by 10 to 15 years by accelerated cardiovascular disease, infection, pulmonary and renal disease, and gastrointestinal bleeding.

SERONEGATIVE ARTHRITIS

The seronegative spondyloarthritis disorders are characterized by inflammation of the axial spine with sacroiliitis and spondylitis, in particular, enthesitis, which is inflammation at the attachments of tendons and ligaments to bones, dactylitis, asymmetric polyarthritis often of the lower limb, eye inflammation and varied mucocutaneous features. They are labelled 'seronegative', as the serum RF is negative.

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Epidemiology

The term 'seronegative spondyloarthritis' covers conditions such as AS, reactive arthritis occurring in the setting of viral or bacterial infection, psoriatic arthritis and arthritis associated with IBD. It is further differentiated into *axial* and *peripheral* spondyloarthritis.

The prevalence of the seronegative spondyloarthritis disorders varies widely and may parallel the prevalence of the HLA-B27 gene.

However, the exact role of HLA-B27 in the pathogenesis of these disorders has not been clearly defined; however, patients with HLA-B27 positivity have a 20-fold risk of developing spondyloarthropathy.⁵

The Assessment of Spondyloarthritis International Society (ASAS) advanced classification criteria for axial and peripheral spondyloarthritis (Fig. 14.3.1). These criteria have better sensitivity and comparable specificity to previous criteria and are well validated.⁶

PSORIATIC ARTHRITIS

Psoriatic arthritis is a heterogeneous disease distinct from other inflammatory arthritides. It occurs in up to 30% of patients with psoriasis, but may affect up to 40% of hospitalized psoriasis patients with widespread skin involvement.⁷ It occurs between the ages of 30 and 60 years,

with an equal prevalence in males and females. It is thought to be inherited in a polygenic pattern significantly influenced by environmental factors, including trauma and infectious agents. The arthropathy pattern may be pauci-articular, but more than five peripheral joints are usually involved.

Clinical features and diagnosis

The diagnosis of psoriatic arthritis is essentially clinical, requiring the demonstration of coexisting synovitis and psoriasis.

Classification criteria for psoriatic arthritis (CASPAR) diagnostic criteria⁸

Established inflammatory joint disease and at least three points from the following features:

- current psoriasis (2 points)
- history of psoriasis (in the absence of current psoriasis) (1 point)
- family history of psoriasis (in the absence of current or past history) (1 point)
- dactylitis (1 point)
- juxta-articular new bone formation (1 point)
- RF negativity (1 point)
- nail dystrophy (1 point)

Five clinical subtypes are recognized, including asymmetric oligoarthritis, symmetric small joint polyarthritis, predominant distal interphalangeal joint involvement, psoriatic spondyloarthropathy and arthritis mutilans. Major extra-articular organ

manifestations, such as aortic insufficiency and pulmonary fibrosis, occur rarely. However, up to 30% of patients have mild inflammation at the eye, most commonly conjunctivitis.

Asymmetric oligoarthritis

This occurs in 30% to 50% of patients.⁹ It presents as an oligoarthritis involving a single large joint, in association with a 'sausage-shaped' or dactylitic digit or toe. Dactylitis occurs due to a combination of arthritis and tenosynovitis. Distal interphalangeal joint involvement is typical, almost invariably associated with psoriatic nail changes of pitting, ridging and onycholysis. Enthesitis occurs most frequently with this form of the disease and commonly manifests as plantar fasciitis or epicondylitis at the elbow.

Symmetric small joint polyarthritis

This occurs in 30% of patients, in a pattern strongly resembling RA, but with distal interphalangeal joint involvement⁹.

Psoriatic spondyloarthritis

This occurs in 5% of patients.⁹ It is often asymptomatic, but may present with inflammatory low back pain due to sacroiliitis in up to 30% of cases.

Arthritis mutilans

'Arthritis mutilans' is a rare (<5% of patients) but well-characterized feature of psoriatic arthritis with severely deforming arthritis including telescoping of the fingers or toes from osteolysis of the metacarpal or metatarsal bones and phalanges.⁹

Dermatological features

Dermatological features include typical erythematous, scaling plaques on the extensor surfaces of the elbows and knees, scalp and ears and nail pitting, ridging and onycholysis with separation of the nail from the underlying nail bed. Nodules and vasculitic features such as digital ulcers are not seen.

Psoriatic arthritis can be difficult to distinguish from the other seronegative spondylarthritides in the absence of dermatological features or a positive family history.

Investigations

ESR and CRP are raised, but the RF and autoantibody screen are negative. Plain x-rays of affected joints may reveal typical radiographic features including soft-tissue swelling, bone proliferation at the base of digital phalanges coupled with resorption of the distal tufts (the 'pencil-in-cup'

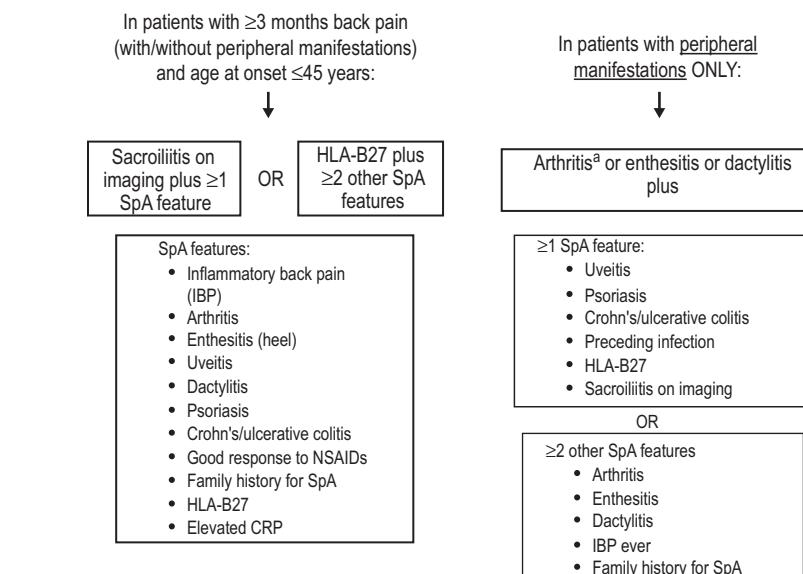


FIG. 14.3.1 Combined use of the Assessment of Spondyloarthritis International Society (ASAS) criteria for axial spondyloarthritis and the ASAS criteria for peripheral SpA in the entire SpA population. ^aPeripheral arthritis: usually predominantly lower limb author asymmetric arthritis combined sensitivity 79.5% and combined specificity 83.3% n=975. CRP, C-reactive protein; HLA, human leucocyte antigen; NSAIDs, non-steroidal anti-inflammatory drugs. (Reproduced with permission from Rudwaleit M, van der Heijde D, Landewé R, et al. The Assessment of SpondyloArthritis International Society classification criteria for peripheral spondyloarthritis and for spondyloarthritis in general. *Ann Rheum Dis.* 2011;70:25–31.)

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deformity) and fluffy periostitis.¹⁰ Chest radiographs are useful as a baseline when clinical examination suggests cardiac or pulmonary involvement.

Emergency management

Emergency treatment involves the exclusion of infection and relief of pain. Prompt rheumatology referral for early institution of DMARDs to prevent joint destruction and maintain joint function. Education, exercise and referral to a multidisciplinary allied health team are also part of the mainstay of ongoing management. Admit patients if their symptoms are severe enough to preclude oral therapy or safe discharge, pending outpatient specialist follow-up.

NSAIDs are useful for acute symptomatic relief. Intra- or peri-articular corticosteroids may be used for short-term relief of painful arthritis or enthesitis; however, exclusion of active infection is paramount. Long-term therapy with DMARDs, such as sulphasalazine or methotrexate, is instituted at specialist review. Oral corticosteroids are usually avoided as their cessation often exacerbates the psoriasis. Therapy with tumour necrosis factor- α (TNF- α) antagonists; interleukin-17A (IL-17A) 12 and 23 antagonists have been approved for rheumatologists under strict access criteria for severe disease resistant to other DMARD therapy.

Emergency management of skin disease includes topical treatments, such as emollients and keratolytic agents.¹¹ Phototherapy and photo-chemotherapy may be instituted on early dermatological consultation.

Prognosis

Psoriatic arthritis generally runs a more benign course than RA; adverse prognostic factors include onset before 20 years of age, erosive disease and extensive skin involvement.⁹

REACTIVE ARTHRITIS

Reactive arthritis is an aseptic peripheral arthritis following certain infections, which include bacterial infections of the urogenital tract usually by *Chlamydia trachomatis* or *Neisseria gonorrhoeae*, or of the gastrointestinal tract with organisms, such as *Shigella*, *Salmonella* and *Campylobacter*. It may also follow bacterial infections such as *Treponema pallidum* and viral infections, such as HIV. The seroconversion illness of HIV has its own constellation of articular symptoms and is considered to be a separate entity.

Epidemiology

The prevalence of reactive arthritis is difficult to define. The male preponderance is up to 9:1

following sexually transmitted infection, but males and females are equally affected following gastrointestinal tract infection.¹² The peak incidence is around age 35 years and up to 75% of patients are HLA-B27 positive.¹² An important exception is with the reactive peripheral arthritis that occurs in 20% of patients with idiopathic IBD, a condition that may mimic gastrointestinal tract infection, but where patients are usually HLA-B27 negative.

Clinical features and diagnosis

The diagnosis of reactive arthritis is clinical. It typically manifests within a month of gastrointestinal or genitourinary infection. Musculoskeletal manifestations include myalgias and asymmetric polyarthritis affecting the knees, ankles and small joints of the feet in particular, although peripheral upper limb involvement is seen. Affected joints demonstrate marked inflammatory features with erythema, swelling, warmth and exquisite pain on active or passive movement. Fever and malaise are common. Exclusion of a septic joint is paramount.

Arthritis and extra-articular manifestations

Symptomatic spondylitis and sacroiliitis cause low back and buttock pain and occur frequently. Dactylitis and enthesitis are characteristic features of this disease with heel pain from plantar fasciitis or Achilles tendinitis.

Extra-articular features include keratoderma blennorrhagica, the scattered, thickened, hyperkeratotic skin lesions with pustules and crusts seen in reactive arthritis and circinate balanitis. Keratoderma blennorrhagica on the soles or palms may coalesce to form plaques virtually indistinguishable from those of psoriasis.¹³ Circinate balanitis causes shallow meatal ulcers that are moist in uncircumcised men or hyperkeratotic and plaque-like in circumcised men.¹³ An inflammatory aortitis occurs in 1% of patients and may result in aortic valvular incompetence and/or heart block.

The peripheral arthritis associated with IBD can be migratory and occurs in a similar distribution. Common features include joint effusions, particularly involving the knee, and sacroiliitis or spondylitis. Unlike peripheral arthritis following genitourinary infection, the spondylitis of IBD-associated arthritis may not settle with treatment of the bowel inflammation. Cutaneous manifestations associated with this form of arthritis occur mainly on the lower limbs and include erythema nodosum and pyoderma gangrenosum.

Investigations

Laboratory

An active inflammatory response is seen in the acute phase with a neutrophil leucocytosis and thrombocytosis and raised ESR and CRP. The presence of a

mild normochromic, normocytic anaemia suggests chronic disease. Send blood for HLA-B27.

Document the preceding gastrointestinal or genitourinary organism by stool culture or cervical/urethral swabs. RF and ANA are often negative.

Joint aspiration

Joint aspiration is vital to exclude intra-articular sepsis (see Chapter 14.2). The synovial fluid may be turbid, viscous and with a neutrophil leucocytosis up to 50,000/mm³, but Gram stain and bacterial culture are negative, and unlike true septic arthritis, the synovial glucose level is not significantly reduced compared to serum levels.¹⁴ Macrophages with intracytoplasmic vacuoles containing ingested neutrophils are occasionally seen.

Imaging

X-ray changes are unusual with acute arthritis, but are seen after several months. As with psoriatic arthritis, a common finding is a 'fluffy' periosteal reaction, particularly at the calcaneus, and evidence of sacroiliitis or spondylitis with bridging syndesmophytes in long-standing disease.

Emergency management

Exclude infection by synovial aspiration and culture with a markedly inflamed joint and consult early with a rheumatologist, particularly in a patient with a first presentation. Admit patients with suspected septic arthritis until it is excluded or if they are unable to tolerate simple oral therapies. Request a cardiology opinion for major cardiac involvement with valvular disease or a conduction abnormality and a gastroenterology opinion when IBD is suspected, although the role of treatment and the effect on the arthropathy is unclear.

Otherwise, provide symptom relief with NSAIDs as the mainstay of treatment. Corticosteroids may be given after rheumatological consultation, either systemic, intra-articular, topically for the skin manifestations. Disease modifying therapy is initiated at specialist follow-up if NSAID therapy fails to control symptoms. Multidisciplinary physical therapy is essential on an outpatient basis.

Give antibiotics, such as doxycycline 100 mg orally bd for 7 days or azithromycin 1 g orally once for documented urethritis or cervicitis, and remember partner contact tracing and treatment involving infectious diseases service.¹⁴

Prognosis

Signs and symptoms usually remit within 6 months. However, up to 50% of patients suffer from recurrent arthritis and up to 30% develop chronic arthritis.¹⁵ Post-dysenteric cases have a better prognosis than post-chlamydial cases. Poor prognostic signs include early onset under the age of 16 years, hip involvement and the presence of dactylitis.

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POLYARTICULAR CRYSTAL ARTHRITIS

Crystal-induced arthritis disorders result from the deposition of crystal in joint spaces, such as in gout or pseudogout. Both diseases cause debilitating joint inflammation resulting from the lysis of neutrophil polymorphs that have ingested monosodium urate in the case of gout, or calcium pyrophosphate crystals in pseudogout. Although usually monoarticular, polyarticular involvement can occur in up to 5% of cases. Exclusion of septic arthritis via joint aspiration is paramount. See Chapter 14.2.

INFECTIOUS POLYARTHRITIS

Septic bacterial arthritis is most often monoarticular, although it can present with polyarticular involvement. Septic screen should be performed, including blood cultures, urine microscopy and culture and chest radiograph. Cardiac echocardiogram is essential to look for vegetations in the presence of a cardiac murmur. Joint aspiration for cell count, gram stain and culture is essential for diagnosis. Infectious polyarthritis may also occur as aseptic manifestation of certain viral infections and following streptococcal infection in acute rheumatic fever (ARF).

Viral arthritis

Arthralgia affecting several joints is common in many viral infections, but few cause frank polyarthritis. In general, these are self-limiting and managed symptomatically. Viruses involved include alphaviruses, such as the Ross River virus (RRV), parvovirus B19, and hepatitis A, B and C viruses.

Alphaviruses

Alphaviruses are a mosquito-borne genus of the Togaviridae family. They are responsible for epidemics of febrile polyarthritis, including RRV, Barmah Forest and Sindbis viruses (SINV) in Australia and West Nile virus in the United States; Chikungunya virus in East Africa, South and Southeast Asia; O'nyong-nyong virus in East Africa and the Mayaro virus in South America.^{16,17}

Ross River virus

RRV is endemic to Australia, New Zealand and South Pacific islands and is the most common arboviral disease in Australia. RRV is transmitted by the *Ochlerotatus* (formerly *Aedes*) *vigilax* mosquito via a marsupial reservoir.¹⁸ Epidemics of acute febrile polyarthritis are most common between January and May, but can occur after periods of heavy rains.

Clinical features and diagnosis

A detailed travel and sexual history is essential. There is usually low-grade fever and other constitutional symptoms. A rash varying in distribution, character and duration occurs up to 2 weeks before, during or after the other features. Polyarticular symptoms are present in most patients with a symmetric arthritis or arthralgia primarily affecting the wrist, knee, ankle and small joints of the extremities. Cervical lymphadenopathy occurs frequently, and paraesthesiae and tenderness of the palms and soles occur in a small percentage of cases.¹⁹

The diagnosis is predominantly clinical, particularly in endemic areas in the event of a local outbreak, and confirmed by serology.

Investigations

Serology testing distinguishes RRV from other causes of febrile polyarthritis, such as Barmah Forest virus. A significant rise in IgM antibody titre to RRV indicates acute infection or the virus itself may be isolated from the serum of acutely unwell patients. Radiographs are unremarkable and unnecessary, as the disease is largely self-limiting.²⁰

Emergency management

Patients with RRV require symptomatic treatment with simple analgesics or NSAIDs. Occasionally, a brief course of low-dose prednisolone may be used. RRV is a notifiable disease.¹⁸ Refer to a rheumatologist if symptoms are severe or refractory to simple treatment measures.

Conventional personal preventative measures, such as protective clothing, effective mosquito repellent and avoidance of mosquito-prone areas should be recommended, as no vaccine currently exists.

Prognosis

RRV is usually self-limiting, but prolonged symptoms may occur and there may be relapses of decreasing intensity, separated by remissions for up to a year or more.

Parvovirus B19

Human parvovirus B19 infection is caused by a small, single-stranded DNA virus that has a predilection for erythroid precursor cells and is transmitted by respiratory secretions. It causes the self-limiting illness *erythema infectiosum* known as 'slapped cheek disease' or 'fifth disease' in children. In adults, however, parvovirus B19 manifests with severe flu-like symptoms, and as many as 75% develop joint symptoms. It may be responsible for up to 12% of adult patients presenting with acute polyarthritis, most notably in those who have frequent exposure to children.²¹

Clinical features and diagnosis

The characteristic 'slapped cheek' rash is usually absent in adults. An acute polyarthritis improves over 2 weeks, with symmetric involvement of peripheral small joints, including the hands (proximal interphalangeal and metacarpophalangeal joints in particular), wrists, knees and ankle joints. Morning stiffness is prominent. These features are similar to those seen in patients with RA.

Uncommon but important extra-articular features of parvovirus B19 infection include²²:

- development of an aplastic crisis in patients with chronic haemolytic anaemia
- bone marrow suppression in immunocompromised patients
- *hydrops fetalis* in women infected during pregnancy
- Henoch–Schönlein purpura
- thrombotic thrombocytopaenic purpura
- granulomatosis with polyangiitis (GPA, formerly known as Wegener granulomatosis) or polyarteritis nodosa (rare).

Investigations

Send an FBC, given the potential for an aplastic crisis and bone marrow suppression. Non-specific markers of inflammation are likely to be elevated. Specific serological diagnosis is made by a high IgM antibody titre specific to the virus and by isolation of the viral DNA by PCR. IgG antibodies to parvovirus B19 indicate past infection. Radiographs of the affected joints are normal.

Emergency management

Rest and NSAIDs are the mainstay of emergency treatment, except in pregnant women when NSAIDs are contraindicated in the third trimester. A short course of prednisolone may be required. Significant extra-articular manifestations may require admission and consultation with the appropriate specialist. Blood transfusion or intravenous immunoglobulin infusions may be necessary.

Prognosis

Joint symptoms are self-limited in the majority of adult patients, but up to 10% may have prolonged relapsing and remitting symptoms lasting up to 9 years.²³

Hepatitis A, B and C viruses

The hepatitis viruses A, B and C all cause viral polyarthritis. Hepatitis B virus (HBV) is responsible for 20% to 25%, and hepatitis A virus (HAV) up to 14% of causes in patients with viral polyarthritis.²⁴ The polyarthritis of HAV tends to occur during the infectious phase and is self-limiting. The polyarthritis of HBV and HCV occurs in early infection during a period of significant viraemia and is thought to be due to immune complexes.

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Clinical features and diagnosis

HBV polyarthritis is acute and severe and manifests in a symmetric, migratory or additive fashion.²⁵ Other large axial joints, in addition to hand joints, may be involved, and significant early morning stiffness is often present. The arthritis may precede the development of jaundice and persist for several weeks after jaundice has developed.

Hepatitis C virus (HCV) polyarthritis is rapidly progressive and symmetrical, involving the hands, wrists, shoulders, knees and hips.²⁵ Carpal tunnel syndrome and tenosynovitis may occur. It is unusual for polyarthritis to be the first manifestation of the underlying disease in either HBV or HCV. Nonetheless, ask about exposure risk factors for these viruses, such as intravenous drug abuse, unprotected sexual intercourse, past blood transfusions, tattoos, as well as about previous jaundice.

Both hepatitis B and hepatitis C disease are associated with a number of important extra-articular, extra-hepatic manifestations that include

- HBV: polyarteritis nodosa, systemic necrotizing vasculitis, membranous glomerulonephritis
- HCV: mixed cryoglobulinaemia causing palpable purpura, arthritis and serum cryoglobulinaemia with cutaneous phenomena, such as Raynaud syndrome and digital ulcers, membranous glomerulonephritis and lymphoma

Laboratory investigations and imaging

Send blood for LFTs for raised transaminases with elevated bilirubin, hepatitis B surface antigen, surface antibody and core antibody. If core hepatitis B core antibody is positive, perform viral DNA quantification by PCR. Check also for anti-HCV IgM and for viral DNA quantification by PCR.

Also check FBC and for ESR, CRP, complement C3 and C4, cryoglobulins and RF in the presence of a rash, ulcers or other vasculitic phenomena.

Radiographs are normal other than showing soft-tissue swelling.

Emergency management

Commence symptomatic treatment with NSAIDs and refer refractory HBV- or HCV-associated polyarthritis to a rheumatology specialist and/or combined hepatology clinic. Disease-modifying agents, such as prednisolone and sulphasalazine, may be used cautiously with careful monitoring of the liver function tests and for increasing viraemia. Refer patients to a gastroenterologist for ongoing management of hepatitis infection and assessment of liver function. Patients with HCV should be commenced on direct acting antivirals.

Prognosis

This varies depending on the underlying disease and on the presence of vasculitic phenomena. The polyarthritis of HBV is usually limited to the pre-icteric phase, but patients with chronic active hepatitis or chronic HBV viraemia may have recurrent arthritis.

RHEUMATIC FEVER

ARF refers to the constellation of non-infectious symptoms occurring after a pharyngeal infection with group A streptococci (GAS). Evidence suggests that it may also occur in high-risk populations following skin infections with GAS.²⁶

Epidemiology

ARF is characterized by inflammation of connective tissue including the joints, subcutaneous tissue, heart and blood vessels. Its prevalence has declined over time in developed countries, but it remains a major public health problem in Indigenous populations in the more socially isolated

parts of Australasia and in developing countries. In fact, the highest documented rates in the world occur in the Aboriginal Australian population and Torres Strait Islander populations of New Zealand and the Pacific Islands.²⁷

ARF is primarily a disease of children aged 5 to 14 years. The annual incidence may reach up to 1.2 per 1000 Aboriginal children.²⁸ However, the polyarthritis of ARF is most common in adolescents and young adults.

Diagnosis and clinical features

The diagnosis of ARF worldwide is made using the 1944 Jones, or more recent World Health Organization major and minor criteria. However, these criteria appear too restrictive for diagnosing ARF in Australian Indigenous populations. Therefore new criteria for use in high- and low-risk populations in Australia have been proposed (Table 14.3.1).²⁸

The polyarthritis of ARF is usually the earliest symptom of the disease and is classically described as migratory, affecting several joints in quick succession for a short time, commencing with the large joints of the lower limb then the large joints of the upper limb.²⁹ Affected joints are painful, but objective signs of inflammation, such as erythema and swelling, are not prominent.

Fever and constitutional symptoms are common. Other important extra-articular major criteria (with polyarthritis) of the disease include the following²⁸:

- carditis: symptomatic pericarditis with pain and/or congestive cardiac failure with breathlessness, new murmurs, cardiomegaly, electrocardiographic evidence of heart block
- Sydenham chorea (St Vitus dance): choreiform movements particularly of the face and upper limbs, emotional lability, rarely transient psychosis

Table 14.3.1 2012 Australian guideline for the diagnosis of acute rheumatic fever

	<i>High-risk groups</i>	<i>All other groups</i>
Initial episode of ARF	Two major or one major and two minor manifestations plus evidence of a preceding GAS infection	Two major or one major and two minor manifestations plus evidence of a preceding GAS infection
Recurrent attack of ARF in a patient with known past ARF or RHD	Two major or one major and two minor or three minor manifestations plus evidence of a preceding GAS infection	Two major or one major and two minor or three minor manifestations plus evidence of a preceding GAS infection
Major manifestations	<ul style="list-style-type: none"> • Carditis, including subclinical evidence of rheumatic valve disease on echocardiogram • Polyarthritis or aseptic monoarthritis or polyarthralgia • Chorea • Erythema marginatum • Subcutaneous nodules 	<ul style="list-style-type: none"> • Carditis, excluding subclinical evidence of rheumatic valve disease on echocardiogram • Polyarthritis • Chorea • <i>Erythema marginatum</i> • Subcutaneous nodules
Minor manifestations	<ul style="list-style-type: none"> • Fever • ESR ≥ 30 mm/h or CRP ≥ 30 mg/L • Prolonged P-R interval on ECG 	<ul style="list-style-type: none"> • Fever • Polyarthralgia or aseptic mono-arthritis • ESR ≥ 30 mm/h or CRP ≥ 30 mg/L • Prolonged P-R interval on ECG

ARF, Acute rheumatic fever; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; GAS, group A streptococci; RHD, rheumatic heart disease.

14.4 MUSCULOSKELETAL AND SOFT-TISSUE EMERGENCIES

- subcutaneous Aschoff nodules: firm, painless, mobile nodules near bony prominences on the extensor surfaces of wrists, elbows and knees
- rash (*erythema marginatum*): occurs in around 5% of ARF

Laboratory investigations and imaging

Measure antistreptolysin O and antideoxyribonuclease B (anti-DNase B) titres.²⁹ As these titres can take 6 weeks after infection to peak, interpretation in the acute phase should be cautious and serial tests should be performed.

Send a throat swab for culture and rapid antigen testing, although the sensitivity and specificity of these tests vary. Other important tests include:

- ESR and CRP, which are almost invariably elevated
- FBC, which may demonstrate a leucocytosis and, less commonly, a normochromic, normocytic anaemia
- ECG to document the P-R interval
- chest x-ray to look for cardiomegaly or symptomatic cardiac failure

Synovial fluid aspirate is usually inflammatory with an elevated white cell count and sterile on

microscopy and culture. Radiographs of affected joints generally demonstrate soft-tissue swelling only.

Emergency management

This depends on establishing the diagnosis and treating the manifestations. Patients are markedly symptomatic and often require admission for initial observation and management. Request rheumatology and infectious disease opinions, and a neurology opinion if chorea is troublesome. The presence of heart block or, more importantly, frank cardiac failure or acute valvular regurgitation mandate cardiology admission.

The polyarthritis of rheumatic fever is exquisitely responsive to NSAID therapy, particularly aspirin, so much so that failure of NSAID therapy rapidly to relieve symptoms should prompt consideration of an alternative diagnosis.²⁸ Give high-dose aspirin at 80 to 100 mg/kg/day in 4 to 5 divided doses in adults, usually for 1 to 2 weeks.²⁸

Commence antibiotic therapy with phenoxy-methylpenicillin 10 mg/kg up to 500 mg orally 12-hourly for 10 days to eradicate streptococcal pharyngitis, after obtaining appropriate diagnostic investigations as detailed previously. Commence

prophylaxis following resolution of the acute episode in high-risk indigenous communities.

Ongoing rheumatology and infectious diseases specialist follow-up is recommended. Note that penicillin reduces the frequency and severity of post-streptococcal rheumatic fever, but has little effect on the course of the immune-complex mediated post-streptococcal glomerulonephritis (PSGN).

Prognosis

Recurrence of ARF commonly occurs within 2 years of the initial attack, despite prophylactic therapy. Most affected connective tissues do not sustain long-lasting damage, with the exception of the heart, which is prone to additive subclinical damage resulting in rheumatic heart disease.

Full references are available at <http://expertconsult.inkling.com>

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14.4 Musculoskeletal and soft-tissue emergencies

Anthony Tzannes

ESSENTIALS

- The mechanism of injury and biomechanics predict the soft-tissue damage caused.
- Soft-tissue injuries can be as debilitating and painful as fractures in the same area, and may take longer to heal.
- The so-called 'minor injury' can be associated with significant and prolonged morbidity that could be permanent if managed incorrectly. Adopting a careful, consistent approach that considers potential pitfalls is important to patient outcome.
- Exclude potentially serious causes of back pain by assessing for 'red flags' in every patient presenting with this complaint.

COMMON CAUSES OF SOFT-TISSUE INJURIES

All injuries have a soft-tissue component. The simplest way of dividing their causes is into 'acute' (specific event that exceeds tissue tolerance) and 'chronic' (repetitive minor damage in excess of ability to heal). Both types may be

further subdivided by the tissue affected (bone, tendon, muscle, etc.).

Acute soft-tissue trauma can also be subdivided by the mechanism:

- Penetrating:
 - puncture versus incised
 - solid object versus fluid stream (high pressure hose, etc.).

- Blunt:
 - crush injury±laceration
 - shear/degloving (open or closed).
- Many of the types of trauma above are covered in other chapters.

General evaluation of a soft-tissue injury

Assessment

History

Obtain a history of:

- the nature of the injury: when, where and how it was sustained with specific attention to the forces involved, especially any potential crush or shear injury with devitalized tissue
- the possibility of a foreign body, wound contamination and/or damage to deeper structures
- patient function pre and post injury
- pain associated with the injury, including time course, nature and aggravating factors
- co-morbidities and drug therapy
- allergies and tetanus immunization status.

14.3 POLYARTHRITIS

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Examination

The extent of any nerve damage should be determined before using local anaesthetic.

Examination should potentially be delayed until after an x-ray if a radiopaque foreign body (metal or glass) is suspected, after giving analgesia.

Tendon damage may be best elucidated after adequate analgesia is obtained so the wound can be adequately explored.

PUNCTURE INJURY**Management**

Refer immediately to the appropriate surgical team all high-pressure gun injuries, such as from grease, paint or oil where the skin has been broken, even if no damage is apparent initially. They require extensive wound debridement and tissue plane cleaning, however innocuous they may seem.¹

Otherwise, clean the wound and evaluate the need for tetanus prophylaxis and antibiotics. A puncture wound to the sole of the foot will require exploration if it has occurred through the sole of footwear, or potentially has a foreign body.

Prophylactic antibiotics are controversial. If prophylaxis is chosen, give amoxicillin/clavulanic acid 875/125 mg bd for 5 days, add pseudomonal cover (e.g. ciprofloxacin 500 mg bd) if it is an at-risk injury such as through footwear.² As these wounds are at a high risk of infection, instruct the patient to return if increasing pain, redness or swelling occurs.

ACUTE MECHANICAL OVERLOAD INJURIES

These include fractures, ligament sprains, muscle strains or tears, and tendon ruptures. Many are covered in [Section 4](#).

See [Table 14.4.1](#) for a classification system for ligamentous sprains.

Table 14.4.1 Classification of ligament sprains/muscle strains

Grade	Features
I	Small number of fibres injured, pain on loading, but no laxity or loss of strength
II	Significant number of fibres injured, with laxity and/or weakness and pain on loading
III	Complete tear with gross laxity and no strength

Management**General principles**

The initial management principles are the same for both ligament sprains and muscular strains. This includes protection, rest, ice, compression and elevation (PRICE) with analgesia, usually a combination of paracetamol 1 g orally qid, plus a non-steroidal anti-inflammatory drug (NSAID), such as ibuprofen 400 mg orally tds (in the absence of NSAID-sensitive asthma, peptic ulcer disease and renal impairment).

Ligament sprain

Ligament sprains that are grade I or II (see [Table 14.4.1](#)) are managed with a protective brace or strapping and reduction in, but not cessation of, physical activity. Consider immobilizing grade III sprains with a splint or plaster of Paris (POP) cast and/or operative repair if there is gross instability and warn the patient that he or she can take up to 3 months or longer to heal. This is of particular relevance to the manual labourer and high-level athlete. Proprioception retraining at physiotherapy has been shown to prevent recurrence in the long term (>1 year) but not mid-term (6 to 9 months)³ in lateral ankle sprains.

Muscle strain

Muscle strains require initial PRICE to minimize bruising and haematoma formation followed by a graded return to activity. Physiotherapy may aid in return of function and prevent re-injury.⁴

Assess the functional limitations imposed by these injuries, particularly in patients who live alone and/or who are elderly and infirm, as loss of independence is likely. A complete muscle tear, especially in an active individual, may benefit from operative repair following referral to an orthopaedic specialist. Consider the need for community services, respite care or admission for those who are initially unable to care for themselves.

Tendon rupture**Evaluation**

Acute rupture of the supraspinatus tendon (see [Chapter 4.1](#)), long head of biceps and Achilles tendon (see [Chapter 4.11](#)) are the most common serious tendon injuries that present to an emergency department (ED). Injury may be secondary to an acute event or chronic overload that is often asymptomatic until a tear occurs, and the extent of the rupture may be partial or complete.

Management

Treatment is aimed at the earliest return to normal function, with the least likelihood of recurrence. Refer a complete tear, particularly in active people, for orthopaedic surgery for consideration of operative repair. Manage partial tears conservatively, but they too may have a

better outcome if repaired surgically, depending on local hospital practice and surgical availability.

One exception is a long head of biceps tendon tear, which usually results in a mostly cosmetic defect—the ‘Popeye’ sign. However, in highly active people or those with associated rotator cuff pathology surgical repair is often indicated.⁵

An ultrasound can confirm the diagnosis. Magnetic resonance imaging (MRI) is equally or more sensitive and specific depending on which tendons are being imaged, although it is much less readily available.

PRETIBIAL LACERATION

These are most common in elderly patients, often from trivial trauma that tears a flap of skin, particularly if taking steroids. Ask about general mobility and safety issues at home.

Management

The majority of these wounds will heal with conservative management. Clean the wound, remove blood clots, trim obviously necrotic tissue and unfurl the rolled edges of the wound to determine actual skin loss. Refer the patient immediately for consideration of debridement +/- early skin grafting if there is large skin loss, gross contamination, major haematoma or marked skin retraction preventing alignment of the skin edges.⁶

Otherwise, lay the flap back over the wound and hold in place with adhesive skin-closure strips (Steristrips). Then cover the wound with a non-adhesive dressing, and apply a firm crêpe bandage and instruct the patient to keep the leg elevated when not walking. Determine the need for tetanus immunization or booster.

Arrange follow-up with either outpatient wound services, or if unavailable, to the ED in 5 days for review and a dressing change, or earlier if blood or serum has seeped through the wound dressing, known as ‘strike-through’, which increases the risk of secondary infection.

DEGLOVING INJURY**Evaluation**

Degloving injuries are caused by either a shearing or traction force on the skin, causing it to be torn from its underlying capillary blood supply. When the skin actually peels off it leaves an obvious exposed open injury, or the skin may remain intact causing a closed injury.

A closed degloving injury is much harder to diagnose⁷ with up to one-third thought to be missed at the time of initial trauma.⁸ It occurs most

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commonly in the hip, thigh or pelvic region and usually in the setting of high energy trauma. The clinical exam is often complicated by underlying bony injuries. The most consistent finding is soft fluctuance and/or hypermobility of the skin. Decreased cutaneous sensation is often but not always present.⁷ The best diagnosis is on imaging; CT is reasonable but MRI is the preferred imaging modality.⁹ Pain may or may not be prominent and/or may relate to an underlying bony injury.

Management

Arrange specialist assessment and admission for all degloving injuries by the appropriate surgical team, usually plastic and/or orthopaedic surgery. Keep any degloved skin, as it may be used as a skin graft.

Do not be tempted simply to replace the skin into its original position and hold it there with sutures or adhesive skin-closure strips (Steri-Strips), as this is inadequate. Degloving injuries are also a high-risk wound for tetanus.

CHRONIC OVERUSE (OVERLOAD) INJURIES

Chronic overuse injuries develop wherever tissue microtrauma occurs at a rate that exceeds

the body's natural ability to heal. Few require emergency treatment, but general knowledge of these conditions is valuable to advise patients on cause and management.

Classification

Bony overuse injuries follow a continuum from pain on activity only, through local tenderness to pain at rest, with loss of function. Many will have led to a stress fracture by the time of presentation to an ED.

Other overuse injuries are classified by the tissue type and the extent of injury and are often best diagnosed by the timing of the pain in relation to physical activity. They are further classified by the presence or absence of inflammation. See Table 14.4.2 for a classification of chronic overuse syndromes.

Management

Most chronic overuse injuries are managed with a decrease in activity and NSAIDs, though their use in stress fractures is controversial.^{10,11} Arrange referral to a physiotherapist or specialty physician, such as sports or performing arts physician, as appropriate. Tendon-related injuries may benefit from a steroid injection, which should only be performed by doctors trained in the technique

(orthopaedic surgeons, rheumatologists, sports physicians or some ED doctors).

Specific chronic overuse injuries that require more extensive management are summarized in Table 14.4.3.

NON-ARTHROSTIC JOINT AND SOFT-TISSUE DISORDERS

General management of non-arthritic joint and soft-tissue disorders

Joint pain, swelling and tenderness mimicking arthritis may be due to inflammation of

Table 14.4.2 Classification of chronic overuse syndromes

Grade	Symptom
I	Pain after activity
II	Pain early on and after activity; activity not limited
III	Pain throughout activity, which is limited
IV	Pain at rest

Table 14.4.3 Stress fractures which require active specialist management

Injury	Associated with	Symptoms	X-ray	Other imaging	Management
Pars interarticularis	Gymnasts, ballet dancers, fast bowlers	Unilateral low back pain, worse on extension	Pars # often seen	CT or MRI definitive, XR+Bone scan alternative option	Avoiding hyper extension for 6/52, consider brace for 6–12/52; core stability retraining once healed
Femoral neck (see Chapter 4.7)	Athletes/military increased activity	Vague thigh/groin pain with loading	Often normal	Bone scan or MRI, CT less sensitive	If <50% of bone fractured, decrease activity, if >50% ORIF
Femoral shaft	Dancers	Vague thigh/knee pain with loading	# Usually visible	CT or bone scan	Lateral cortex—ORIF, medial cortex (much rarer) non-weightbearing 6/52
Anterior cortex of mid-tibia (see Chapter 4.10)	Distance runners, ballet dancers	Progressive anterior leg pain with activity	Anterior # line, thickened cortex	Bone scan? Non-union versus recent injury	Decrease activity, intermedullary nail if progresses
Talus (see Chapter 4.12)	Repeated falls/jumping from height	Foot/ankle pain worse with weightbearing	Usually normal	Bone scan, CT or MRI	6/52 non-weightbearing in POP
Navicular	Increased running/marching	Vague midfoot pain with point tenderness over navicular	May show #	Bone scan, CT or MRI	6–8/52 non-weightbearing, ORIF if fails to heal
Base 2nd metatarsal	Ballet dancers	Forefoot pain on exercise	# Usually visible	Bone scan, CT or MRI but usually not needed	Non-weightbearing on crutches for 4–6/52
Base 5th metatarsal (see Chapter 4.12)	Ballet dancers	Midfoot pain with activity	# Usually visible	Bone scan, CT or MRI but usually not needed	Non-weightbearing with POP for 6/52 or direct ORIF as often fail to heal
Sesamoid bone of hallux	Increased running/marching	Forefoot pain, tender/swelling over ball of foot	Often hard to interpret	Bone scan or MRI	6/52 Non-weightbearing with crutches then orthotics to correct biomechanics

CT, Computed tomography; MRI, magnetic resonance imaging; ORIF, open reduction internal fixation; POP, plaster of Paris; XR, x-ray; 6/52, 6 weeks.

periarticular structures. Most patients can be treated with NSAIDs, such as ibuprofen 200 to 400 mg orally tds or naproxen 250 mg orally bd and/or with paracetamol.

Underlying or secondary true arthritis also may be present and complicate the presentation. Joint aspiration is indicated to rule out a septic arthritis and, when this is suspected, follow local guidelines as to who performs it. Refer the patient in whom a septic joint has been excluded back to the general practitioner (GP) or outpatients unless mobility is so significantly affected that he or she requires admission.

Do not perform a steroid injection in the ED, as complications, such as septic arthritis and joint destruction, do occur. This is best left to the specialist who undertakes long-term care. Some of the more common presentations include the following.

Torticollis ('wry neck')

Diagnosis

Torticollis is abnormal unilateral neck muscle spasm, resulting in the head being held in a bent or twisted position. The aim of the history and examination is to exclude a serious underlying cause such as local sepsis/abscess, recent trauma, cervical disc prolapse, acute drug dystonia, raised intracranial pressure, or even a carotid artery dissection.¹²

Management

Benign 'wry neck' most commonly occurs on waking after sleeping in an awkward position or follows unaccustomed activity or minor trauma. Arrange for cervical imaging if there is a history of possible bony trauma or cervical pathology. Give benzotropine 1 to 2 mg intravenously when drug-induced dystonia is suspected.

Once serious causes have been excluded, use NSAIDs +/– paracetamol. Recommend gentle manipulation or muscle energy techniques to slowly work loose the muscles in spasm. Discharge the patient back to the GP with analgesia and ongoing exercises/stretches to maintain neck alignment.

Adhesive Capsulitis (Frozen shoulder)

Diagnosis

Frozen shoulder (adhesive capsulitis) has a natural history lasting 1 to 5 years, with an average duration of 2.5 years. It begins with an acutely painful period of 3 to 9 months with a progressively decreasing range of motion at the glenohumeral joint, and a 'freezing phase' over 4 to 12 months starting soon after the pain. Pain tends to be worse at night or when lying flat. The decreased range

of motion usually resolves in the 'thawing' phase, but this may take from 1 to 4 years.

A frozen shoulder may occur spontaneously, but more commonly follows local trauma (which can be trivial), non-shoulder surgery, immobilization, a cerebrovascular accident or shingles. There is an increased risk in diabetic patients where the condition may present bilaterally, in smokers, with hyperlipidaemia and in those on treatment with protease inhibitors. It is more common in females with a peak incidence age of 55 years and in the non-dominant arm.

On examination, the most sensitive sign is loss of passive external rotation at the glenohumeral joint. Test for this by first immobilizing the scapula by placing a hand over the top of the shoulder to exclude scapulothoracic movement.

TESTING PASSIVE EXTERNAL ROTATION OF THE GLENOHUMERAL JOINT – ADDITIONAL ONLINE MATERIAL

Management

Treatment options depend on the stage of the disease. The initial painful phase can be temporarily improved by intra-articular or oral steroids; NSAIDS may also have a role in symptom relief. Once the freezing stage has been reached then orthopaedics procedures to release the contracted capsule are potentially of benefit. Physiotherapy has conflicting evidence, with some studies showing prolongation of impaired function and others showing some improvement, usually when the patient is in the thawing stage.¹³

Supraspinatus tendonitis

Diagnosis and management

Supraspinatus tendonitis is one of the causes of the 'painful arc' occurring between 60 degrees and 120 degrees of shoulder abduction. Perform a shoulder x-ray, which may reveal calcification in the supraspinatus tendon and/or 'hooking' of the acromion, decreasing the subacromial space and predisposing to this condition.¹⁴ Patients may present at the time of acute rupture of calcific material into the subacromial bursa, which causes significant pain.¹⁵ Ultrasound is used for diagnosis and to facilitate aspiration and local steroid injection.

Give an anti-inflammatory analgesic and consider referral to the orthopaedic or rheumatology clinic, especially if calcific tendonitis is present.¹⁴ A 1.25 mg/h glyceryl trinitrate patch over the subacromial space has been shown to be more effective than physical therapy alone in decreasing pain in non-calcific tendonitis.¹⁶

PAINFUL ARC

Subacromial bursitis

Diagnosis and management

Subacromial bursitis may follow rupture of calcific material into the subacromial bursa that again causes a 'painful arc' on attempted shoulder abduction or constant severe pain in the shoulder. Manage as for supraspinatus tendonitis, above.

Tennis and golfer's elbow

Diagnosis and management

Tennis elbow (incorrectly termed lateral epicondylitis) causes pain over the lateral epicondyle of the humerus from chronic angiofibroblastic tendinosis. There is disorganized tissue and neovascularization but minimal actual inflammation of the extensor origin of the forearm muscles involved in repetitive movements, such as using a screwdriver or playing tennis. Advise the patient to avoid the activity causing the pain and to rest the arm.

Give an anti-inflammatory analgesic and refer for physiotherapy. Eccentric and isometric exercises are most effective in treating and preventing recurrence.¹⁷ A tension strap also can be used to control symptoms, particularly when a patient presents within the first 6 weeks. A local steroid injection often reduces short-term pain and improves movement in the first 6 weeks, but has a worse longer-term outcome.¹⁸

Golfer's elbow (medial epicondylitis) is a similar condition affecting the medial epicondyle and the flexor origin. Management is the same.

Olecranon bursitis

Diagnosis and management

Painful swelling of the olecranon bursa is due to local trauma, gout or infection, usually with *Staphylococcus aureus*. Aspiration under sterile conditions for microscopy (looking for crystals and/or bacteria) and culture is indicated where possible as physical exam is poorly sensitive for differentiating septic from traumatic bursitis. Imaging is indicated when a foreign body is suspected.¹⁹

Refer the patient for drainage of the bursa under anaesthesia and/or ultrasound guidance if significant bacterial infection or a foreign body is confirmed, or if a septic arthritis is suspected due to markedly reduced movement at the elbow (see Chapter 14.2). Otherwise, give an anti-staphylococcal antibiotic, such as di- or flucloxacillin 500 mg orally qid for 10 days in an immunocompetent patient +/– a non-steroidal anti-inflammatory analgesic and refer back to the

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GP.¹⁹ Immunosuppressed patients warrant initial intravenous therapy if a septic bursitis cannot be excluded.

Prepatellar bursitis (housemaid's knee)

Diagnosis and management

This is a prepatellar bursitis secondary to friction or, occasionally, infection. Treat by giving an anti-inflammatory analgesic, avoiding further trauma.²⁰ If initial treatment fails and infection has been excluded, consider a steroid injection²⁰ by an orthopaedic or rheumatology specialist, or by arrangement with the patient's GP. When local infection is suspected, aspirate, if possible, for culture, microscopy and crystals, and start an anti-staphylococcal antibiotic, such as di- or flucloxacillin 500 mg orally qid for 10 days and refer back to the GP.

Refer the patient to the orthopaedic specialist for intravenous antibiotics and/or local drainage if systemic infection is suspected.

De Quervain stenosing tenosynovitis

Diagnosis and management

This causes tenderness over the radial styloid, a palpable nodule from thickening of the fibrous sheaths of the abductor pollicis longus and extensor pollicis brevis tendons and pain on moving the thumb. Treat by resting the thumb in a splint and by using an anti-inflammatory analgesic.²¹

Refer to a rheumatology specialist for consideration of a local steroid injection, although it may require surgical release of the tendon sheaths if the local steroid injection fails.²¹

Plantar fasciitis

Diagnosis and management

Plantar fasciitis presents as a painful midfoot, especially in the sole or arch, which is worse on first weight bearing and improves after 10 to 15 minutes of walking, and recurs during load bearing for an extended period. It is one of the most common causes of recurrent foot pain and may be one manifestation of the spondyloarthropathy seen in Reiter syndrome, ankylosing spondylitis and psoriatic arthritis (see Chapter 14.3). It also can be triggered by an acute increase in exercise. On examination, there is tenderness of the plantar fascia, especially at the calcaneal attachment.²²

An x-ray may reveal a bony spur extending along the plantar fascia, but this has no bearing on the initial management. There is poor evidence for any specific therapy; however, expert opinion recommends orthoses (over-the-counter has been found to be better than custom fitted in one study), reduction in activity and NSAIDs.²²

Carpal tunnel syndrome

Diagnosis and management

This is a compressive neuropathy of the median nerve at the wrist, most commonly affecting middle-aged females. Secondary causes include rheumatoid arthritis, diabetes, post-trauma, such as a Colles fracture, pregnancy and—rarely—myxoedema, acromegaly and amyloidosis. However, most cases are idiopathic or related to minor repetitive trauma.²³

Patients complain of pain and burning paraesthesia in the distribution of the median nerve in the hand, primarily the thumb, index, middle and lateral aspect of the ring finger. It is typically worse at night or following repetitive strain, especially with higher loads or vibrating tools.²³

Perform Phalen's test by reproducing paraesthesia in the distribution of the median nerve following 60 degrees of wrist hyperflexion, or look for Tinel's sign eliciting median nerve paraesthesia by tapping on the volar aspect of the wrist over the median nerve. Test for reduced sensation over the palmar aspect of the affected digits and weakness of thumb abduction, associated with thenar muscle wasting in chronic cases.

Treat with an anti-inflammatory analgesic and immobilize the wrist in a volar splint in the neutral position, particularly at night. Refer resistant cases to an orthopaedic specialist for consideration of steroid injection or carpal tunnel decompression.²³

BACK PAIN

This is a common problem that usually simply requires analgesia and patient education. Assessment is targeted at determining whether concerning features, 'red flags', are present which mandate further investigation. Back pain may be subdivided into four major categories:

- direct major spinal trauma
- indirect mechanical back trauma (non-specific low back pain)
- back pain with radiculopathy
- back pain with focal 'hard' neurology, or a specific serious cause suspected.

Direct major thoracic and lumbosacral spine trauma is covered in Chapter 3.3.

Back pain 'red flags'

Every patient presenting to the ED with acute low back pain must be assessed for the presence of 'red flag' symptoms or signs suggesting a potentially serious underlying cause²⁴:

- Signs and symptoms of infection and/or high-risk factors for spinal infection
- Signs and symptoms of spondyloarthritis
- New or progressive neurological deficit:

- History of malignancy
- Significant trauma
- Unexpected weight loss
- Elderly, corticosteroid use and/or other osteoporotic risk factors.

Although the majority will end up having a diagnosis of musculoskeletal pain, laboratory testing and/or imaging is indicated when red flags are present. See Table 14.4.4 for the differential diagnosis and investigation.

Indirect mechanical back trauma (non-specific low back pain)

Clinical features

History

Bending, lifting, straining, coughing or sneezing may precipitate acute, severe low back pain, causing intense muscle spasm or even complete immobility. It is common for patients to have apparently minor back discomfort on one day, then wake with severe spasm the next.

Examination

This is focused on excluding any focal 'hard' neurology or radiculopathy. Giving adequate analgesia so that pain does not limit strength is an important part of the assessment. See Chapter 3.3 for a description of the myotomes, dermatomes and nerve roots in the leg.

Hard neurology is characterized by the loss of sensation, reflexes or true weakness. A radiculopathy is characterized by pain or subjective altered sensation following a dermatome. These should both be absent. Imaging is not usually indicated unless symptoms are continuous for greater than 6 weeks and are not previously investigated.

Management

The mainstay of management is patient education along with adequate analgesia to allow active physical therapy.²⁵ The ED management consists of excluding more serious causes, then educating and reassuring the patient while ensuring adequate analgesia to allow movement. Analgesic best evidence is for NSAIDs in isolation.²⁵ Paracetamol as a sole agent has been found not to be effective at the 3-week follow-up and is not recommended by some guidelines.²⁶ However, if stronger analgesia is required it should be used as the short-term effect on pain was not studied. Muscle relaxants have been found to be effective for short-term analgesia but often have significant side effects; if needed, try baclofen 10mg tds.²⁷ Opiates are not recommended²⁵ but are often required for the subset of patients who have presented to an ED; aim to minimize duration of therapy with these agents. Short-acting opiates may be required to allow adequate physical exam by ensuring

Table 14.4.4 Differential diagnosis and investigation of serious disorders causing back pain

Suspected diagnosis	History/symptoms/findings	Investigations
Infection Osteomyelitis Discitis Epidural abscess	Fever IVDU Immunosuppression Recent instrumentation or infection Hard or progressive neurology	FBC/CRP/ESR ESR most sensitive Blood culture MRI best imaging
Cancer Primary Secondary	Previous cancer Unexplained weight loss Age >50 (65 in some series) Failure to improve after 4–6 weeks	XR MRI if neurology
Spinal cord compression Cauda equina Infections as above	Urinary retention Incontinence (bladder or bowel) Saddle anaesthesia Sensory &/or motor level (NB often patchy in cauda equina or epidural abscess)	MRI
Fracture	Osteoporosis Long term steroid use Pain significant at rest	XR + CT if >50% height loss or retropulsed fragments
Ankylosing spondylitis	Age <30 Pain worse at night Morning stiffness Improves with exercise	ESR/CRP HLA-B27 Pelvis XR
Spinal stenosis	Leg pain >> back pain Pseudoclaudication No pain when patient is seated Thigh pain after 30s lumbar extension	CT MRI if neurology

CRP, C-reactive protein; CT, computer aided tomography; ESR, erythrocyte sedimentation rate; FBC, full blood count; IVDU, intravenous drug user; MRI, magnetic resonance imaging; XR, x-ray.

strength is not limited by pain. Benzodiazepines are often used²⁸ but have not been found to be effective by any well-performed studies²⁹; only consider their use as an adjunct in the setting of high patient anxiety.

Patients who are able to mobilize without more complex analgesic regimes may be discharged to the care of their GP for ongoing follow-up and education concerning posture and lifting. Patients who require ongoing opiate analgesia will require admission, either to an ED short-stay ward for nursing care and regular analgesia prior to physiotherapy review, or to an inpatient ward according to hospital policy, most commonly under orthopaedics or general medicine.

Back pain with radiculopathy

Clinical features

These patients not only have a similar presentation to those with non-specific low back pain, but also have neuropathic pain following one or more lower leg dermatomes. Examination may reveal subjectively altered sensation but with intact sharp/dull (or hot/cold), 2-point discrimination and proprioception. Straight-leg raising may exacerbate radicular symptoms. Strength and reflexes are also intact, with no reported incontinence or urinary retention.

Imaging is again not indicated unless symptoms are progressing with increasing numbers of dermatomes or there are continuous symptoms for more than 6 weeks.

Management

Management is the same as for non-specific back pain, with the addition of more specific neuropathic pain analgesia, such as pregabalin 25 to 75 mg bd or amitriptyline 10 to 25 mg nocte (lower doses in older patients +/- tapentadol SR 50 mg bd or tramadol 100 to 200 mg SR bd).

Back pain with focal 'hard' neurology, or a specific serious cause suspected

This small group of patients with hard neurology consisting of true weakness, loss of sensation and/or reflexes requires further investigation and specialist referral (usually neurosurgery or orthopaedics). The timing of this investigation will depend on the acuity and extent of the symptoms or signs. Acute onset or ongoing progression mandate emergent investigation and referral for treatment. Subacute or chronic symptoms (especially if from a single nerve root) may be investigated and managed on a less urgent basis in discussion with the specialist team, particularly if they are unlikely to be reversible.

Other patients with 'red flag' symptoms or signs also must be investigated urgently (see Table 14.4.4). They may have any of the following conditions.

Spinal infection

Clinical features

Spinal infections include epidural abscess, discitis and vertebral osteomyelitis. Risk factors are recent instrumentation (prolonged epidural catheter > surgery > brief, such as obstetric epidural catheter), immunosuppression, alcoholism, diabetes, intravenous drug use, contiguous infection or distal infection with bacteraemia. The classic progression of symptoms is from back pain to radiculopathy, to weakness, to paralysis with progression from radiculopathy to paralysis sometimes occurring over hours. Fever is absent in over one-third of cases.

Investigations

A normal white cell count (WCC), erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) virtually exclude the diagnosis, with ESR being the most sensitive and WCC the least. Blood cultures should be taken, although CT-guided or surgical specimens are more likely to culture the causative microbe. MRI is the imaging modality of choice to confirm or exclude the diagnosis.

Management

Progressive neurology requires urgent operative intervention with the decision on which antibiotic(s) prior to surgery discussed with the treating team. In patients without neurology, the treating team may elect to manage conservatively. Empirical antibiotic therapy is targeted at skin flora, including methicillin-resistant *Staphylococcus aureus* (MRSA) and dental flora, unless it is suspected that it has spread from a focal infection, such as *Escherichia coli* or *Streptococcus pneumoniae*.

Spinal cancer

Clinical features

Acute symptoms are most likely in the setting of previous cancer, particularly those that metastasize to bone (lung, breast, prostate, renal, thyroid and melanoma). Unexplained weight loss, age >50 years and symptoms failing to improve after 1 month, are risk factors. Examination should thus include skin (melanoma), breasts, chest, abdomen and prostate to look for a primary tumour.

Investigations

Plain x-ray may be adequate to find a bony lesion, but more information with high sensitivity is obtained from CT scanning. An MRI is indicated if there is any focal neurology.

14.4 MUSCULOSKELETAL AND SOFT-TISSUE EMERGENCIES

Management

If cancer is found or is highly suspicious, admit the patient to hospital. Spinal cord compression may respond to radiotherapy and a pathological fracture may require stabilization. Otherwise, management is with analgesia, and the investigation is aimed at determining the primary tumour, which will dictate the definitive treatment.

Fracture (vertebral compression)

Clinical features

Suspect this with significant pain at rest, long-term steroid use or known osteoporosis even with minor trauma. Examination is aimed at excluding focal neurological complications.

Investigations

Plain x-ray is the initial investigation. CT is indicated if there is greater than 50% vertebral height loss or retropulsion of fragments into the spinal canal is noted.

Management

Analgesia is as per non-specific back pain. It is extremely rare for these injuries to be unstable or to require immobilization or surgical stabilization, although admission for analgesia and bedrest may be necessary.

Spinal cord compression or cauda equina syndrome

Clinical features

Spinal cord compression or cauda equina syndrome (lesion at or below the first lumbar vertebra) may be due to tumour, infection or central disc prolapse. Urinary retention is the most sensitive sign of cauda equina syndrome, which is seen in $\approx 90\%$ of cases. A history of incontinence and perineal or perianal 'saddle

area' anaesthesia or bilateral leg weakness may also occur. The neurology findings will correspond to a specific level in the case of spinal cord compression, but may be inconsistent and patchy in cauda equina syndrome.

Investigation

Urgent MRI is the investigation of choice, with CT of some value, particularly if bony injury is suspected or if MRI is unavailable. Imaging should not delay urgent transfer to definitive treatment under the care of a spinal surgeon.

Management

Urgent surgery. Corticosteroids are not supported unless due to a steroid-responsive tumour.

Ankylosing spondylitis

Clinical features

Ankylosing spondylitis is a chronic inflammatory enthesopathy affecting the axial skeleton. It usually occurs in males (5:1) below the age of 30 years, causing pain that improves with exercise and worsens with rest, sometimes resulting in waking in the second half of the night due to discomfort. Examination may be unremarkable or show a general decreased range of spinal motion in more advanced cases.

Investigations

The ESR and CRP are usually raised. HLA-B27 is sensitive for the disease and is present in around 95% of Caucasian and Chinese patients. Pelvic x-ray often shows sacroiliitis.

Management

Commence NSAIDs at a maximum dose and refer to rheumatology outpatients follow-up. Regular physiotherapy including hydrotherapy is essential.

CONTROVERSIES

- Indications for surgical versus conservative management for soft tissue or chronic overuse injuries, particularly in elite athletes/young manual workers to reduce the time to return to elite or work activity.
- Who should perform joint aspiration and/or intra-articular/intralesional steroid injections and their safety.
- Sensitivity of inflammatory markers to exclude spinal infection.

Full references are available at <http://expertconsult.inkling.com>

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14.4 MUSCULOSKELETAL AND SOFT-TISSUE EMERGENCIES

Testing passive external rotation of the glenohumeral joint (eFigs. 14.4.1 and 14.4.2)

Have the patient sit or stand comfortably with their arm by their side. The exam is most easily performed with the examiner standing either behind the shoulder to be examined or slightly further to the side. It can be done from in front of the patient, in which case the actions of each hand will need to be reversed

Place the opposite hand (i.e. if examining a right shoulder, use your left hand) over the top of the shoulder to prevent movement of the scapula.

Use the other hand to gently grasp the patient's forearm just distal to the elbow and flex the patient's elbow to 90 degrees.

Then assess the passive range of motion of external rotation at the glenohumeral joint.

Painful arc of the shoulder

The patient actively abducts their shoulder from by their side to overhead. Pain through the arc of 60 to 120 degrees abduction is indicative of subacromial pathology (e.g. supraspinatus tendonitis, subacromial bursitis). Pain in the last 10 to 15 degrees is indicative of acromio-clavicular joint pathology.

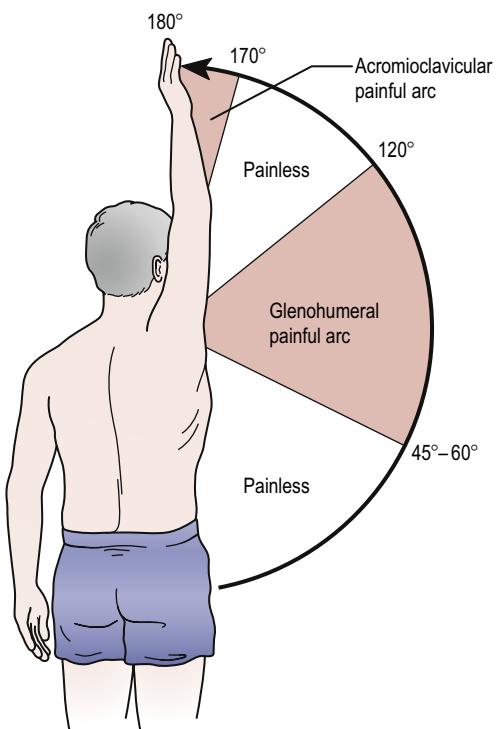


FIG. 14.4.1 Painful arc of the glenohumeral joint on abduction ~60 to 120 degrees is due to subacromial pathology, ~170 to 180 degrees is due to acromio-clavicular joint pathology. (From Magee DJ. *Orthopedic Physical Assessment*. 4th ed. Philadelphia, PA: Saunders; 2002, with permission.)

14.4 MUSCULOSKELETAL AND SOFT-TISSUE EMERGENCIES



FIG. 14.4.2 Testing passive external rotation of the glenohumeral joint while standing behind (A) or in front of the patient (B). The patient's elbow is kept by their side during the test and scapulothoracic movement is prevented/detected by the hand placed over the shoulder.

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SECTION 15

DERMATOLOGY EMERGENCIES

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15.1 Emergency dermatology 540

15.1 Emergency dermatology

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ESSENTIALS

- 1 Emergency dermatology presentations may be divided into potentially life-threatening dermatoses, vesiculo-bullous conditions, petechial and purpuric rashes, and inflammatory dermatoses such as eczema, urticaria and psoriasis.
- 2 Potentially life-threatening presentations include Stevens-Johnson syndrome, toxic epidermal necrolysis (TEN), Sweet syndrome, drug rash with eosinophilia and systemic symptoms (DRESS) and erythroderma.
- 3 Petechial or purpuric rashes may represent cutaneous or systemic vasculitis, or coagulopathy; investigations are targeted at internal organ involvement, and management is multidisciplinary.
- 4 Cutaneous infections may be a primary presentation or a secondary complication of a primary dermatosis.

Introduction

The pattern and form of acute dermatological conditions that present to the emergency department (ED) are confusing in that the clinical features, such as vasodilation, exfoliation, blistering or necrosis, are the common endpoint of many different inflammatory processes in the skin.

The pathological process involves cytokines or chemokines and their effects create the visible response(s). The important clinical differences seen in these acute reactions should be recognized by the trained observer (Tables 15.1.1 and 15.1.2). This chapter aims to provide a clinical pathway from taking an appropriate history to having knowledge of the distinguishing clinical features of the likely differential diagnoses. The emergency presentations discussed are limited to specific dermatological conditions that may be seen in an ED as a true urgency.

It is important to use other resources with this chapter, such as a dermatology atlas or specialized texts, to provide greater detail on the conditions mentioned. The presentation of skin and soft-tissue infections (Chapter 9.5) and anaphylaxis (Chapter 2.8) are covered elsewhere.

POTENTIALLY LIFE-THREATENING DERMATOSES

Stevens-Johnson syndrome and toxic epidermal necrolysis

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are acute severe cutaneous presentations characterized by extensive necrosis and detachment of the epidermis. Confusion exists between these

two diagnoses and erythema multiforme (EM). EM was previously considered a variant of SJS/TEN, but it is now commonly accepted that they are clinically distinct disorders with different aetiologies and prognosis. Most consider EM minor and major to be related to infections (e.g. herpes simplex virus [HSV]); whereas SJS/TEN are variants of the same disorder defined by severity and are usually caused by drugs. SJS is also known to be triggered by mycoplasma infections. The distinction between EM major, SJS and early TEN is not important in the emergency setting; rather it is the recognition of a potentially serious dermatosis that is important, and the need for comprehensive assessment and monitoring.

The difference between SJS and TEN is defined by the extent of skin involvement. SJS affects 10% or less of the total body surface area (TBSA), whereas TEN affects more than 30% TBSA (Fig. 15.1.1). 'TEN/SJS overlap' refers to patients where there is between 10% and 30% TBSA involvement. The extent of necrolysis must be carefully evaluated since it is a major prognostic factor. Patients with HIV, over age 65 and those with malignancy are at increased risk of TEN.

Clinical features

Clinical features of SJS/TEN include a prodrome with upper respiratory tract (URT)-like symptoms, fever, malaise, vomiting and diarrhoea. Skin pain may herald the development of SJS/TEN and is a sensitive sign of impending epidermal detachment. Symmetrical erythematous macules, mainly localized on the trunk and proximal limbs, evolve progressively to dusky erythema and confluent flaccid blisters leading to epidermal detachment.

15.1 EMERGENCY DERMATOLOGY

Table 15.1.1 Definition of macroscopic skin pathological lesions

Papule	Circumscribed firm raised elevation, less than 0.5 cm in diameter
Nodule	A solid or firm mass more than 0.5 cm in the skin, which can be observed as an elevation or can be palpated
Purpura	Red-purple discolouration of skin or mucous membranes due to extravasation of red blood cells
Pustule	An accumulation of yellow-white fluid within a vesicle or papule; may be centred around a pore, such as a hair follicle or sweat glands, and sometimes appears in normal skin, including the palms and soles
Vesicle (s)	A visible accumulation of fluid in a papule of <5 mm The fluid is clear, serous-like and is located within or beneath the epidermis
Bulla (ae)	Large fluid-containing lesion of >5 mm
Plaque	An area or sheet of skin elevated and with a distinct edge, of any shape and usually wider than 1 cm

(Modified with permission from Rook AJ, Burton JL, Champion RH, Ebling FJG. Diagnosis of skin disease. In: Bologna J, Jorizzo J, Rapini R, eds. *Textbook of Dermatology*. Oxford: Blackwell Scientific; 1992.)

Table 15.1.2 Definitions of patterns in skin disorders

Annular	Ring-like or part of a circle
Linear	Line-like
Arcuate	Arch-like
Grouped	Local collection of similar lesions
Unilateral	One side
Symmetrical	Both sides



FIG. 15.1.1 Toxic epidermal necrolysis.

Box 15.1.1 SCORTEN severity score for toxic epidermal necrolysis

- Age >40 years
 - Heart rate >120/min
 - Presence of cancer or haematological malignancy
 - Epidermal detachment involving body surface area >10% on day 1
 - Blood urea nitrogen >10 mmol/L (28 mg/dL)
 - Glucose >14 mmol/L (252 mg/dL)
 - Bicarbonate <20 mEq/L
- (One point is given for each variable)

Table 15.1.3 SCORTEN mortality prediction

Score	Mortality (%)
0–1	3.2
2	12.1
3	35.3
4	58.3
5 or greater	90.0

(Reproduced with permission from Guégan S, Bastuji-Garin S, Poszepczynska-Guigné E, et al. Performance of the SCORTEN during the first five days of hospitalization to predict the prognosis of epidermal necrolysis. *J Invest Dermatol*. 2006;126:272–276.)

prognosis. Arrange assessment and treatment by the ophthalmology and ear, nose and throat teams for ocular and oral/pharyngeal involvement, respectively; urological and/or gynaecological review of patients with TEN is essential to prevent genito-urinary scarring.

TEN may continue to evolve and extend over days, unlike a burn, where the initial insult occurs at a defined time. The SCORTEN severity scoring system for TEN (Box 15.1.1) is similar in concept to the Ranson's score for pancreatitis. Calculate the SCORTEN severity score within 24 hours of admission and again on day 3 to aid the prediction of possible death (Table 15.1.3).

Erythema multiforme

While not life threatening, EM is part of the differential of a potentially life-threatening reaction, such as SJS/TEN. EM is an acute usually mild, self-limited cutaneous and/or mucocutaneous syndrome that presents with the rapid onset of lesions within a few days, favouring acral sites. These are often mildly pruritic or painful papular or urticarial lesions, as well as the classical 'target' lesions, but with only one mucous membrane involved (EM major) or none (EM minor). Typically, the oral mucosa is involved showing a few, discrete, mildly symptomatic erosions. Rarely, the eye, nasal, urethral or anal mucosa may be involved. A mild prodrome may precede development of the rash.



FIG. 15.1.2 Erythema multiforme.

Most cases of EM are due to infection, most commonly HSV or mycoplasma. Drugs are now considered to be an uncommon cause (Fig. 15.1.2).

Investigations

Send a baseline FBE, U&E, LFT and CRP, as well as a skin biopsy if the diagnosis is uncertain, swabs for HSV PCR. Request a CXR and mycoplasma serology if there are respiratory symptoms.

Management

Usually, only symptomatic treatment is required with topical steroids, antihistamines, antiseptic mouthwashes and local anaesthetic preparations for oral involvement. For severe cases, treat EM with a systemic steroid, such as prednisolone (0.5 to 1 mg/kg/day). In recurrent EM due to HSV, oral antivirals are effective at preventing relapse.

Sweet syndrome

Sweet syndrome (acute febrile neutrophilic dermatosis) may resemble severe EM in the acute oedematous phase, presenting variably with fevers, arthralgias, sterile potentially painful pustules, plaques or nodules over the head, trunk and arms. The red-purple plaques/nodules are often referred to as 'juicy' indicating they are soft and pus-filled though not truly fluctuant.

Sweet syndrome is often a relapsing-remitting presentation that may be associated with an underlying haematological malignancy inflammatory bowel disease, rheumatoid arthritis or other connective tissue disease, pregnancy or infection, such as *Streptococcus* or *Yersinia* (Fig. 15.1.3).



FIG. 15.1.3 Sweet syndrome.

Sweet syndrome is highly responsive to systemic steroids; however, any underlying association must be sought and excluded by appropriate investigations.

Drug rash with eosinophilia

Drug rash with eosinophilia and systemic symptom (DRESS) is a severe skin reaction to a drug with systemic manifestations that carries significant morbidity and a mortality rate of 10%. It typically occurs within 2 to 6 weeks of drug initiation. It has been reported with the antiepileptics (phenytoin, carbamazepine, phenobarbital), lamotrigine, sulphonamides (including sulphamethoxazole and trimethoprim combinations and dapsone), minocycline, allopurinol, terbinafine, abacavir and nevirapine. Up to 70% cross-reactivity occurs between different aromatic anticonvulsants, which should therefore be avoided if someone has previously had a major reaction to an aromatic antiepileptic.

Fever and rash are the most common symptoms. Cutaneous involvement is often polymorphic usually starting as a morbilliform rash, which may later become oedematous, exfoliative or erythrodermic, and/or include non-follicular pustules. Often, rash involving the face indicates a more serious drug reaction and facial oedema and lymphadenopathy are frequent hallmarks of this syndrome.

Prominent eosinophilia is a characteristic feature that occurs in 60% to 70% of cases. Potentially serious internal organ involvement, such as hepatitis, nephritis, pneumonitis, myocarditis, thyroiditis and encephalitis can occur. Fever, skin rash and organ involvement may

fluctuate and persist for weeks or months after drug withdrawal, with the delayed onset of sequelae reported.

Investigations

Diagnosis can be difficult because of the polymorphic rash and variable organ involvement. A skin biopsy should be taken for histopathology and, although not diagnostic, histological features of a drug reaction will assist in making the diagnosis. Also request a baseline FBE, U&E and LFT. Immunoglobulins and viral serology (Epstein–Barr virus, cytomegalovirus, human herpesvirus 6 or 7 [HHV6, HHV7]) should be sent, as transient hypogammaglobulinaemia and viral reactivation may be associated with fluctuations in symptoms. Other investigations should be as directed for systemic involvement, including baseline CXR, electrocardiogram (ECG) and Thyroid Stimulating Hormone (TSH).

Management

This usually includes admission to hospital and ceasing the suspected drug. Corticosteroids are the first line of therapy despite no consensus on dose or regimen; a starting dose of 0.5 mg to 1 mg/kg/day is reasonable. Fluctuation in symptoms and relapse can occur when the dosage is tapered. As a result, steroid therapy sometimes has to be maintained for several weeks, even months and a steroid-sparing agent may be required. Topical steroids should always be implemented to assist in systemic steroid tapering. Intravenous immunoglobulin (IVIG) may be required in cases of DRESS with severe systemic involvement such as severe hepatitis.

Erythroderma

The causes of erythroderma include eczema (40%), psoriasis (22%), drugs (15%), lymphoma (Sezary syndrome) (10%) and idiopathic (8%). Seek a history of previous skin disease, recent medications or recent changes to skin management, assess hydration and cardiac status, check for oedema, respiratory infection and a deep vein thrombosis (DVT).

Complications of erythroderma

Include:

- high output cardiac failure
- transepidermal water loss causing intravascular hypovolaemia (dehydration)
- hypoalbuminaemia contributing to intravascular dehydration
- electrolyte imbalance
- hypothermia/temperature dysregulation
- thrombophlebitis/DVT
- infection, both cutaneous and respiratory, with pneumonia a major cause of death

15.1 EMERGENCY DERMATOLOGY

Table 15.1.4 Causes of petechiae or purpura

Non-thrombocytopenic	Non-palpable purpura					
	Thrombocytopaenic disorders					
	With splenomegaly	Abnormal marrow	Normal marrow	Without splenomegaly	Abnormal marrow	Palpable purpura (vasculitis)
Cutaneous disorders	Liver disease with portal hypertension	Leukaemia Lymphoma Myeloid metaplasia	Immune: Idiopathic thrombocytopaenic purpura, drugs, infections including HIV Non-immune: Vasculitis, sepsis, disseminated intravascular coagulation, haemolytic-uraemic syndrome, thrombotic thrombocytopaenic purpura	Cytotoxics Aplasia, fibrosis or infiltration Alcohol, thiazides	Polyarteritis nodosa (PAN) Leucocytoclastic (allergic) Henoch–Schönlein purpura Infective: <ul style="list-style-type: none">• Meningococcaemia• Gonococcaemia• Other infections<ul style="list-style-type: none">• Staphylococcus• Rickettsia (Rocky Mountain spotted fever)• Enteroviruses Embolic	
• Trauma						
• Steroids, old age						
Systemic disorders	Myeloproliferative disorders					
• Uraemia						
• von Willebrand disease	Lymphoproliferative disorders					
• Scurvy, amyloid	Hypersplenism					

Investigations

Request an FBE, U&E, LFTs and blood cultures if the patient's temperature is $>38^{\circ}\text{C}$, or if the patient appears unwell with rigors, even if the temperature is normal, as the patient may have become poikilothermic but is still septic.

Send skin swabs for Microscopy/Culture/Sensitivities (MCS) and request a CXR. Arrange biopsy of the skin if the cause of the erythroderma is uncertain.

Management

Arrange to admit the patient. Treatment is general and supportive and includes:

- attention to temperature control, avoiding hypothermia
- Intravenous fluid replacement with careful charting of the fluid balance, monitoring urine output in particular
- referral to dietitian for high protein diet in the first 24 hours
- DVT prophylaxis.
- Specific treatment includes:
 - bath oil daily in bath or shower
 - wet wraps three times a day (TDS):
 - A. topical corticosteroid (as appropriate) applied liberally
 - B. 50% white soft paraffin, 50% liquid paraffin applied liberally
 - C. wet tubular bandage or full-length pyjamas
 - D. dry tubular bandage or full-length pyjamas
 - antibiotics for proven infection.

Supervision should be under the direction of the dermatology team. Intensive care may be necessary.

OTHER BULLOUS AND VESICULAR CONDITIONS

There are many causes of blistering skin rashes that range from common and harmless (but still distressing) to the uncommon and potentially life



FIG. 15.1.4 Bullous pemphigoid.

threatening. See Table 15.1.4 for the differential diagnosis of a vesicobullous rash.

Always ask about recent drug ingestion and about drug allergy in the event that a bacterial skin infection is diagnosed and antibiotics are required.

Pemphigus vulgaris

Pemphigus vulgaris is characterized by flaccid bullae and **erosions**, together with oral ulceration. The Nikolsky sign is positive, though true vesicles and bullae are often rare as they often break easily to form erosions. The scalp, oral mucosa and genitals are commonly involved. Vegetating lesions, particularly in flexures, such as the axillae or on the scalp, may occur as 'pemphigus vegetans'.

Investigations

Send blood for U&E, LFTs and random blood glucose (RBC) as a baseline and for thiopurine methyl-transferase (TPMT) levels, reduction of which increases the risk of toxicity if adjuvant immunosuppression with azathioprine if required.

Send a serum autoantibody profile for antiskin antibodies ('anti-epithelial antibodies') directed against desmoglein 1 and 3. Arrange a biopsy of lesional skin for histology and perilesional skin, which should be sent **fresh** and not in formalin, for direct immunofluorescence. An alternative medium is Michel's if fresh transport is not possible.

Management

Start high-dose prednisolone initially at a dose of up to 1 mg/kg/day to achieve remission. Admit the patient under the care of a Dermatologist for consideration of other therapies, such as immunosuppression with mycophenolate mofetil, azathioprine, IVIG or rituximab.

Bullous pemphigoid

The usual presentation is an older patient with tense skin bullae that may occur on an erythematous base or from normal skin. Itch is a common symptom. Blisters may be small (vesicles) or large (bullae) and heal with scarring (Fig. 15.1.4).

Investigations

Send for FBC, electrolytes, urea and creatinine (EUCs), LFTs and RBG level as a baseline, plus serum for indirect immunofluorescence for autoantibodies to Bullous Pemphigoid Antigens 1 & 2 ('anti-basement membrane zone' antibodies). Also send a TPMT level, as adjuvant immunosuppression with azathioprine may be required. Arrange biopsy of an uricated or bullous lesion for histology and perilesional skin for direct immunofluorescence. If this is not possible, blister fluid may be sent for indirect immunofluorescence.

Management

Start prednisolone at a moderate dose, such as 0.5 to 0.75 mg/kg daily. A tetracycline antibiotic, such as doxycycline 100 mg daily and nicotinamide 500 mcg orally tds, may be used for their anti-inflammatory properties as adjuvant therapy. Admit patients for supportive care if blistering is widespread.

In more severe disease, steroid-sparing agents, such as azathioprine, methotrexate or mycophenolate mofetil, may be required. Superpotent topical steroids are also effective and may be used as monotherapy for localized disease.

PETECHIAL AND PURPURIC RASHES

Petechiae, bruising and ecchymoses

Consider and exclude potentially life-threatening causes, such as thrombocytopenia and vasculitis, platelet abnormalities or over-anticoagulation (see Box 15.1.2 for causes of a petechial or purpuric rash). Take a full drug history, including anticoagulant medications, and ask about systemic symptoms including fever, bleeding tendency, travel history, alcohol abuse and known HIV disease.

'Senile purpura' are usually due to sun damage and ageing with subsequent loss of dermal support for blood vessels, which then bleed into the skin. Sometimes they can be dramatic but are always benign and resolve. When simple trauma is considered, remember non-accidental injury in all cases where the history is suspicious, 'hollow' or changes over time.

Cutaneous vasculitis

There are many potential causes of cutaneous vasculitis, such as drug-induced, viral and bacterial infections, autoimmune and connective tissue diseases including systemic lupus erythematosus (SLE), rheumatoid arthritis and inflammatory bowel disease, systemic vasculitis such as the antinuclear cytoplasmic antibodies

(ANCA)-associated vasculitides, and polyarteritis nodosa. Rarely, malignancies and leukaemia may trigger a paraneoplastic vasculitis.

However, 50% of all cases of cutaneous small vessel vasculitis remain of undetermined aetiology or 'idiopathic' after extensive investigation, and are presumed to be of post-infectious origin. Cutaneous vasculitis is clinically best diagnosed when lesions are palpable and on the lower limbs, although they may spread to the buttocks and arms (Fig. 15.1.5). Sharp edges with stellate or irregular shapes (referred to as 'retiform purpura') indicate full thickness ischaemia and are a sinister sign of small-medium vessel thrombo-embolic occlusions; for example, meningococcal infection, and calciphylaxis in, for instance, chronic renal failure.

Pyoderma gangrenosum

An acute presentation of pyoderma gangrenosum is frequently a differential diagnosis of cutaneous vasculitis. It may begin as a discrete painful

haemorrhagic pustule or grouped lesions that rapidly ulcerate, usually on the lower leg, causing larger lesions with neutrophilic inflammation with abscesses and necrosis, but no vasculitis on biopsy. It may be associated with inflammatory bowel disease, rheumatoid arthritis, blood dyscrasias, Behçet syndrome and malignancy, such as myeloma and leukaemia (Fig. 15.1.6).

Investigations for vasculitis

Send blood for a vasculitis screen including FBC, ESR, CRP, U&E, LFTs, hepatitis B and C serology, ANA, rheumatoid factor, ANCA, antistreptolysin O (ASO) titre, cryoglobulin screen, anticardiolipin and antiphospholipid screen, serum protein electrophoresis and complement (C₃/C₄) levels.

Send two sets of blood cultures prior to any antibiotic therapy, such as ceftriaxone 2 g intravenously, if meningococcal infection is possible. Send a fresh urine specimen for phase contrast

Box 15.1.2 Causes of a vesicular or bullous skin rash

Most common	Less common	Rare
Viral:	Erythema multiforme major ('target lesions' rash, plus one mucous membrane involved) or erythema multiforme minor (1–2 cm 'target lesions' only):	Porphyria cutanea tarda
• herpes zoster	• mycoplasma pneumonia	Epidermolysis bullosa
• herpes simplex	• herpes simplex	
Impetigo	• drugs such as sulphur, penicillins	
Scabies	• idiopathic (50%)	
Insect bites and papular urticaria	SJS and TEN with epidermal detachment and mucosal erosions:	
Bullous eczema and pompholyx	• drugs such as anticonvulsants, sulphonamides, NSAIDs and penicillins	
Drugs:	Staphylococcal scalded-skin syndrome (children)	
• sulphuramides	Dermatitis herpetiformis (gluten sensitivity)	
• penicillin	Pemphigus and pemphigoid	
• barbiturates		

NSAIDs, Non-steroidal anti-inflammatory drugs; SJS, Stevens–Johnson syndrome; TEN, toxic epidermal necrolysis.



FIG. 15.1.5 Palpable purpura due to vasculitis.

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microscopy, looking specifically for glomerular red cells and casts indicating renal involvement.

Arrange a biopsy, although this is usually performed after admission or dermatology referral to clinic. Send a fresh specimen for both immunofluorescence (Henoch–Schönlein purpura suspected) and culture (infection suspected), as well as a specimen in formalin for histology.

Management

Potential triggers (see above) should be sought and treated appropriately. General measures include rest and elevation of the legs, compression stockings and topical steroids. If systemic treatment is required, NSAIDs may be trialled before prednisolone. Antibiotics, steroids and cytotoxic immunosuppression are indicated based on the aetiology and severity of the disease, in consultation with a dermatologist.



FIG. 15.1.6 Pyoderma gangrenosum.

PRURITIC (ITCHY) Dermatoses

Itch can be localized or generalized and may present with or without rash. While not an urgent problem, itch must be recognized as being distressing to the patient. The causes are many and varied and the prevalence of chronic itch (like chronic pain) increases with age. See [Box 15.1.3](#) for causes of pruritus with or without skin disease.

Urticaria

Urticaria may be acute, relapsing or chronic ([Fig. 15.1.7](#)). It may also be a warning of impending anaphylaxis that necessitates immediate assessment for upper airway swelling, wheeze and/or hypotension (see Anaphylaxis, [Chapter 2.8](#)).

The causes of urticaria are heterogeneous and include immunological such as Immunoglobulin E (IgE-related), immune-complex or autoimmune; or non-immunological including physical, such as cold, heat, sweating, exercise, pressure, sunlight, water and vibration; drug-related, such

Box 15.1.3 Causes of pruritus with, and without, skin disease

With skin disease	Without skin disease
Drugs, scabies, pediculosis, insect bites, parasites (roundworm)	Hepatobiliary—jaundice, including primary biliary cirrhosis
Eczema	Chronic renal failure
Contact dermatitis	Haematological: <ul style="list-style-type: none"> • lymphoma • polycythaemia rubra vera
Urticaria	Endocrine: <ul style="list-style-type: none"> • myxoedema • thyrotoxicosis
Lichen planus	Carcinoma: <ul style="list-style-type: none"> • lung • stomach
Pityriasis rosea ('Herald' patch)	Drugs
Dermatitis herpetiformis (gluten sensitivity)	



FIG. 15.1.7 Urticaria.

as NSAIDs and radiocontrast media; or food and food additives. Alternatively, urticaria may be related to an underlying systemic condition such as infection, SLE or other vasculitis, malignancy including lymphoma, or urticaria pigmentosa (mastocytosis).

However, in many acute cases, no clear cause is found, and it is labelled 'idiopathic'. In chronic urticaria, defined as lasting more than 6 weeks, there is frequently no known aetiology, although autoimmune causes are eventually found in 30% to 40%. Classic urticaria appears as welts that are migratory and pruritic, and resolve without purpura/scars. High-dose antihistamines (2 to 4x the usual dose) are essential with or without concomitant oral prednisolone.

Scabies

Scabies is a common parasitic infection that must be considered in any patient presenting with itch. It is more common in the elderly, particularly nursing home residents, and returned travellers (both domestic and international.) Scabies may present with an eczematous and/or urticarial picture, usually without a pre-existing history of eczema. Diagnosis requires careful examination of finger web spaces, flexures, wrists and the instep of the feet, for scabies burrows, and the penis and scrotum for scabetic nodules.

Crusted 'Norwegian' scabies is predisposed to by glucocorticoid therapy, organ transplant and HIV infection and in the elderly. Application of 5% permethrin cream from neck down for 42 hours, and repeated in 1 week, is first-line therapy. Oral ivermectin (200 mcg/kg) PO stat and repeated in 1 week should be considered as second-line therapy or in severe cases ([Fig. 15.1.8](#)).

Tinea

Tinea incognito refers to tinea corporis, which has been suppressed and modified in appearance due to the inappropriate use of topical steroids. The topical steroid suppresses the erythema and allows for excessive growth of the causative fungus. It is common in the feet (tinea pedis), hands (tinea manus) and genitals/buttocks (tinea cruris) especially in diabetics, the elderly and immunocompromised patients.

Investigations for pruritus

Send blood for the following:

- FBE for eosinophilia (a non-specific finding seen in atopy, scabies and parasitic infections) and to look for iron-deficiency anaemia
- iron studies for deficiency (a very common cause of pruritus)
- glucose level to screen for diabetes



FIG. 15.1.8 Crusted 'Norwegian' scabies.

- EUC to exclude renal failure
- LFTs to exclude hepatic impairment with jaundice, including primary biliary cirrhosis
- serum protein electrophoresis to look for a monoclonal gammopathy, particularly in patients over 70 years
- thyroid stimulating hormone to exclude hypothyroidism or hyperthyroidism
- coeliac serology, such as IgG immunoglobulin A (IgA) tissue transglutaminase antibodies.

Take skin scrapes from any suspicious areas for fungal culture and microscopy. In suspected scabies, send material to look for scabies mites, eggs or faeces on microscopy.

Management

General measures include avoiding triggers, in particular overheating and over-drying. Rehydrating the skin with good emollient is essential. Antihistamines for short-term use, particularly if sleep is impaired, such as promethazine 10 mg 8-hourly or chlorpheniramine 4 mg 6-hourly, with a clear warning to avoid alcohol and not to drive or operate machinery.

Attempt to identify a cause in every case. **Resist prescribing prednisolone for an itchy dermatosis when no cause has been identified.** Arrange appropriate investigations and refer the patient for dermatological follow-up.

ECZEMA AND PSORIASIS

Eczema

Atopic eczema is a common skin complaint often affecting the flexures (Fig. 15.1.9). It may present as an emergency in a number of ways. See Table 15.1.5 for an overview of aetiology, clinical features and management principles.



FIG. 15.1.9 Atopic flexural eczema.

Eczema is one of the most common causes of erythroderma. See earlier for management principles, which should always involve a dermatologist and may require intensive care unit admission.

Discoid eczema

Discoid eczema presents as discrete coin-like or 'nummular' erythematous plaques that may develop significant exudate and crusting. 'Satellite' lesions are common and skin involvement is often progressive, as one area of involvement 'drives' other areas of skin to become eczematous.

Investigation

Take swabs to exclude staphylococcal super-infection.

Management

Prescribe in bulk quantities a potent topical steroid, such as mometasone furoate 0.1% or betamethasone dipropionate 0.05% cream or ointment. Advise the patient that GENEROUS application once or twice daily may be required until all active eczema is resolved. Aggressive initial management for 2 or more weeks may be required, before gradually tapering topical steroids. Bleach baths are critical (12 mL/10 L water, bath oil and bath salts) as are emollients.

Allergic contact dermatitis

Allergy to plants typically presents in a 'streaky' or linear pattern. A severe facial flare of eczema may suggest an airborne allergen as a trigger. The use of hair dyes following a 'henna tattoo' (which may have been applied months or years before) can result in severe scalp and facial dermatitis, as henna used on hair is adulterated with paraphenylenediamine. The patient becomes sensitized to this compound, which is found in most hair dyes.

Some allergens are activated by the ultraviolet (UV) in sunlight to become symptomatic. This occurs in phytophotodermatitis (often a streaky or linear dermatitis on exposed areas that may be blistered or hyperpigmented), which is seen after contact with photosensitizing compounds found naturally in some plants, fruit and vegetables. Nickel sensitivity is a common cause of reactions to jewellery, particularly costume jewellery and, occasionally, to the clasp of a bra. These causes may or may not be obvious to the patient, so a careful focused history is essential.

Irritant contact dermatitis

The hands are commonly involved and may become secondarily infected. Patients may be severely incapacitated if both hands are affected and may need admission. Patients commonly have an atopic background, especially atopic eczema. Ask the patient how many times he or she washes the hands each day, as irritant contact dermatitis is common in health care workers, new parents and avid gardeners. Soap-free cleansers are critical, as are hand gloves and moisturizers.

Eczema herpeticum

Eczema herpeticum is a widespread herpes simplex infection complicating a pre-existing skin disease, most often atopic eczema. Consider this in any patient with an acute flare of eczema, particularly if the skin is painful. It presents as an acute eruption of monomorphic vesicles and/or erosions often with purulent exudate and crusting, but not necessarily with herpetiform grouping.

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Table 15.1.5 Atopic eczema: acute attacks and complications

	Infective eczema		Erythroderma	Acute eczema	
	Eczema herpeticum	Impetiginized eczema	Unstable eczema	Psychological	Contact
Cause	Infection with herpes simplex, varicella, which can rapidly disseminate over the skin	Staphylococcal	Due to many factors systemic or external	Stressors	Allergen?
Examination	Grouped locally or generally Pinhead-sized papules or vesicles Clear or closed pustules Excoriated sharply defined circular erosions	Discharge and weeping Yellow and crusted blisters or erosions	Total body redness Scale or weeping. Pruritis Hypothermia Fever, sepsis	Severe red pruritus Disturbed sleep	Sharp edges Localized
Management	Antivirals if severe, early and eyes at risk	Oral antibiotics. Antiseptic (tricosan) soaks and wet dressings	Admission Oral steroids Ciclosporin	Admission topicals Oral steroids Paraffin, etc.	Oral steroids Admission

A preceding herpetic cold sore may or may not have been present. Some episodes present as a severe systemic illness with high fever, malaise and a widespread generalized eruption. However, there may be no systemic disturbance and the eruption may be quite localized, often to areas of pre-existing eczema.

Ocular HSV infection should be suspected if there is periorbital involvement or if ocular symptoms are present, such as eyelid oedema, tearing, photophobia, chemosis or preauricular lymphadenopathy, whether the eruption involves the face or not. An urgent ophthalmology opinion should be sought for complications, such as corneal ulceration, scarring and blindness.

Investigations

Viral swabs for PCR should be taken of vesicle fluid or the base of an erosion to confirm the diagnosis of HSV. Bacterial superinfection is common, so send a swab for bacterial MCS as well.

Management

Antiviral therapy is essential, such as valaciclovir 1 g TDS for 7 days. Antiviral prophylaxis may be required for recurrent attacks. If secondary bacterial infection is suspected, start an anti-staphylococcal antibiotic, such as cephalexin 1 g BD for 5 days. Optimizing the topical management of eczema is also critical.

Psoriasis

Psoriasis may present acutely in the following patterns:

- Erythroderma: an unstable state that may be caused by systemic or external factors, including treatment. Clinically, it is indistinguishable from the other causes of erythroderma, as there is total body redness with no typical features of psoriasis. At presentation, hypothermia, sepsis and high-output cardiac failure must be recognized.
- Pustular psoriasis: triggered by systemic or external factors (including pregnancy), topi-



FIG. 15.1.10 Generalized psoriasis.

cal treatments, medication and oral steroids. Examination reveals yellow sterile pustules on plaques, diffuse generalized (Fig. 15.1.10) or localized red areas beginning around the paronychium of the digits or pulp. Arthritis may be present, and consider Reiter syndrome if there is a history of gastrointestinal or genitourinary symptoms. Hypocalcaemia may develop if the pustular psoriasis is generalized.

- Immune-activated psoriasis flares: caused by bacterial or viral infective foci in respiratory, bowel, gallbladder or urinary bladder sites. Typically, there are new guttate lesions or flares in old psoriatic plaques. Often there have been similarly triggered attacks in the past. Streptococcal pharyngitis is a common precipitant.
- Flare or rebound psoriasis: following cessation or poor compliance with therapy or after treatment with oral steroids.

- Palmoplantar psoriasis: may be pustular or may show a keratoderma (thickened skin), which can be difficult to distinguish from eczema, or even inflammatory tinea pedis. Patients are debilitated and unable to walk or care for themselves and therefore may require admission.

Investigations for acute psoriasis

Send blood for FBE, urea, electrolytes and creatinine (UEC) and LFTs, including a serum calcium (which may be low with pustular psoriasis). Send other investigations for systemic complications such as infection, including a skin swab and/or blood cultures, as well as monitoring for the side effects of therapy. A skin biopsy is usually performed in the ward or dermatology clinic if the diagnosis is in doubt.

Management

Treatments include UV therapy, methotrexate, cyclosporin, acitretin or biological therapy. These all require a dermatology consultation and careful review of past treatment. Admission is required if the patient has extensive areas involved, is systemically unwell or unable to manage at home.

Rotating therapies in psoriasis may be beneficial and a past treatment failure does not necessarily indicate that treatment will always be ineffective.

OTHER DERMATOSES

Skin cancer

Patients may present to an ED with lesions they, or a concerned family member or partner, are worried about. Important differential diagnoses not to miss include melanoma and non-melanoma skin cancer, including squamous cell and basal cell carcinoma. Refer the patient for prompt assessment by a dermatologist if the lesion looks suspicious, which will usually require a biopsy.

Herpes zoster

The first manifestation of herpes zoster is usually pain, which may be severe and accompanied by fever, headache, malaise and regional lymphadenopathy. Closely grouped red papules evolve to classical vesicles and then often pustules, in a dermatomal distribution. Rarely, the eruption may be multi-dermatomal or bilateral, particularly if the patient is immunosuppressed.

Diagnosis can be a challenge unless the dermatomal distribution of the eruption is appreciated. Vesicles on the side of the nose indicate involvement of the nasociliary branch of the ophthalmic division of the trigeminal nerve, which also innervates the cornea. Nasal herpetic infection (Hutchinson sign) may precede or accompany ophthalmic involvement, which necessitates urgent ophthalmological referral. Vesicles within the external auditory meatus associated with deep ear pain and lower motor neuron facial nerve palsy is the classic triad of Ramsay Hunt syndrome. Early diagnosis, and treatment with oral prednisolone and antivirals, is indicated.

Investigations

Take swabs for bacterial MCS and viral PCR for VZV to confirm the diagnosis.

Management

Prompt treatment with antiviral medication, such as famciclovir 250 mg tds, when seen within 72 hours of vesicle eruption, may prevent post-herpetic neuralgia.

CONTROVERSIES

- The treatment of TEN is controversial, with IVIG, prednisolone and cyclosporin at one time or another being advocated and then discredited. Currently, evidence suggests that IVIG improves survival. Qualifying criteria for IVIG therapy for TEN or SJS/TEN overlap and include: (1) diagnosis by a dermatologist, (2) body surface area of 10% or more, and (3) evidence of rapid evolution. IVIG should be initiated as quickly as possible, preferably within 24 hours of diagnosis. As it does not always limit the progression of TEN, further investigation is required. Several studies have concluded that corticosteroids did not stop the progression of the disease and were even associated with increased mortality and adverse effects, particularly sepsis.
- The use of immunomodifying agents and immunosuppressants, with their potential for toxicity, opportunistic infections, unusual side effects or severe rebound of cutaneous disease following cessation or poor compliance.
- The take-up of teledermatology makes it easier to obtain a second opinion in isolated areas or to triage patients better for dermatological review. Studies have now shown that teledermatology can provide rapid and accurate diagnosis and treatment advice for dermatological presentations to ED. Research is in progress to improve telemedicine services.

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SECTION
16

OCULAR EMERGENCIES

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16.1 Ocular emergencies

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ESSENTIALS

- 1** Always test and record visual acuity: use pinhole if usual spectacles are not available.
- 2** Chloramphenicol eyedrops are not a universal panacea.
- 3** Pain: sharp/scratchy = anterior (cornea or conjunctiva); aching = intraocular (intraocular pressure or inflammation)

Trauma

- 1** Computed tomography scan/x-ray where bony or globe penetration injury is suspected.
- 2** Remove prolapsed ocular tissue or protruding foreign bodies only in an operating theatre
- 3** Copious free irrigation for all corneal acid or alkali burns.

Unilateral red eye

- 1** Bacterial keratitis requires specific, intensive, antibiotic eyedrops.
- 2** Acute angle closure produces a hard, inflamed eye with a steamy cornea and a fixed, mid-dilated pupil.

Loss of vision

- 1** Triage cases of sudden vision change with care: painless can still be urgent.
- 2** Test the pupils for a relative afferent pupillary defect, which is an objective sign.
- 3** Local ocular pathology does not cause a visual field defect respecting a vertical midline.
- 4** Central retinal artery occlusion and endophthalmitis require immediate referral to an ophthalmologist.
- 5** Recent onset of distorted vision requires ophthalmic review within a few days to exclude exudative age-related macular degeneration.
- 6** New onset of floaters, particularly in association with flashes, requires dilated examination to exclude retinal detachment.
- 7** Elderly patients with acute visual failure have giant cell arteritis until proven otherwise and need oral steroid cover until the diagnosis is excluded.

Introduction

Acute ocular presentations are common. A seemingly trivial trauma may mask a more serious underlying injury. Similarly, a relatively transient episode of visual loss with no abnormality found on examination may herald blinding disease. Therefore all eye presentations in an emergency department (ED) should be carefully triaged and evaluated with the necessary equipment. Determine the patient's prior visual status, including the wearing of glasses or contact lenses and the use of any ocular medication, which can provide useful hints.

Basic ocular testing equipment should include:

- Snellen 6-m chart
- black occlusive paddle with multiple pinhole perforations
- slit-lamp biomicroscope: to examine the anterior segment and for removal of foreign bodies
- portable slit lamp: to examine reclining patients
- intraocular pressure (IOP)-measuring device (e.g. Tono-pen or iCare tonometers, which are portable, accurate and easily used)
- Fundus biomicroscopy lens or direct ophthalmoscope

Visual acuity testing

Vision is tested by a distance Snellen chart, using a pinhole device, if necessary, to provide 'corrected' vision: 'The patient sitting at 6 metres sees what a normal person sees at ... (record value)' (e.g. 6/18). Vision less than 6/60 Snellen may be graded by the patient's ability to count fingers (CF) at a measured distance, discern hand movements (HM) or to project the direction of a light (PL) from various angles. The eye not being tested must be completely shielded by an opaque occluder.

Emergency eye trolley setup

Examining equipment

- Torch
- Magnifying loupe
- Desmarres lid retractors/lid speculum
- Sterile dressing packs
- Normal saline for irrigation
- Fluorescein strips (sterile)
- Topical anaesthetic (e.g. tetracaine 1%).

Treating

- Mydriatics (dilating): tropicamide 1%, cyclopentolate 1%
- Miotic (constricting): pilocarpine 2%
- Antibiotic ointment (e.g. chloramphenicol)
- Pressure control: acetazolamide 250 mg tablets; ampoules 500 mg (Diamox)
- Eye pads, plastic shields, skin adhesive tape
- Cotton-tipped applicators (sterile)
- 25 G, 23 G disposable hypodermic needles (foreign body removal).

OCULAR TRAUMA

History

The incidence of injuries varies with the environment and protective measures taken. The major injuries result from blunt trauma or penetrating injuries to the globe, with or without the retention of a foreign body. Mechanical interference with eye movement may result from orbital injury, either haematoma or interference with muscle function. Similarly, neuro-trauma may disturb the visual pathways or ocular motor nerves.

Examination

After an eye toilet to remove any debris, clot or glass from the eyelids, acuity is tested. Fresh local anaesthetic drops—preferably single use Minims—may be instilled to ease discomfort. Reassurance and extreme gentleness in subsequently examining the eye will allow a more definite assessment to be made. With penetrating trauma, any external pressure on the eye may result in ocular structures being squeezed out of the wound, drastically worsening the prognosis. Desmarres retractors (*Fig. 16.1.1*) can be useful to open the lids yet avoid globe pressure. To open lids that are adherent due to blood or discharge, gently bathe with sterile saline. Wipe the eyelid skin dry and apply gentle distractive pressure to skin below the brow and below the lower lid (i.e. over bony orbital rim) to open the lids.

Investigation

If a penetrating injury is suspected, perform a computed tomography (CT) scan or x-ray to exclude a radiopaque intraocular foreign body



FIG. 16.1.1 Desmarres retractors for opening eyelids.

(IOFB). If there is any possibility of metallic IOFB, magnetic resonance imaging (MRI) scans are contraindicated. When an adequate examination cannot be made, or where occult perforation is suspected, examination under anaesthesia is necessary.

Management of specific injuries

Superficial injury

Corneal abrasion

The corneal epithelium is easily dislodged by a glancing blow from fingernails, twigs, stones or a paper edge. The trauma produces an acute sensation of a foreign body, with light sensitivity and excessive tearing. Lash ingrowth (**trichiasis**) may cause small abrasions.

Stain with fluorescein and measure the size of the epithelial defect. Antibiotic ointment (chloramphenicol) is instilled and an eye pad applied if a local anaesthetic is used. The condition heals spontaneously within 24 to 48 hours. Pain is due to the epithelial defect and also to reflex ciliary spasm, which may require short-acting cycloplegics, such as cyclopentolate 1%, in addition to oral analgesia.

Recent publications have suggested that topical **local anaesthetic** can safely be used for short periods as analgesia.¹ This is in contrast to a long-standing edict against such use—due to toxic effects that may delay corneal healing^{2,3}—and represents a divergence in practice between emergency physicians and ophthalmologists.⁴ The handful of small, controlled trials has yielded equivocal evidence on safety and efficacy.¹ As neither patient attendance for follow-up nor discarding of excess drops can be guaranteed, ongoing caution is urged as blinding side effects

have been documented from overuse of topical anaesthetic.⁵ Use is absolutely contra-indicated in pre-existing dry-eye conditions (e.g. Sjogren syndrome).⁶ If deployed, use should be strictly for no more than 24 hours and the eye must remain protectively covered throughout.

Corneal foreign body

Small ferrous particles rapidly oxidize when adherent to the corneal epithelium, producing a surrounding rust ring within hours. Remove rusted particles with adequate topical anaesthesia and a bevel-up 25-gauge needle under a slit-lamp microscope. A difficult or adherent rust ring can be loosened by applying antibiotic ointment and padding for 24 hours, after which it is easily shelled out with the edge of a similar needle. Mechanical dental burrs can be difficult to sterilize and may cause large areas of epithelial removal and delay the patient's return to work. Wooden splinters are particularly dangerous as they may easily penetrate the eye and cause violent suppuration. In all suspected foreign body injuries, evert the upper and lower lids and examine with suitable lighting, magnification and fluorescein. The conjunctival fornices may be swept gently with a moist cotton bud under topical anaesthesia.

Technique for upper eyelid eversion: the patient must look down at all times; grasp the upper lid lashes and draw the lid down, then with a cotton bud in the other hand, depress the lid 11 mm above the central lid margin (i.e. above the tarsal plate) and counter-rotate the grasped lashes and lid around this cotton-bud fulcrum. The lashes may be held against the superior orbital margin with a finger and the cotton bud removed. When the examination is complete, release the lid and allow the patient finally to look up and the lid will revert to the normal position.

Contact lens wear

Contact lens wearers may present with a foreign body sensation from multiple potential causes. Fluorescein staining and upper lid eversion will identify a 'lost' lens. Unless microbial keratitis is suspected, most cases should be told to desist with contact lens wear and be directed back to their primary eye-care provider.

Conjunctival laceration

Unless large, this rarely requires suturing. However, it is vital to ensure that this superficial laceration does not hide a deeper penetration of the globe. After instillation of local anaesthetic, the conjunctiva may be gently moved aside with a cotton bud to examine the bed of the laceration.

Penetrating injury

A careful history of possible penetrating trauma is crucial. Occupational trauma may be due to

16.1 OCULAR EMERGENCIES

high-speed penetrating metal fragments. Agricultural trauma often involves heavily contaminated implements. Seatbelt legislation has markedly reduced the incidence of penetrating eye injuries in road trauma, but eye problems can occur from airbag deployment and still occur from violent head and facial trauma.^{7,8}

The eye is examined gently without pressure, as previously described. The penetration may be evidenced by an obvious laceration or the presence of prolapsed tissue with collapse of the globe. Conjunctival oedema (chemosis) and low IOP may indicate an occult perforation or bursting injury.

When a penetrating injury is either suspected or established, the patient must be transferred without delay to a centre where appropriate surgical facilities are available. During transport, cover the eye with a sterile pad and a plastic shield; prevent vomiting with anti-emetics; fast the patient and give intravenous fluids as necessary. Extruded tissue or projectiles should not be removed: intraocular contents will surely follow. Removal can only be undertaken in the controlled environment of an operating theatre. Prognosis depends on the extent of globe disruption.

Blunt injury

Concussion of the globe may cause tearing of the iris root, resulting in blood in the anterior chamber (**hyphaema**). A hyphaema greater than one-third of the anterior chamber usually indicates some damage to the drainage angle and may also be associated with concussive lens damage. Uninterrupted absorption of the hyphaema is essential. Traditional treatment has been admission to hospital and sedation, with the affected eye padded and the patient nursed semi-recumbent to encourage sedimentation of the blood in the anterior chamber to clear as much of the angle as possible. The application of Atropine 1% drops to 'splint' the ocular interior is logical but theoretically risks a re-bleed with the initial dilating effect.

A hyphaema may cause considerable pain due to raised IOP. To lower the pressure, oral or intravenous acetazolamide 500 mg is initially required, with topical IOP-lowering drops in the medium term. Pain is relieved by paracetamol or narcotics, with anti-emetics if necessary. Anti-platelet agents in any form should be avoided due to increased risk of secondary haemorrhage.

Bleeding recurs in up to 10% of patients, usually due to early mobilization in those with extensive iris damage, so that the patient should ideally remain rested until the blood has completely cleared from the anterior chamber. Subsequent ophthalmic follow-up will include assessment of the drainage angle for glaucoma risk and a fundus exam to exclude a traumatic retinal tear.

Smaller hyphaemas may be managed on an outpatient basis, perhaps with rest at home and the use of atropine drops, but can be sensibly considered only if daily IOP monitoring is not required.

Blunt trauma may be associated with assorted facial fractures including **orbital blow-out fracture**. Symptoms may include (particularly) vertical diplopia in the case of orbital floor fractures. Urgent repair is seldom required except where CT scanning demonstrates muscle entrapment in association with bradycardia, nausea and vomiting (**oculo-vagal reflex**), or in a young person with marked motility restriction and little external evidence of trauma ('**white-eyed blowout**').⁹ Indications for subacute surgical repair are residual, functionally significant diplopia (primary position or downgaze) or uncosmetic enophthalmos.

Chemical burns

The first principle of management—at the location where the injury was sustained—is copious irrigation of the eyes for at least 10 minutes with clean running water. *Do not delay* to await the availability of proprietary eye irrigants. Chemical trauma requires priority assessment on arrival at an emergency centre and immediate irrigation if this has not been done or has been inadequate, with the aim of achieving a neutral pH.

Alcohol and solvent burns occur from splashes while painting and cleaning. Although the epithelium is frequently burnt, it regenerates rapidly. The condition is very painful initially, but heals with a topical antibiotic and patching for 48 hours.

Alkali and **acid** burns are potentially more serious because of the ability of the burning agent to alter the pH in the anterior chamber of the eye and inflict chemical damage on the iris and lens. Caustic soda, lime and plaster—commonly used in industry—may inflict painful, deep and destructive ocular burns. Splashes of acids, such as sulphuric and hydrochloric, if concentrated, will cause equally destructive injury.

To assess the ocular burn, use topical anaesthetic drops and fluorescein staining to determine the area of surface injury; evert the eyelids, examine the fornices carefully and sweep gently with a cotton bud to ensure there is no particulate caustic agent remaining. Compress limbal blood vessels with a cotton bud: extensive stasis in peri-limbal vessels is a poor prognostic sign.

Chemical burns where the epithelium is intact or minimally disturbed can usually wait 24 hours before review by an ophthalmologist. Burns involving more than one-third of the epithelium and the corneal edge, with any clouding of the cornea, are potentially more serious as subsequent melting of the cornea by collagenase action may ensue. These burns should all be further irrigated in the ED with a buffered sterile solution, such as Ringer lactated solution

(Hartmann solution). The irrigation should continue until the tears are neutral to litmus testing.

More serious caustic injuries have shown a significant improvement in outcome with the introduction of 10% citrate and ascorbate drops, commencing 2-hourly for 48 hours and reducing over the week, in combination with 1 g oral ascorbic acid daily. This regimen has an inhibitory effect on corneal melting. Topical antibiotic (e.g. chloramphenicol) is used; topical steroid is used under ophthalmic supervision.¹⁰

Flash burns

Exposure of the eyes to prolonged or severe ultraviolet radiation results in widespread punctate epithelial loss from the corneal surface. This is most frequently seen in welders who have not used sufficient eye protection while working, or in adjacent, unprotected observers. Patients complain of delayed onset of moderate to severe ocular discomfort with excessive watering and foreign body sensation.

Ocular examination shows widespread punctate fluorescein staining, usually with no ulceration and no evidence of foreign body present. Apart from welding, other instances in which excessive ultraviolet radiation may be encountered are in alpine snowfields and tanning beds.

Treatment is supportive with oral analgesia, topical lubricants and explanation of the cause and likely time course. The symptoms generally settle within 24 to 48 hours as the epithelium recovers. Caution is urged in any decision to dispense local anaesthetic drops for analgesia, as noted previously.

UNILATERAL RED EYE

Any history of predisposing trauma should be obvious: these conditions have been outlined in the previous section. The type of pain can be useful in distinguishing the location of pathology: a sharp or scratchy discomfort implicates cornea or conjunctiva, whereas a deep-seated aching pain is likely intraocular inflammation or elevated IOP.

Acute infectious keratitis

The usually smooth surface of the corneal epithelium hinders the adherence of infectious agents and the rapid repair of any defect in the epithelium limits the likelihood of penetration by such pathogens. The flow of tears over the surface washes debris away and contains antibodies and lysozymes. If these defences are impaired in any way, there is the possibility of penetration into the corneal stroma, and active infection may occur.

Bacterial keratitis is characterized by a focus of infection with an associated inflammatory

response. Patients complain of sharp pain, redness, watering and a decrease in visual acuity. Fluorescein staining shows an area of ulceration over the infection, which appears as an opacity or area of whiteness within the cornea. Marked conjunctival and episcleral injection results in a unilateral red eye. Evidence of intraocular inflammation is usually present, with cells and flare being seen in the anterior chamber with oblique, narrow-beam slit-lamp examination. In severe cases, a collection of inflammatory cells can be seen in the inferior part of the anterior chamber as a sediment, called a **hypopyon**.

An attempt should be made to identify the infectious agent prior to commencing appropriate antibiotic treatment:

Corneal scraping technique

A specimen is taken via a scraping for microbiological assessment, including Gram staining and culture. Under topical anaesthetic, using a preservative-free single-use dispenser of benoxinate or tetracaine, a sterile, bevel-up 25 or 23 G needle held flat to the corneal surface is used to gather a small specimen from the local infiltrate. This is transferred directly to glass slides and also plated on to HB and chocolate agar plates for culture. Fungal cultures may be indicated.

Antibiotic therapy is not delayed until the results are available, but is commenced on a broad-spectrum basis, such as the intensive use of a fluoroquinolone eye drop (e.g. G. ciprofloxacin or ofloxacin) on an hourly basis. Chloramphenicol drops qid are not adequate treatment. Daily monitoring with slit-lamp examination is mandatory and severe infections require hospital admission. This regimen can be modified when culture and sensitivity results are available.

Herpes simplex keratitis usually presents initially as an infection of the epithelial cell layer, although with recurrent episodes, stromal involvement may be seen. It is most often a unilateral infection. As with other herpetic infections, it is not possible to eradicate the virus, but limitation of inflammatory-mediated damage is important. Patients complain of a scratchy, foreign body sensation, redness, watering and a variable decrease in visual acuity. On examination, the areas of infected epithelium can be seen as a branching irregularity or **dendrite** on the surface of the eye (Fig. 16.1.2). Multiple dendrites may be scattered over the surface, particularly in immunocompromised patients. These are best seen when the cornea is stained with fluorescein and viewed with the slit lamp.

Treatment is directed to clearing the virus from the cornea to promote epithelial healing and to limit stromal involvement and damaging corneal inflammation. A single pass with a sterile cotton bud rolled across the ulcer will deplete the viral load; an antiviral ointment (aciclovir) is

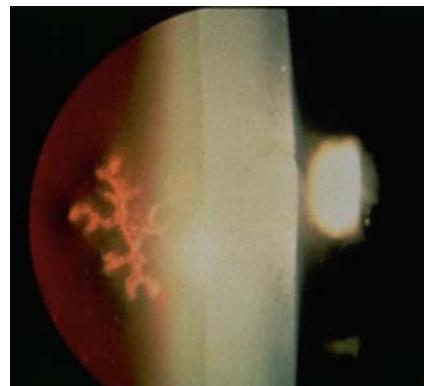


FIG. 16.1.2 Herpetic dendrite.

then instilled five times daily until there is resolution of the epithelial lesions and then ceased as long-term usage may be toxic to the unaffected corneal epithelium. Steroid eye drops are contraindicated except under the strict supervision of an ophthalmologist.

Adenoviral conjunctivitis

This highly contagious conjunctival infection is a common cause of viral conjunctivitis.

Initial presentation is usually a short history with a complaint of discomfort or swelling, watery discharge, redness, and ocular foreign body sensation. Commonly unilateral on initial presentation, it may ultimately extend contralaterally. There is often a history of either recent upper respiratory tract infection or contact with someone with a current episode of adenoviral infection.

Examination shows a follicular pattern of conjunctivitis, particularly in the sub-tarsal conjunctiva. In severe cases, subconjunctival haemorrhage and pseudomembrane formation can occur. There may be crusting of the lid margin and eyelashes. Uncommonly, the cornea can be involved with focal subepithelial infiltrates noted with minimal overlying epithelial disturbance. This is an immune response and can affect the visual acuity if in the visual axis. There is no evidence of intraocular inflammation. **Tender pre-auricular lymphadenopathy** on the affected side is characteristic.

It is an acute, self-limiting disease (2 to 3 weeks) for which no specific treatment is required (or available): there is no evidence that topical antibiotics or antiviral agents affect the course of the infection. Lid hygiene, lubricants and cold compresses may be helpful for symptomatic relief. **Topical steroid eyedrops are only given under strict ophthalmic supervision for corneal infiltrates if vision is affected.** Highlight the contagious nature of this condition and enforce standard restrictions on shared linen, towels, etc.

Acute iritis

Acute anterior uveitis (AAU) is an inflammatory response in the iris and ciliary body. As part of this response there is an increase in vascular dilatation and permeability with the release of inflammatory mediators and cells.

Acute iritis (AI) is usually an idiopathic condition with no systemic cause or association. Less commonly, associated conditions may include HLA-B27-related disease including ankylosing spondylitis, sarcoidosis, inflammatory bowel disease (including ulcerative colitis and Crohn disease), connective tissue disorders and ocular infection, including herpetic disease, toxoplasmosis, syphilis and tuberculosis. A complete history will often give clues to these associations, which are teased out in the post-acute phase.

AI is generally unilateral, although bilateral involvement is seen. It is characterized by pain, redness and visual disturbance. The pain is aching and constant, with photophobia due to pupillary movements in an inflamed iris. Dilatation of the conjunctival and episcleral vessels is apparent, particularly in the vessels adjacent to the corneal limbus, often referred to as **limbal flush**. Visual acuity can be reduced by varying degrees depending on the severity of inflammation. The pupil is constricted (**miosis**) due to irritation, but may be irregular due to 'sticky' iris adhering to the anterior lens surface (**posterior synechiae**).

Slit-lamp examination of the anterior segment with a narrow, oblique beam will reveal evidence of increased vascular permeability, seen as fibrin clumps, flare and inflammatory cells in the aqueous released from the vessels. In some cases, small collections of neutrophils can be seen aggregating on the posterior surface of the cornea as **keratic precipitates** (Fig. 16.1.3). The IOP may be raised.

In cases of severe inflammation, cells can accumulate in the inferior anterior chamber and a sediment level can be seen as a hypopyon. The presence of a hypopyon should lead to a search for an infectious cause, generally either keratitis or endophthalmitis.

In all cases of iritis is essential that a complete fundal examination be performed through a pharmacologically dilated pupil in order to determine the presence of inflammatory disease in the posterior segment. Thus a timely ophthalmic referral is indicated.

Treatment of AI is directed towards resolution of the inflammatory response and limiting any ocular damage from this inflammation. The mainstay of treatment is intensive, topical steroid eye drops (prednisolone acetate 1%, up to hourly in severe cases). In severe cases, orbital steroid injections or oral steroids may be necessary. Mydriatic eye drops (G. tropicamide 1% or cyclopentolate 1%) are used to break any lens–iris

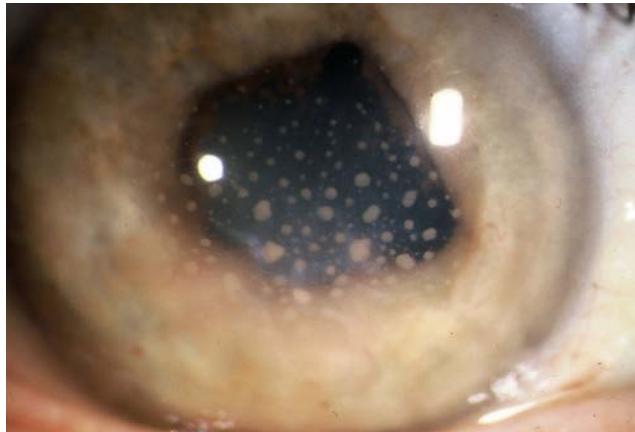


FIG. 16.1.3 Anterior uveitis with keratic precipitates and adhesions between the iris and anterior lens surface (posterior synechiae).

adhesions and to limit the extent of permanent adhesions. In 'splinting' the iris, these drops also provide pain relief by limiting pupil movement.

As the degree of inflammation decreases on slit-lamp examination, the topical treatment is decreased in frequency. The long-term use of topical steroid drops is not without risk and can be associated with the development of glaucoma, cataract and concurrent ocular surface infection, such as herpes simplex keratitis.

Endophthalmitis

Endophthalmitis is characterized by progressive inflammation of the vitreous and aqueous humours of the eye. Although it usually presents with reduced vision, ocular redness and ocular pain, characteristically in the presence of hypopyon and hazy ocular media, any of these features may be absent. The term 'endophthalmitis' is usually used to refer to cases of inflammation secondary to infection. 'Endogenous endophthalmitis' refers to cases of haematogenous spread of infection, while 'exogenous endophthalmitis' is used where infection is due to ocular trauma, intraocular surgery or intravitreal injection. Endogenous endophthalmitis may be bilateral.

Endophthalmitis must be urgently treated by an ophthalmologist to avoid loss of vision and of the eye itself. Especially in exogenous cases, this usually starts with the procedure of 'tap and inject'. This refers to obtaining a vitreous and often aqueous aspirate for microbiology and culture and often other testing for diagnostic purposes, followed by intravitreal injection of antibiotics. In endogenous cases a systemic work-up for the source of infection should be performed. Recently an increasing number of patients—particularly diabetics—with pyogenic liver abscesses due to *Klebsiella pneumoniae* have been developing severe endogenous

endophthalmitis^{11,12}: beware the septic patient complaining of reduced vision.

Although the choice of intravitreal antibiotics is governed by the clinical situation, the standard initial treatment is with vancomycin and ceftazidime. Consideration should also be given to the possibility of fungal infection, which would require antifungal agents. Vitrectomy surgery is sometimes required in more severe cases to reduce the infectious and inflammatory burden in the avascular vitreous gel.

The retina may also be affected by viruses, especially in immunosuppressed states. The most common scenarios are cytomegalovirus **retinitis**, characterized by haemorrhages in areas of retinal opacity known as a 'cottage cheese with ketchup' appearance, and **acute retinal necrosis** (ARN), which features zonal retinal necrotic opacity and often severe ocular inflammation, and which most commonly arises from herpes zoster or herpes simplex infection.

Acute primary angle-closure (glaucoma)

Acute primary angle-closure (APAC) is characterized by an acute impairment of the outflow of aqueous from the anterior chamber in an anatomically predisposed (crowded) eye. This results in a rapid and severe elevation in IOP. Population mean IOP lies between 10 and 21 mm Hg but, in cases of APAC, can rise to >60 mm Hg. This is manifested as severe **pain**, blurring of vision and redness. The pain may be severe enough to cause nausea and vomiting and may be poorly localized to the eye. Visual disturbance can be preceded by **halos** around lights and, in established cases, is due to corneal oedema. Relative hypoxia of the pupillary sphincter due to elevated pressure results in a pupil unresponsive to light stimulation. The pupil is classically fixed and **mid-dilated** (in contrast to the miosis

of iritis). The associated inflammation induces congestion of conjunctival and episcleral vessels. (The term 'acute angle-closure glaucoma' is no longer regarded as accurate, as there may be no optic nerve head cupping or visual field loss—the features that define glaucoma—at the acute presentation.)

Treatment of APAC is aimed at lowering the IOP and allowing the flow of aqueous from the posterior to the anterior chamber. Acetazolamide 500 mg intravenously and/or topical apraclonidine (lopipidine) or brimonidine (Alphagan) may be effective in acutely lowering the pressure and thereby reducing pain. If ineffective, subsequent constriction of the pupil with 2% pilocarpine, a parasympathomimetic, may alleviate the forward bowing of the iris, relieve the pupil block and re-establish aqueous flow and angle drainage. One drop is initially instilled every 5 minutes for 15 minutes and then half-hourly. However, if the pressure is very high the ischaemia induced will render the pupillary sphincter unresponsive to the pilocarpine. In these cases, it may be necessary to move to early laser treatment.

A laser peripheral iridotomy (PI) is performed using the yttrium:aluminium:garnet (YAG) laser to allow aqueous permanently to bypass the pupil and remove the risk of further episodes of APAC. This may be done acutely if corneal oedema does not preclude an adequate view. The anatomical predisposition to APAC is usually bilateral: miotics (G. pilocarpine 2% qid) are also instilled in the unaffected eye until YAG PI can be done (electively).

Laser iridoplasty—an alternative technique used when corneal oedema is severe—requires specific expertise.

SUDDEN LOSS OF VISION

Introduction

Acute visual failure is any acute loss of visual acuity, visual field or colour vision. Most of the sinister causes of acute visual failure are *painless* (Table 16.1.1) and the absence of apparent distress may result in the patient being triaged in error to a non-acute review. Effective emergency management depends upon rapid recognition of those conditions for which acute therapy is available (Table 16.1.2). Some conditions have no effective therapy or are more appropriately managed on an outpatient basis.

Clinical assessment

Fundus examination can be challenging for non-ophthalmologists. History can thus be crucial in distinguishing the varying causes of vision loss and thus directing care.

16.1 OCULAR EMERGENCIES

Table 16.1.1 Symptoms significant for cause in sudden vision loss

Symptom	Condition
Floaters (if recent onset)	Posterior vitreous detachment Vitreous haemorrhage Retinal detachment
Flashes (especially temporal)	Retinal detachment Migraine aura
Shadow (billowing curtain/cloud)	Retinal detachment Vitreous haemorrhage
Distortion	Exudative macula disease
Amaurosis fugax	Retinal artery occlusion Anterior ischaemic optic neuropathy
Pain on eye movement	Optic neuritis
Visual field loss	
Horizontal hemifield	Anterior ischaemic optic neuropathy Branch retinal vein occlusion Branch retinal artery occlusion
Vertical hemifield (bilateral)	Retrochiasmal CVA/compression
Whole-field (unilateral)	Vitreous haemorrhage Central retinal artery occlusion Anterior ischaemic optic neuropathy Central retinal vein occlusion Retinal detachment
Bilateral total loss of vision	Bilateral occipital infarction Toxic (methanol/quinine)

Table 16.1.2 Sudden vision loss for which acute therapy is available

Condition	Therapy
Central (or branch) retinal artery occlusion	Acetazolamide CO_2 rebreathing Pulsed ocular compression Anterior chamber paracentesis
Anterior ischaemic optic neuropathy	Steroids
Exudative age-related macular degeneration	Anti-VEGF injections Laser
Retinal detachment	Surgery
Endophthalmitis	Intravitreal antibiotics Surgery

Anti-VEGF, Anti-vascular endothelial growth factor.

History

Particular attention should be paid to the rapidity of onset, and the degree and location in space of visual loss, previous episodes and associated symptoms. (One should distinguish in the history between acute onset and acute discovery of visual loss, as a patient may discover decreased vision from, e.g. a cataract, by inadvertently covering one eye for the first time.)

Examination

Testing of the visual acuity and visual field will clarify uni- or binocular involvement.

Examination of the pupils is mandatory before pharmacological dilatation. *Test for a relative afferent pupillary defect (RAPD), one of the few objective signs.* When required, pupils will dilate in 10 to 15 minutes with tropicamide 1.0% drops, which last 1 to 2 hours. Pupils should not be dilated if the patient requires monitoring for a head injury.

Bilateral vision loss

Bilateral visual field loss usually implicates a retrochiasmal and, therefore, a non-ocular cause. However, this visual field defect will respect a vertical midline. In contrast, the retinal nerve fibre

layer and retinal vascular elements within the eye are distributed around a horizontal midline and may thus involve a superior or inferior (i.e. horizontal) hemifield. *Localized ocular pathology does not cause a visual field defect respecting a vertical midline.*

Bilateral acute, complete, visual failure is uncommon. Bilateral occipital infarction may present with bilateral blindness, but pupil responses would be expected to be intact. Rapidly progressive bilateral sequential visual loss from temporal arteritis is occasionally encountered. Other pre-chiasmal causes of bilateral, simultaneous, ocular involvement include toxic causes, such as poisoning with either **quinine** or **methanol**, where the patient presents with bilateral blindness and fixed, widely dilated pupils. Visual recovery in these cases is variable and the efficacy of a range of therapeutic interventions is controversial.^{13,14}

Central retinal artery occlusion

The history is typically of sudden, painless loss of vision in the affected eye over seconds. This may have been preceded by episodes of transient loss of vision (**amaurosis fugax**) in the previous days or weeks. The mean age of presentation is in the 70s. Men are more frequently affected and the patient may be a 'vasculopath'. Carotid disease is frequently implicated, with an embolus often being the cause of the obstruction, but its absence does not preclude the diagnosis, as the obstruction may lie behind the lamina cribrosa. Check the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) when an embolus is not seen, as temporal arteritis causes 5% of cases of central retinal artery occlusion (CRAO).

The visual acuity is drastically reduced, often to the level of light perception, with an RAPD present on the affected side. Fundus examination shows creamy-white retinal oedema (cloudy swelling) with a central red fovea—the 'cherry-red spot'—caused by the absence of oedema in the thinner retina at the fovea. The arterioles may be attenuated, with segmentation ('cattle-trucking') of the blood column. An embolus may be seen at any point along the retinal arterioles, from the disc to the periphery.

Acute treatment proceeds on the assumption that the cause is embolic. Therefore the principles of therapy are to vasodilate the retinal arterial circulation in order to promote dislodgement of the embolus from a proximal position and encourage its movement downstream to a less strategic site. All the measures currently used are directed to lowering the IOP, thereby relieving the compressive effect on the intraocular vasculature. Intravenous or oral acetazolamide 500 mg will lower IOP within 15 to 30 minutes; pulsed ocular compression ('ocular massage') involves cyclical

16.1 OCULAR EMERGENCIES

sustained compression of the globe for 10 to 15 seconds before sudden release of this compression, continuing for 5 to 10 minutes. The release of pressure may result in a momentary marked increase in the perfusion pressure gradient and dislodge an embolus. The use of carbogen gas (95% oxygen/5% carbon dioxide) is now largely historical, but carbon dioxide rebreathing may be tried for its central vasodilatory effect. Definitive reduction of IOP is achieved with anterior chamber paracentesis, a technique that requires the specific expertise of an ophthalmologist. Trials of timely intra-arterial fibrinolytic therapy have so far shown a discouraging level of co-morbidity from the treatment.^{15,16} The place of hyperbaric therapy remains uncertain.¹⁷ Visual outcomes are generally poor in CRAO, but occasional successes justify aggressive intervention if the patient presents within 12 hours. Non-acute management must include investigations to define the embolic source.

Central (branch) retinal vein occlusion

Central or branch retinal vein occlusion (CRVO) may present as a painless blurring of vision that is not sudden. Patients are usually in the older age group, often with systemic hypertension, diabetes mellitus and glaucoma. Visual acuity varies with severity, as does the presence of an RAPD. The characteristic fundus appearance is of extensive intraretinal haemorrhage with a variable number of cotton wool spots ('margherita pizza'). There may be disc oedema, with venous tortuosity and a generally congested appearance. If an insufficiently wide fundus view is obtained, the patient may be misdiagnosed with 'papilloedema' and subjected to unnecessary investigations.

There is no emergency management specific to the vein occlusion that will positively influence the visual outcome—systemic hypertension and raised IOP rarely require acute control—and the patient should therefore be referred to the next ophthalmic outpatient clinic.

Age-related macular degeneration

In 10% to 20% of cases of age-related macular degeneration (AMD), exudative (or 'wet') macular changes are seen due to the presence of choroidal neovascularization (CNV). These patients may present with painless blur of the central vision, and 'metamorphopsia', which is a complaint that objects that they know to be straight appear curved. Visual acuity is reduced, depending on the stage of the disease; an RAPD is rarely seen owing to the relatively small area of retina involved, which may manifest as a central scotoma on field testing. Macular drusen (yellow

spots), retinal thickening and haemorrhage may be seen, with at least drusen usually also seen in the fellow eye.

Acute symptoms must not be dismissed. With appropriate treatment, central vision may be preserved in a proportion of these patients. Therefore ophthalmic review within 2 to 4 days is appropriate. Recent advances in treatment with anti-vascular endothelial growth factor agents, such as ranibizumab (Lucentis), bevacizumab (Avastin) and afiblivercept (Eylea) have revolutionized the prognosis, and often sight can now be preserved¹⁸.

Acute vitreo-retinal problems

Posterior vitreous detachment

Shrinkage and detachment of the vitreous is common in the older population and produces a new onset of floaters, which are wispy spots, threads or 'spider webs' in the vision. As part of this process, vitreous traction on the retina may produce flashes of light (photopsia) seen particularly in the temporal periphery of vision in that eye. These flashes can usually be distinguished from the visual aura of migraine. While posterior vitreous detachment (PVD) is usually not serious in its own right, early dilated examination of the retinal periphery is needed to exclude retinal tears, which predispose to detachment. Pigmented cells ('tobacco dust' or Shafer sign) in the anterior vitreous are associated with the presence of a retinal tear and therefore heighten the urgency of referral.

Retinal detachment

Acute retinal detachment (RD) is usually a result of a retinal tear or hole formation, with seepage of fluid into the subretinal space and lifting of the retina. Exudative and tractional RDs are less common and are associated with underlying pathology. A detached retina shows a visual field defect, which will be described as a shadow or curtain, corresponding to the area of detachment; that is, inferior field defect equals superior RD. Vision loss is painless. There may be an RAPD, depending on the amount of retina involved. Treatment will usually require surgery. If the visual acuity is normal, the macula is likely still attached, and referral to an ophthalmologist specializing in vitreo-retinal surgery is urgent in order to preserve central vision.

Vitreous haemorrhage

The common causes are proliferative diabetic retinopathy, chronic branch retinal vein occlusion, PVD or trauma. Patients with an acute vitreous haemorrhage (VH) may have symptoms varying from a few floaters causing blurred vision to a total loss of vision to a level of light perception,

depending on the density of the haemorrhage. Any loss of vision is painless. The red reflex may be poor and the view of the retina may be similarly impaired. Media opacities do not affect pupil light reflexes, so the presence of an RAPD suggests that the underlying retina is damaged or detached.

The patient should be referred for early ophthalmic assessment—urgent if an RAPD is present—which may include B scan ultrasonography to exclude RD if the retinal view is inadequate. Anticoagulants should be avoided where possible.

Giant cell arteritis

Arteritic **anterior ischaemic optic neuropathy** (AION) is the feared visual loss of giant cell (temporal) arteritis (GCA). The patient is commonly in his or her mid-70s or older and is more often female. Presentation is with profound vision loss in one eye. This may have been preceded by brief premonitory visual obscurations or double vision, to which the patient may not have ascribed significance. Systematic questioning may reveal specific features, such as jaw claudication, headache, scalp tenderness, anorexia, malaise, weight loss or night sweats, and there may be a history of polymyalgia rheumatica in up to 50% of cases. GCA is a systemic illness with the potential for devastating visual loss, as well as long-term life-threatening non-ophthalmic complications.

Vision may be reduced at presentation to the level of perception of light only. An RAPD will be present and the optic disc is almost invariably oedematous, but the fundus may be otherwise normal. Total field loss in the affected eye is usual. Evidence of decreased acuity, colour vision deficits and disc oedema also should be sought in the other eye. Palpation of the temporal arteries will often be abnormal, with the pulses perhaps absent or the arteries thickened and tender.

Clinical suspicion requires blood to be drawn for ESR and CRP. Steroid treatment should then be started on an urgent basis and must not be delayed or deferred until after temporal artery biopsy. The biopsy will remain positive for at least several days despite steroids. Elevation of both ESR and CRP is highly specific for a diagnosis of GCA, but does not avoid the need for biopsy.¹⁹ Urgent referral to an ophthalmologist is required.

Prednisolone 1 mg/kg daily is an accepted dose, although recent experience has suggested that 'pulse' methylprednisolone 500 mg intravenously daily or twice daily over 1 to 2 hours is safe and more efficacious in suppressing the inflammation, and this has become standard therapy in a number of centres. This is generally used for 3 days and oral prednisolone is then substituted.^{20,21} Weaning oral treatment will be prolonged (at least 6 months) and should be undertaken in cooperation with a physician,

with attention also directed to the avoidance of steroid complications in this aged patient group.

Non-arteritic AION is classically seen in males in their late 50s and 60s who have a history of cardiac or vascular disease, hypertension, diabetes or smoking. The visual presentation may be similar to that seen with GCA—although the visual acuity and field loss may not be as profound (may be a hemifield loss) and the specific systemic symptoms are absent—so that management must be as for arteritic AION until GCA is excluded. The condition was well-known prior to the advent of sildenafil (Viagra), which has been inconclusively implicated in some cases.²²

Optic neuritis

Optic neuritis classically presents in young females and may be the first presentation of a demyelinating illness. Visual symptoms are not usually sudden and presentation is thus seldom acute. The vision declines gradually over days, perhaps to the level of 6/36 to 6/60, with loss of colour vision being prominent. The common visual field defect is a central scotoma, but many variations are possible and an RAPD should always be present. If disc oedema is not seen, the diagnosis may be retrobulbar neuritis. There may be pain on medial or superior eye movement.

Good spontaneous recovery has made the value of treating optic neuritis controversial: the results of the Optic Neuritis Treatment Trial suggested that there is no place for oral prednisolone alone in management. The benefit of 'pulse' intravenous methylprednisolone seems restricted to shortening the acute episode, without influencing the possibility of progression to multiple sclerosis or the final visual outcome.²³ However, there is usually no role for acute intervention, and referral within a day or two to a neurologist or ophthalmologist is satisfactory.

CONTROVERSIES

- Local anaesthetic drops in treatment of corneal abrasions
- Emerging evidence of eye injuries from vehicle air bag deployment
- Role of hyperbaric oxygen or intra-arterial fibrinolysis in CRAO
- Role of sildenafil in causing non-arteritic AION

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SECTION
17

DENTAL EMERGENCIES

Edited by Peter Cameron

17.1 Dental emergencies 557

17.1 Dental emergencies

Ian Hewson

ESSENTIALS

- 1** An avulsed tooth reimplanted within 30 minutes has a 90% chance of survival.
- 2** Dental caries is the most common cause of dental emergency attendance.
- 3** Dental caries requires analgesia in the emergency department and referral to a dentist for definitive care. Antibiotics are not required unless the caries is complicated by abscess.

Anatomy

The tooth consists of the crown, which is exposed, and the root, which lies within the socket covered by the gum; the latter serves to anchor the tooth. The gingival pulp carries the neurovascular structures via the root canal and is covered by dentine which, in turn, is covered by enamel, the hardest substance in the body (Fig. 17.1.1).

The deciduous teeth are 20 in number and erupt between the ages of 6 months and 2 years. The permanent dentition begins to erupt at around age 6 and, in the adult, consists of 32 teeth.

Dental caries

The most common cause of toothache or odontalgia is caries. Dental caries-related emergencies account for up to 52% of first contact with a dentist for children below the age of 3 years.¹ Dental caries is the cause of emergency visits to a dentist in 73% of paediatric patients.² Pain associated with dental caries is of a dull, throbbing nature, localized to a specific area and aggravated by changes in temperature in the oral cavity (hypersensitivity to hot and cold food or fluids).

Examination reveals tenderness of the offending tooth when tapped with a tongue depressor or mirror. Management includes symptomatic pain relief using analgesics, such as paracetamol with or without codeine, non-steroidal anti-inflammatory drugs (NSAIDs) and urgent referral to the dentist.

Periodontal emergencies

Pain is the most common cause of self-referral to the emergency department for dental problems. The common conditions causing dental pain are acute apical periodontitis and reversible and irreversible pulpitis resulting from dental caries.³ Symptoms include painful, swollen gums with or without halitosis. On occasion, frank pus or bleeding from the gums may be the presenting symptom. At all stages, varying degrees of pain associated with inflammation are present.⁴

Infected gums can be an early clinical sign of undiagnosed diabetes, acute myeloid leukaemia (AML), HIV and graft-versus-host disease in bone marrow transplantation.

Management includes diagnosis of the periodontal disease and the offending tooth. Symptomatic pain relief can be achieved with

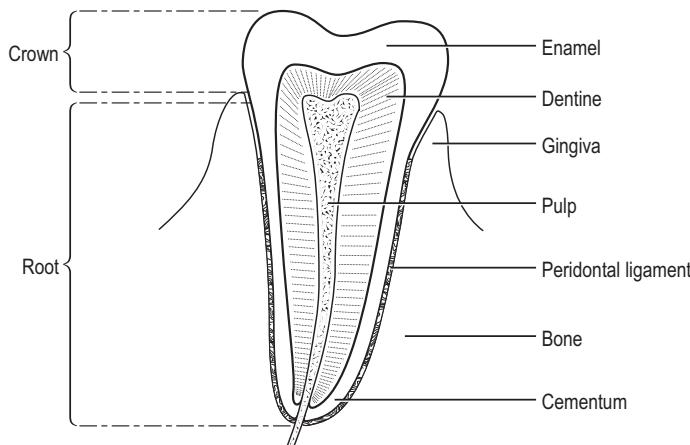


FIG. 17.1.1 The anatomy of a tooth. (From an original drawing by Ian Miller RN.)

analgesics, NSAIDs and warm saline rinses. Routine antibiotic therapy is not required unless there is evidence of gross infection locally, regional lymphadenopathy or fever. In all cases, urgent review by the dentist is mandatory.

Acute necrotizing ulcerative gingivitis (ANUG) is a severe form of gingivitis that could be related to stress and needs antibiotic cover and urgent referral to the dentist.

Alveolar osteitis (dry socket)

Dry socket occurs between 2 and 5 days following dental extraction. The dull throbbing pain is due to the collection of necrotic clot and debris in the socket. The condition is diagnosed on the history and examination, which confirms the acutely tender extraction site.

Treatment consists of irrigation (2% chlorhexidine) of the extraction site to remove the necrotic material and packing the socket with sterile gauze soaked in local anaesthetic, such as cophenylcaine, or placing alvogyl into the socket (butamben, iodoform and eugenol) followed by urgent dental review.⁵

Post-dental extraction bleeding

Bleeding from the socket within 48 hours after extraction results from reactionary haemorrhage due to opening up of the small divided blood vessels. Bleeding after 5 days is secondary haemorrhage due to infection that has destroyed the organizing blood clot.

General causes, such as hypertension and warfarin therapy, must be addressed to control the bleeding.

Management is essentially reassurance and careful suctioning to clear the debris and clot in the socket; this is followed by packing with gauze soaked in lignocaine with adrenaline or cophenylcaine and pressure. Or Surgicel may be placed into the socket.

Dilute aminocaproic acid (IV Amicar) 5 mL in 10 mL of normal saline may be used to rinse the mouth. Use Amicar or tranexamic acid-soaked gauze to bite on, applying direct pressure for about 30 minutes and repeat as required to control the bleeding. Occasionally the gingival flaps may have to be sutured under local anaesthetic.

Traumatic dental emergencies

Tooth avulsion is probably the most serious tooth injury. An avulsed tooth, if reimplanted in the socket within 30 minutes, has a 90% chance of survival.⁶ The mechanism of injury in such cases is usually either an accidental sports-related facial injury or an assault.

Management

If the patient makes telephone contact with the emergency department, he or she is advised to locate the tooth because, even if the crown is broken, the root may be intact. The tooth should not be handled by the root to avoid damage to the periodontal ligament fibres; it is washed in running cold water and replaced in the socket. If this is not possible, the patient should place the tooth in the cheek or under the tongue and proceed immediately to the dentist. Do not scrub the tooth.^{7,8}

The best transportation medium for an avulsed tooth is saliva. Cold milk or iced salt water are suitable alternatives. If the tooth can be replaced in the socket, this is the perfect environment even if it is not stable in the socket.

When the patient arrives in the emergency department with the tooth, clean it by holding it by the crown in sterile saline or Ringer solution; any foreign debris should be removed with forceps. The tooth should not be allowed to dry. Following irrigation, the tooth should be placed in the socket as close to its original position as possible and the patient referred to a dentist for stabilization with an arch bar or orthodontic bands.

The complications of reimplantation are ankylosis and loss of viability.

The 2010 Dental Trauma Guide by the Danish Dental Association supported by the International Association of Dental Traumatology provides an interactive drop-down menu on how to deal with every possible dental trauma.⁹

Dentoalveolar trauma in children

Concussion and subluxation

Concussion is an injury to the tooth without displacement or mobility. Subluxation is when the tooth is mobile but not displaced.

Management

This includes periapical x-rays as baseline, soft diet for a week and local dentist follow-up.

Intrusive luxation

This is the most common injury to upper primary incisors after a fall.

Management

If the crown is visible, allow the tooth to re-erupt. If the whole tooth is intruded, extraction is required, as it might otherwise affect the permanent dentition underneath.

Extrusive and lateral subluxation

If there is excessive mobility or displacement, extraction is recommended.

Avulsion

Avulsed primary teeth should not be reimplanted. Unless there is extensive soft-tissue damage, antibiotics are not required.

Dental fractures

The incidence of fractured teeth is reported to be 5 and 4.4 per 100 adults per year for all teeth and posterior teeth, respectively.¹⁰ Based on these statistics, it can be deduced that the likelihood of experiencing a fractured frontal/anterior tooth is about 1 in 20 in a given year in adults and 1 in 23 for posterior teeth.

Traumatic injuries to the teeth have been classified as follows¹¹:

- Class I: Simple fracture of the enamel of the crown
- Class II: Extensive fracture of the crown involving dentine
- Class III: Extensive fracture of the crown involving dentine and dental pulp
- Class IV: Extensive involvement and exposure of the entire pulp
- Class V: Totally avulsed or luxated tooth
- Class VI: Fracture of the root with or without loss of crown structure
- Class VII: Displacement of tooth without fracture of crown or root
- Class VIII: Fracture of the crown in its entirety (Fig. 17.1.2)

Management

Emergency management includes reassurance, adequate analgesia, replacement of an avulsed tooth in the socket and immediate referral to a dentist for further evaluation and appropriate management.

Specific treatment depends on the type of fracture¹²:

- Class I: Treated by smoothing the enamel margins and applying topical fluoride to the fracture site.

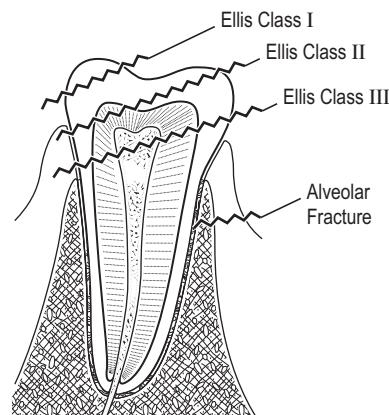


FIG. 17.1.2 Ellis classification. (From an original drawing by Ian Miller RN.)

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- Class IIA: Calcium hydroxide dressing is applied as a bandage to provide a stable form of temporary restoration, which will be replaced by a more aesthetic restoration as soon as the vitality of the pulp is assured.
- Class III: If seen within 6 hours of the accident, it should be treated with calcium hydroxide direct pulp capping. If more than 6 hours but less than 24 hours have elapsed, pulpotomy is advised. If more than 24 hours have elapsed, since the accident, the treatment is total pulpectomy.
- Class IV: Treated with conventional filling for permanent teeth and total pulpectomy for a primary tooth.
- Class V: Managed as for an avulsed tooth.
- Class VI: If the pulp is necrotic, pulpectomy and root canal therapy are appropriate.
- Class VII: If the tooth is intruded, it should be extracted (deciduous teeth only). If driven through the labial plate of bone, it should be extracted; if not, it should be left alone to re-erupt. If the tooth is extruded, slowly move it back to its original position using finger pressure. Primary teeth, if mobile 2 weeks after the injury, should be extracted. Parents should be warned about possible damage to the developing permanent tooth.
- Class VIII: In a permanent tooth, pulpotomy or pulpectomy is appropriate. Primary teeth with this amount of destruction should be extracted.
- When a tooth is missing following facial trauma, a thorough intraoral examination is followed by appropriate radiographs to avoid missing an intruded tooth. When full intrusion of a tooth is suspected, a facial computed tomography (CT) scan may aid definite diagnosis.¹³

Temporomandibular dislocation

Temporomandibular dislocation can result from congenital weakness of ligaments, iatrogenic causes (traumatic extractions, prolonged dental procedures and direct laryngoscopy), trauma, drugs, epilepsy and even simple yawning. The dislocation may be unilateral but is more commonly bilateral. The condyle is most frequently dislocated anterior to the articular eminence.

The patient presents with an open bite and malocclusion. If unilateral, the mandible deviates to the unaffected side. The patient complains of severe pain in the ear and is unable to open or close the mouth fully. Management includes diagnosis and reduction. The patient is seated, with posterior head support, and the muscle spasm is overcome

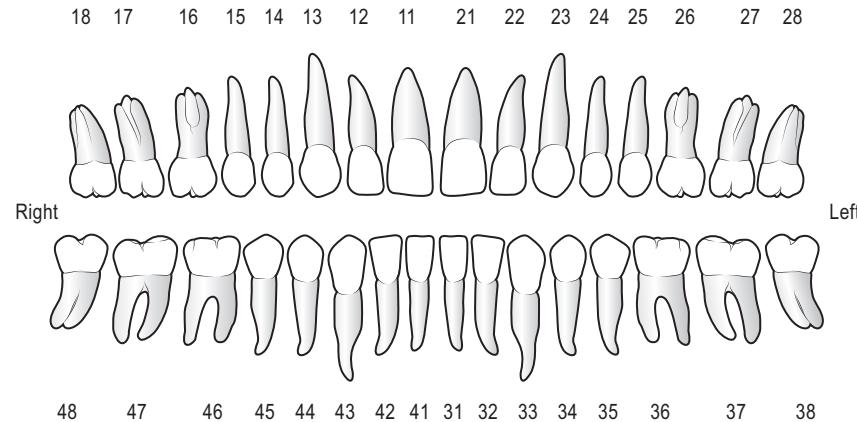


FIG. 17.1.3 Dental nomenclature. (From the FDI World Dental Federation Two-Digit Notation. ISO 3950:2009: Dentistry—Designation system for teeth and areas of the oral cavity.)

by using intravenous benzodiazepines, such as midazolam, and narcotic analgesia, such as fentanyl.

The mandible is held by the clinician with both hands, with the gloved thumbs placed intraorally just lateral to the lower molars. The mandibular condyle is then manipulated in a downward and backward direction below the articular eminence. In bilateral dislocation, it may be easier to reduce one side at a time using a lateral rocking motion.

Following the procedure, a post-reduction radiograph is taken to confirm enlocation. The patient is discharged with a supportive bandage to the mandible and a soft diet for the next few days is advised. Follow-up by the maxillofacial surgeon is essential, as temporomandibular dysfunction due to damage to the fibrous cartilage can lead to ongoing symptoms or recurrent dislocations.

Dental infection and abscess (odontogenic infection)

Dento-facial infections usually arise from necrotic pulps, periodontal pockets or peri-coronitis.

The symptoms are pain and swelling of the adjacent gingival tissue with facial swelling and fever.

Examination reveals erythema and tender swelling of the gingiva and, in severe cases, frank pus with halitosis. The offending tooth is tender on percussion.

Gingival probing, x-rays and orthopantomography (OPG) confirm the diagnosis.

Management

Periapical abscess requires root canal (endodontic) treatment and, in severe cases, extraction.

Periodontal abscess requires scaling and root planing (periodontal) treatment and, in severe cases, extraction.

Complications include the spread of infection into the submental, submandibular and parapharyngeal spaces of the neck as well as Ludwig angina (cellulitis of the floor of the mouth). If a collection is diagnosed on the CT scan, this requires intravenous antibiotic therapy and drainage.

Dental nomenclature

The international numbering system of teeth should be strictly adhered to in any form of communication. The mouth is divided into four quadrants: the right maxillary as 1, left maxillary as 2, left mandibular as 3 and the right mandibular as 4 (Fig. 17.1.3).

There are five primary teeth and eight permanent teeth in each quadrant.

CONTROVERSIES

- Dental services are generally not part of acute health service funding; therefore low-income patients may have to experience the medical complications of poor dental hygiene before being able to access appropriate care.
- Oil of cloves originated from India and was traditionally used topically for relief of dental pain, such as dry socket, prior to the availability of safe, approved topical anaesthetic agents. However, this oil is highly toxic to human cells even at relatively low concentrations.
- Even small amounts of clove oil (e.g. 0.03% [v/v]) can be life-threatening if ingested.

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SECTION 18

EAR, NOSE AND THROAT EMERGENCIES

Edited by Peter Cameron

18.1 Ear, nose and throat emergencies 561

18.1 Ear, nose and throat emergencies

Carmel Crock • Nadine de Alwis

ESSENTIALS

- 1** Make sure that the ear-nose-throat (ENT) supplies in your emergency department are well stocked and maintained.
- 2** Develop agreed pathways/protocols with your local ENT department for common and serious presentations.
- 3** A foreign body in the ear requiresatraumatic removal with appropriate equipment and a cooperative patient. Refer to ENT if you anticipate difficulty.
- 4** Exclude a perilymphatic fistula in blunt and penetrating ear trauma, which may be suggested by sensorineural hearing loss and dizziness.
- 5** Idiopathic sudden sensorineural hearing loss is an emergency treated with oral steroids.
- 6** Exclude septal haematoma in a fractured nose, as delayed diagnosis may lead to a saddle-nose deformity.
- 7** Fish bones commonly lodge in the tonsillar bed or at the base of the tongue. Refer to ENT for nasoendoscopy if you are unable to localize the bone and the patient is symptomatic.
- 8** Suspect supraglottitis in adults with sore throat, painful swallowing and minimal signs in the pharynx. Meningococcal strains are on the rise. Refer to ENT for nasoendoscopy.

Introduction

Ear-nose-throat (ENT) emergencies are common in emergency departments. The key to their successful management is the availability of appropriate ENT equipment (**Box 18.1.1**) and familiarity and practice in its use.

THE EAR

Perichondritis

This presents as painful swelling and redness of the pinna with sparing of the lobule. It may

occur after minor trauma, high chondral piercing, a subperichondrial haematoma or severe otitis externa (OE). It can lead to liquefaction necrosis of the cartilage and severe cosmetic deformity of the ear. The primary organism is *Pseudomonas aeruginosa*. Urgent evaluation by ENT should occur. Depending on severity, treatment is with ciprofloxacin 750 mg PO bd (CC) in adult for 1 week with close follow-up or admission for ticarcillin/clavulanate 3.1 g IV q4–6h (CC). Remove involved piercings.

Swelling and redness of the pinna involving the lobule suggests pinna cellulitis, which is treated with anti-staphylococcal antibiotics.

Box 18.1.1 Ear-nose-throat equipment

Ear

Otoscope
Portable headlight
Ear speculae and pneumatic attachment (Seigel)
512-Hz Tuning fork
Houseaursuckers: 11, 14, and 17 gauge, with adaptors
Merocel Otowick (Pope wick)
Alligator and cupped crocodile forceps
Jobson-Horne probe (wax curette)
Right-angled hook
Ear swabs

Nose/throat

Protective gown, gloves, eye protection (goggles)
Nasal speculae: Thudicum or Killian
Cophenylcaine (lignocaine/phenylephrine) spray and 1:10,000 adrenaline
Spray nozzles
Cotton wool balls
Nasal sucker (Frazier/Ferguson)
Cotton buds
Tilley forceps (nasal packing)
Silver nitrate sticks
Nasal packs: Rapid Rhino (single balloon anterior 5.5 cm, 7.5 cm and double balloon posterior 9 cm), Merocel (3.5 cm, 8 cm), Kaltostat rope
Absorbable packing e.g. Surgicel, Surgicel Fibrillar, Nasopore, Nasopore forte
Foley catheter and umbilical clamp
Tongue depressor
Large cotton swab sticks
Magill forceps and gauze
Laryngeal mirror and anti-fog solution
Curved artery forceps
#11 blade and scalpel handle

Perichondritis should be distinguished from relapsing polychondritis, an autoimmune condition affecting cartilages of the ear, often

bilaterally, the nose and sometimes laryngeal and costal cartilages.

Acute otitis externa ('swimmer's ear')

This is an infection of the external auditory canal, often caused by swimming, ear syringing, or the use of cotton buds or a hearing aid. Bacterial OE is often caused by *Pseudomonas aeruginosa* or *Staphylococcus aureus*. In about 10% of cases the cause is fungal, such as *Aspergillus* or *Candida* spp.¹

Features include severe otalgia, discharge, pain on traction of the pinna (this helps distinguish it from otitis media), canal debris and, in more severe cases, canal oedema with little or no view of the tympanic membrane. Suspect fungal infection in patients without water exposure who have used anti-bacterial ototopicals and in those with recurrent OE (especially in diabetics). Fungus may also be involved if there is prominent itch, much debris (often grey/black) and less canal oedema.

Treatment involves removing debris from the canal and assessing whether the tympanic membrane is intact (it may not be possible to see this) as well as prescribing antibiotic or antifungal drops, advising the patient on water precautions and avoiding the use of cotton buds. An ear swab is not normally taken on initial presentation.

Canal debris can be removed with tissue spears (to wick moisture, not to rotate within the canal) or by suction under direct vision using a headlight, aural speculum and metallic house suction catheter (if trained for this procedure). The tympanic membrane is examined and pneumatic otoscopy performed. Fungal OE can cause perforation of the tympanic membrane.

If the discharge is purulent and voluminous and the ear canal is not oedematous, suspect an acute or chronic suppurative otitis media or cholesteatoma.

If the tympanic membrane is intact, framycetin sulphate/gramicidin/dexamethasone (Sofradex) is prescribed for likely bacterial OE. For fungal OE, treatment may include Locacorten-Vioform or Otocomb drops (the latter are thick and tend to block the ear), Otocomb ointment or clotrimazole cream packing with ENT follow-up in 14 days. Ciprofloxacin 0.3% (Ciloxan) (CC) is used if there is perforation of the tympanic membrane.

If there is marked canal oedema, an otowick is inserted to deliver drops and ciprofloxacin/hydrocortisone (Ciproxin HC) used, with ENT review for wick removal in 2 days.

Instruct patients not to allow water in their ears for 2 weeks. A cotton wool ball covered in Vaseline and placed in the external meatus is one effective means. Avoid non-disposable ear plugs.

Differential diagnoses

Occasionally there will be acute otitis media (AOM) with perforation and secondary OE, and both oral antibiotics and ear drops may be required.

In diabetics, the elderly or immunocompromised patients with a discharging ear, consider malignant OE (skull base osteomyelitis), which can be fatal. Presentation includes dull earache, especially at night, pain on chewing, persistent ear discharge and treatment failure. The pathognomonic sign is granulation tissue in the floor of the ear canal. There may be associated cranial nerve palsies (VII, IX, XII). Refer suspected cases to ENT.

A squamous cell carcinoma or basal cell carcinoma of the external ear canal may present as OE, particularly in the elderly.

Furuncle

A furuncle (boil) in the external ear canal presents as an exquisitely tender, localized swelling and is commonly caused by *S. aureus*. Management includes insertion of an otowick, Sofradex ear drops, oral flucloxacillin 500 mg qid (CC) for 5 days and oral analgesia, with ENT follow-up. Incision and drainage under local anaesthetic may be required if there is fluctuance.

Acute otitis media

Presentation is with symptoms of an upper respiratory tract infection, severe otalgia and blocked sensation. It is clinically defined as a red, bulging tympanic membrane. There should be poor or no mobility of the tympanic membrane on pneumatic otoscopy. A tympanic membrane perforation may occur, with otorrhoea. Tuning fork tests demonstrate a conductive hearing loss, with Weber lateralizing to the affected ear. Facial nerve function should be documented. Some unsteadiness may occur; if this is severe, suspect complications.

Initially manage with regular simple analgesia. Commence antibiotics if bilateral or severe infection, unresolving infection after 48 hours of observation or if this is the only hearing ear. Give amoxicillin 500 mg tds (CC) 3 times a day for 5 days. If response is inadequate after 48 to 72 hours, upgrade to augmentin duo forte. If unresolving within 48 to 72 hours of commencing the upgrade, refer urgently to ENT for consideration of a grommet. Rare causes of atypical AOM include autoimmune or vasculitic conditions, syphilis and tuberculosis.

Complications of AOM should be sought and excluded. These include tympanic membrane perforation, suppurative labyrinthitis, mastoiditis with subperiosteal abscess, meningitis, facial nerve palsy, otic hydrocephalus, petrous apicitis,

cerebral abscess and venous sinus thrombosis. Seek immediate ENT advice for suspected complications.

Acute mastoiditis

Particularly in children, mastoiditis can still occur secondary to partially treated AOM; it presents with swelling, redness and tenderness over the mastoid with the pinna pushed forward. Refer to ENT for computed tomography (CT) scan of the temporal bones, intravenous antibiotics and consideration for surgery.

Idiopathic sudden sensorineural hearing loss

This is an otologic emergency. The patient may wake and notice a sudden hearing loss or may present with a blocked ear, unaware of any hearing loss. There is often associated tinnitus and mild disequilibrium. A tuning fork test shows the Weber test lateralizing to the unaffected ear. Whisper voice testing confirms hearing loss.

The cause is unknown but may be vascular, viral or autoimmune in origin. Consider herpes zoster oticus if there is otalgia or vesicles are seen on the pinna or in the canal. If tuning fork testing is consistent with a sudden sensorineural hearing loss (SSNHL), the patient is commenced empirically on oral prednisolone 1 mg/kg up to 60 mg daily (CC) (for 7 days then reducing over a week) and urgent audiogram and ENT follow-up planned for the same or following day. Intratympanic steroids may be used by ENT if there are contraindications to oral steroids. Outpatient magnetic resonance imaging (MRI) is performed to rule out an acoustic neuroma. Sixty percent of patients with idiopathic SSNHL regain some hearing over time.

Acute facial (seventh) nerve palsy

Determine whether this is an upper or lower motor neuron (LMN) palsy. The cause of upper motor neuron (UMN) seventh nerve palsy is often a stroke. There is sparing of forehead muscles and there may be other neurological signs. In LMN seventh nerve palsy, the entire side of the face is affected, including the forehead muscles. The House-Brackmann scoring system should be used to record the degree of facial palsy.

Causes of acute LMN seventh nerve palsy include Bell palsy, Ramsay-Hunt syndrome (herpes zoster oticus), AOM, cholesteatoma, trauma (temporal bone fracture) and rarely autoimmune conditions, vasculitic conditions and infections such as HIV, Epstein-Barr virus (EBV) and syphilis. A parotid tumour, metastatic perineural invasion

18.1 EAR, NOSE AND THROAT EMERGENCIES

and facial schwannoma can cause acute palsy if there is a sudden bleed into the mass but generally these cause slowly progressive, partial facial palsy.

Bell palsy is a diagnosis of exclusion. It is an acute, unilateral, usually complete paralysis and should always show some recovery with time. Symptoms include pain behind the ear, hyperacusis and abnormal taste. It may be viral in origin. Treatment is with oral prednisolone 1 mg/kg up to 70 mg (CC) for 5 days. There is low-quality evidence for benefit from antivirals, but it is an option if commenced within 72 hours of onset.² If there is incomplete eye closure, ocular lubricants and ophthalmology referral is required. Eighty percent of patients recover fully within 3 months. If there is no recovery, refer to ENT, and an MRI is warranted.

Ramsay-Hunt syndrome (herpes zoster oticus) usually presents with severe otalgia followed by vesicles on the pinna and/or in the canal. There is often sensorineural hearing loss and a dense facial palsy. Prognosis is poorer than with Bell palsy. Treatment is with an antiviral within 72 hours of the appearance of the rash (famciclovir 250 mg tds (CC) for 7 days or valaciclovir 1 g tds (CC) for 7 days) and oral prednisolone as above.

Ear trauma

In trauma to or around the ear, consider the possibility of cervical spine and head injury.

Base-of-skull fractures

Suspect this if the mechanism of injury is a high-speed motor vehicle accident, fall from a significant height, heavy crush injury or multitrauma. Clinical signs include raccoon eyes, the Battle sign and clear or bloody otorrhoea or rhinorrhoea with a halo sign on the bed sheet.

Anterior fractures mainly involve the cribriform plate; if there is also a dural tear, this will present with cerebrospinal fluid (CSF) rhinorrhoea. Do not insert a nasogastric tube if this is suspected.

Lateral fractures involve the temporal bone. Order a CT of the petrous temporal bone or reconstruction CT of the brain. Fractures that spare the otic capsule are more common and can include the ear canal, perforate the eardrum and disrupt the ossicles. Otic capsule involving fractures are more likely to cause facial palsy, CSF otorrhoea, perilymphatic fistula and sensorineural hearing loss but are less common. In all head trauma, document facial nerve function and inspect the ear. Complete facial palsy of immediate onset requires urgent surgical decompression by ENT. Any delayed or incomplete palsy can be managed with steroids and timely review by ENT, with an audiogram when possible.

Subperichondrial haematoma of the pinna

This results from blunt trauma to the pinna. It can lead to necrosis of the cartilage, causing a deformity known as 'cauliflower ear'. Refer to ENT for surgical incision and drainage. Small collections can be drained by needle aspiration or stab incision using sterile technique; however, these tend to recur if the dressing is inadequate. Larger collections involving multiple subunits of the pinna should be drained under general anaesthesia.

After needle aspiration or stab incision, apply a conforming pressure dressing, give oral flucloxacillin 500 mg qid (NDA), and arrange review in 24 hours. Do not suture the dressing through the cartilage, as this may cause perichondritis. Materials such as paraffin-soaked ribbon gauze, Bismuth subnitrate, Iodoform and Paraffin Paste (BIPP) gauze and Xeroform dressing can be moulded and lightly tacked to the overlying skin with a nylon suture. Over this a mastoid pressure dressing can be applied and removed by the patient in 24 to 48 hours and then replaced with a soft headband for 1 week. The conforming dressing can be removed after 1 week and the soft headband should be used over the ear whilst sleeping for further 1 to 2 weeks. Contact sport should be avoided for 3 weeks to prevent recurrence.

Lacerations to the auricle

Refer wounds involving the ear cartilage to ENT or plastic surgery for repair. Simple skin lacerations involving the auricle can be sutured (using 5-0 or 6-0 non-absorbable nylon). Give tetanus prophylaxis as indicated and oral flucloxacillin 500 mg qid for 5 days (NDA).

Foreign body in ear

In adults, common foreign bodies in the ear are cotton bud tips, rubber pieces of hearing aids, pieces of silicone ear plugs and live insects. Live insects should be drowned using olive oil, Woxsol or lignocaine 2%.

A foreign body (FB) in the ear should be removed atraumatically under direct vision with a head light, the largest appropriate ear speculum and a cooperative patient. Crocodile forceps, a right-angle hook or metal suction catheter can be used, depending on the type of FB. Hard beads should not be grabbed with crocodile forceps, as they can be pushed in further; use a hook instead. After removal, document the appearance of the tympanic membrane and whether it is intact.

If the practitioner is not experienced in use of the equipment or the foreign body is impacted, the patient can be referred to ENT for its removal. This is not an emergency.

Barotrauma

This can occur on descent of a plane or during scuba diving, causing a haemotympanum, which causes otalgia and a blocked sensation; however, it usually resolves spontaneously. More severe barotrauma may result in perforation of the tympanic membrane and rupture of the oval or round window, resulting in a perilymphatic fistula. This is suggested by sensorineural hearing loss, a positive fistula test, vomiting, dizziness, unsteadiness and a positive Hallpike test. If these features are present, refer urgently to ENT.

Acoustic trauma

Exposure to a sudden loud noise may cause temporary or permanent hearing loss, which may present as tinnitus with or without otalgia and sensitivity to noise. Refer patient for a formal audiogram and an ENT opinion. Steroids may be required. Counsel the patient on hearing protection to prevent further damage.

Traumatic tympanic membrane perforation

This may occur in the setting of a blast injury, diving, slap to the ear or a penetrating injury such as from a cotton bud or sharp plant. Exclude perilymphatic fistula, especially in postero-inferior perforations.³

For penetrating perforations arrange an urgent audiogram (same or next day). If a perilymphatic fistula is suspected, arrange urgent ENT referral for possible surgical exploration.

For non-penetrating injuries without clinical evidence of sensorineural hearing loss or lasting dizziness, an audiogram can be arranged in 6 weeks' time to objectively document that the perforation has healed.

Advise the patient to keep the ear dry and arrange ENT follow-up.

THE NOSE

Epistaxis

Epistaxis is a common presentation, particularly in elderly patients on antiplatelet and anticoagulant medication. Over 90% of epistaxis is anterior, arising from the Little area antero-inferiorly on the nasal septum, and it can be controlled with simple measures. In the elderly with significant bleeding, assessment and treatment of epistaxis will progress simultaneously. Assess airway, breathing and circulation and insert intravenous lines, taking blood (including full blood count, group and hold and coagulation studies with or without liver function tests, depending on history)

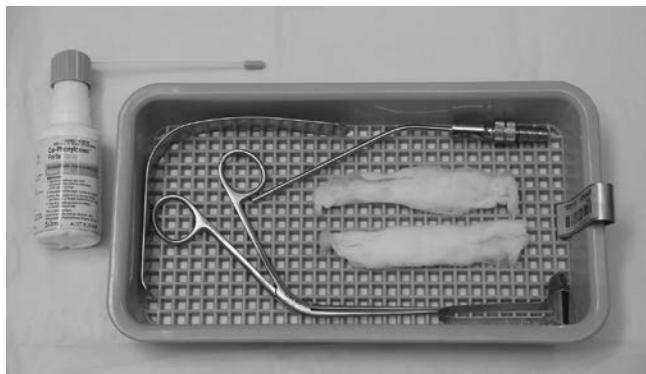


FIG. 18.1.1 Epistaxis tray.

and commence intravenous fluid. Ask the patient or nurse to commence first aid, applying continuous, firm pressure to the anterior nares for 10 to 15 minutes. After donning a gown, gloves and eye shield/goggles, mask and headlight, open an epistaxis tray (Fig. 18.1.1) containing a tongue depressor, nasal speculum and nasal suction catheter and nasal packing (Tillley) forceps. Unroll two cotton wool balls and spray with lignocaine/phenylephrine (Cophenylcaine) until soaked (maximum 10 sprays in patients with cardiovascular disease). These will be used as nasal packs, providing topical local anaesthesia, vasoconstriction and decongestion of the nasal mucosa. Use the nasal speculum and suction catheter to suction clots from the nose and gently pack both sides of the nose with Cophenylcaine-soaked cotton wool. Any nasal packing can cause a vagal response.

Using the tongue depressor, examine the back of the throat for posterior bleeding. Wait for 10 to 15 minutes, then remove the cophenylcaine-soaked cotton wool and seek the source of bleeding. If the bleeding recommences, repack the nose, as earlier. This process may need to be repeated several times until the bleeding slows or stops.

If the bleeding site can be clearly identified (as by touching it with a cotton bud tip and causing bleeding), it can be cauterized using a silver nitrate stick in a rosette fashion. Make sure that the site is not bleeding at the time of cautery and that the silver nitrate does not run onto the face, as it can then cause a superficial burn and stain the skin. Avoid cautery to both sides of the nasal septum, as this can result in septal necrosis and perforation. Surgicel can be applied over the cauterized site and barrier ointment, such as Nasalate or mupurocin 2%, prescribed. The patient can be discharged if there is no further bleeding after 1 to 2 hours including ambulation within the department.

For patients on an antiplatelet or anticoagulant, consider avoiding cautery and packing the nose with absorbable packing, such as Surgicel fibrillar or Nasopore, to avoid the need for removal. Check the International Normalized Ratio (INR) of patients on warfarin and manage over-coagulation.

If anterior epistaxis cannot be controlled by the outlined measures, a nasal pack such as a Rapid Rhino™ can be used, inserted parallel to the nasal floor and slowly inflated with air. A nasal tampon (Meroce) is an alternative, but it is more traumatic and requires lubrication. Commence oral cephalixin 500 mg bd (CC) to avoid toxic shock syndrome. Admit all patients with bilateral packs and the elderly or patients with obstructive sleep apnoea/respiratory disease/multiple comorbidities and unilateral packs. Uncomplicated patients with unilateral packs can be discharged and reviewed in 48 hours for removal of the pack.

In posterior epistaxis, bleeding is often from both nostrils and down the back of the throat. Most epistaxis, however, is still anterior, with failed anterior packing most commonly due to inadequate suctioning of the posterior blood clot prior to nasal packing rather than true posterior bleeding. A 9-cm Rapid Rhino 900™, which has both anterior and posterior balloons, can be used, or a Foley catheter plus anterior nasal packing with ribbon gauze, secured with an umbilical clamp. If the bleeding cannot be controlled, the patient may have to undergo surgery for ligation of the sphenopalatine artery and rarely the anterior ethmoid artery.

Patients who have had functional endoscopic sinus surgery, septoplasty and turbinectomy can present with heavy bleeding. Management should involve resuscitation measures, initial packing of the nose with cophenylcaine-soaked cotton wool, followed by Nasopore. Rapid Rhino may be necessary to control bleeding while awaiting ENT arrival. Patients who have had septoplasty and require a nasal pack should have bilateral packing. On occasions, return to surgery to control the bleeding is required.

Topical application of the injectable preparation of tranexamic acid in epistaxis has been described, using cotton pledges^{4,5}; however, a recent Cochrane review did not recommend its routine use in non-surgical bleeding.⁶

Instruct patients on appropriate first aid (sitting with head forward, ice to suck and on back of neck, pinching the soft part of the nose together

for 15 minutes), to refrain from hot drinks and hot showers for 24 hours, avoid blowing the nose, and to avoid straining as well as heavy exercise for 2 weeks.

Acute rhinosinusitis

With a presentation of nasal congestion, discharge, facial pain or pressure, it can be difficult to distinguish acute bacterial rhinosinusitis from more common viral rhinosinusitis, which resolves in 7 to 10 days without treatment. Symptomatic treatment involves regular oral analgesia, saline nasal spray, topical nasal steroid spray, and topical nasal decongestant for 3 days. If symptoms are severe, prolonged (>7 days) or worsening in an adult, consider oral amoxicillin 500 mg tds for 5 days as first line treatment. If nil improvement within 48hrs then upgrade to oral amoxycillin with clavulanic acid 875/125mg bd for 5 days. If there are any signs of complications such as unilateral periorbital oedema, then refer to ENT and commence IV broad spectrum antibiotics and IV dexamethasone as instructed.⁷

Complications include preseptal and orbital cellulitis, sub-perisosteal abscess, cerebral abscess and dural venous sinus thrombosis. Severe invasive fungal sinus infections (e.g. mucormycosis) can occur in the immunocompromised, including diabetics, requiring urgent ENT and infectious disease management. This can be a life-threatening emergency and usually presents with pain out of proportion to the clinical signs. A pale or dusky appearance of the nasal mucosa may be all that is seen, so clinical suspicion must remain high in immunocompromised hosts. If such a patient is presenting late, frank necrosis may be seen, along with orbital and cranial nerve involvement, although at this stage the mortality nears 80%.

Fractured nose

Nasal bone fracture, common after blunt trauma including contact sports and fights, is a clinical diagnosis and x-rays are unnecessary; however exclude other facial fractures, cervical spine and head injury. CSF rhinorrhoea suggests fracture of the cribriform plate. Refer immediately to ENT if there is gross deformity, open fracture or septal haematoma, which is managed with incision and drainage. A septal haematoma is a red boggy swelling over the septum, diagnosed by gentle pressure with the tip of a cotton bud. Delayed diagnosis of septal haematoma may result in necrosis of the nasal cartilage and a 'saddle nose' deformity.

If there are no indications for immediate referral, refer to ENT for review within 5-7 days. This allows time for reduction of the swelling and enables proper assessment for consideration of manipulation under anaesthesia, ideally within 2 weeks of injury date.

Nasal vestibulitis

Nasal vestibulitis presents with crusting within the nose. Management is with local antibiotic ointment such as mupirocin 2%. It can lead to nasal cellulitis requiring systemic anti-staphylococcal antibiotics and prompt intravenous treatment if there is no improvement on oral therapy. This area is part of the 'danger space of the face,' as infections can spread via valveless venous channels from the superficial to the deep venous system, rarely leading to cavernous sinus thrombosis, which is nearly always fatal.

THE THROAT

Pharyngitis/Tonsillitis

A simple sore throat is often viral and antibiotics are not warranted; however, it can be difficult to distinguish viral from bacterial infection. If the patient looks unwell or has severe symptoms and signs—such as high fever, drooling, new-onset snoring, stridor, torticollis, trismus, voice change, severe adenopathy and dehydration—treat with an antibiotic, such as phenoxymethypenicillin 500 mg (child: 15 mg/kg up to 500 mg) q6h (NDA) for 10 days. A throat swab should be taken for emerging beta lactamase-producing group A streptococcal strains. If culture is negative and the patient is improving, antibiotics can be ceased. Treat with antibiotics all indigenous Australians, patients who have had previous rheumatic fever and the immunocompromised.

Epstein-Barr virus (infectious mononucleosis) can present in young adults with severe sore throat and confluent white exudative tonsillitis. Amoxicillin should be avoided in EBV as it can cause a morbilliform rash. Treat with intravenous fluids and paracetamol. Occasionally intravenous dexamethasone is warranted for symptomatic relief. A Monospot test can be used to confirm the diagnosis; although a negative test dose cannot exclude EBV, but serology can. Viral infections can predispose to secondary bacterial infection; thus, if there are upper airway obstructive symptoms or symptoms persist or are worsening, treat with antibiotics.

In all cases of tonsillitis, if there is difficulty tolerating oral fluids, dehydration or a complication is suspected, consider admission for intravenous paracetamol, fluids, dexamethasone 8 mg stat, benzylpenicillin 1.2 g q6h. Rarely, grossly enlarged tonsils can cause upper airway obstruction and admission to a high-dependency unit (HDU) is warranted.

Quinsy (peritonsillar abscess)

Presentation is with unilateral throat pain, fever for 3 days or more, muffled 'hot potato' voice and trismus. There is unilateral swelling of the soft palate, with the tonsils displaced inferomedially and the uvula displaced to the contralateral side.

Management is aspiration or incision and drainage under local anaesthesia, in most institutions performed by ENT. Admit and give intravenous benzylpenicillin 1.2 g qid (NDA) and intravenous metronidazole 500 mg tds (NDA).

In patients over 40 years of age, especially smokers, consider squamous cell carcinoma of the tonsils and ENT follow up is recommended.

Epiglottitis/Supraglottitis

Epiglottitis, previously mainly a childhood disease, has become rare since introduction of *Haemophilus influenzae* B vaccine.

Supraglottitis, infection and swelling of the tissues above the vocal cords including the epiglottis, occurs mainly in adults. Organisms are varied, including *Streptococcus pneumoniae* and viruses. Presentation is with sore throat, odynophagia, dysphonia and sometimes stridor.⁸ Have a high index of suspicion in adults with painful swallowing, a hoarse voice and minimal signs in the pharynx to explain the symptoms; refer to ENT for flexible nasoendoscopy. Supraglottitis can on occasion cause airway compromise in adults. Management includes close monitoring of the airway, admission to an HDU or intensive care unit (ICU) under ENT, intravenous ceftazidime 1 g daily for (NDA) 5 days (NDA) and intravenous dexamethasone 8 mg stat then regular dosing (NDA).⁹ There is emerging meningococcal supraglottitis in the unvaccinated adult population.

Post-tonsillectomy bleeding

Classified as primary (within 24 hours post-operatively) or secondary (after 24 hours, normally day 5 to 10 and related to infection), post-tonsillectomy bleeding can rarely cause death from airway obstruction or haemorrhagic shock.

With an increase in day-case tonsillectomy, emergency departments are likely to see an increase in presentations due to primary post-tonsillectomy bleeds. These require a return to surgery.

Notify ENT, summon senior help, insert large-bore intravenous access and take blood for full blood count, coagulation studies, group and hold. Give bolus intravenous normal saline 20 mL/kg and intravenous paracetamol. Sit the patient upright to facilitate removal of blood.

If the patient is not actively bleeding, do not attempt to remove blood clot visible on the tonsillar bed; instead, await ENT arrival.

In brisk active bleeding, suction blood and, if a bleeding point on tonsillar fossa can be visualized, firmly apply a large cotton swab stick soaked in 1:10,000 adrenaline (or gauze soaked in 1:10,000 adrenaline held with Magill forceps) and apply pressure for 20 minutes.

If bleeding cannot be controlled with these measures, urgent return to surgery is warranted. Intravenous tranexamic acid 1 g (15mg/kg) may be given. Although there is no direct evidence for its use in post-tonsillectomy bleeding, it has been shown to reduce the need for transfusion in post-surgical bleeding.

Foreign body in throat

Oropharyngeal foreign body

Chicken or fish bones may lodge in the tonsils (commonest site), tongue base, vallecula or pyriform fossae. Rare serious complications include perforation, retropharyngeal infection and mediastinitis.

History is crucial, with onset of discomfort at the time of eating and pinpoint pain suggestive of a FB. There may be local tenderness on moving the larynx. The patient may clearly indicate the site of lodgement by pointing to a site on the neck. Using a headlight and tongue depressor, inspect the tonsils and tongue base. Tilley forceps can be used to remove a bone visible in the tonsils or tongue base.

Use a laryngeal mirror to inspect the vallecula and pyriform fossae. If no FB is seen and the patient remains symptomatic, refer to ENT for nasoendoscopy. If no bone is seen on nasoendoscopy and the history is suggestive, ENT will consider non-contrast CT of the neck.

Oesophageal foreign body

An oesophageal food bolus or bone may cause partial or complete obstruction, with inability to swallow saliva.

A lateral neck x-ray will show fish bones, when present, 20% of the time; however, subtle signs such as loss of the cervical lordosis may indicate oesophageal FB. In symptomatic patients, refer to ENT for nasoendoscopy. ENT may consider a CT of the neck or may perform rigid oesophagoscopy, depending on the history and examination (laryngeal crepitus or pain on moving the larynx, drooling, inability to swallow saliva). Soft oesophageal FBs can be dealt with by gastroenterology, but sharp objects should be referred to ENT with the aim of removal within 24 hours. Referral pathway depends on local protocols.

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SECTION 19

OBSTETRICS AND GYNAECOLOGY EMERGENCIES

Edited by Biswadev Mitra

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19.1 Pelvic pain

Anusch Yazdani

ESSENTIALS

- 1** History, abdominal and age-appropriate pelvic examination guide diagnosis.
- 2** History and examination can be supplemented, but not replaced, with appropriate investigations.
- 3** A normal pelvic examination should not preclude gynaecological referral, even in the absence of other findings.
- 4** The possibility of pregnancy must be considered in *all* patients of reproductive age with abdominal or pelvic pain under the following well-iterated tenets:
 - All female patients are pregnant until proven otherwise.
 - All pregnant patients have an ectopic pregnancy until proven otherwise.
- 5** Give effective analgesia with the regular administration of non-steroidal anti-inflammatory drugs (NSAIDs).

Presentation

This chapter outlines the initial presentation and management of the most common gynaecological conditions associated with acute and chronic pelvic pain.

History

A detailed pain history is essential in the assessment of abdominopelvic pain. This should include the site, severity, onset and time course, character, radiation, associated symptoms, radiation or shift and exacerbating or relieving factors.

As such, parietal pelvic pain may be well localized and occur secondary to peritoneal irritation, such as in appendicitis and mittelschmerz. More generalized and diffuse abdominal pain may be associated with intraperitoneal blood or inflammation resulting from an ectopic pregnancy or a tubo-ovarian abscess. Severity of pain is best assessed by the impact of the pain on function, such as activities of daily living or acute incapacitation.

Pain of abrupt onset is associated with sudden events, such as ovarian cyst rupture or adnexal torsion. Gradually worsening pain is suggestive of a long-term process, such as endometriosis or chronic pelvic inflammatory disease (PID). Pain with sexual intercourse (dyspareunia) may be associated with any pelvic process, including adnexal pathology and endometriosis.

Introduction

Pelvic and lower abdominal pain in female patients is a complex and challenging complaint. It is the second most common gynaecological symptom after vaginal bleeding, and the large differential diagnosis for female pelvic pain makes a definitive diagnosis in the emergency department (ED) difficult. A systematic approach is essential.

The emergency physician should aim to stabilize the haemodynamically unstable patient, provide adequate analgesia where appropriate,

identify conditions that require early surgical intervention and expedite the investigation and further management of females with pelvic pain.

Classification

Pelvic pain is traditionally classified as either acute or chronic. Conditions causing pelvic pain can be life threatening or inconsequential, gynaecological or non-gynaecological and/or non-organic. These presentations are often complex and require ongoing care and management, often by multiple specialties.

Table 19.1.1 Causes of acute pelvic pain

Gynaecological	Non-gynaecological		
	Intestinal	Urological	Other
Complication of pregnancy: ectopic, miscarriage	Appendicitis	Cystitis	Hernia
Complication of ovarian and adnexal cysts and masses	Diverticulitis	Acute urinary retention	Pelvic vein thrombophlebitis
Pelvic inflammatory disease	Inflammatory bowel disease	Urolithiasis	
Adnexal torsion	Gastroenteritis	Pyelonephritis	
Leiomyoma complication	Bowel obstruction Constipation		

Pain radiation may provide a clue to the underlying origin, such as pain referred via the hypogastric nerve plexus to the lower abdomen from the uterine fundus, adnexae and bladder dome. The S2–4 sacral nerve roots transmit pain from the lower uterine segment, cervix, bladder trigone and rectum to the lower back, buttocks, perineum and legs. A history of associated urological, gastrointestinal and musculoskeletal symptoms is essential.

Sexual and reproductive history

The reproductive history should focus on the current menstrual pattern and any relation to pain, the last normal menstrual period (LNMP), menarche, menopause, pregnancies (regardless of outcome) and previous gynaecological surgery. A sexual history, taken appropriately and with due consideration to privacy and confidentiality, should include time of last intercourse, contraception, number of partners, possibility of physical or sexual abuse and sexually transmitted diseases (STDs).

Psychosocial impact

Finally, the clinician should particularly consider psychosocial factors in the evaluation of chronic pain. The symptoms of fatigue, loss of energy and depressed mood are commonly associated with chronic pelvic pain; thus a screen for anxiety, depressive and somatoform disorders is essential.

Enquire about relationship distress, the partner's understanding and response to the pain and the family's response to how the patient is managing her pain.

Examination

Examination starts with an assessment of the body habitus and an establishment of baseline observations, including height, weight, temperature, pulse and blood pressure, which may indicate life-threatening haemorrhage, such as an ectopic pregnancy or overwhelming sepsis

associated with a tubo-ovarian abscess. The examination then proceeds in a systematic manner from the hands to the feet. As in all intimate examinations, it is important to provide early analgesia and establish rapport with the patient, who may be reticent, frightened or embarrassed.

Abdominal examination

Commence the abdominal examination with inspection for distension associated with obstruction, ascites or abdominal masses. Palpation and percussion can delineate areas of generalized or localized tenderness and may replicate the patient's pain. Check for hernias, inguinal nodes and other non-gynaecological causes for the patient's symptoms at the same time (Table 19.1.1).

Pelvic examination

In the sexually active patient, a pelvic examination is an important differentiator of the aetiology of pain. However, it is not mandatory when the diagnosis is certain – for example, in early-pregnancy bleeding (see Chapter 19.4). Perform this only in the presence of a chaperone, after providing a careful explanation of the procedure and obtaining consent.

It is important to note that bimanual examination has been shown to have limited sensitivity and specificity in the evaluation of pelvic organs, independent of the experience the examiner. The overall accuracy of pelvic examination under anaesthesia compared with operative findings has been estimated at 70% for specialists and 60% for medical students. Not surprisingly, there is lower sensitivity for the detection of adnexal pathology compared with the assessment uterine size or contour. Similarly, even in specialized endometriosis units, the sensitivity and specificity of vaginal examination for retro-cervical and recto-vaginal disease is only around 70%.

However, as a low-cost, low-risk intervention, it is recommended that a vaginal examination be considered as part of the assessment of the infertile couple. The pelvic examination guides the suspicion of pelvic pathology, which will then

increase the predictive value of any subsequent targeted investigations, such as ultrasound.

The pelvic examination includes the following:

- Visual examination of the vulva and urethral meatus to identify varicosities, infection or abnormal lesions.
- Speculum examination to visualize the cervix, cervical os and the vaginal vault. Note any vaginal discharge and take endocervical and vaginal swabs. However, performance of a routine cervical screening test is *not* encouraged.
- Bimanual (vagino-abdominal) examination to examine the cervix, uterus and adnexae.

The uterus is normally mobile, but conditions such as endometriosis or adhesions may cause fixation. An enlarged uterus is associated with pregnancy, fibroids or adenomyosis. The uterine axis is dependent on a number of other local pelvic factors such as the content of the bladder or bowel. A retroverted uterus can be normal, but a fixed retroverted uterus is classically associated with pouch-of-Douglas pathology, such as endometriosis.

Uterine tenderness occurs with any cause of pelvic peritonism but also conditions such as adenomyosis or fibroid degeneration. An open cervical os may be associated with the passage of intrauterine pathology, such as a failed pregnancy or clots. Cervical excitation (pain on moving the cervix) is non-specific and associated with any condition producing pelvic peritonism, such as blood or other irritants in the peritoneal cavity, including PID (see Chapter 19.2). Palpable adnexal masses are associated with more gross pathology, such as an ovarian cyst.

A normal pelvic examination does not exclude pelvic pathology but guides the selection of further definitive investigations, such as an ultrasound scan (USS) or laparoscopy.

Rectal examination

A rectal examination, where appropriate, completes the pelvic examination. This should be performed only once, preferably by the doctor providing continued clinical care. Practitioners should take note of stool consistency, faecal occult blood and the presence of a mass lesion. A rectovaginal examination allows palpation of the posterior cul-de-sac for ovarian masses, the posterior wall of the uterus and the uterosacral ligaments for nodularity and tenderness in association with endometriosis.

Laboratory investigations

Laboratory investigations depend on the history and physical examination and are tailored to the individual patient. They include the following.

Urinalysis

Urinary beta subunit of human chorionic gonadotrophin (β -hCG) is rapid, inexpensive and accurate. This should be performed in all female patients of childbearing age. The presence of leucocytes in the urine may indicate infection with a sensitivity of around 70% to 75%, but it may also be associated with inflammation of adjacent pelvic organs. The presence of red cells may indicate urolithiasis.

The urine should be sent for microscopy, culture and sensitivity if urinary tract pathology is suspected. The urine should also be sent for chlamydial and gonorrhoea polymerase chain reaction (PCR) in suspected PID (see Chapter 19.2).

Microbiological swabs

Take endocervical swabs for chlamydia, gonorrhoea and *Ureaplasma* during the speculum examination. Specific viral and bacterial swabs vulval swabs should be taken only in the presence of a vulval lesion, such as suspected herpes simplex infection.

Blood tests

Beta human chorionic gonadotrophin

The β -hCG is produced by the outer layer of cells of the gestational sac (the syncytiotrophoblast) and may be detected as early as 9 days after fertilization (see Chapter 19.4). False-positive and even false-negative serum and urine tests do occur but are extremely rare.

Full blood count, erythrocyte

sedimentation rate and C-reactive protein

A full blood count may show anaemia. A leucocytosis may indicate underlying infection or inflammation. An elevated erythrocyte sedimentation rate (ESR) or C-reactive protein is a non-specific marker of acute inflammation and would be included in the clinical diagnosis of PID at some centres.

Tumour markers

Tumour markers have a limited role in the evaluation of pelvic pain in the ED. Markers such as CA 125 may be sent in the evaluation of an adnexal mass or when endometriosis is suspected. Serial levels improve the sensitivity and specificity of such markers, usually on an outpatient basis.

Imaging

Ultrasound scan

Ultrasound should be considered a non- or minimally invasive extension of the physical examination. Other than the pregnancy test, this is the single most useful investigation in the diagnosis of acute gynaecological presentations.

Ultrasound determines normal anatomical findings, such as uterine size; the thickness and morphology of the endometrium, myometrium and adnexae; as well as pathology, such as fibroids, ovarian cysts, endometrioma, hydro/pyoosalpinges, tubo-ovarian masses and tumours.

USS is more accurate at predicting abnormal pelvic pathology, as confirmed by laparoscopy, than pelvic examination alone. Bedside operators familiar with the transabdominal and transvaginal (endocavitory) ultrasonographic examination can obtain more accurate information faster, thereby improving time to consultation or discharge. However, there are pitfalls associated with missing uncommon diagnoses. Such investigations should be followed up by a formal ultrasound.

Computed tomography scan

A computed tomography (CT) scan has poor soft tissue resolution and therefore a limited role in the assessment of pelvic pain. It may be helpful in the definition an abdominopelvic mass that cannot be assessed by USS, the identification of a urinary calculus, a Spigelian hernia or appendicitis. The radiation risk should be considered, particularly if a repeat scan is needed.

Magnetic resonance imaging

Magnetic resonance imaging (MRI) most appropriately defines adenomyosis, congenital reproductive abnormalities and endometriotic lesions. Although this modality has a limited role in an emergent ED assessment, it has a specific role in the evaluation of acute pain in the adolescent and in advanced gestation.

DIFFERENTIAL DIAGNOSIS

Patients attending the ED present with

- acute pelvic pain
- chronic pelvic pain

Importantly, patients with chronic pelvic pain may present acutely with a de novo pathology or an acute exacerbation of chronic pain.

Acute pelvic pain

Table 19.1 lists conditions that present to the ED with acute pelvic pain. The causes may be considered under the following.

Pregnancy-related

A pregnancy test must be performed in all women of reproductive age; if diagnosed, an ectopic pregnancy must then be excluded (see Chapter 19.4).

Pelvic inflammatory disease

See Chapter 19.2 on the evaluation of PID.

Adnexal mass or cyst

Ovarian mass or cyst

• 'Functional' ovarian cysts are either follicular cysts that develop during the first 14 days of the menstrual cycle prior to ovulation or luteal cysts that develop following ovulation. Such cysts are usually asymptomatic unless a complication, such as haemorrhage, rupture or torsion occurs. As these cysts are related to normal ovarian activity, an ovarian cyst in the postmenopausal woman should never be considered 'functional'.

- Neoplastic masses may be benign or malignant. Features that increase the risk of malignancy include being post-menopausal, the presence of ascites and increasing size or complexity of the lesion.
- Infective masses usually arise as part of a tubo-ovarian mass in association with PID.
- Endometrioma are deposits of endometriosis in association with the ovary, forming a collection of altered blood and cellular debris, hence the term 'chocolate cyst'.

Non-ovarian adnexal mass or cyst

- Para-ovarian and paratubal cysts are related to either the ovary or, more commonly, the fallopian tube.
- A hydrosalpinx arises in the blocked fallopian tube.

Any of these structures may present acutely due to rupture, haemorrhage or torsion.

Rupture of an ovarian cyst

Follicular cyst expansion and/or rupture at ovulation is accompanied by ovarian bleeding and peritoneal irritation, known as mittelschmerz, during the mid-cycle. Rupture of a corpus luteum cyst usually occurs between days 20 and 26 of the menstrual cycle and is associated with intraperitoneal bleeding. Rarely, such bleeding may be catastrophic, particularly if the patient is anticoagulated or has a coagulopathy.

An USS differentiates a ruptured ectopic pregnancy from a bleeding corpus luteum cyst, although they may coexist.

Intra-ovarian haemorrhage

Haemorrhage may occur into a functional cyst or tumour. The sudden onset of sharp unilateral pain with increasing intensity results from ovarian capsule distension. There may be localized or generalized peritonism dependent on the degree of peritoneal irritation and haemorrhagic extravasation. Pelvic examination may reveal a focal expanding adnexal mass, which is confirmed by USS.

Haemorrhagic ovarian cysts may be managed conservatively. Indications for intervention include haemodynamic instability, failure to obtain adequate analgesia and failure of symptom resolution.

Torsion of adnexae

The adnexae include the ovary and fallopian tube. Torsion occurs when these structures twist on their supportive appendages, compromising their vascular supply. This most commonly occurs in the third decade of life and accounts for 3% to 5% of emergency gynaecological surgery.

Over 90% of cases of adnexal torsion are associated with cystic tumours or simple cysts of the ovary. Torsion of the fallopian tube is less common and is associated with a hydrosalpinx, tubal ligation and pelvic adhesions. Both adnexal torsion and torsion of the fallopian tube present with an enlarging adnexal mass secondary to venous obstruction and secondary oedema.

Pain associated with adnexal torsion is commonly sudden in onset, sharp, unilateral and increasingly severe on a background of a dull pelvic ache. Classically it radiates from the pelvis to the flank ('reverse renal colic') and is associated with nausea, vomiting, low-grade pyrexia and urinary symptoms secondary to bladder irritation. Late cases can present with ovarian necrosis, frank peritonitis and shock.

Ovarian infection

This may rarely occur as a primary event with mumps or tuberculosis; most commonly it occurs in the setting of PID with the formation of a tubo-ovarian abscess (see [Chapter 19.2](#)).

Chronic pelvic pain

Chronic pain has been defined as pain lasting for more than 6 months, but is now recognised as pain that extends beyond a period of healing and levels of pathology that are often low and insufficient to explain the presentation. It affects millions of women worldwide and accounts for 10% of gynaecology outpatient attendances.

The commonest diagnoses associated with chronic pelvic pain are endometriosis and pelvic adhesions. However, up to 60% of patients have no visible pathology at laparoscopy and 25% remain without a definitive diagnosis.

Patients may present to the ED with an unrelated acute cause of pelvic pain, an acute exacerbation of their chronic condition or the inability to manage their debilitating condition.

Cyclic pelvic pain

Cyclic pelvic pain occurs in 30% to 50% of women of reproductive age and interferes with normal daily activities in up to 12% of cases. Cyclic pain is typically related to ovulation or menstruation, but many nongynaecological conditions can have cyclical exacerbations. Many conditions that cause cyclic pain, such as endometriosis, may ultimately come to cause acyclic, chronic pain ([Table 19.1.2](#)).

Table 19.1.2 Causes of cyclic and acyclic pelvic pain

Cyclic	Acyclic
Mittelschmerz	Chronic PID
Endometriosis ^a	Pelvic adhesions
Adenomyosis	Uterine prolapse
Cervical stenosis ^a	Chronic urethritis
	Diverticulitis
Leiomyoma (fibroid)	Irritable bowel syndrome
Primary dysmenorrhoea	Levator syndrome
	Detrusor instability
	Interstitial cystitis
	Abdominal hernia
	Abdominal wall myofascial pain
	Abuse syndromes: physical and sexual
	Depression

PID, pelvic inflammatory disease

^aMay become 'acyclic'.

Mittelschmerz

Mittelschmerz is the transient mid-cycle pain occurring at or after ovulation; it is related to increasing ovarian capsular pressure due to ovulation. The pain is typically poorly defined but becomes localized following follicular rupture and the release of fluid and/or blood, causing peritoneal irritation.

There are usually minimal findings on physical examination. Mittelschmerz is a clinical diagnosis, but USS may reveal the presence of a recently ruptured follicle. Regular NSAIDs and reassurance should be provided. Although the pain on presentation may be severe, it usually resolves spontaneously.

Endometriosis

Endometriosis is defined as the presence of ectopic endometrial glands and stroma outside the uterine cavity. Initially, the pain may be cyclic and associated with menses; as the disease progresses, however, the pain often becomes continuous and acyclic.

Endometriosis affects women of reproductive age and is the second most common cause of cyclic pain in this age group. Up to 60% of patients investigated for infertility and pain are found to have endometriosis.

Typically the pain commences a few days prior to the menses and extends variably into or beyond this period. Persistent unilateral mid-cycle pain is suggestive of an endometrioma.

Patients commonly present with dysmenorrhoea (75%), dyspareunia (20%), tenesmus or an adnexal mass (endometrioma).

Adenomyosis

Adenomyosis is a benign condition characterized by the extension of endometrial glands and stroma into the myometrium. The majority (>80%) of cases involve multiparous women in the fourth and fifth decades of life. Patients usually present with menorrhagia and dysmenorrhoea.

Pelvic examination reveals a symmetrically enlarged, slightly tender uterus with a diffusely boggy consistency. Rarely, a distinct mass (adenomyoma) may be palpated or imaged.

USS may reveal generalized uterine enlargement with an indistinct endomyometrial junction. MRI will more clearly demonstrate the pathology but is rarely indicated in the ED assessment.

The definitive diagnosis is usually made by histology, most typically at hysterectomy.

Leiomyomata (fibroids)

Leiomyomata or fibroids are benign tumours of myometrial origin. They are the most common pelvic tumour and occur in 25% of Caucasian women and 50% of black women. Their aetiology is unknown but they enlarge in pregnancy and regress after menopause.

Symptoms relate to the space-occupying effect of the lesion and may lead to chronic pelvic pain with or without bleeding. Acute pain occurs with torsion or degeneration; torsion usually involves pedunculated subserosal lesions. Degeneration results from the rapidly expanding lesion restricting its own blood supply and may occur during pregnancy as a differential of acute pelvic pain.

Primary dysmenorrhoea

This is painful menstruation in the absence of pelvic pathology and is a diagnosis of exclusion. Primary dysmenorrhoea is associated with the release of prostaglandins, principally PGF_{2α}, from the endometrium during menstruation. This causes uterine contractions, arteriolar vasoconstriction and uterine ischaemia, with the most intense pain occurring as the menstrual flow is subsiding. Primary dysmenorrhoea usually coincides with the onset of ovulatory cycles 4 to 12 months after menarche and affects up to 10% of young nulliparous women.

Primary dysmenorrhoea is associated with spasmodic, crampy lower abdominal pain radiating to the lower back and upper thighs and lasts for 24 to 48 hours. Associated symptoms include headache, nausea and vomiting. Symptoms may be alleviated by the regular administration of NSAIDs or by suppressing ovulation with the oral contraceptive pill.

19.2 PELVIC INFLAMMATORY DISEASE

Acyclic pelvic pain

Chronic pelvic inflammatory disease

See Chapter 19.2.

Pelvic adhesions

Adhesions occur when anatomical structures are abnormally bound to one another by bands of fibrous tissue. They are believed to account for pain suffered by up to 33% of patients with chronic pelvic pain, although their exact role is uncertain. They are associated with PID, endometriosis, abdominal surgery, perforated appendix and inflammatory bowel disease.

Adhesions contain nerve fibres and some of the pain perceived by patients may relate to this nerve tissue. The pain is often consistent in location and aggravated by sudden movements, intercourse or physical activity. Laparoscopy is the gold standard for its diagnosis and treatment.

Psychological

There is an association between chronic pelvic pain and somatization disorders. In addition, many women with chronic pelvic pain have suffered physical, sexual and emotional abuse and psychiatric disease is often related.

Conclusion

Female pelvic pain is a complex and challenging problem in the ED. A systematic evaluation may find a diagnosis in acute pelvic pain, but chronic conditions require review and follow-up by a specialist unit.

The resuscitation of the acutely unwell patient, exclusion of pregnancy-related problems, provision of adequate analgesia, prompt initiation of appropriate investigations and specialist referral for ongoing evaluation are fundamental to the management of gynaecological pelvic pain.

CONTROVERSIES

- Accuracy of emergency physician-focused pelvic ultrasound scan to evaluate pelvic pain
- Diagnosis and management of acute-on-chronic and chronic pelvic pain syndromes

Further reading

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19.2 Pelvic inflammatory disease

Erica Kreismann • Gar Ming Chan

ESSENTIALS

- Pelvic inflammatory disease (PID) is infection and/or inflammation of the upper genital tract.
- The clinical features cover a spectrum of presentations that depend on the extent of infection and/or inflammation, the anatomical structures involved and the specific micro-organisms.
- Chlamydia trachomatis* is the most common pathogen identified in sexually transmitted PID. Other pathogens include *Neisseria gonorrhoeae* and mixed anaerobes.
- The sequelae of PID include ectopic pregnancy, infertility and chronic pelvic pain.
- Screening high-risk patients for sexually transmitted infections reduces the incidence of PID.

Introduction

Pelvic inflammatory disease (PID) refers to a clinical syndrome resulting from infection or inflammation involving the usually sterile upper genital tract in women. Although infection can be secondary to pregnancy, instrumentation or other primary abdominal infection, the term PID is primarily reserved for an infection initiated by a sexually transmitted infection (STI). Despite differing aetiologies, these can have similar clinical presentations and are often distinguishable through thorough history taking and physical examination.

Most cases of PID are caused by the ascent of microorganisms from the vagina and endocervix into the upper genital tract.¹ The passage of organisms through the cervix is facilitated by disruption of the cervical barrier (e.g. by an STI, *Chlamydia trachomatis* and *Neisseria gonorrhoeae*, or by a surgical procedure). The majority of PID cases (85%) are caused by sexually transmitted (ST) pathogens, whereas less than 15% are associated with enteric organisms (*Escherichia coli*, *Bacteroides fragilis*, group B streptococcus, *Campylobacter*) or respiratory pathogens (*Haemophilus influenzae*, group A streptococcus, and *Staphylococcus aureus*).

Early identification and treatment are important to reduce the serious sequelae of PID, which can be debilitating; including endometriosis, salpingitis, oophoritis, peritonitis, peri-hepatitis (Fitz-Hugh–Curtis syndrome [FHCS]), tubo-ovarian abscess, ectopic pregnancy, chronic pelvic pain and infertility.

Epidemiology

The true incidence of PID is indeterminable as there are no standardized clinical criteria for diagnosis. Additionally, asymptomatic or subclinical PID as well as under-diagnoses are known to occur.

Up to 300,000 women are treated as outpatients and 10,000 are admitted to Australian hospitals each year with a diagnosis of PID. The highest reported incidence involves patients between ages 20 and 29 years. The rate of hospitalization is up to nine times higher in the indigenous population.

Risk factors

Risk factors for PID include any sexually active female with multiple partners, age below 25 years, history of PID or STIs and procedures or conditions that involve disruption of the normal cervical barrier. Chlamydial infection is the most common cause of sexually transmitted PID in Australia. The presence of an intrauterine contraceptive device (IUCD) increases the risk of PID.

in the first 3 weeks following insertion.² There is also an increased risk of PID during or shortly after the menses.³

Presentation

No symptom or sign is pathognomonic of PID and the diagnosis of PID includes a spectrum of clinical conditions determined partly by the anatomical location of the infection and by the pathogen involved. Clinical diagnosis remains the most important practical approach.

The assessment of a patient with suspected PID must involve the exclusion of other possible diagnoses, such as ectopic pregnancy, endometriosis, ruptured ovarian cyst, appendicitis and urinary tract infection. However, in view of the significant sequelae of untreated PID, the current recommendation is to consider treatment in an at-risk woman with adnexal tenderness if no other cause for the local signs can be found.⁴

History

The history should assess recognized risk factors for STIs, such as young age at first sexual intercourse, younger age, high frequency of sexual intercourse, multiple sexual partners and non-barrier methods of contraception. History should also enquire about non-sexually transmitted causes, such as recent uterine instrumentation, including operative termination of pregnancy.

Abdominal pain of less than 3 weeks' duration is the most sensitive symptom of PID; the pain is usually suprapubic and diffuse but may lateralize. However, significant lateralization suggests an alternate diagnosis or a tubo-ovarian abscess. Other symptoms may include a new or changed vaginal discharge, dyspareunia, post-coital and/or intermenstrual bleeding.

Examination

Adnexal tenderness on bimanual examination is the most sensitive examination finding and is present in 95% of cases but has a specificity of only 3.8%.⁴ Other examination findings with high sensitivity include lower abdominal, cervical motion or uterine tenderness. However, as isolated findings, each of these lacks sensitivity.

Rebound tenderness, fever, and decreased bowel sounds may be present. While the presence of fever is associated with a more severe infection, the absence of fever does not exclude the diagnosis.

Fitz-Hugh–Curtis syndrome (perihepatitis)

FHCS is a perihepatitis with focal peritonitis resulting from the transcoelomic spread of inflammatory peritoneal fluid to the subphrenic and sub-diaphragmatic spaces. It occurs in approximately 10% cases of acute PID, and whereas FHCS is

usually an incidental finding in patients with PID, occasionally right-upper-quadrant (RUQ) pain is the presenting symptom and the diagnosis is often considered only when upper abdominal ultrasound rules out biliary tract disease.⁵

Investigations

Haematology

There are no specific laboratory tests to diagnose PID. The white cell count, erythrocyte sedimentation rate and C-reactive protein are all raised as non-specific markers of inflammation but lack sensitivity and specificity for the diagnosis.

Biochemistry

Check a beta subunit of human chorionic gonadotrophin (β -HCG) level on all women of childbearing age. Although PID is uncommon in pregnancy, especially after the first trimester, the diagnosis of PID in pregnancy has significant implications.

Pelvic pain secondary to a complication of pregnancy, such as an ectopic pregnancy, is an important differential diagnosis.

Microbiology

Collect and send endo-cervical swabs for microscopy and culture and polymerase chain reaction (PCR) or the nucleic acid amplification test (NAAT) for *N. gonorrhoeae* and *C. trachomatis*. A positive result retrospectively supports the diagnosis of PID, defines antibiotic sensitivities and identifies the need to treat partner(s) with sexual contact over at least 6 months.⁶ However, a negative result does not exclude the diagnosis, as the sensitivity of microscopy is only 60%.⁶

The presence of either purulent discharge or white blood cells (WBCs) in the vaginal discharge is a sensitive marker for PID. The diagnosis of PID is thus unlikely if the cervical discharge appears normal and there are no WBCs in a wet slide preparation.⁷ All patients who are diagnosed with acute PID should be considered for a full sexual health evaluation, including hepatitis B, syphilis and HIV serology, plus partner contact tracing.⁸

Ultrasound

Ultrasound, particularly transvaginal, is valuable in the assessment of suspected PID to identify complications such as tubo-ovarian abscess and to exclude other causes of pelvic pain. However, ultrasound features, such as free fluid in the pouch of Douglas, lack sensitivity in the diagnosis of mild to moderate PID.

Laparoscopy

Laparoscopy is no longer considered to be a gold standard for the diagnosis of PID as,

although it has a specificity approaching 100%, the sensitivity is as low as 50% to 80%. The main indications for laparoscopy include acute pain of uncertain origin and the diagnosis of chronic pelvic pain.

Differential diagnosis

Important differential diagnoses include ectopic pregnancy, endometriosis, complications of ovarian cysts and tumours, appendicitis, diverticulitis and urinary tract infection.

Management

The presumptive diagnosis of PID is made in high-risk female patients (see earlier discussion of risk factors) who present with lower abdominal or pelvic pain unattributed to other aetiologies and who have cervical motion, adnexal, or uterine tenderness on examination. The sensitivity of this clinical diagnosis is only 65% to 90%;⁶ however, because of the serious potential reproductive sequelae, the initiation of empiric antibiotic therapy is warranted. Patients with mild to moderate PID may be treated as outpatients. There is no evidence of improved outcomes between inpatient and outpatient treatment with respect to fertility, chronic pelvic pain or recurrence of PID.⁹

Indications for inpatient treatment include severe PID, inability to tolerate oral antibiotics, failed oral therapy and/or compliance issues, pregnancy and when a surgical emergency cannot be excluded.

Antibiotic therapy

Sexually acquired pelvic inflammatory disease

- Mild to moderate infection:* ceftriaxone 500 mg IM or IV as a single dose and azithromycin 1 g PO as a single dose plus metronidazole 400 mg PO q 12 h for 14 days plus azithromycin 1 g PO as a single dose plus either doxycycline 100 mg PO q 12 h for 14 days or (for women who are pregnant or patients suspected of being non-compliant with doxycycline) azithromycin 1 g PO as a single dose 1 week later.
- Severe infection:* ceftriaxone 2 g IV qd plus azithromycin 500 mg IV qd plus metronidazole 500 mg IV q 12 h.¹⁰

If there is strong clinical suspicion of sexually transmitted infection, contact tracing and presumptive treatment of sexual contacts with azithromycin (1 g PO as a single dose) should be initiated. Sexual contacts should also be investigated for *C. trachomatis*, *N. gonorrhoeae* and *M. genitalium*.

19.3 ABNORMAL VAGINAL BLEEDING IN THE NON-PREGNANT PATIENT

Non-sexually acquired pelvic inflammatory disease

- Mild-to-moderate infection:** amoxicillin plus clavulanate 875/125 mg PO bd for 14 days, plus doxycycline 100 mg PO q 12 h for 14 days.
- Severe infection:** amoxicillin or ampicillin 2 g IV 6-hourly, plus gentamicin IV plus metronidazole 500 mg IV bd.

Disposition

Patients discharged on oral medication should be reviewed within 24 to 48 hours to assess the response to therapy. All patients with sexually acquired PID should be counselled regarding safe sex practices and other sexual health issues, such as hepatitis B and human papillomavirus vaccination.

Prognosis

Women with PID are at increased risk of ectopic pregnancy, chronic pelvic pain and infertility.

CONTROVERSIES

- Clinical criteria for the initiation of treatment in PID
- The role of ultrasound in the primary diagnosis of PID
- Indications for laparoscopy in PID

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19.3 Abnormal vaginal bleeding in the non-pregnant patient

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ESSENTIALS

- Start the assessment of any patient with vaginal bleeding by excluding pregnancy.
- Locate the anatomical site of bleeding and assess the severity looking for signs of hypovolemia and shock.
- Familiarize yourself with the PALM-COEIN classification system.
- Consider coagulopathy as a cause of heavy uterine bleeding in all patients, especially adolescents.

Introduction

Vaginal bleeding is often divided into two major categories: bleeding which occurs in a pregnant patient and bleeding in the non-pregnant patient. Therefore, in conjunction with determining hemodynamic stability, the first step for a patient presenting with vaginal bleeding is to exclude pregnancy. See Chapters 19.4 and 19.5 if the woman is pregnant.

In this chapter, we will deal exclusively with bleeding in non-pregnant women. Abnormal

vaginal bleeding is the most common reason women seek gynaecologic care.¹ Bleeding may be from the uterus, lower genital tract (vulva, vagina, cervix) or from systemic causes. The PALM-COEIN acronym was introduced in 2011 by the International Federation of Gynecology and Obstetrics (FIGO) with a goal of avoiding confusing or poorly defined terminology in the classification of acute abnormal uterine bleeding. With this system, aetiologies are classified as structural or nonstructural: PALM for structural (polyp, adenomyosis, leiomyoma, malignancy

and hyperplasia) and COEIN for nonstructural (coagulopathy, ovulatory dysfunction, endometrial, iatrogenic, not otherwise classified).

Physiological uterine bleeding

Physiological uterine bleeding is associated with ovulatory menstrual cycles, which occur at regular intervals every 21 to 35 days, and last for 3 to 7 days. The average volume of blood loss is 30 to 40 mL (each normal sized tampon or pad holds 5cc when soaked through) with >80 mL being defined as menorrhagia.

The menstrual cycle is controlled by the hypothalamic–pituitary–ovarian (HPO) axis. During the first 14 days, oestrogen is produced by the developing follicle, leading to proliferation of the endometrium, which reaches a thickness of 3 to 5 mm. Oestrogen acts on the pituitary gland to cause the release of follicle stimulating hormone (FSH) and luteinizing hormone (LH), which result in ovulation. The corpus luteum then releases progesterone in excess of oestrogen.

Progesterone causes stabilization of the endometrium during the secretory phase of the menstrual cycle. In the absence of fertilization, there is involution of the corpus luteum and a

fall in oestrogen and progesterone levels. This results in vasoconstriction within the endometrium, which consequently becomes ischaemic and is shed as normal menstrual bleeding.

Pathological uterine bleeding

Pathological causes include infection, structural abnormalities, such as polyps, fibroids, arteriovenous malformations (AVM) or malignancy, drugs, hyperprolactinaemia, coagulopathy and thyroid endocrinopathy. Terms associated with abnormal uterine bleeding are inconsistently defined, but may be broadly considered as abnormal uterine bleeding with ovulatory menstrual cycles and abnormal uterine bleeding with anovulatory menstrual cycles.

Abnormal uterine bleeding with ovulatory menstrual cycles

The most common cause of abnormal uterine bleeding is menorrhagia occurring in ovulatory menstrual cycles. This presents as regular heavy bleeding and may result in anaemia. In these women, the menstrual blood has been shown to have increased fibrinolytic activity and/or increased prostaglandins.

Abnormal uterine bleeding with anovulatory menstrual cycles

Abnormal uterine bleeding or metrorrhagia due to anovulatory menstrual cycles, sometimes referred to as dysfunctional uterine bleeding (DUB), presents as irregular bleeding of variable volume. In anovulatory menstrual cycles and other high oestrogen states, there is a relative lack of progesterone to oppose the oestrogenic stimulation of the endometrium. This results in excessive proliferation and occasionally hyperplasia/metaplasia of the endometrium. The endometrium also becomes 'unstable' and prone to erratic sloughing.

Clinically, this presents as irregular, often heavy, menstrual bleeding. Anovulatory cycles are due to immaturity or disturbance of the normal HPO axis. This is seen at the extremes of reproductive ages, in the first decade after menarche and in premenopausal women, as well as in polycystic ovary syndrome (PCOS) and during times of either physical or emotional stress.

CAUSES OF ABNORMAL VAGINAL BLEEDING

It is essential initially to review all the possible causes of vaginal bleeding which may be considered by pathophysiology and/or pathological location ([Box 19.3.1](#)).

History

A careful menstrual history helps determine the cause of the vaginal bleeding. A history of vaginal

Box 19.3.1 Differential diagnosis of abnormal vaginal bleeding

- Ovulatory bleeding 'menorrhagia'
Anovulatory bleeding: sometimes known as dysfunctional uterine bleeding (DUB)
- Uterine and ovarian pathology:
uterine fibroids (pelvic pain, dysmenorrhoea) endometriosis; adenomyosis (dysmenorrhoea, dyspareunia, pelvic pain, infertility) pelvic inflammatory disease and pelvic infection (fever, vaginal discharge, pelvic pain, intermenstrual and postcoital bleeding) endometrial polyps (intermenstrual bleeding) endometrial hyperplasia; endometrial carcinoma (pelvic pain, abnormal bleeding, postcoital bleeding)
polycystic ovary syndrome (irregular bleeding, infertility and hirsutism)
- Systemic disease:
coagulation disorder; bleeding diathesis such as von Willebrand disease
liver or renal disease
hypothyroidism (fatigue, constipation, coarse features, alopecia)
- Iatrogenic cause:
anticoagulation
intrauterine device
chemotherapy
sex steroids

trauma may indicate vulval or vaginal wall bleeding. The vaginal trauma may be associated with either consensual or non-consensual intercourse or a vaginal foreign body. Exposure in utero to diethyl stilboestrol (DES) should raise suspicion of vaginal malignancy.

The patient's estimate of the amount of vaginal bleeding is often inaccurate and has limited use in diagnosis, other than the presence of clots, which is abnormal and suggests heavy bleeding.² Ask about additional information, including known gynaecological cancer, a known bleeding disorder or a family history of a bleeding diathesis and exogenous sex steroid use. Up to 13% of women with heavy menstrual bleeding have some variant of von Willebrand disease, and up to 20% of women may have an underlying coagulation disorder.³

Postcoital or intermenstrual bleeding

Postcoital or intermenstrual bleeding may be symptomatic of cervical or uterine pathology. Common causes include ectropion or polyps on the cervix, infection or malignancy causing bleeding from the vagina, cervix or uterus.

Postmenopausal bleeding

Postmenopausal bleeding is related to vaginal or uterine conditions, which include infection, atrophy, trauma or malignancy. All postmenopausal bleeding is abnormal and requires follow-up

evaluation for endometrial cancer. Risk factors for uterine malignancy include obesity, age >40 years, nulliparity, tamoxifen use, infertility and chronic anovulatory cycles.

Anovulatory bleeding

A diagnosis of anovulatory bleeding is classically made from the history of irregular menses with periods of amenorrhoea followed by heavy bleeding, in the absence of features suggesting a structural or a histological uterine abnormality.² A menstrual cycle of less than 21 days or more than 35 days, even if regular, is usually anovulatory.

Physical examination

First determine the haemodynamic stability of the patient. Physiological menorrhagia alone is rarely a cause of shock and other diagnoses, such as cervical malignancy or endometrial AVM, should be considered. Also look for evidence of anaemia, petechiae suggesting a bleeding tendency and thyroid endocrinopathy.

Abdominal and pelvic examination

Palpate the abdomen to assess for uterine enlargement. Inspect the vulva for local causes of bleeding, including trauma and infection. Vaginal speculum examination should include assessment of the vaginal walls and the cervix, ideally, with a clear plastic speculum for ease of view. Speculum examination will also allow an assessment of the site and amount of bleeding. Bimanual examination is indicated to assess for local tenderness, uterine size and/or masses and adnexal masses or cervical motion tenderness.

Investigations

These are based around laboratory tests and ultrasound scanning.

Laboratory investigations

- Serum or urinary β-hCG pregnancy test. Perform this immediately on all women of childbearing age, even in the face of assurances from the patient that pregnancy could not be possible. Urine pregnancy tests are highly sensitive, detecting β-hCG levels as low as 25 IU/L.
- Full blood count. Perform this in all patients to identify anaemia. Add iron studies if the blood count shows a hypochromic, microcytic picture.
- Thyroid function tests. These are only indicated in women with menorrhagia and anovulatory bleeding or with clear evidence of thyroid endocrinopathy (see Chapter 11.3). Do not send routinely.

19.3 ABNORMAL VAGINAL BLEEDING IN THE NON-PREGNANT PATIENT

- Coagulation profile.** Perform on all adolescents and any women with unusually heavy uterine bleeding.

Radiology

- Ultrasound is requested to assess the pelvic organs. Particular attention is paid to the myometrium looking for fibroids or adenomyosis, the endometrial thickness and the endometrial cavity for polyps or retained products of conception (positive β -hCG).
- Ultrasound may also identify an AVM, which may be congenital or acquired either postpartum or, more commonly, post-instrumentation of the uterus.

Management

Management may be considered as general supportive measures and then specific treatment.

General supportive measures

Resuscitation should proceed in the usual manner with initial therapy determined by the degree of haemodynamic instability or severity of anaemia.

Specific treatment for structural lesions

Vaginal wall bleeding

Vaginal wall bleeding secondary to trauma generally settles spontaneously. Examination under anaesthesia (EUA) is indicated for vaginal trauma if the laceration extends beyond the mucosa or if examination is too uncomfortable for the woman.

Cervical bleeding

Cervical bleeding rarely requires immediate therapy. However, cervical bleeding from malignancy may occasionally be difficult to control as lesions tend to be friable. Attempt cautery with silver nitrate and, if this fails to control the bleeding, consider placing a vaginal pack. Refer the patient immediately to the gynaecology team.

Specific treatment for vaginal and endometrial infection

Vaginal and endometrial infections are dealt with as outlined in Chapter 19.2. Arrange for the partner(s) to have contact tracing and simultaneous antibiotic treatment as necessary.

Specific treatment for menorrhagia associated with ovulatory cycles

Choice of treatment depends on clinical stability, acuity of presentation, suspected aetiology of bleeding, comorbidities and desire for future fertility. Medical therapy is considered the first line for initial treatment.

Medical Management

Hormonal management is often the preferred initial treatment in patients without suspected bleeding disorders. Options include combined oral contraceptives, oral progestins or IV conjugated equine estrogen.³

Oral progestins, such as norethisterone 5 mg bd or tds or medroxyprogesterone acetate 10 mg one to three times a day, on days 1 to 21 of a 28-day cycle reduce blood loss by up to 83%, although adherence can be poor due to nausea, lethargy, headache, bloating with fluid retention and acne.⁴ In addition, treatment should be limited to less than 6 months because of the risk of hypo-oestrogenism.

Levonorgestrel-releasing intrauterine system

While not commonly placed in the emergency department (ED), we must be aware, as acute care providers, of the option of a levonorgestrel-releasing intrauterine system (LNG-IUS). It can be used to treat heavy menstrual bleeding associated with ovulatory or anovulatory cycles and has high patient satisfaction rates. It reduces bleeding more effectively than a 21-day course of norethisterone and avoids the systemic effects of oral progestins.⁴

Tranexamic acid

Tranexamic acid is a plasminogen activator inhibitor that promotes local haemostasis. Recommendation is for either oral or IV tranexamic acid, and it is considered first line in the acute setting.¹ To 1.5 g orally, 6- to 8-hourly for the first 3 to 5 days of menstruation.⁴ Side effects include nausea and leg cramps, but it is generally well tolerated. Although long-term studies have not shown an increase in thromboembolic events, active thromboembolic disease is a contraindication to use.⁵ It reduces blood loss by around 47%.⁴

Non-steroidal anti-inflammatory drugs

Non-steroidal anti-inflammatory drugs (NSAIDs) block prostaglandin PGE₂, a vasodilator found in excess in patients with menorrhagia.⁶ The efficacy of NSAIDs is less than other therapies with only a 29% reduction in blood loss. However, they are well tolerated and are particularly helpful if there is associated dysmenorrhoea.

Usual doses are mefenamic acid 500 mg tds, naproxen 250 mg tds or ibuprofen 400 mg tds.

Combined oral contraceptive

As a longer-term therapy, the combined oral contraceptive pill reduces the mean menstrual blood loss by about 43% using a pill containing 35 µg of ethinyloestradiol. Contraindications include the desire for fertility and all contraindications to oestrogens.

Specific treatment for heavy anovulatory uterine bleeding

Acute irregular heavy bleeding is most commonly secondary to anovulatory bleeding. There are many different treatment regimens and ED physicians should select a range of agents with which to become familiar.^{2,3,7,8} The underlying pathology is a relative lack of progesterone and so treatment should include progestin therapy to stabilize the endometrium. This may be combined with tranexamic acid and/or an NSAID, which decreases the amount of blood loss. If anovulatory cycles are expected to continue, then progestin therapy may need to be long term.

Progestin therapy

Medroxyprogesterone 10 mg orally, once daily for the same 12 days of each calendar month or norethisterone 5 mg orally, once daily for the same 12 days of each calendar month.⁴ Side effects include bloating, headache, acne and breast tenderness.

Tranexamic acid and non-steroidal anti-inflammatory drugs

These can be added to progestin therapy for heavy anovulatory bleeding.

Combined oral contraceptive pill

The combined oral contraceptive pill (COCP) may be used to decrease blood loss in ovulatory cycles and to regulate and decrease blood loss in anovulatory cycles. It also provides contraception. Start a monophasic COCP that includes at least 30 µg of ethynodiol dienoate and a progestin.

Consider histological assessment of the endometrium in patients over 35 years of age, prior to commencing hormone therapy. An antiemetic is recommended with hormonal therapy.

Other treatments not usually commenced in the emergency department

Surgical procedures

Dilatation and curettage (D&C) is a method of endometrial sampling and not a long-term treatment for menorrhagia or irregular menstrual cycles. The procedure is often combined with hysteroscopy, which allows visual assessment of the uterine cavity and biopsy if indicated. If structural abnormalities are revealed, polypectomy or myomectomy may be required. Other surgical interventions to be considered are uterine artery embolization, endometrial ablation and hysterectomy, and these should be discussed directly with the consulting gynaecologist and patient.

Other drug treatments

Other treatments that are not usually commenced in the ED include the levonorgestrel-releasing intrauterine system, such as Mirena,

or long-acting progestogens, such as medroxyprogesterone acetate (Depo-Provera), which may prove successful if oral agents fail.

Gonadotrophin-releasing hormone (GnRH) analogues should only be commenced by a gynaecologist when other medical and surgical treatments are contraindicated or prior to proposed surgery.

Disposition

Admit patients with haemodynamic instability or profound anaemia. Consult the gynaecology team if a significant underlying cause for the abnormal bleeding is likely. However, most patients may be discharged and followed up in an outpatient clinic.

CONTROVERSIES

- Precise regimen for progestins in the management of anovulatory bleeding.
- Indications for endometrial sampling, especially in postmenopausal women.
- Role of surgical versus medical therapy in the long-term management of menorrhagia.

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19.4 Ectopic pregnancy and bleeding in early pregnancy

Gim Tan

ESSENTIALS

1 Approximately 25% of all clinically diagnosed pregnancies are associated with bleeding in the first 12 weeks, of which approximately 50% of cases will be due to a failed pregnancy.

2 Ectopic pregnancy occurs at a rate of around 1:1000 diagnosed pregnancies.

3 The management of ectopic pregnancy and failed pregnancy may be surgical, medical or conservative.

Introduction

Bleeding in early pregnancy is a common problem affecting approximately 25% of all clinically diagnosed pregnancies, and, of these, approximately 50% will have bleeding due to a failed pregnancy.¹ Other causes of bleeding include ectopic pregnancy and molar pregnancy; however, most bleeding is incidental or physiological and has no bearing on the outcome of the pregnancy.

Terminology

The terminology used to describe early pregnancy bleeding conditions is defined as follows.

Miscarriage

A miscarriage is defined as pregnancy loss occurring before 20 completed weeks' gestation or a foetus less than 400 g weight, if the gestation is unknown.

Threatened miscarriage

A threatened miscarriage is any vaginal bleeding other than spotting before 20 weeks' gestation.

Inevitable miscarriage

Inevitable miscarriage is a miscarriage that is imminent or in the process of happening.

Complete miscarriage

A complete miscarriage is when all products of conception have been expelled.

Failed pregnancy

A failed pregnancy is defined on ultrasound criteria. These include the finding of a crown rump length (CRL) greater than 6 to 10 mm with no cardiac activity or a gestational sac equal to or greater than 20 to 25 mm with no foetal pole (previously referred to as an anembryonic pregnancy or a blighted ovum).

A failed pregnancy may then remain in the uterus (previously termed a missed abortion) or may progress to either an incomplete or complete miscarriage, as defined by the presence or absence of pregnancy-related tissue in the uterus.

Pregnancy of unknown location

A pregnancy of unknown location refers to the situation where the beta subunit of human chorionic gonadotrophin (β -hCG) is elevated, but no pregnancy can be identified on ultrasound.

Ectopic pregnancy

An ectopic pregnancy is a pregnancy that is implanted outside of the normal uterine cavity. The most common location for an ectopic pregnancy is in the fallopian tube. Other sites include cervix ($\approx 1\%$), ovary (1% to 3%), interstitial (1% to 3%), abdomen (1%) and, rarely, in a uterine scar.

The natural history of an ectopic pregnancy may be one of resorption, spontaneous miscarriage (vaginal or tubal) or it may continue to grow and disrupt the surrounding structures (rupture).

History

History should include the date of the last normal menstrual period (LNMP) and a complete obstetric and gynaecological history, including the use of assisted reproductive technology (ART). Risk factors for ectopic pregnancy include a past history of tubal damage, a previous ectopic pregnancy, pelvic infection, tubal surgery, assisted reproductive technology, increased

19.4 ECTOPIC PREGNANCY AND BLEEDING IN EARLY PREGNANCY

age, smoking and progesterone-only contraception. Intrauterine contraceptive devices (IUDs) decreases the chance of intrauterine pregnancies, but whether they increase the likelihood of an ectopic pregnancy is currently debated.²

When estimating the amount of vaginal bleeding, it is useful to quantify the blood loss compared with the woman's normal menstrual loss. Heavy bleeding and the passage of clots are more common with failed intrauterine pregnancy, as ectopic pregnancy is rarely associated with heavy bleeding.

However, the history of passage of foetal products should not be used as the basis for diagnosis of a miscarriage. Blood clots or a decidua cast may be misinterpreted as the products of conception. In addition, the correct identification of the products of conception does not exclude the possibility of a live twin or of a coexistent ectopic pregnancy (known as a heterotopic pregnancy).

Examination

Determination of the patient's haemodynamic status and the rate of ongoing bleeding are a priority. Hypotension, tachycardia and signs of peritoneal irritation suggest a ruptured ectopic pregnancy or bleeding from a corpus luteal cyst. A complete physical examination should be performed, including assessment of the woman's mental state, as pregnancy loss may have a profound psychological impact on some women. The role of pelvic examination in the assessment of early pregnancy bleeding is limited, providing that there is prompt access to transvaginal ultrasound examination. Pelvic examination does not provide further diagnostic information over ultrasonography used in conjunction with beta human chorionic gonadotropin assays. When performed, bimanual examination can localize tenderness and identify adnexal masses and can also give an estimate of the size of the uterus. However, bimanual examination lacks sensitivity and specificity in identification of a small, unruptured ectopic pregnancy and gives no information about the viability of the pregnancy. Speculum examination is indicated only in those presenting with severe bleeding or hypotension, as removal of obstructing endocervical products can be a crucial resuscitative measure.³

Investigations

Biochemistry

Beta subunit of human chorionic gonadotrophin

The β-hCG is produced by the outer layer of cells of the gestational sac (the syncytiotrophoblast) and may be detected as early as 9 days after fertilization. The β-hCG level increases by

approximately 1.66 times every 48 hours, then plateaus, before falling at around 12 weeks to a lower level.

At any stage of the pregnancy there is always a large range of normal values and a single value cannot be used to determine the location or viability of the pregnancy. There is also potentially significant laboratory-to-laboratory variation, and as such, serial hormone levels may only be compared if they are from the same laboratory.

The half-life of β-hCG is approximately 48 hours, which results in the β-hCG level remaining elevated for a number of weeks post-miscarriage or termination. Therefore a positive pregnancy test or a single β-hCG level is unreliable to confirm ongoing pregnancy and cannot be used to identify retained products of conception. High levels of β-hCG may be associated with multiple or molar pregnancies.

Urine pregnancy test

Urine pregnancy tests are sensitive to a β-hCG level of 25 to 60 IU/L. Thus false negatives may rarely occur in the setting of early pregnancy or dilute urine.

Haematology

A full blood count and cross-match should be arranged for haemodynamically unstable patients. Blood group and Rhesus factor should be determined on all patients.

Ultrasound

Ultrasound should be performed in every patient to identify the anatomical location of the pregnancy and to assess foetal viability. The introduction of emergency department (ED) ultrasound provides a cost-effective method for the assessment of a patient presenting with bleeding in early pregnancy, but it does not preclude a formal ultrasound

Transvaginal ultrasound

A gestational sac can be identified as early as 31 days' gestation using transvaginal ultrasound. A yolk sac can be identified within the gestational sac at 5 to 6 weeks when the β-hCG is around 1500 IU/L (except in the case of anembryonic pregnancy). Embryonic cardiac activity should be identified by approximately 39 days' (5.5 weeks') gestation, at which stage the crown rump length of the embryo is approximately 5 mm.

Transabdominal ultrasound

The findings on transabdominal ultrasound are similar approximately 1 week later. Previously a β-hCG of approximately 1500 IU was called the discriminatory zone, meaning that if no pregnancy was identified in the uterus at this level, then an ectopic pregnancy could be diagnosed. However, trans-abdominal ultrasound is still

valuable even when the β-hCG level is less than 1000 IU/L, as direct or indirect signs of an ectopic pregnancy can often be found at levels lower than 1500 IU.⁴

The two most common errors in the interpretation of early pregnancy ultrasound include the misidentification of a pseudo-sac or an endometrial cyst as an early gestational sac. A pseudo-sac is a small collection of fluid seen in the uterine cavity, often in association with an ectopic pregnancy. Secondly, assuming that an ultrasound finding of a uterus with no signs of pregnancy is a complete miscarriage, rather than correctly identifying the situation as that of a pregnancy of unknown location. One study of 152 women with a history and examination supporting a complete miscarriage had a 6% rate of ectopic pregnancy.

Heterotopic pregnancy

Identification of an intrauterine pregnancy does not exclude a coexistent ectopic (heterotopic) pregnancy. The incidence of heterotopic pregnancy in the general population is around 1:3889 but, in patients who have undergone ART, the incidence is as high as 1:100 to 1:500.⁵ Thus, in the patient with risk factors and clinical features of an ectopic pregnancy, finding an intrauterine gestation cannot rule out a coexistent ectopic pregnancy.

Management

Rh(D) immunoglobulin

All patients should have their blood group and Rhesus (Rh) factor determined. As little as 0.1 mL of Rh(D) positive foetal blood will cause maternal Rh iso-immunization. In the first trimester, a dose of 250 IU Rh(D) immunoglobulin is given when there has been a miscarriage, termination of pregnancy (medical or surgical), ectopic pregnancy and chorionic villous sampling within 72 hours of onset of the bleeding. There is insufficient evidence that threatened miscarriage in the first 12 weeks necessitates anti-D. Further doses may be required in repeat or prolonged bleeding.

A dose of 625 IU Rh(D) is recommended for obstetric haemorrhage in the second and third trimester. Blood should be taken for Rh antibody titre prior to administration of anti-D, in order to detect those who have already become immunized.

ECTOPIC PREGNANCY

Haemodynamically unstable patient

A haemodynamically unstable patient with suspected ectopic pregnancy should be resuscitated and referred for surgical intervention. A ruptured

corpus luteal cyst may rarely cause similar haemodynamic compromise and is also diagnosed at laparoscopy.

Haemodynamically stable patient

The management options for a haemodynamically stable patient with an ectopic pregnancy found on ultrasound include observation, medical treatment or surgical intervention.

Factors to be considered in reaching a management decision include the location of the ectopic pregnancy, the β -hCG level, the size of the ectopic pregnancy, the presence of foetal cardiac activity and patient factors.

Selection criteria for conservative or medical management depend upon the gynaecological team, but may include stable patients with a low β -hCG (<1000 IU/L) which is falling, non-tubal ectopic pregnancy or a small tubal ectopic pregnancy (<3 cm) with no cardiac activity and a β -hCG level less than 5000 IU/L.

MISCARRIAGE

Haemodynamically unstable patient

Any patient with heavy vaginal bleeding, hypotension and bradycardia should have an immediate speculum examination as, occasionally, the products of conception cause dilatation of the cervix, which leads to cervical shock, a form of neurocardiogenic shock. Removal of the clot and products of conception from the cervical os usually results in cessation of bleeding and reversal of the shock.

Haemodynamic compromise may also be secondary to significant blood loss related to the miscarriage. Fluid resuscitation should be instituted simultaneously with attempts to control the bleeding by removal of blood clot and the products of conception from the cervix and vagina. Uterine contraction may be induced by administering ergometrine 200 µg IM if removal of clot and tissue fail to control the bleeding. Emergency surgical evacuation of the uterus is then required.

Haemodynamically stable patient

A haemodynamically stable patient with threatened miscarriage is treated expectantly. For other types of miscarriages, expectant, surgical or medical management (such as prostaglandin E1) may be considered in consultation with the gynaecology service. Expectant management is contraindicated if the woman has an increased risk of haemorrhage, if she has had an adverse or traumatic pregnancy related experience such as a stillbirth or miscarriage, if she is on anticoagulants or there is infection present. Currently, there is insufficient evidence to support the superiority of any one of these three treatment options. Although studies have assessed the time to achieve complete miscarriage and the frequency of complications, they suffer from different inclusion criteria and duration of conservative management.

Conservative management is usually associated with slightly longer duration of bleeding and pain and possibly the need for transfusion. The incidence of infection was similar or higher in the surgical group. Complications of surgery, such as cervical trauma, uterine perforation and intrauterine adhesions, were uncommon.

The woman's preference should be a consideration in recommending a treatment option and the haemodynamically stable patient may be discharged for ongoing care by the gynaecology team. Discharge advice should include explicit indications of when to return, such as heavy bleeding or signs of infection, and advice regarding pelvic rest and a clear follow-up plan.

Prognosis

Approximately 50% of patients with bleeding in early pregnancy will proceed to term. Only 60% of women with an ectopic pregnancy will conceive again naturally, and will have a recurrent ectopic rate of 25% to 30% in subsequent pregnancies.

Disposition

Patients with a threatened miscarriage and an ultrasound confirming a live intrauterine gestation have an 85% to 90% chance of the

pregnancy progressing to term. Poor prognostic indicators include advanced maternal age, ultrasound findings of an enlarged yolk sac and foetal bradycardia after 7 weeks' gestation. Patients should be advised to avoid sexual intercourse and not to use tampons until after the bleeding has settled. There is no evidence to support improved pregnancy outcomes from recommending bed rest. Referral for counselling or psychological support may be indicated in some women.

Investigation for an underlying cause is generally not indicated until after a third consecutive miscarriage. These include anatomical uterine abnormalities, thrombophilic disorders such as antiphospholipid syndrome and Factor V Leiden, chromosomal abnormalities, immune disorders, hormonal disorders, infection and environmental and lifestyle factors.

Patients with a non-viable intrauterine pregnancy or an ectopic pregnancy are referred to a gynaecology service for ongoing management.

CONTROVERSIES

- Role of point of care ultrasound within the ED
- Indications for anti-D immunoglobulin
- Management of patients with pregnancy of unknown location
- Best practice for emptying the uterus following a failed pregnancy
- Best practice for managing an ectopic pregnancy

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19.5 Bleeding after the first trimester of pregnancy

Fatima Rahman

ESSENTIALS

- 1** Up to 5% of pregnant women will have significant bleeding after 20 weeks' gestation.
- 2** Resuscitation of the mother followed by ultrasound localization of the placenta are the priorities of management for patients with heavy vaginal bleeding after 20 weeks' gestation.
- 3** Secondary postpartum haemorrhage is commonly caused by endometritis or retained products of conception.

Introduction

Pregnancy is measured in trimesters from the first day of the last menstrual period, totalling 40 weeks. The first trimester of pregnancy is week 1 through week 12, or about 3 months. Vaginal bleeding after the first trimester may be due to a number of causes. The most common is classified as 'incidental', where the bleeding is not directly related to pregnancy.

Antepartum haemorrhage

Bleeding from the genital tract that occurs after 20 weeks' gestation and before the onset of labour is classified as an antepartum haemorrhage (APH). APH complicates 2% to 5% of all pregnancies. It is associated with increased perinatal morbidity and mortality and contributes significantly to health care utilization.¹

Postpartum haemorrhage

Primary post-partum haemorrhage (PPH) is defined as heavy (>500 mL) vaginal bleeding within 24 hours of delivery and is discussed in Chapter 19.7.

Secondary postpartum haemorrhage

Secondary PPH is defined as bleeding >24 hours, or up to 6 weeks after delivery, most commonly as a result of infection or retained products of conception.

ANTEPARTUM HAEMORRHAGE

Differential diagnosis

Incidental causes

These include bleeding from the lower genital tract, most commonly from physiological cervical erosion or ectropion, where the bleeding

may be either spontaneous or post-traumatic, such as post-coital. Other causes that need to be excluded include bleeding from cervical polyps, cervical malignancy and cervical or vaginal infection.

Bleeding from haemorrhoids or vulval varices may also be mistakenly reported as vaginal bleeding.

Placenta praevia

Placenta praevia occurs when the placenta is situated in the lower uterine segment in the third trimester of pregnancy. It occurs in 0.5% of term pregnancies.² Bleeding in this situation is usually bright red and painless, unless associated with labour contractions and often presents with several small 'warning' bleeds.

Placental abruption complicates around 1% of pregnancies. Bleeding occurs from a normally situated placenta. This may be a marginal bleed (from the placental edge) or in association with significant placental separation.

Bleeding may be revealed when blood escapes through the vagina, or it may be concealed behind the placenta, with no evidence of bleeding from the vagina. A placental abruption may follow relatively minor blunt trauma, such as a fall onto the abdomen, or a shearing force, such as that applied in a motor vehicle deceleration crash. Placental abruption may also occur spontaneously associated with hypertension, pre-eclampsia, thrombophilia or with cocaine use.³

Vasa praevia

This is the presence of foetal vessels running in the amniotic membranes distant from the placental mass and across the cervical os, such as with a succenture lobe of placenta or a villamentous insertion of the cord, so that an earlier ultrasound may have described a fundal placenta. These

vessels occasionally rupture, often in association with rupture of the amniotic membranes.

When this happens, the bleeding is from the foetus, which may quickly lead to foetal compromise. The first indication of this may be foetal bradycardia or other abnormalities of the foetal heart rate seen on cardiotocographic (CTG) tracing.

Physiological

Vaginal blood mixed with mucus is called a 'show' and is due to the mucus plug or operculum within the endocervical canal dislodging as the cervix begins to dilate. This usually occurs at the time of, or within a few days of, the onset of labour and is not significant unless the pregnancy is preterm or associated with rupture of the membranes. As a general guide, when a woman needs to wear a pad to soak up blood, she should be assessed as having an APH.

History

The history should specifically include the following details:

- Timing and amount of blood loss—for example, number of pads with an estimate of the blood staining on each pad
- Associated pain or contractions—for example, constant abdominal or lower back pain (suggestive of abruption). Painless bleeding suggests placenta praevia
- Provoking factors—for example, trauma or sexual intercourse
- Foetal movements since bleeding commenced
- Previous episodes of bleeding in pregnancy
- Prior cervical damage (risk factor for cervical incompetence)

Examination

Assess the mother as a priority. A relatively low blood pressure with a systolic of 90 mm Hg and a resting tachycardia of up to 100 bpm is normal in pregnancy.

Examination after 30 weeks' gestation should be performed in a supine position with the right hip elevated by a pillow to give a 15-degree tilt of the pelvis to the left. This avoids the problem of vena caval compression (supine hypotension syndrome) from pressure of the gravid uterus reducing inferior vena caval venous return.

Speculum or digital vaginal examination

Speculum or digital vaginal examination should never be performed until the site of the placenta is determined by ultrasound, to avoid disrupting a low-lying placenta and precipitating torrential haemorrhage.

Once an ultrasound scan has excluded a low-lying placenta, an experienced operator may proceed to a speculum examination to look for liquor within the vagina in suspected rupture of the membranes, or to assess the cervix to localize the site of bleeding and to look for cervical dilatation.

A sterile speculum examination is indicated, again by an experienced operator, if preterm pre-labour rupture of the membranes is possible, to decrease the risk of introducing infection.

Digital vaginal examination should be performed to assess the cervix for dilatation if labour is suspected.

Ideally, a CTG should be applied to assess the status of the foetus beyond 24 weeks' gestation. Auscultation of the foetal heart for several minutes should be attempted if this is not available. The baseline rate and variations related to contractions are important. The normal range of the foetal heart rate is 120 to 160 bpm, but a healthy term or post-term foetus may have a heart rate of between 100 and 120 bpm. Decelerations of the foetal heart rate may indicate foetal distress.

Investigations

Laboratory blood tests

Blood should be taken for baseline haemoglobin and platelet count, coagulation screen, Kleihauer test, blood group, Rhesus factor, Rhesus antibodies and a cross-match.

A pre-eclampsia screen should be ordered if the patient is hypertensive, including liver function tests and uric acid, as well as the platelet count.

Ultrasound

Ultrasound is used to assess foetal gestation, presentation, liquor volume and placental position. Many 'low-lying' placentas at 18 weeks are no longer classified as placenta praevia by 30 to 32 weeks, owing to the differential growth of the lower uterine segment as pregnancy progresses. A placental edge at least 2 cm away from the cervical os at term is considered safe to allow a planned vaginal delivery.

As only 50% of placental abruptions will be seen on ultrasound, it is unreliable for excluding this problem with the diagnosis usually made on clinical grounds alone. Transvaginal ultrasound with an empty bladder is best to visualize the cervix to look for shortening or 'beaking' of the

amniotic sac into the internal os, which are signs of early cervical incompetence.

Management

Analgesia and anti-emetics should be offered. The need for analgesia should raise concerns for a moderate or severe placental abruption, or that the woman is in labour.

Incidental causes of bleeding usually require no specific therapy apart from explanation and reassurance.

Minor amounts of bleeding due to placenta praevia distant from term are managed by close observation, usually initially as an inpatient or later as an outpatient.

Small placental abruptions may also be managed conservatively with serial ultrasound scans to monitor foetal growth and regular CTG assessments. Delivery is usually advised round 37 weeks to pre-empt a massive placental abruption developing. Sometimes, a small retroplacental clot will cause weakening of the amniotic membranes and subsequent rupture of the amniotic sac 1 to 2 weeks after the initial bleed.

Massive antepartum haemorrhage, often with foetal demise when associated with placental separation, requires urgent delivery, possibly by caesarean section. Hypovolaemia and coagulopathies are treated as per usual guidelines.

Prognosis

A decision needs to be made in a hospital where there are no obstetric or neonatal facilities about when to transfer a patient to an obstetric unit. Corticosteroids should be administered to the mother if the foetus is between 23 and 34 weeks and delivery can be delayed for 24 hours. Two intramuscular doses of betamethasone or dexamethasone given over 24 hours decreases the baby's risk of developing respiratory distress syndrome, necrotizing enterocolitis and intraventricular haemorrhages.⁴

Administer 625IU anti-D as an intramuscular injection if the woman is Rhesus D negative.

If birth is imminent at a gestation less than 30 weeks gestation, consider a magnesium sulphate infusion for foetal neuroprotection.⁵ Discussion about dose and timing should be with the obstetric staff receiving the woman if transfer is being planned.

The current survival rate of a baby admitted to a neonatal intensive care unit (NICU) is 40%, 50%, 60% and 70% at 24, 25, 26 and 27 weeks, respectively.⁴

Disposition

Depending on the underlying cause, women who have experienced a non-life-threatening

APH, who are clinically stable, may be discharged home with outpatient review.

SECONDARY POSTPARTUM HAEMORRHAGE

Introduction

Secondary PPH is defined as excessive or prolonged bleeding from 24 hours to 6 weeks' postpartum. Normal lochia is moderately heavy, red vaginal loss for some days that settles to light bleeding or spotting by 2 to 4 weeks. Some women have a persistent brownish vaginal discharge for up to 8 weeks.⁶

Differential diagnosis

Common causes of secondary PPH include retained products of conception and endometritis. The bleeding is usually prolonged, moderate blood loss or a recurrence of blood loss after an initial decline.

Less common causes of secondary PPH include trophoblastic disease, uterine arteriovenous malformation (AVM) and any of the incidental causes outlined in the previous section. Reactivation of bleeding from an episiotomy or vaginal laceration may also be responsible. Annoying spotting may occur for several weeks in women using progestogen-only contraception, especially when concurrently breastfeeding, in the setting of an oestrogen-deficient endometrium.

History

Distinguishing endometritis from retained products may be difficult clinically and the two conditions often coexist. Endometritis may follow any type of delivery, but is more common in women with a history of prolonged rupture of the membranes and multiple vaginal examinations during labour.

Examination

Abdominal examination may show subinvolution of the uterus with retained tissue, while offensive lochia, uterine tenderness and systemic signs of infection support the diagnosis of endometritis.

An AVM presents with heavy vaginal bleeding and, occasionally, haemodynamic compromise.

Investigations

Full blood examination and two paired sets of blood cultures are indicated if the woman is

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clinically septic. Send cervical swabs for microscopy and culture and *Chlamydia trachomatis* detection to help guide the management of endometritis.

Ultrasound is necessary to quantify the amount of retained products of conception and to confirm a diagnosis of an AVM.

Treatment

Empirical treatment with amoxicillin/clavulanic acid 875 mg/125 mg bd PO for 5 to 7 days as an outpatient is appropriate if endometritis is suspected but the woman is systemically well.⁷ Erythromycin may be substituted in penicillin-sensitive patients. Admit systemically unwell patients for intravenous antibiotics.

Perform an ultrasound examination if bleeding persists to look for retained products. Patients with small amounts of retained products may be treated conservatively. Uterine curettage in the postpartum period is associated with the risks of uterine perforation or Asherman syndrome (formation of scar tissue in the uterine cavity) due to intrauterine adhesions and/or fibrosis.

CONTROVERSIES

- Suppression of labour in patients with APH
- Timing of delivery in patients with mild APH due to placental abruption
- The timing and interpretation of ultrasound investigation in patients with secondary PPH

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19.6 Pre-eclampsia and eclampsia

Marian Lee

ESSENTIALS

- 1** Pre-eclampsia is hypertension with organ-system dysfunction unique to the second half of pregnancy.
- 2** Maternal and foetal demise are inevitable and can only be stopped by pregnancy termination.
- 3** Early diagnosis is crucial as the rate of deterioration is unpredictable.
- 4** Eclampsia is a seizure complicating pre-eclampsia and leads to high maternal and foetal morbidity and mortality.

Introduction

Pre-eclampsia is a hypertensive disorder unique to pregnancy. Maternal and foetal morbidity and mortality are high with pregnancy termination the only definitive treatment. In Australia, severe pre-eclampsia occurs in 1% to 2% of all pregnancies and accounts for 15% of maternal mortality. The perinatal mortality is 10% and accounts for 5% to 10% of pre-term deliveries.¹

Definitions²

The blood pressure (BP) in a normal pregnancy falls in the first trimester, reaching a nadir in the second, and returns to the normal range by the third trimester. Hypertension is a BP of >140/90 mm Hg. A change of >30/15 mm Hg from the preconception level should prompt close monitoring. The four hypertensive disorders in pregnancy are:

- Chronic hypertension: predates the pregnancy.
- Gestational hypertension: during pregnancy and resolves within 6 weeks post-partum.
- Pre-eclampsia: hypertension with organ-system dysfunction occurring at >20 weeks gestation and up to 6 weeks post-partum.
- Pre-eclampsia superimposed on chronic hypertension.

Pathophysiology^{3,4}

The pathogenesis of pre-eclampsia remains unclear, and some of the current thinking is discussed.

Abnormal placentation

In normal pregnancy, foetal trophoblasts migrate into the endometrial and myometrial spiral

arteries, causing their remodelling into low resistance–high capacitance vessels. Trophoblasts in pre-eclamptic pregnancies do not migrate beyond the endometrial spiral arteries. They remain as high resistance vessels that jeopardize the blood supply to the placenta.

Endothelial dysfunction

The systemic effects are thought to result from endothelial dysfunction leading to high systemic vascular resistance. The end result is hypoperfusion of organ-systems. The cause is thought to be an imbalance between angiogenic and antiangiogenic factors.

Immunological cause

An immunological cause without definite evidence has been proposed for the following risk factors: first pregnancy, multiple pregnancy, pregnancy with a different partner or when the inter-pregnancy period is beyond 10 years with the same partner. See Box 19.6.1 for other risk factors.

Clinical features

Pre-eclampsia causes multiple organ-system dysfunctions that may not be evident on presentation. Checking the BP in patients of >20/40 weeks gestation is an essential component of the assessment. Hypertension detected must trigger the inclusion of preeclampsia in the differential diagnoses. The following are clinical features

Box 19.6.1

- Age >40 years
- BMI >30kg/m²
- Gestational hypertension
- Past history of pre-eclampsia
- Family history
- Antiphospholipid syndrome
- Diabetes

that may be encountered. More than one organ system may be affected in pre-eclampsia.

Neurological

Neurological features are related to cerebral oedema. Headaches, visual symptoms, confusion and papilloedema should be sought. Stroke may also occur. Seizure, known as eclampsia, is the most time critical complication, with a high maternal and foetal mortality and morbidity.

Eclampsia is a self-limiting seizure that occurs as a complication of preeclampsia. It can occur any time after 20 weeks gestation and up to 6 weeks post-partum. However, it is less common after 24 hours post-partum. It is not always associated with hypertension but more likely to occur with severe preeclampsia with BP of >170/110 mm Hg, which accounts for two-thirds of cases. The rest have a lower BP, including a normal BP.⁵ The magnitude of the BP is not a reliable way of predicting eclampsia, and unfortunately, there is no reliable way to detect its imminent onset. Persistent headache, visual disturbances, neurological deficit or hyper-reflexia should trigger preventive measures,² as there is a high risk of intracerebral haemorrhage in eclampsia. Eclampsia is the most important differential diagnosis to consider in pre-eclampsia. However, other causes of seizures need to be sought, especially when seizure occurs beyond the first 24 hours post-partum.

Cardiovascular^{6,7}

In normal pregnancy, the fall in the diastolic BP and systemic vascular resistance (SVR) is coupled with a raised cardiac output. In pre-eclamptic pregnancies, the SVR is increased and coupled with a reduced cardiac output. There is left ventricular diastolic dysfunction. In practice, this means that patients are at risk of acute pulmonary oedema with injudicious intravenous fluid therapy.

Gastrointestinal

Pre-eclampsia may present with severe or persistent epigastric or right upper quadrant pain. A transaminitis twice the normal range may be found in isolation or associated with other features of the HELLP syndrome (HELLP stands for haemolysis, elevated liver enzymes

and low platelets) discussed below. Biliary tract disease and fatty liver of pregnancy are alternative diagnoses.

The following features of pre-eclampsia need to be sought through investigations.

Renal²

Evidence of renal involvement needs to be sought in patients with oedema.

Proteinuria

The current practice is to use a spot urine protein/urine creatinine ratio to quantify the amount of proteinuria. Significant proteinuria is a ratio >30 mg/mol. Replacing the previous criteria of a 24-hour urine sample means early diagnosis can be made in the emergency department (ED).

Urine output

Oliguria is defined as <500 mL/day. It is acceptable to use 80 mL/4 hours in the ED.

Serum creatinine

Renal involvement is present when the serum creatinine is greater than 90 mmol/L. In normal pregnancy, serum creatinine lies in the lower normal range.

The differential diagnosis for renal insufficiency and hypertension are the vasculitic disorders, in particular Systemic Lupus Erythematosus (SLE) and antiphospholipid syndrome.

Haematological²

This has two components: haemolysis and thrombocytopenia.

Haemolysis

Consistent with haemolysis are schistocytes on the blood film, raised serum bilirubin, LDH >600U/L and a low serum haptoglobin.

Thrombocytopenia

In normal pregnancy (1%), the platelet count can be as low as 100,000 × 10⁹/L. Hence thrombocytopenia is defined as <100,000 × 10⁹/L and should prompt a search for disseminated intravascular coagulation (DIC). Differential diagnoses to consider are thrombotic thrombocytopenic purpura and haemolytic uraemic syndrome.

HELLP syndrome²

HELLP is a marker of severe preeclampsia. The full syndrome is uncommon, and two of the three components are adequate for the diagnosis. The elevated liver enzymes refer to transaminitis that is at least twice normal. The differential diagnoses are fatty liver of pregnancy and biliary tract disease.

The foetus²

Evaluation of the foetus must be part of the evaluation for preeclampsia. Evidence of placental dysfunction is indicated by oligohydramnios and abnormal umbilical artery Doppler for reduced blood flow. Foetal well-being is gauged by cardiotocography.

Recognition of severe pre-eclampsia^{2,6}

Early diagnosis of severe pre-eclampsia is crucial to management. The rate of deterioration is unpredictable. The following are features of severe pre-eclampsia.

1. Hypertension: SBP >160 mm Hg, DBP >110 mm Hg
2. Persistent cerebral or visual symptoms
3. Eclampsia
4. Acute left heart failure—acute pulmonary oedema
5. Persistent RUQ and/or epigastric pain with no alternative diagnosis
6. HELLP syndrome
7. Foetal growth restriction

Management

Once the diagnosis is made, the aim is to optimize maternal and foetal well-being prior to the inevitable termination of the pregnancy. The following is a prioritized management plan.

Eclampsia²

The specific priority beyond initial assessment and stabilization of the airway, ventilation and circulation is terminating the seizure, if present.

Stop the seizure

Benzodiazepines are the first-line drugs. Diazepam up to a dose of 10 mg is used intravenously. Clonazepam 2 mg, 5 minutely is an alternative.

Prevent further seizure

Mg₂SO₄ is used for the acute treatment of eclampsia after benzodiazepines, given as a loading dose and followed by an infusion. It is also used to prevent eclampsia in patients with clinical features consistent with severe preeclampsia.⁶

The mechanism of action is not well understood. It is given as a loading dose of 4 gram IV diluted in 100 mL of Normal Saline given over 15 minutes followed by an infusion at of 2g/h. For further seizures, another bolus of 2 to 4 grams is given over 10 minutes, together with a benzodiazepine.

The therapeutic range based on clinical experience, is 2.0 to 3.5 mmol/L. An IV bolus of 4 to 6 grams achieves this serum level within 30 minutes. An infusion of 2g/h leads to a serum level between 2.0 and 3.0 mmol/L.⁸ It can be given intramuscularly with less predictable serum levels.

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Table 19.6.1 Adverse effects of magnesium by serum levels

Serum Level	Toxic effect
3.2–5.0 mmol/L	Loss of deep tendon reflexes
4.0–6.0 mmol/L	Slurred speech and respiratory depression
≥20 mmol/L	Cardiac arrest

Monitoring for Mg toxicity symptoms is necessary. The adverse effects are related to serum concentration (Table 19.6.1).⁶

Aside from the potential toxicity, MgSO₄ causes uterine atony and contributes to post-partum haemorrhage.

Treat the hypertension^{2,6}

The target BP is <160/100 mm Hg. No single antihypertensive is recommended. They are categorized into first and second-line drugs. Labetolol and hydralazine are both available in intravenous form, and their doses are given in the following discussion. Using the most familiar and appropriate drug in either category is recommended.

First-line antihypertensives: labetolol, methyldopa, oxprenolol Labetolol is an alpha and beta antagonist. It is contraindicated in asthmatics and cardiac failure. It may cause bradycardia and hypotension. It is given 20 mg IV, 10 minutes, up to a maximum dose of 300 mg.⁹ The onset of action is within 5 minutes.

Second-line antihypertensives: hydralazine, nifedipine and prazosin Hydralazine is a directly acting vasodilator. When compared to labetolol, it has a poorer adverse effect profile. Hydralazine may cause maternal hypotension with a reflex tachycardia. It is given 5 mg IV or IM. Repeat at doses of 5 to 10 mg 30 minutes, up to a maximum dose of 20 mg.⁹ The onset is 20 minutes.

Antihypertensives not recommended are ACEI and angiotensin receptor blockers due to risk of foetal renal injury; spironolactone due to antiandrogenic foetal effects and β-blockers may cause congenital anomalies.⁶

Pregnancy termination

The best time to deliver the foetus requires a balance of maternal and foetal risks.

Useful definitions² Immediate delivery is within a period of 48 hours.

Expectant delivery is beyond this period.

Maternal risks Pre-eclampsia leads to inevitable maternal deterioration manifesting as severe organ-system dysfunction such as eclampsia, acute pulmonary oedema, HELLP syndrome and placental abruption.

Foetal risks² Gestational age is central to the evaluation of the foetal risks and benefits of delaying delivery.

Less than 24 weeks: Delaying delivery is outweighed by the high maternal risks.

24 to 32 weeks: The foetal risks are respiratory distress syndrome, longer ICU admission and higher risk of caesarean section. The maternal risks are continuing deterioration of organ-systems.

>32 weeks: the optimal gestation for delivery for both maternal and foetal outcome is 36 weeks.

Delivery The role of the emergency physician is to diagnose and manage the acute complications of pre-eclampsia. Optimization of maternal and foetal well-being prior to delivery are done in collaboration with the obstetric and neonatal team.

Treatment of the hypertension

A BP of >160/100 mm Hg is significant hypertension and signifies severe pre-eclampsia. Urgent treatment is indicated to prevent eclampsia, intracerebral haemorrhage, posterior reversible encephalopathy syndrome and hypertensive encephalopathy (see the previous discussion for antihypertensives used).

General maternal management

Fluid management^{2,3}

There is a risk of acute pulmonary oedema. Fluid challenges are given in volumes of 250 mL for hypoperfusion with careful monitoring. Otherwise, it is given at maintenance rate. Hypotension may not respond to intravenous fluids. Metaraminol and adrenaline are considered safe in pre-eclampsia.²

Thrombocytopenia

There is a risk of peripartum bleeding for platelet count of <50,000 × 10⁹/μL. Platelet transfusion is given at the time of delivery or for invasive procedures.

Foetal well-being²

Foetal monitoring and two specific agents are used to improve foetal outcome in pre-term delivery.

A single dose of betamethasone or dexamethasone is used pre-natally for pregnancy <34/40 weeks gestation, given ideally at 48 hours prior to delivery. This reduces the risk of neonatal death, respiratory distress syndrome and cerebral haemorrhage. The optimal steroid with its dosage regime is not known.^{2,10}

MgSO₄ is recommended for foetal neuroprotection for pre-term delivery at <30/40 weeks gestation. It reduces the risk of cerebral palsy.²

Summary

Pre-eclampsia leads to inevitable maternal and foetal morbidity and mortality. In the ED, the emphasis is on early diagnosis, treatment of acute complications, prevention of further deterioration and facilitating timely termination of the pregnancy. Early collaboration with the obstetric and neonatal team is essential.

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19.7 Emergency delivery and complications

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ESSENTIALS

- 1** Perform a rapid assessment of any pregnant patient arriving in labour at the emergency department to decide the most appropriate site for management.
- 2** Emergency department staff must be prepared to provide newborn resuscitation following an emergency delivery. Preparedness for newborn resuscitation requires preparation of a suitable area with ability to provide radiant heat, special equipment and trained dedicated personnel as well as a structured approach to assessment and intervention.
- 3** Necessary equipment, drugs and protocols must be immediately available within emergency departments so that unexpected deliveries can be managed safely.
- 4** Be prepared to manage sudden complications of delivery, such as shoulder dystocia, breech delivery or postpartum haemorrhage.
- 5** Establish and maintain lines of communication with regional obstetric services so that decisions regarding the management of labour and transfer of mothers and babies are optimum.

Introduction

Occasionally a doctor working in an emergency department (ED) is faced with a patient in labour and required to manage a spontaneous vaginal delivery. This situation is generally accompanied by much anxiety on the part of the ED medical and nursing staff, but it is important that a calm, systematic approach be taken to minimize the risk of an adverse foetal or maternal outcome.

This chapter describes the management of a normal delivery in the ED and provides a brief outline of the recognition and management of abnormal deliveries and selected peri-partum complications.

Setting

There are a number of settings when childbirth may have to occur in an ED. Pregnant patients at different gestational ages may present to the ED at varying stages of labour.

Whenever a woman in the third trimester of pregnancy seeks treatment in the ED, the possibility that she is in labour must be considered. A wide array of non-specific symptoms may herald the onset of labour. Abdominal pain, back pain, cramping, nausea, vomiting, urinary urgency, stress incontinence and anxiety can be symptoms of labour.

The immediate management of a woman in labour will depend on the availability of obstetric services, the gestational age, known antenatal history and past obstetric history and on both the stage of labour and its anticipated speed of progression.

All ED deliveries should be considered high risk. Antepartum haemorrhage, premature rupture of membranes (PROM), eclampsia, premature labour, abruptio placentae, malpresentation, and umbilical cord emergencies are over-represented in the ED population.

Safe transfer to a delivery suite when there is adequate time is always preferable to delivery in the ED.

Women with the urge to push or with the head of the infant crowning are at imminent risk of delivery, which should then take place in the ED. If there is no delivery suite available, or a patient arrives with full cervical dilatation, the foetal presenting part is on the perineal verge and there is no time for transfer to an appropriate facility, arrangements must be made to perform the delivery rapidly in the ED. In these situations, the emergency physician should prepare for two patients, both potentially needing emergency care.

Precipitate labour

Patients who have precipitate labour—an extremely rapid labour lasting less than 3 hours

from onset of contractions to delivery, which is more common in the multiparous—may have to stop in the ED even when en route to the delivery suite or another hospital because of the rapidity of the labour.

Concealed or unrecognized pregnancy

The diagnosis of a concealed or unrecognized pregnancy may also be made in the ED. Concealed pregnancies occur most commonly in teenage girls who do not tell anyone that they are pregnant and receive no antenatal care. Unrecognized pregnancy occurs most commonly in obese females who may present to the ED complaining of abdominal pain or a vaginal discharge and are found to be pregnant and/or in labour. Women with intellectual impairment or mental illness are another group who may present with an unrecognized pregnancy.

'Born before arrival'

The term 'precipitous birth' or 'born before arrival' (BBA) is commonly associated with precipitate labour and refers to women who deliver their baby prior to arrival at a hospital, usually without the assistance of a trained person. On arrival in the ED, both the mother and baby require assessment and may need resuscitation and completion of the third stage of labour. The term *precipitous birth* is also commonly used to describe deliveries that occur in the emergency department or areas outside of a labour and delivery suite.

The incidence of BBA is low but depends on the population studied. In Australia, the incidence of precipitate labour is approximately 1% to 2% in spontaneous non-augmented labours.

History

Assessment of the patient in labour in the ED includes obtaining information regarding gestational age, antenatal care, progression of the pregnancy and past obstetric and a medical history. Always enquire if the patient has a copy of her antenatal care record with her. Take a careful history regarding the onset and timing of contractions and the presence and nature of fetal movements in addition to a history of vaginal bleeding or discharge, which may represent the rupture of membranes.

Delivery in a hospital where there is no delivery suite should include immediate contact by

telephone with the nearest or most appropriate obstetric unit to obtain advice and organize postpartum transfer of the mother and newborn.

Gestational age

The gestational age may be determined from the last normal menstrual period (LNMP) if this is known. The Naegle rule is the most common method of pregnancy dating. The estimated date of delivery (EDD) is calculated by counting back 3 months from the last menstrual period and adding 7 days. As an example, if the last menstrual period was December 20, then the EDD will be September 27. This method assumes that the patient has a 28-day menstrual cycle with fertilization occurring on day 14. Inaccuracy occurs because many women do not have regular 28-day cycles or do not conceive on day 14 and many others are not certain of the date of their last period.

Antenatal ultrasound

Antenatal ultrasound is useful in gauging the estimated date of delivery where dates are uncertain, noting that scans performed later in the pregnancy are less accurate in dating the gestational age of the baby than those performed early. Additionally, a rough estimate of the gestational age of the baby can be made by abdominal examination. At 20 weeks' gestation, the uterine fundus reaches the umbilicus. Approximately 1 cm of fundal height is added per week of gestation until 36 weeks. At that time, the fundal height decreases as the foetus drops into the pelvis. These estimates can help to establish gestational age rapidly.

Past obstetric history

The past obstetric history should include the duration and description of previous labours, the types of deliveries and the size of previous babies, in addition to a history of a previous caesarean section, the use of forceps or vacuum extraction, previous stillbirth, and history of abnormal presentation (e.g. breech presentation), shoulder dystocia, prolonged delivery of the placenta or a postpartum haemorrhage.

Maternal medical conditions

Maternal conditions—such as cardiac and respiratory disease, diabetes, bleeding conditions, hepatitis B and herpes simplex infection—should be documented. Record all drugs, whether prescribed, over-the-counter or illicit, that the patient is taking as well as any allergies. The presence of any bleeding or other complications during the pregnancy should also be noted. Obtain the results of antenatal investigations, including a full blood count, blood group, hepatitis B status, HIV, syphilis serology and any record of group B streptococcal bacteraemia or colonization.

Examination

General examination

A general physical and obstetric examination to confirm the progression of labour, the number of babies and the presence or absence of any complications related to the pregnancy and labour is made. In hospitals where there is a delivery suite, a member of that unit (usually a midwife) is called to attend the ED either to assist with immediate transfer to the delivery suite if possible or with the assessment and conduct of the labour within the ED. Occasionally a member of the ED staff will hold a midwife certificate, and this staff member should be tasked to assist with labour and delivery.

The general examination includes particular emphasis on vital signs and the abdominal and pelvic examination. Examine the patient's heart and chest and perform a urinalysis looking for evidence of infection, glucose or proteinuria, which may be associated with pre-eclampsia (see Chapter 19.6 Pre-eclampsia and Eclampsia).

Abdominal examination

Perform an abdominal examination to ascertain the height of the fundus, the lie and presentation of the foetus and to make an assessment of the engagement of the presenting part. The term *presenting part* refers to the foetal anatomic part proceeding first into and through the pelvic inlet. Most commonly, the foetal head is presenting, which is referred to as a cephalic (or vertex) presentation. The presence of scars and extra-uterine masses should be noted. Also assess the frequency, regularity, duration and intensity of uterine contractions.

Braxton Hicks contractions, or false labour, must be differentiated from true labour. Braxton Hicks contractions do not escalate in frequency or duration, in contrast to the contractions of true labour. By definition, these contractions are associated with minimal or no cervical dilation or effacement. Any discomfort associated with false labour is usually relieved with mild analgesia, ambulation or change in activity.

Unlike false labour, true labour is characterized by cyclic uterine contractions of increasing frequency, duration, and strength culminating in delivery of the foetus and placenta. In contrast to Braxton Hicks contractions, true labour causes cervical dilation to begin, marking the first stage of labour.

In the third trimester or during labour, ultrasonography can provide crucial information pertaining to impending delivery. When an ultrasonographer is available and if time permits, foetal viability, gestational age, and a survey of fetal and placental anatomy, lie and presentation may be obtained. The use of bedside trans-abdominal ultrasonography by emergency clinicians to

evaluate such parameters expeditiously continues to rise as this modality becomes increasingly available and operator skill improves.¹

Fetal heart rate

Count the foetal heart rate between contractions for 1 minute using an ordinary stethoscope, Pinard or a Doppler stethoscope. The heart rate should be between 110 and 160 beats per minute. Count the fetal heart rate for at least 30 seconds following a contraction. Slowing of the foetal heart rate during and immediately following a contraction is not uncommon and normally represents physiological reflexes associated with head compression. Persisting bradycardia greater than 30 seconds after a contraction may indicate umbilical cord compression or utero-placental insufficiency. Recommended management is to give the mother oxygen and position her in the left lateral position to ensure that uterine blood flow and fetal oxygenation is optimized.

If post-contraction bradycardias persist despite these measures, give an intravenous fluid bolus and seek specialist obstetric advice. Note any vaginal bleeding or discharge and record the amount, remembering that haemorrhage may also be concealed. Assess the colour and character of any amniotic fluid looking for evidence of meconium staining.

Vaginal examination

Perform an aseptic vaginal examination with the patient in the dorsal lithotomy position to assess the effacement, consistency and dilatation of the cervix, the nature and position of the presenting part (i.e. vertex or breech) and to exclude a cord prolapse. If unsure of the nature of the presenting part, a portable ultrasound can aid in diagnosis.

The exception to performing a vaginal examination is the gravid patient with active vaginal bleeding. Such a patient should be evaluated with an ultrasound to exclude *placenta praevia* before performing any pelvic examination.

If the membranes are intact and the labour is progressing satisfactorily, there is no indication to rupture them as there is an increased risk of cord prolapse when the presenting part is not well engaged in the pelvis. After the vaginal examination, apply a sterile perineal pad and allow the mother to assume whichever position gives her the most comfort while avoiding a totally supine position, as this has the potential for inferior vena cava (IVC) compression by the gravid uterus.

Transferring the patient

After this assessment, the decision whether to transfer the patient to a delivery suite either within the hospital or at a distant hospital must be made. Cervical dilatation greater than 6 cm in a multiparous patient and 7 to 8 cm in a primipara

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Table 19.7.1 Equipment and drugs required for emergency delivery

Equipment	Drugs
Three clamps – straight or curved (e.g. Pean)	Adrenaline 1:10,000
Episiotomy scissors	Oxytocin 10 units
Scissors	Ergometrine 250 µg
Suture repair set	Vitamin K 1 mg
Absorbable suture material	Lignocaine 1%
Sterile drapes	Naloxone 400 µg/1 mL
Huck towels	Glucose 10%
Sterile gloves	
Soap solution	
Sterile bowls	
Neonatal resuscitation equipment , including appropriately sized suction catheters, oropharyngeal airways, masks, self-inflating bag (approximately 240 mL), endotracheal tubes, stylets, laryngoscopes, end-tidal CO ₂ detector device, neonatal oxygen saturation probe	
Umbilical vein catheters, overhead warmer, clock with timer in seconds, warmed towels, and feeding tubes for gastric decompression	

makes transfer to a distant hospital a hazardous process because of the risk of rapid progression to full cervical dilatation and imminent delivery of the baby.

The availability and type of transport and personnel and the distance to be travelled must be carefully considered. Consult with the obstetric unit regarding the safety of transfer and make arrangements for reception of the patient. Consider contacting specialty neonatal transport services if problems are anticipated or the baby is premature.

Management

Preparation for delivery

Ongoing assessment of the maternal temperature, blood pressure, heart rate and contractions should be performed and recorded. Fetal heart rate should be counted every 15 to 30 minutes up to full cervical dilatation and every 5 minutes thereafter. The fetal heart rate is best measured with a Doppler device, commencing toward the end of a contraction and continuing for at least 30 seconds after the contraction has finished.

Unless there is a clear indication for an intravenous line, such as a history of postpartum haemorrhage or antepartum haemorrhage, bleeding tendency, evidence of pre-eclampsia or history of a previous caesarean section, placement of such a line for the normal delivery is unnecessary. Perform simple venipuncture for a haemoglobin, blood glucose and blood group and put some blood aside for cross-matching.

Equipment and drugs

Obtain a delivery pack, sterile surgical instruments and oxytocic drugs and place nearby ([Table 19.7.1](#)). Resuscitation equipment and drugs should be available. Assemble personnel with clear task delegation, remembering that reassurance and emotional support for the mother and the mother's partner is crucial during the entire labour. A specific member of staff may be delegated to provide this.

If a midwife or doctor experienced in delivery is available, he or she should assume control of the procedure and continue assessing the progression of labour and conduct the delivery of both the baby and the placenta. A doctor or nurse with some experience in neonatal or paediatric resuscitation should perform a rapid assessment of the newborn immediately after the delivery to ascertain the need for resuscitation.

Conduct of labour

Labour is divided into three stages: the first stage is from the onset of regular contractions to full (10 cm) dilatation of the cervix. The second stage is from full dilatation of the cervix to delivery of the baby and the third stage is from the birth of the baby until delivery of the placenta. A full description of the detailed management of the three stages of labour is beyond the scope of this chapter, but a brief summary of the management of a normal vertex delivery is described.

First stage

Examine the patient abdominally and vaginally as necessary to follow the progress of the labour.

As mentioned earlier, regularly perform measurement and recording of maternal vital signs and fetal heart rate. Gently wash the perineum with a non-irritating solution. Shaving, urinary catheterization or enema administration are not required.

The duration of the first stage of labour averages 8 hours in nulliparous women and 5 hours in multiparous women. During this time, frequent assessment of foetal well-being is important.

Analgesia

Analgesics are helpful for the patient with significant discomfort and are generally not injurious to the foetus. The timing and dose of analgesia must be decided with due regard to the stage and rate of progression of labour in addition to the mother's wishes and birth plan.

Inhaled nitrous oxide is simply delivered, acts quickly, is rapidly eliminated and does not affect the foetus. It is usually provided initially in a dose of 50% N₂O mixed with 50% oxygen, but the N₂O dose can be increased to 70% maximum by delivery systems available in many EDs.

Opiate analgesia is also commonly used, although is generally not recommended within 4 hours of predicted delivery, meaning that it is unlikely to be used in a precipitous delivery in the ED. Morphine is preferred to pethidine, as the active metabolite of intramuscular pethidine has a longer half-life in the newborn compared with intramuscular morphine. Major opiate side effects include maternal drowsiness, nausea and vomiting. Although there is no clear evidence of major adverse effects at birth, the timing of any opiates given during labour should be considered and the newborn assessed for possible secondary respiratory depression or hypothermia.

Second stage

The second stage of labour is characterized by a fully dilated cervix and accompanied by the mother's urge to bear down and push with each uterine contraction. The median duration of this stage is 50 minutes in nulliparous women and 20 minutes in multiparous women, with the anticipation of a more rapid progression for low-birth-weight premature infants.

Spontaneous delivery of the foetus presenting by vertex is divided into three phases: delivery of the head, delivery of the shoulders and delivery of the body and legs. The second stage of labour begins when the cervix is fully dilated and delivery will occur when the presenting part reaches the pelvic floor.

As the second stage of labour progresses, preparations for delivery should be under way. A radiant warmer should be available and heated. Neonatal resuscitation adjuncts should be available and a suitably experienced staff member tasked and prepared to provide immediate assessment and care of the newborn. A nurse

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should be at the bedside to coach and provide reassurance to the mother.

The vulva and perineum are cleared and gently washed with sterile water or saline. A repeated sterile examination to assess labour progression and confirm presentation may be performed. Drape the patient in such a manner that there is a clear view of the perineum.

Maternal position

Either a dorsal lithotomy or lateral Sims position may be used for delivery. The dorsal lithotomy position is recommended for inexperienced operators as it is easier to visualize and to manually control the delivery process or perform an episiotomy. In the dorsal lithotomy position, the mother should be tilted over to the left side, using a pillow or soft wedge, to avoid compression of the inferior vena cava by the gravid uterus and possible maternal hypotension and fetal hypoxia.

Episiotomy

When the presenting part distends the perineum, delivery is imminent. Consider an episiotomy at this time, but this should not be routine with a controlled delivery. It should be routinely performed only for specific indications, such as shoulder dystocia or breech delivery. The term *episiotomy* refers to a surgical incision of the perineum performed by the birth assistant just prior to delivery. The primary reason for this is to prevent a larger spontaneous, irregular laceration of the perineum, particularly one that extends into the rectum. It is performed with scissors when the perineum is stretched and distended, just prior to crowning of the fetal head, following infiltration of a posterior area of the peritoneum with 5 to 10 mL of 1% lignocaine (lidocaine) between contractions.

A mediolateral perineal incision is recommended, beginning at the posterior fourchette and extended towards the ischiorectal fossa. A midline episiotomy is no longer recommended due to an increased risk of tears extending through to the rectum. The patient should be encouraged to bear down during contractions and to rest in between.

Delivery of the head

Calm communication between the physician and mother is the best way to maintain control of the delivery. Delivery of the head must be controlled by the birth assistant so that the head extends slowly after crowning and does not 'pop out' of the vagina, which would increase the risk of perineal injury. Placing the palm of one hand over the head to control its extension most easily achieves this. At this point, the patient should cease actively pushing and may have to be instructed to pant or breathe through her nose in order to overcome a desire to push. The birth

assistant's second hand, covered with a sterile gauze pad or towel, may be used gently to lift the baby's chin, which can be felt in the space between the anus and the coccyx.

As the occiput descends under the symphysis pubis, extension of the head occurs and progressively the forehead, nose, mouth and finally chin emerge. Suctioning of the nasopharynx and oropharynx prior to birth of the shoulders and trunk is not required even in the presence of meconium-stained liquor.² In 25% to 30% of patients, the umbilical cord is looped around the neck (nuchal cord); this should be checked. Usually, it is only loosely looped and can be drawn over the head. If that is unsuccessful, another method is to bring the cord caudally over the shoulders and deliver the baby through the cord and then unwind it after delivery. If this is not possible (e.g. it is too tight or has too many loops), double clamp the cord 2 to 3 cm apart and divide the cord between the clamps. Release of additional loops is now straightforward by unwinding the clamped ends around the neck. Recheck the neck, because the cord may be wrapped more than once. Then deliver the infant expeditiously.

Restitution and delivery of the shoulders

The baby's head, having been delivered face down in the most common occipito-anterior position, is allowed to 'restitute' (or correct) to one or the other lateral position. Once the head has restituted, the shoulders will lie in an antero-posterior plane within the pelvis. Delivery of the shoulders is now affected, taking great care not to allow the perineum to tear. Usually the anterior shoulder slips under the symphysis pubis with the next contraction. Gentle downward traction on the head promotes delivery of the anterior shoulder. Do not use excessive force, as this may result in a brachial plexus injury.

On delivery of the anterior shoulder, lifting the baby up will deliver the posterior shoulder, followed by the body and lower limbs. If delay occurs in delivery of the shoulders, the potential for shoulder dystocia should be considered.

Grasp the baby firmly with one hand, securing the infant behind the neck, with the other hand encircling both ankles; then place the baby on the mother's abdomen. The baby is slippery as a result of being covered with vernix and should never be held with one hand alone. Dry the baby and wrap it in a warm blanket to minimize heat loss; also record the time of birth.

As the infant clears the perineum, attention focuses on the umbilical cord. The infant should be kept low or at the level of the perineum to promote blood flow into the infant from the placenta. The cord is now clamped and cut. Clamps should be placed 4 or 5 cm apart, with

the proximal clamp 10 cm from the infant's abdomen. An adequate umbilical stump is important for venous access if the neonate should require resuscitation.

Clamping the cord

There is no need to cut the cord immediately if the baby appears vigorous and breathes spontaneously. Delayed cord clamping, defined as waiting to clamp the umbilical cord for 1 to 3 minutes after birth or until cord pulsation has ceased, is associated with benefits, as more blood is transferred from the placenta to the baby. Benefits include higher birth weight, higher haemoglobin concentration, improved iron stores at 6 months, and improved respiratory transition.^{3,4}

Delayed cord clamping is indicated with all deliveries unless urgent resuscitation is needed. Clamps should be placed 2 or 3 cm apart, with the proximal clamp more than 5 cm from the infant's abdomen. An adequate umbilical stump is important for venous access if the neonate requires resuscitation.

Immediately following birth, the vigorous newborn should be placed directly in contact with the mother's skin and covered with a blanket. Skin-to-skin contact is associated with decreased time to the first feeding, improved breastfeeding initiation and continuation, higher blood glucose level, decreased crying, and decreased hypothermia.⁵ Maintain warmth by drying the baby with pre-warmed towels or blankets.

If the baby requires resuscitation, then the evidence favouring delayed cord clamping over rapidly commencing resuscitation is less clear. Quickly clamp the cord following delivery and transfer the baby for further assessment and resuscitation to a resuscitation trolley that has a radiant heat source.

Apgar score

Apgar scoring is used to provide a rough estimate of the baby's immediate adaptation to extrauterine life. The score allows easy communication of a baby's status between providers and indicates a basic prognosis for the newborn. It is obtained at 1 minute and 5 minutes after birth, with a score from 0 to 10.

The following acronym approach can be used to remember the five categories, with each scored on a scale from 0 to 2:

A: Appearance (0: pale or blue; 1: pink body, blue extremities; 2: pink body and extremities)

P: Pulse (0: absent; 1: less than 100 beats/min; 2: more than 100 beats/min)

G: Grimace (0: absent; 1: grimace or notable facial movement; 2: cough, sneezes, or pulls away)

A: Activity (0: absent; 1: some flexion of extremities; 2: active and spontaneous movements of limbs)

R: Respiration (0: absent; 1: slow and irregular; 2: good breathing with crying)

Note that if the baby requires resuscitation, waiting to do an Apgar score at 1 minute is not indicated.

The Apgar score can be calculated after delivery and resuscitation are complete.

Use of oxytocics

After every ED delivery, particularly deliveries that are precipitous or that occur in an out-of-hospital setting, the mother should be examined for the possibility of twins. Ongoing labour may be confused with postpartum cramping, only to have twin B and all the potential complications surprise the emergency clinician. This is particularly relevant for women with inadequate prenatal care and low-birth-weight infants.

Following the birth of the baby, when an antenatal ultrasound result is unavailable, palpate the mother's abdomen to exclude the possibility of a second foetus and administer an oxytocic agent if no such foetus is present.

Oxytocics aid in placental separation and reduce post-partum bleeding. The most common is oxytocin at a dose of 10 units given intramuscularly or 5 units intravenously as a slow bolus. An alternative is ergometrine in a dose of 250 µg intramuscularly or administered slowly intravenously. However, because this agent is associated with nausea, vomiting and hypertension, it is unsuitable for use in pre-eclampsia, eclampsia or hypertension. There is no significant advantage to the combination of oxytocin and ergometrine, and its use is associated with increased adverse effects relating to ergometrine.⁴

Third stage

The third stage of labour involves the delivery of the placenta and frequent checks of the tone and height of the uterine fundus. After administration of the oxytocic agent, look for signs of separation of the placenta from the uterine wall. Three classic signs of placental separation are (1) lengthening of the umbilical cord; (2) a gush of blood from the vagina, signifying separation of the placenta from the uterine wall; and (3) a change in the shape of the uterine fundus from discoid to globular, with elevation of the fundal height.

These signs usually occur within 5 to 10 minutes of the delivery of the infant but may extend to 30 minutes. Beyond 18 minutes, the risk of postpartum haemorrhage increases, and it is up to six times more likely after 30 minutes. Any attempt to deliver the placenta before it separates is contraindicated. Following separation and once the uterus is firmly contracted, apply

controlled traction on the cord in a backward and downward direction with one hand while the other is placed suprapubically to support the uterus. Cease traction if the cord feels as though it were tearing.

Placental inspection

As the placenta appears at the introitus, traction is applied in an upward direction and the placenta is grasped and gently rotated to ensure that the membranes are delivered without tearing. Examination of the umbilical cord and placenta is an essential part of the delivery process, and any abnormalities should be noted at this time.

Inspect the placenta and membranes to look for any missing segments or cotyledons, or evidence of a missing succenturiate 'accessory' lobe; these may prevent the uterus from contracting properly if they remain within the uterus.

The umbilical cord is normally a three-vessel structure, with two umbilical arteries on either side of the single umbilical vein.

Uterine tone

The first hour after delivery of the placenta is a critical period during which postpartum haemorrhage is most likely to occur. The uterus is evaluated frequently for tone and massaged trans-abdominally if any sign of relaxation exists.

Rub over the uterus to facilitate contraction and expulsion of clots. A common cause of postpartum haemorrhage is incomplete uterine contraction as a result of clots or tissue remaining within the cavity, which may be expelled by massaging the fundus or by manual removal under anaesthesia. Further oxytocics may be necessary.

Bleeding may also occur from other sites, so always perform a careful examination of the cervix, vagina, episiotomy wound and perineum following delivery. Full examination of the cervix for ongoing bleeding will require anaesthesia. The episiotomy wound and any other lacerations may be repaired using a continuous technique with a synthetic absorbable suture.

Observations

Observations taken following the birth of the baby should include the following:

- Maternal—temperature, pulse, blood pressure, uterine tone, lochia and fundal height
- Examination of placenta and membranes—assessment of their condition and structure, cord vessels and completeness
- Maternal emotional/psychological condition in response to labour and birth
- Successful bladder emptying

Newborn care

Keep the baby warm and dry and record the baby's vital signs, Apgar scores and weight. If vitamin K is available, administer it to the baby as

a deep intramuscular 1-mg injection for prophylaxis of haemorrhagic disease of the newborn.

Disposition

Disposition of mother and baby to an obstetric unit either within the hospital or at a distant hospital should then be made once both are stable. The important information that should be provided includes the time of birth, drugs given to mother or baby, estimated maternal blood loss and the Apgar scores of the baby. Include the results of any blood tests and a copy of the observations. If either mother or baby is unstable, early consultation with the appropriate referral service is mandatory regarding the optimum timing and nature of the transfer.

Complications of delivery

Breech delivery

When a foetus is in a noncephalic or nonvertex presentation, it is considered a malpresentation.

Breech presentation refers to a foetus with the feet or buttocks presenting in the pelvic inlet; this is the most common type of malpresentation.

Breech presentation occurs in 3% to 4% of all deliveries, reducing in incidence with advancing gestation. It is associated with a morbidity rate three to four times greater than that of a normal cephalic delivery.

Breech presentation is more common with prematurity, as the final natural rotation in the pelvis may not have occurred. Therefore this and is associated with a greater incidence of foetal distress and umbilical cord prolapse. The most feared complication of a vaginal breech delivery is head entrapment, which can lead to foetal asphyxiation and death.⁵

In the normal cephalic presentation, the head maximally dilates the birth canal, allowing the rest of the body to descend unobstructed. However, with a breech presentation, the head emerges last and can become entrapped by incomplete cervical dilatation. Delivery of a breech presentation is often performed by caesarean section when available.

Circumstances such as precipitous delivery, lack of prenatal care, prematurity and the mother's preference for vaginal delivery can place an emergency medicine physician in the situation of managing a breech delivery. The following is relevant to the ED when vaginal delivery is imminent without obstetric backup or if the physician is concerned about foetal demise.

Management of breech delivery

Immediate obstetric expertise should be requested urgently while preparations are made for neonatal resuscitation. It is critical for the emergency physician to avoid manipulating the

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foetus but rather to allow the delivery to occur spontaneously as far as possible.

Perform an episiotomy as the foetal anus is climbing the perineum. Allow maternal effort to deliver the baby spontaneously to the umbilicus, delivering the legs with knee flexion. Do not apply traction to the foetus, as this may cause foetal head extension, which leads to entrapment of the head and greatly increases the risk of asphyxiation.⁶

A loop of umbilical cord may be pulled down and allowed to hang. The mother is encouraged to bear down until the trunk becomes visible up to the scapula. Then rotate the trunk until the anterior shoulder delivers. Subsequent rotation of the trunk in the opposite direction results in delivery of the posterior shoulder.

Once the shoulders have been delivered, an assistant should provide downward pressure in the suprapubic area to keep the foetal head flexed while the assistant delivers the head either with the application of forceps or by placing the left hand into the vagina and pressing on the maxilla to cause further neck flexion while the other hand grasps a shoulder and applies firm traction in the line of the baby's hips, taking care not to extend the head. The combined neck flexion, traction on the foetus toward the hip/pelvis and the suprapubic pressure on the mother/uterus allows for delivery of the head of a breech infant (Mauriceau Smellie Veit manoeuvre).

Shoulder dystocia

Shoulder dystocia is a relatively uncommon and unpredictable obstetric emergency. From a clinical standpoint, a shoulder dystocia is most often diagnosed when the typical gentle downward traction on the foetal head that is used to deliver the anterior shoulder is unsuccessful in delivering the anterior shoulder under the pubic symphysis.

It is one of the more frightening complications of vaginal delivery and, while some at-risk patients may be identified, it is frequently unexpected. Estimates of its incidence are between 0.2% and 3.0%, depending on the exact definition used.⁷ Important steps in management are recognizing the at-risk patient, calling for assistance early and understanding the manoeuvres to deliver the foetus. At-risk patients may have a large baby or gestational diabetes or be experiencing a precipitous birth.

One risk factor for shoulder dystocia that deserves attention is the mother's history of a shoulder dystocia, because recurrence rates are increased in a subsequent pregnancy, particularly when the foetus is of similar or greater size.

Investigators have attempted to determine whether, using known risk factors, shoulder dystocia can be accurately predicted. Their conclusion was that although a number of factors are associated with an increased risk of shoulder

dystocia, none are of sufficient sensitivity or positive predictive value to allow their use clinically and thus to reliably and accurately identify the occurrence of shoulder dystocia.

Notably, the most relevant risk factor for an emergency physician performing emergency delivery is in fact a precipitous delivery—which is frequently the antecedent to the mother delivering in the ED in the first place. However, in many cases there are no predisposing factors.

Recognizing shoulder dystocia

As it is not possible to predict which deliveries will be complicated by shoulder dystocia, the emergency physician must be prepared for it.

Normally the shoulders negotiate the maternal pelvis in sequential fashion, anterior shoulder first. With shoulder dystocia, both shoulders attempt to clear the maternal pelvis simultaneously.

Following delivery of the foetal head, the anterior shoulder either does not deliver spontaneously or with gentle traction by the birthing assistant. Instead, the anterior shoulder becomes caught immediately above the symphysis. The first sign of shoulder dystocia is retraction of the foetal chin into the perineum, following the delivery of the head (the 'turtle sign').

In addition to the turtle sign, examination often reveals that the foetal shoulders are on a vertical axis rather than oblique. These findings, in combination with an arrested delivery, confirm the diagnosis of shoulder dystocia.

Delivery in less than 5 minutes is essential to prevent asphyxia as a consequence of compression of the umbilical cord, compression of the carotid vessels and potential premature separation of the placenta.

Adverse events with shoulder dystocia

Reported maternal complications related to shoulder dystocia have included third- or fourth-degree perineal lacerations, postpartum haemorrhage, vaginal or cervical lacerations, and symphyseal separation with lateral femoral cutaneous neuropathy.

Self-limiting neonatal complications include clavicular and humeral fracture, which occur in approximately 5% to 10% of shoulder dystocia cases. In addition, brachial plexus palsies resulting from lateral traction on the foetal head during delivery – predominantly of the Erb-Duchenne (C5 through C6) or the Klumpke (C8 through T1) type – occur in 10% to 20% of neonates born after a shoulder dystocia. Fortunately most of these neurological conditions resolve over time, with an estimated rate of persistence of 1% to 5%.

Other long-term neonatal complications that have been reported to occur, albeit infrequently, include permanent central neurologic injury and death.⁸

Treatment of shoulder dystocia

Once shoulder dystocia is recognized, either by a 'turtle' sign or the lack of delivery of the anterior shoulder after typical gentle downward traction on the foetal head, alleviating manoeuvres should be used.

An episiotomy may be considered if not already performed. Although an episiotomy is not a mandatory procedure, many operators may decide, given the individual circumstances, that an episiotomy will allow other manoeuvres to be accomplished more easily or effectively.

These manoeuvres include some combination of the McRoberts manoeuvre, suprapubic pressure, foetal rotation or delivery of the foetal posterior arm.

The McRoberts manoeuvre is generally recommended as the first technique and describes the exaggerated abduction and hyperflexion of the maternal thighs upon the abdomen. When a woman is placed in this position, the actual dimensions of the maternal pelvis are not changed; instead, the symphysis pubis is caudally rotated and the sacrum is flattened; these changes in pelvic orientation are believed to facilitate delivery.^{7,8}

The addition of downward suprapubic pressure applied just proximal to the symphysis by an assistant—either continuously or in a rocking motion—is commonly used in association with the McRoberts manoeuvre. Suprapubic pressure adducts the shoulders and disimpacts the baby from the pubic symphysis into an oblique position. These two manoeuvres result in successful shoulder delivery in over 50% of episodes.

Additional manoeuvres include the Woods corkscrew and the Rubin II manoeuvres, which seek to rotate the shoulder girdle into a different orientation and free the anterior shoulder from under the symphysis pubis. Both these rotational manoeuvres require the physician's hands to be placed into the vagina and a large episiotomy.

Another type of alleviating action is the delivery of the posterior arm. To perform this manoeuvre, the clinician should apply pressure at the antecubital fossa to flex the foetal forearm and then sweep the arm across the foetal chest, with ultimate delivery of the arm over the perineum. After delivery of the arm, there is a 20% reduction in shoulder diameter, thereby allowing the dystocia to be relieved.

Further alternatives include placing the mother 'on all fours' in a hands and knees position, which can facilitate spontaneous delivery. The Zavanelli manoeuvre involves replacing the head in the birth canal and proceeding to immediate emergency caesarean section.

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Postpartum haemorrhage

Postpartum haemorrhage (PPH) is the most common complication of labour and delivery, with primary PPH defined as excessive bleeding in the first 24 hours after birth. In an emergent situation, diagnosis generally occurs through estimation of blood volume loss and haemodynamic changes in response such as hypotension, tachycardia and oliguria.

PPH of more than 500 mL after vaginal delivery affects 5% to 10% of all deliveries and accounts for up to 25% of obstetric deaths.⁴

PPH is divided into two categories; the primary category includes blood loss that occurs within the first 24 hours and the secondary category is haemorrhage 24 hours to 6 weeks after delivery.

Other definitions of PPH include blood loss in excess of 500 mL after vaginal birth or more than 1000 mL after caesarean section. Severe PPH is blood loss greater than or equal to 1000 mL while a critical or major PPH is blood loss of greater than 2500 mL.⁴

The consequences of postpartum haemorrhage are related to the degree of blood loss and the timeliness of resuscitative measures. The uterus at full gestation receives 600 mL of blood per minute, placing the woman at risk for massive amounts of blood loss in a short time. Therefore this is a true obstetric emergency.

Pregnancy has a couple of advantages when compared with other clinical scenarios, both related to maternal age and pregnancy-related maternal adaptation; these include volume expansion. The average maternal age at delivery is 24 years, and occurs at a time in life when women are at their peak physiological condition.⁴ Women at this age are typically healthy and do not have significant comorbidities.

Unlike other patient populations, women who are pregnant handle moderate amounts of haemorrhage well and usually recover unscathed. More importantly than this, the adaptation of blood volume to pregnancy confers a protective advantage against excessive blood loss that is unique.

This volume expansion begins at the end of the first trimester and results in a 50% increase in the blood volume, which leads to an additional 1000 to 1500 mL of circulating blood at the time of delivery. Considering that the average blood loss at vaginal delivery is 500 mL and at caesarean delivery is 1000 mL, most women have ample reserve at term for routine blood loss and moderate amounts of haemorrhage.

Bearing these facts in mind, it is important to remember that blood loss is frequently underestimated and PPH may be first detected by haemodynamic compromise. Once the patient shows signs of haemodynamic compromise, more than 1500 mL of blood volume may have been lost.

Table 19.7.2 Risk factors for PPH

Risk factors	Aetiology
Antenatal	
Increased maternal age—more than 35 years	Tone
Asian ethnicity	Tone/trauma
Obesity—body mass index (BMI) of more than 35	Tone
Grand multiparity—uncertain as mixed findings	Tone/tissue
Existing uterine abnormalities (e.g. anatomical anomalies, fibroids)	Tone
Maternal blood disorders: von Willebrand disease, idiopathic thrombocytopaenic purpura, thrombocytopaenia caused by pre-eclampsia/gestational hypertension, disseminated intravascular coagulation (DIC)	Thrombin
History of previous postpartum haemorrhage or retained placenta	Tone/tissue
Anaemia of less than 9 g/dL at onset of labour	No reserve
Antepartum haemorrhage associated with suspected or proven placental abruption, known placenta praevia	Tissue/tone/thrombin
Over-distension of the uterus: multiple pregnancy, polyhydramnios, macrosomia—greater than 4 kg	Tone
Intrauterine fetal death	Thrombin
Intrapartum	
Prolonged labour—first, second or third stage	Tone/tissue
Chorioamnionitis, pyrexia in labour (e.g. prolonged membrane rupture)	Tone/thrombin
Amniotic fluid embolism/DIC	Thrombin
Uterine inversion	Trauma/tone
Genital tract trauma (e.g. episiotomy, ruptured uterus)	Trauma
Postnatal	
Retained products (e.g. placenta, cotyledons or succenturiate lobe, membranes or clots)	Tissue
Amniotic fluid embolism/DIC	Thrombin
Drug-induced hypotonia (e.g. anaesthetic, magnesium sulphate)	Tone
Bladder distension preventing uterine contraction (e.g. obstructed Indwelling Catheter (IDC), unable to void)	Tone

(Modified from Queensland Maternity and Neonatal Clinical Guideline: PPH, with permission from the Queensland Maternity and Neonatal Clinical Guidelines Program).

The role of permissive hypotension in the maternity patient is uncertain because there is concern that it may compromise foetal well-being and uterine contractility in the postpartum period.

The common causes of PPH are referred to as the 'four Ts', which, in order of decreasing frequency, are as follows:

- Tone (70%)
 - atonic uterus
- Trauma (20%)
 - Laceration of the cervix, vagina and perineum
 - Uterine rupture or inversion
 - Non-genital tract trauma (e.g. subcapsular liver rupture)
- Tissue (10%)

- Retained products, placental (cotyledons or succenturiate lobe), membranes or clots, abnormal placenta
- Thrombin (<1%)
- Coagulation abnormalities

Management of postpartum haemorrhage

Prevention is essential by identifying the at-risk patient (Table 19.7.2). The aggressive use of oxytocin along with active management of the third stage of labour are important. These measures reduce the incidence of PPH by 40%. The initial response to PPH requires a multidisciplinary team approach to restore the woman's haemodynamic state while simultaneously identifying and treating the cause of bleeding.

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The first key to management of PPH is to recognize its occurrence in a timely fashion. Bleeding often begins at the time of placental separation, and although it can be brisk and obvious, it is sometimes more subtle and can be steady and relentless. In the face of other bodily fluids associated with delivery, including amniotic fluid and urine, the amount of blood loss is often underestimated.⁹

It is important to factor in blood-loss volumes in blood-soaked linen and dressings. The steady bleeding seen initially may appear moderate but can persist until serious hypovolaemia has occurred. Further complicating this is the failure of the pulse and blood pressure to change significantly until large amounts of blood have been lost. Once PPH has been identified, resuscitative measures should be quickly taken, including obtaining intravenous access with two large-bore intravenous lines for rapid infusion of crystalloid and blood, placement of a Foley catheter to monitor urine output, and an effort made to identify the cause (i.e. uterine atony, genital laceration, or other diagnoses). Surgical and anaesthesia teams should be mobilized as needed.

Blood should be taken for measurement of haematocrit, electrolytes, renal and hepatic function, coagulation testing, fibrinogen levels and blood cross-matching.

Intravenous crystalloid up to 1 to 2 L may be used initially and will be effective in mild cases of haemorrhage. Colloid fluids may also be used but have no demonstrable advantage over crystalloids. Very brisk haemorrhage or significant haemodynamic compromise should prompt consideration of the early use of blood rather than repeated doses of crystalloid. If bleeding or haemodynamic instability is ongoing following up to 2 L of intravenous crystalloid, blood should be given. O-negative blood may be required initially, followed by group-specific or fully cross-matched blood. Fresh frozen plasma (FFP), platelets and cryoprecipitate may all be indicated in severe PPH, with initiation of the department's massive transfusion protocol (MTP).

The purpose of the MTP is to trigger a multidisciplinary response to critical bleeding. Transfusion support must occur simultaneously with measures to arrest bleeding. Obstetric haemorrhage is often underestimated and may be concealed by delays in recognition and response, thus contributing to the severity of haemorrhage and to maternal morbidity and mortality. Profound coagulopathy and DIC may develop rapidly and early.

Currently there is no evidence or consensus to guide the optimal ratio of blood component replacement in obstetric haemorrhage; the usual practice is to use similar ratios as for trauma.¹⁰

The Queensland Maternity Clinical Guidelines for Management of Primary Postpartum

Haemorrhage⁴ advocate the use of a massive haemorrhage protocol in situations where there is

- Active bleeding and the use of four units of red blood cells (RBCs) within 4 hours plus haemodynamic instability
- Estimated blood loss greater than 2.5 L
- Clinical or laboratory signs of coagulopathy

The massive haemorrhage protocol incorporates early administration of intravenous tranexamic acid (1 g IV over 10 minutes), multiple units of RBCs and the use of other products. FFP is given to correct coagulopathy (target international normalized ratio [INR] <1.5), platelets to keep platelet count above $50 \times 10^9/L$, and fibrinogen concentrate or cryoprecipitate to maintain serum fibrinogen above 2.5 g/L.

Tranexamic acid may be beneficial in reducing the risk of death due to post-partum haemorrhage. Recombinant activated factor VII may also be used, although generally after discussion with a haematologist. There is no evidence to suggest that dose and timing of rFVIIa in the critically bleeding maternity patient should differ from that of standard massive haemorrhage protocols.¹⁰

Before massaging the fundus, ensure that the placenta has been delivered and is complete. An adherent or incomplete placenta in the setting of PPH may necessitate transfer to the operating suite for operative removal. If the placenta is delivered and complete, check that third-stage oxytocin has been given and massage the uterine fundus to promote contraction. Expel any uterine blood clots and make sure that the bladder is empty.

Make sure that a careful inspection of the vagina, cervix and perineum has been made to confirm or exclude genital trauma as a cause of ongoing bleeding. Clamp obvious arterial vessels and repair lacerations. Transfer to an operating suite may be necessary to allow a full inspection of the vagina, cervix and uterus and effective repair. Suspect uterine rupture in a patient with severe abdominal pain.

Uterine atony

Accounting for approximately 70% of cases, the most common cause of serious immediate postpartum haemorrhage is laxity of the uterus after delivery. Normally, postpartum bleeding from the placental implantation site is limited by contraction of the myometrium, constricting the spiral arteries. If the uterus does not contract, ongoing haemorrhage will occur.

On examination, the uterus is palpable as a soft boggy mass. The treatment of uterine atony is usually medical and consists of administration of oxytocin and/or prostaglandin derivatives. In addition, bimanual compression is performed, a relatively easy technique that controls most uterine haemorrhage. In this technique, the posterior aspect of the uterine fundus is massaged

through the abdomen while the anterior wall of the uterus is massaged through the vagina with the other hand. This should be done while medical treatment is being given.

Give five units of oxytocin IV over 1 to 2 minutes followed by an infusion of 5 to 10 IU/h (30 units of oxytocin in 500 mL of 0.9% saline at 83–167 mL/h). Other drugs used for uterine atony include misoprostol 800 to 1000 µg PR and/or ergometrine 250 µg by the intravenous or intramuscular route.

Second-line drugs, such as PGF₂-α 250 µg IM or intramyometrially may be used up to a maximum of 2 mg, which is successful in 60% to 85% cases of refractory uterine atony. Side effects include nausea, vomiting, diarrhoea, pyrexia, hypertension and bronchoconstriction. Its use is therefore contraindicated in women with asthma and hypertension.

Persisting uterine atony necessitates immediate transfer to theatre to identify and remove retained products; whilst also employing bimanual uterine compression as a temporizing measure.

Additional measures in the operating theatre include the use of a Bakri balloon—a 24-Fr 54-cm silicone catheter with a filling capacity of 500 mL, which acts as an intra-uterine balloon tamponade.

Coagulopathy

Coagulopathies must be considered and should be specifically looked for with testing and managed with products as described earlier.

All women with severe PPH should be evaluated for disseminated intravascular coagulation (DIC). DIC can occur as a consequence of placental abruption, eclampsia, amniotic fluid embolism, postpartum infections, and dilution of clotting factors caused by aggressive volume resuscitation.

Other surgical causes

Continuing severe PPH and haemodynamic instability after management of all of reversible causes requires urgent surgery with possible laparotomy. Causes include uterine rupture or inversion and persistent atony, or causes such as subcapsular liver rupture or amniotic fluid embolism. Surgical procedures for intractable bleeding include placement of B-Lynch compression sutures to the uterus, bilateral uterine artery ligation, angiographic embolization of bleeding vessels and hysterectomy.

NEONATAL RESUSCITATION

Approximately 10% of infants require some assistance to begin breathing at birth, although less than 1% require extensive resuscitation. Of those requiring some assistance, the majority simply

require basic manoeuvres, such as stimulation, airway positioning and transient mask ventilation. Few require intubation and ventilation, and the need for chest compressions and medications is uncommon.¹¹

The need for resuscitation may be completely unexpected; therefore prior preparation to manage a newborn requiring resuscitation is essential. This includes suitable equipment and training and an appropriate location to conduct resuscitation. Early contact should be made with the neonatal or paediatric team to plan for transfer or retrieval if necessary.

Neonates in need of resuscitation

The need for resuscitation in the newborn is more likely in circumstances such as preterm birth, absent or minimal antenatal care, maternal illness, complicated or prolonged delivery, antepartum haemorrhage, multiple births, previous neonatal death and a precipitate birth. This suggests that all ED deliveries should be treated as possibly of high risk, with appropriate preparations made to provide neonatal resuscitation.

Assessment and resuscitation of the newborn

The initial assessment should focus on tone, breathing and heart rate; subsequent assessment during resuscitation is based on the infant's heart rate, breathing, tone and oxygenation. The Australian Resuscitation Council Neonatal Resuscitation Flowchart illustrates the assessment and resuscitation of a newborn baby (Fig. 19.7.1).

Infants who are born at term, have had low or no risk factors for needing resuscitation, are breathing or crying and have good tone should be dried and kept warm. These actions can be provided on the mother's chest and do not require separation of mother and baby. Poor tone and minimal response should be managed with brisk but gentle drying with a soft towel to stimulate the infant to breathe.

Oxygenation

Oxygenation is assessed using pulse oximetry, noting that the healthy term newborn takes up to 10 minutes to achieve oxygen saturations of 85% to 90%. Although insufficient oxygenation can impair organ function or cause permanent injury, there is increasing evidence that even brief exposure to excessive oxygenation is harmful to the newborn during and after resuscitation. Emergency physicians should recognize this aspect of a newborn's normal respiratory physiology and not provide high-dose oxygen in an attempt to attain unnecessarily high oxygen saturations. A guide to expected oxygenation saturations in the first 10 minutes

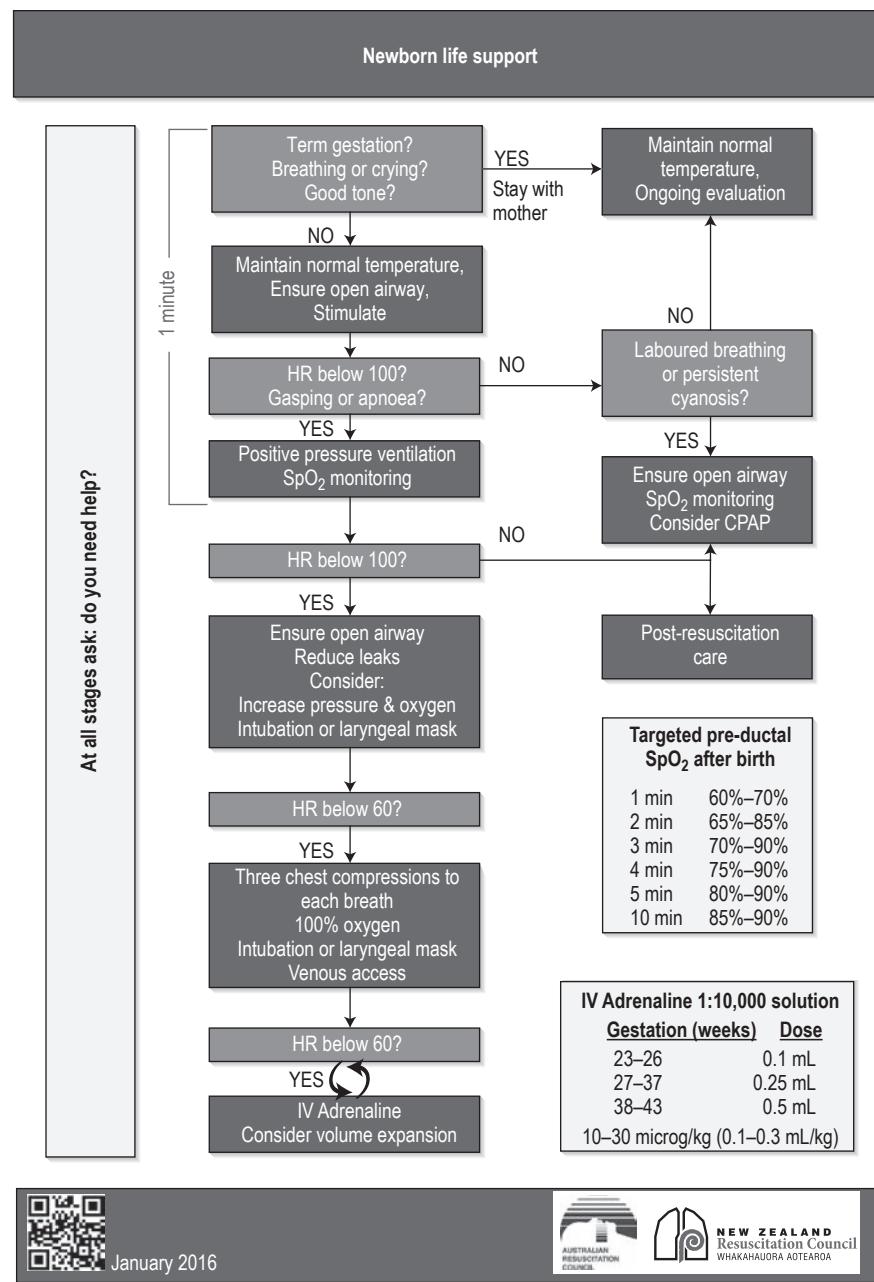


FIG. 19.7.1 Neonatal resuscitation flowchart. (From the Australian Resuscitation Council ANZCOR Neonatal Guidelines.)

after birth is listed on the Australian Resuscitation Council Neonatal Resuscitation Flowchart (see Fig. 19.7.1).

Air should be given initially for ventilation of the term infant while pulse oximetry is commenced. Supplemental oxygen delivered by a blender with air is used when the infant's oxygen saturations do not reach the lower end of the target saturations despite effective ventilation. Increased concentrations of oxygen should be used if the infant's heart rate fails to increase or oxygenation as measured by oximetry remains lower than expected.

Attempting to increase the oxygen saturation over 90% in a newborn is potentially harmful. In all cases, the first priority is to ensure adequate inflation of the lungs followed by increasing the concentration of inspired oxygen only if needed.

Positive-pressure ventilation

If the infant remains apnoeic or its breathing is inadequate, positive-pressure ventilation is started using a self-inflating bag, T-piece device or a flow-inflating bag via a face mask or even an endotracheal tube. Persistent apnoea, particularly associated with hypotonia and a heart rate below

19.7 EMERGENCY DELIVERY AND COMPLICATIONS

100 beats per minute, is an ominous sign. The main measure of effectiveness of ventilation is a prompt and sustained improvement in heart rate. This can be determined by listening to the heart with a stethoscope or initially by feeling for pulsations at the base of the umbilical cord. It should be consistently above 100 beats per minute within 1 minute of birth in a non-compromised infant. Rates below 100 beats per minute are managed with ventilation, whereas a rate below 60 per minute requires both positive-pressure ventilation and chest compressions.

There are few indications for intubation and ventilation in the newborn population. If adequate ventilation is being obtained with a bag and mask, intubation is generally not needed.

Endotracheal tube (ETT) internal diameter in millimetres can be calculated as gestational age in weeks divided by 10. Typically a 2.5-mm tube is appropriate for infants weighing less than 1 kg; a 3.0-mm tube is suitable for infants weighing 1 to 2 kg; a 3.0-mm tube is used for infants weighing 1 to 2 kg; a 3.5-mm tube is used for infants weighing 2 to 3 kg; and a 3.5- or 4.0-mm tube is used for infants weighing more than 3 kg.

Newborn intubation is generally performed using uncuffed tubes, but the use of a 3.5- or 4.0-mm cuffed tube is acceptable for larger babies.

Chest compressions

The preferred technique for chest compression is an 'encircling technique' with two thumbs on the lower third of the sternum, with the fingers surrounding the thorax to support the back. A chest compression should be performed each half second with a half-second pause after each third compression to deliver a breath, resulting in a 3:1 ratio with a total of 90 compressions and 30 breaths per minute.¹¹

Once chest compressions have been commenced, they should be performed with as little interruption as possible. Do not stop unless assessment is needed to make treatment decisions. Signs of improvement in spontaneous cardiac output may include improvement in spontaneous heart rate, a rise in oxygen saturation, and commencement of some spontaneous movement or breaths. Chest compressions should continue until it is obvious that the heart rate is greater than 60 per minute.

As soon as a decision has been made to perform chest compressions, preparation should commence to establish vascular access and administer intravenous adrenaline.¹¹

Adrenaline

Medications and fluids are rarely indicated for the resuscitation of newborn infants. Bradycardia is usually caused by hypoxia and inadequate ventilation. Apnoea is due to insufficient oxygenation

of the brain stem. Therefore establishing adequate ventilation is the most important step to improve the heart rate. However, if the heart rate remains below 60 per minute despite adequate ventilation (the chest is seen to move with inflations) and chest compressions, adrenaline (epinephrine) may be needed. Because this will exert part of its effect by action on the heart, it is important to give it as close to the heart as possible. An umbilical vein catheter is the most rapidly accessible intravascular route for adrenaline (epinephrine) and it can also be used for fluid administration.

Ventilation and chest compressions must be delivered continuously during preparation to administer intravenous medication or fluids.¹¹

Adrenaline is recommended if the heart rate remains below 60 beats per minute despite effective ventilation and chest compressions. The recommended intravenous adrenaline dose is 10 to 30 µg/kg (0.1–0.3 mL/kg of a 1:10 000 adrenaline solution) followed by a small saline flush. This dose is repeated if the heart rate remains below 60 beats per minute despite effective ventilation and cardiac compressions. Higher doses of adrenaline are not recommended.

The preferred route of administration of adrenaline is via the umbilical vein through an umbilical catheter.

If umbilical catheters are not available, a nasogastric feeding tube (size 6) or an 18-gauge cannula without a needle are suitable alternatives. In circumstances where umbilical vein catheterization fails, intraosseous access or peripheral vein access are valid alternatives; however, these are more technically challenging in the newborn.

There is little research to support the use of endotracheal adrenaline and there are concerns that even in higher doses it may still result in lower levels of adrenaline than if it were delivered via the intravenous route. If vascular access cannot be obtained, endotracheal adrenaline (epinephrine) may be considered. If the endotracheal dose fails to increase heart rate to more than 60 beats per minute, an intravascular dose should be given as soon as feasible.

If the endotracheal route is used, a dose of 50 to 100 µg/kg (0.5 to 1 mL/kg of a 1:10 000 solution) is recommended.

Intravenous fluids

Consider intravenous fluids when there is suspected blood loss and/or the infant appears shocked (pale, with poor perfusion and a weak pulse) and has not responded adequately to the other resuscitative measures already outlined. Isotonic crystalloid (e.g. 0.9% sodium chloride or Hartmann's solution) should be used in the

first instance, but in the setting of critical blood loss, this may have to be followed with red cells and other blood products suitable for emergency transfusion.

The initial dose is 10 mL/kg given by intravenous push. This dose may be repeated after observation of the response.

Naloxone

Naloxone is not used routinely as part of the initial resuscitation of newborns with respiratory depression in the delivery room. It may be considered in continuing respiratory depression following restoration of heart rate and colour by standard resuscitation methods if it is thought that this may be secondary maternal opioid medications—especially if administered within the previous 4 hours. The current recommended dose of naloxone is 0.2 mg given intramuscularly in a full-term baby. Smaller doses of 10 µg/kg given intravenously will also reverse opioid sedation, but the effect will last only a short time compared with the larger intramuscular dose.²

Meconium-stained liquor

Meconium-stained liquor (light-green tinge) is relatively common, occurring in up to 10% of births. Notwithstanding this, meconium aspiration is a rare event and has usually occurred in utero before delivery. Suctioning the infant's mouth and pharynx before delivery of the shoulders makes no difference to the outcomes of babies with meconium-stained liquor and is not recommended. Similarly, routine endotracheal intubation and endotracheal suctioning of babies with meconium-stained liquor who are vigorous (breathing or crying, good muscle tone) is discouraged, as it does not alter the outcome and may cause harm.

In the non-vigorous baby with depressed vital signs, the emphasis should be on initiating respiration rather than on clearance of meconium. In a non-vigorous infant and the presence of thick meconium with the potential to block the airway, endotracheal intubation and suction of meconium may serve to clear the airway and allow respiration or ventilation, but it should not delay the initiation of ventilation. If the endotracheal tube is then removed there is no need to repeat this intervention and efforts should then be directed to establishing respirations.

Blood glucose and temperature must be checked in any baby undergoing resuscitative measures. Neonatal hypoglycaemia (Blood Sugar Level (BSL) <2.6 mmol/L) may be corrected by the administration of a bolus of 2.0 mL/kg of 10% glucose solution. Although it is important to avoid hypothermia in newborns by employing a radiant heat source, drying the baby and

wrapping in a warm, dry towel or blanket with the head covered, ideally by a hat or beanie, is also important.

Neonatal transfer

Neonates requiring resuscitation following emergency delivery will have to be referred to a regional or tertiary neonatal unit for ongoing care. Transfer of these babies requires careful communication and coordination between the two centres, with transport usually undertaken by a specialized neonatal transport team.

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SECTION 20

PSYCHIATRIC EMERGENCIES

Edited by Biswadev Mitra

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20.1 Mental state assessment

Blair Hobbs

ESSENTIALS

1 The number of patients presenting to the emergency department (ED) with mental health problems is increasing.

2 Regardless of diagnosis and presentation, an initial assessment must be performed within the first few minutes of an individual's arrival in the ED, taking into account the risk of

- Suicide and self-harm
- Violence or other forms of assault
- Absconding

3 The role of organic illness presenting as a mental disorder should not be forgotten.

4 Substance use/misuse resulting in presentations to EDs appears to be increasing.

- Lack of social supports including suitable housing
 - Lack of alternatives to care
 - Round-the-clock accessibility of the ED⁵
- The Australian Institute of Health and Welfare report into Mental Health Services 2016-17 revealed 276,954 presentations to Australian EDs in which the primary problem was thought to be a mental health disorder.³ A little under 4% of Australian public hospital ED presentations are due to a mental health complaint, correlating well with other studies and US figures, which estimate that 2% to 6% of emergency medicine presentations are primarily due to mental health disorders, although this figure is likely to under-represent the overall number of people presenting to an ED with a mental health problem.³⁻⁶

Two-thirds of these people are between the ages of 15 and 44 years (compared with 42% for the general population presenting to a suburban ED); 29% have anxiety and neurotic disorders; 21% mental and behavioural disorders due to psychoactive substance abuse; 19% mood disorders and 17% schizophrenia or delusional disorders.⁵ It is estimated that 17.7% of adult Australians admitted to hospital report a mental health issue in the previous 12 months. An estimated 0.4% to 0.7% of the adult population suffer from a psychotic episode in any given year.¹⁻²

Mental health issues are highly prevalent and relevant to the work of emergency clinicians. In many cases, these patients' mental illness goes unrecognized, or they may present with an active medical condition and a mental health diagnosis may not be recorded by hospital data collection methods.⁶

Epidemiology

Mental health disorders are among the three leading causes of total burden of disease and injury in Australia, alongside cancer and cardiovascular disease.^{1,2} These mental issues are among leading causes of non-fatal disease burden in the Australian population. Mental health disorders are highly prevalent, with 4 million Australians estimated to have experienced a common mental disorder in 2015. Mental illness can be disabling and costly in both human and socioeconomic terms.^{1,3}

In terms of disability, it has been estimated that having a major depressive disorder is the equivalent of having congestive cardiac failure or chronic severe asthma. The prevalence of this is projected to increase significantly over the next decade.³

Suicide is the third overall leading cause of death for men across all age groups.² The prevalence of suicide is approximately 16 for every 100,000 men and approximately 5 per 100,000 women. The highest rate of suicide occurs in men over the age of 85 years (37.6 per 100,000). A significant proportion of people who commit suicide have had contact with a health provider in the preceding 12 months, often in an ED.⁴

Over the 8 years to 2014, ED presentations rose 14.8% in the United States, whereas mental health presentations for the same time period rose 44%, contributing significantly to ED overcrowding.⁵ This trend has been mirrored in Australia.

Contributing to this may be the following:

- Lack of private health insurance
- Rising substance use

Introduction to the mental state examination

It is common for emergency department staff to report a lack of confidence and skill dealing with a population of patients unfamiliar to them.⁷⁻⁹ Recent Australian studies have shown ED clinicians are most concerned about knowledge gaps in risk assessment, particularly related to self-harm, violence and aggression, and distinguishing psychiatric from physical illness.⁹ ED clinicians routinely report the need for more education on mental health-related presentations.¹⁰⁻¹¹ A high proportion of mental health-related presentations to EDs involve drug and alcohol intoxication. This may complicate the assessment and treatment of mental health problems, often lengthening the stay of these patients within the ED and delaying their disposition.^{5,7}

There is a risk of mental health patients being assigned to lower triage categories and experiencing longer waits to be seen by staff than mainstream patients, and there is more variation in triage categorization for mental health patients.¹¹ With this in mind, there has been much work over recent years to improve the quality of care and experience for people presenting to an ED with a mental health problem.¹²

Bias, Stigma and Discrimination

People with mental illness experience discrimination and difficulties accessing necessary treatment. An interviewer needs to be aware of their own values and beliefs and how this may influence a mental state assessment. If a health professional notices their decision-making is affected by a negative attitude toward the patient, they should seek assistance from a senior colleague. (Box 20.1.1).

ABCs of the mental state examination

At the point of triage, initial risk assessment should be conducted to identify any imminent and/or life-threatening risks to the patient or staff. The triage nurse and treating doctor should obtain a brief collateral history from emergency services and/or significant others and devise an initial treatment plan in order to ensure the safety of the patient, staff and others in the ED. Regardless of risk or patient behaviour, all assessments

Box 20.1.1 Factors that may drive bias and discrimination

- Religious beliefs
- Race/ethnicity/cultural beliefs and practices
- Political opinion
- Philosophical beliefs
- Sexual preference or orientation
- Intellectual disability
- Drug and alcohol use

and interventions should balance the safety of patient and staff with respect and dignity.¹³⁻¹⁵

The ABC of Mental Health Assessment is based on¹³:

- Appearance, affect and mood
- Behaviour
- Communication, conversation and cognition

If the situation is relatively controlled, the formal mental health assessment should then take place. Further information is gathered from community-based resources such as a general practitioner. A provisional assessment and management plan is developed in conjunction with the mental health team and appropriate disposition is arranged (Fig. 20.1.1).

Triage

The Mental Health Triage Scale (Table 20.1.1) has been developed and modified to be included in the Australian Triage Scale (ATS).¹³⁻¹⁵ It provides symptom and behavioural descriptors for the triage nurse to determine the level of risk or

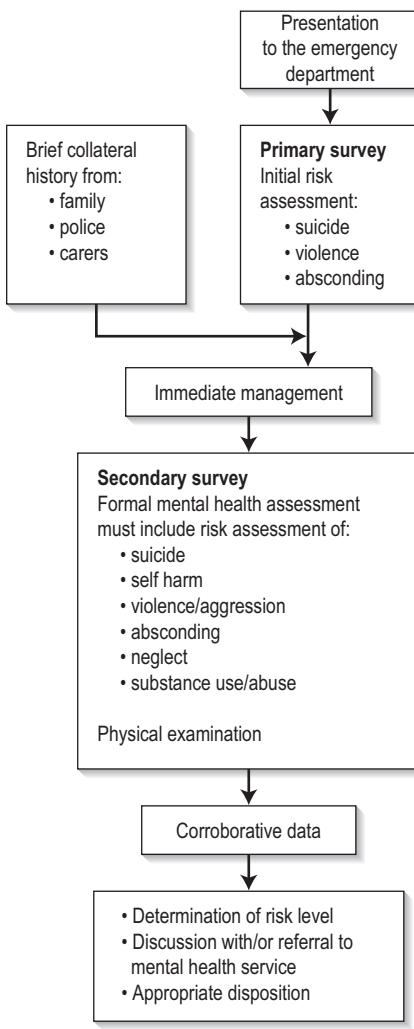


FIG. 20.1.1 The mental health assessment process.

urgency required to manage risks such as suicide and self-harm, violence and absconding. It is also important for the triage nurse to determine whether the patient is intoxicated, as this is a significant contributing risk factor. From this, the triage nurse determines the ATS category, urgency of initial treatment and most appropriate clinical area for the patient to receive further treatment. Having timely access to the patient's clinical file with reference to previous psychiatric history, risk and past behaviours is also helpful. The local mental health service may be able to provide further information or tell you whether the patient is known to them.

Many hospital EDs have developed a triage risk-assessment form or screening tool. For ease of use, many of these have included 'tick box' areas designed to identify risk factors for dangerous behaviour. A compilation of multiple assessment tools used throughout Australia is shown in Boxes 20.1.2 to 20.1.4.^{7,13-15}

It is recommended that any patient who presents as a high or imminent risk be seen in a timely manner. Some EDs have teams specifically assigned to respond to high-risk behavioural disturbance in a co-ordinated and standardized manner. These teams may include a mental health clinician, security or police, depending on the resources available to the hospital. As a last resort, the use of sedation or restraint may be required and used according to legislation and local policy. A collaborative approach to assessment and treatment by ED and mental health clinicians will help to ensure a streamlined and safe pathway of care through an often chaotic and congested department.

Aims of the mental health assessment

The aims of the formal mental health assessment are to determine the following:

- Does the patient have a mental illness?
- Is there a question of safety for the patient or for others?

Table 20.1.1 The mental health triage scale

ATS 2	Patient is violent, aggressive or suicidal or is a danger to self or others Requires police escort/restraint
ATS 3	Very distressed or acutely psychotic Likely to become aggressive May be a danger to self or others
ATS 4	Long-standing or semi-urgent mental health problem and/or has supporting agency/escort present
ATS 5	Patient has a long-standing non-acute mental health disorder but has no support agency Many require referral to an appropriate community resource

20.1 MENTAL STATE ASSESSMENT

PSYCHIATRIC EMERGENCIES

Box 20.1.2 Brief screening suicide risk template

Mental state

- Active disease
- Psychosis
- Hopelessness/despair/guilt/shame
- Anger/agitation
- Impulsivity

Suicide attempts/thoughts

- Continual/specific thoughts
- Formulated plan
- Intent
- Past history of attempt with high lethality
- Means
- Suicide note
- Risk of being found
- Organizing personal affairs

Substance abuse

- Current misuse

Supports

- Lack of or hostile relationships

Loss

- Recent major loss (even perceived): significant relationship, job, housing, financial difficulties, independence
 - Recent/new diagnosis of major illness or chronic illness
- Patients then stratified into high, medium or low risk

- What is the patient's view of his or her health problem or illness?
- What is the patient's view of treatment and how willing is he or she to cooperate?
- Can the treatment be provided in the community or is hospitalization required?

The formal psychiatric interview

Introduction

The central components to a psychiatric assessment are the patient history and the mental state examination (MSE).

Taking a patient's history requires gathering all the relevant details pertaining to the patient's current presentation to the ED and doing this succinctly. Obtaining a history enables the clinician to identify what the problem is; the nature, duration and severity of any symptoms; and what has precipitated the presentation to the ED at this time. While taking a history, it is imperative to observe and listen, demonstrating empathy, establishing rapport and endeavouring to develop a collaborative approach to treatment. Using skills of observation, listening and enquiry, the clinician can construct an MSE in order to identify possible diagnoses and risks. By identifying the main problem or problems and themes in the first few minutes of the interview, the ED clinician can identify the possible diagnosis and then focus the questioning on exploring this further.

The environment in which the MSE is conducted is an important consideration. Behaviourally disturbed people are often fearful and overwhelmed; they may find the highly stimulating environment of an ED to be threatening. The interview space should be quiet and private, making the patient feel safe, and the interviewer should avoid interruptions as much as possible. These prerequisites are difficult to attain in an increasingly busy ED. Wherever appropriate, the interviewer should sit at the same level as the patient, although depending on the context or level of risk, standing may be reasonable. The interviewer must demonstrate respect, genuineness and empathy. His or her voice should be quiet and calming, especially when seeking to calm the hyper-aroused patient. The interviewer should use non-judgmental language and open-ended questions.^{13,16}

It is important that the interviewer also feel safe and secure. If any risk is felt, the interviewer should have security or police present in the room or just outside. The interviewer may ask to have the patient searched for items of potential risk, according to legislation and hospital policy; this may include weapons or medications that the patient is at risk of ingesting. The interviewer should also note the nearest duress alarm and may choose to wear a personal alarm if available. The interviewer should sit within easy access of an exit and should never be boxed into a corner.

If the interviewer begins to feel uncomfortable, there is always the option of leaving and returning to complete the assessment at a later stage. All threats, attempts and gestures suggestive of violence should be treated seriously.

Aspects of the interview: direct questioning

Basic demographic information

The formal interview aims to identify a diagnosis and the necessary treatment for that diagnosis. Traditionally, patient care has been problem-based and centred on the alleviation of distressing symptoms and returning patients to baseline functioning. In recent years there has been a shift in focus from paternal models of care that are historically risk-averse and bio-medically directed to a recovery-orientated approach to care. A recovery focus has been adopted in policy at hospital, state and national levels. Recovery promotes the self-advocacy and empowerment of patients to make decisions about their treatment. Clinicians should have a collaborative discussion with each patient to identify the goals of his or her treatment and desired health outcome. In some cases advanced care directives or statements will have to be considered in treatment decisions.

It is wise to establish rapport with the patient with a personal introduction and an explanation of the purpose of the interview. The interviewer can begin by asking a series of non-threatening questions, for example, regarding demographics. This information is often required, as many mental health services rely on a patient's residential location to determine follow-up services.

These questions help by building a profile of lifestyle, relationships and thought processes. Likelihood of success or failure of particular treatment modalities may be assisted by knowledge of previous hospital admissions, both general hospital and mental health (Box 20.1.5).

The process of MH assessment differs slightly from that of a general medical assessment. In a MH assessment, as well as noting the content of responses, the interviewer also assesses how thoughts are processed and what meaning they may have. The interviewer attempts to interpret the patient's thought patterns to help formulate a diagnosis and understanding of the patient's experience.

Presenting complaint

The patient is asked to recall the sequence of events leading to presentation to the ED. The interviewer should explore the circumstances of the behaviour, reasons for it, degree of planning or impulsivity and its context. Were drugs and alcohol involved? Was there a recent precipitating event? It is often useful to get the patient to recall the previous 48 to 72 hours leading up to the event.¹⁷

This usually leads to questioning regarding current difficulties. The interviewer should explore the nature of current problems. There may be financial

Box 20.1.3 Aggression risk tool

- Alert on chart
 - Previous history of violence/threatening behaviour, verbal or physical
 - Aggressive behaviour/thoughts
 - Homicidal ideation
 - Use of weapons previously
 - Access to weapons
 - Intoxicated
- Patients then stratified into high, medium or low risk

Box 20.1.4 Risk of absconding

Mode of arrival

- Police
 - Handcuffed
 - Family/carer coercion
 - Voluntary
 - Past history of absconding behaviour
 - Alert on chart
 - Verbalizing intent to leave
 - Lack of insight into illness
 - Poor/non-compliance with medication
- Patients then stratified into high, medium or low risk

Box 20.1.5 Demographic information required

- Age/date of birth
- Address
- Accommodation history
- Other persons in household
- Occupation
- Occupational history
- Social resources:
 - family, friends, partners
 - social history
- Past medical history
- Previous hospital admissions
- Previous mental health admissions:
 - length of stay
 - type of treatment: medication/ECT
 - medications on discharge
 - follow-up arrangements
- Forensic history:
 - trouble with police
 - jail terms/convictions
- Alcohol
- Drug use
- Tobacco use
- Gambling

or legal problems, isolation, bereavement, impending or actual loss, or diagnosis of major illness. Have there been any recent changes and who are the patient's usual support people? An exploration of significant relationships is important, along with the depth and duration of these relationships. It is useful to gain an understanding of the patient's usual coping methods and personality style.

Mood and affect

There should be formal questioning regarding the patient's mood (inner feelings) and whether it is in keeping with affect (outer expression). The mood may be incongruent with affect, swing wildly between extremes (labile) or be inappropriate.

Mood is assessed by asking the patient to subjectively describe it (e.g. sad, happy, angry); and it may be helpful to obtain a subjective rating out of ten. Mood can also be objectively assessed by asking about the patient's ability to cope with activities of daily living, such as eating, weight loss or gain, sleep (early morning wakening or trouble getting to sleep) and general hygiene. The patient's ability to concentrate may also diminish with increasing mood disturbance, reflected by the ability to perform usual activities.

This may lead to direct questioning regarding future outlook and thoughts of suicide. It is important to be direct in asking the patient about suicide and whether there is a formulated plan to accomplish this. A well thought out plan with clear means of carrying it out requires further exploration and intervention by a mental health professional.

Delusions and hallucinations

Delusions and hallucinations are features of psychotic disorders. The patient may be reluctant

to disclose intimate thoughts and beliefs to the interviewer, especially if he or she is suspicious or mistrustful owing to a psychotic illness.

Hallucinations may be auditory, visual, tactile, olfactory, somatic or gustatory. The context in which they occur should be explored. Visual and tactile hallucinations are more commonly associated with organic pathology or drug-related presentations. Auditory hallucinations are common in chronic forms of psychosis, such as schizophrenia. Hypnagogic (occurring just before sleep) and hypnopompic (occurring on wakening) hallucinations are more benign than others. Common hallucinatory or delusional themes are persecutory, paranoid, religious, grandiose, controlling, somatizing and suicidal.

Insight and judgement

Insight involves the person's view and understanding of what is happening and why. This may include the following:

- Denial of illness
- Awareness of being sick and needing help but denying it at the same time
- Awareness of being sick but blaming it on external factors
- Awareness that illness is due to something unknown within the patient
- Intellectual insight: understanding of illness but reluctance to apply this to personal circumstances
- Insightful: good awareness of motives and feelings, illness, treatment and implications of decisions

It is important to gain an understanding of the patient's attitudes, views and motives in relation to his or her illness and proposed treatment. This will help to determine appropriate treatment and management, level of supervision required and the likelihood of adherence with treatment.

Aspects of the interview: observation

Key elements

Undertaking an MSE relies on the interviewer actively observing the patient's behaviour and conversation and interpreting his or her thoughts and comments. A summary is given in Box 20.1.6.

There are a multitude of acronyms for remembering the various elements of the MSE. Listed here are two.

The ABCs of the MSE¹⁴:

- Appearance
 - Affect and mood
 - Behaviour
 - Conversation and communication
- GFCMA – 'Got four clients on Monday afternoon'¹⁶:
- General appearance
 - Form of thought
 - Content of thought

Box 20.1.6 Overview of mental state examination

General description:

- appearance
- behaviour
- attitudes

Mood and affect:

- mood
- affect
- appropriateness
- motivation/energy
- appetite
- sleep

Speech:

- rate
- volume
- tone

Perception:

- hallucinations

Thought process:

- form fluency, organised or disorganised

Thought content:

- delusions
- suicidal or homicidal ideas
- hopeless/helpless/guilty

Cognition:

- consciousness
- orientation
- memory
- attention
- insight and judgement

- Mood and affect
- Attitude

Appearance, attitude and behaviour

This considers the patient's ability to care for himself or herself. Box 20.1.7 lists features that may require particular attention. Attitude is important, as it may indicate how cooperative a person will be with care and treatment. Abnormal posturing and unusual or repetitive behaviours should be noted. These may indicate increasing thought disturbance. With increasing aggression and agitation, there may be motor restlessness, pacing and hand wringing. Tension may escalate rapidly and steps should be taken early to defuse the situation.

The interviewer should note the rate, volume and rhythmicity of speech. This can range from being completely mute through monosyllabic answers to rapid, loud speech indicative of pressure of speech. The tone, inflection, content and structure of speech should be noted. The interviewer should determine if the speech is fluent, if the thoughts behind it are logical and whether it flows appropriately for the situation.

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Box 20.1.7 Appearance, attitude and behaviour

General:

- clothing
- application
- appropriate for climate?

Cleanliness:

- general grooming (hair, nails)
- tattoos, track marks on arms

Eye contact:

- intense stare
- avoids direct gaze
- decreases with increasing anxiety

Facial expression:

- variation in facial expression, voice, use of hands and body movements

Reaction to interviewer:

- aggressive, submissive, cooperative, guarded, evasive, passive or hostile

Motor:

- restless
- repetitive behaviour (e.g. rocking, hand wringing)
- tremor
- posturing
- tics
- tardive dyskinesia

Speech:

- rate, volume and rhythm
- mute
- poverty of speech (slow, monosyllabic responses)
- pressure of speech (extremely rapid, loud speech)
- normal inflection or flat and monotonous

Thought disorder

This is characteristic of psychosis. It is conversation that is illogical or lacks cohesion, sequence or connection of ideas. It varies in severity from milder forms of circumstantiality to derailment and word salad at the severe end of the spectrum. Flight of ideas is a common characteristic of mania, whereas poverty of thought or thought blocking can occur in schizophrenia or catatonia. A list with explanations is given in [Table 20.1.2](#).

Thought content

The interviewer identifies the prominent themes being expressed by the patient. These may revolve around feelings of hopelessness or helplessness, suicide, grief and loss, persecution, being controlled or under surveillance, religious or grandiose ideas, delusions of poverty or nihilism (the belief that part of the self does not exist, is dead or is decaying).

Table 20.1.2 Thought disorders

Circumstantiality	Delays in reaching goals by long-winded explanations, but eventually gets there
Distractible speech	Changes topic according to what is happening around the patient
Loosening of associations	Logical thought progression does not occur and ideas shift from one subject to another with little or no association between them
Flight of ideas	Fragmented, rapid thoughts that the patient cannot express fully as they are occurring at such a rapid rate
Tangentiality	Responses that superficially appear appropriate but are completely irrelevant or oblique; never arrives at the point
Clanging	Speech where words are chosen because they rhyme and do not make sense
Neologisms	Creation of new words with no meaning except to the patient
Thought blocking	Interruption to thought process where thoughts are absent for a few seconds and are unable to be retrieved

Perception

Auditory hallucinations are the most common form of hallucinations in mental illness. A patient may be actively hallucinating despite denying this on questioning. It is important to note if the patient's eyes suddenly switch direction for no apparent reason or if he or she appears to be listening to a voice. These movements are often quite subtle and easily missed if observation is not active. Note the content or type of voice being heard, such as command hallucinations, where the patient may feel compelled to act on a specific instruction that could lead to dangerous actions.

Cognitive assessment and physical examination

Screening of cognitive function and a physical examination are an integral part of the psychiatric assessment. The interviewer should ensure that the patient does not have an acute confusional state secondary to a physical condition that may account for a behavioural problem.

A number of tools are available to assess cognitive functioning.^{13,17} These comprise assessments of orientation, concentration, attention, memory, language and abstraction. The presence of impaired cognitive function or an intellectual disability will influence decisions about diagnosis, treatment and disposition. Approximately 20% of mental health patients have a concurrent active medical disorder requiring treatment and possibly contributing to the acute behavioural disturbance.⁶ Investigations depend on patient history and physical examination but may include electrolytes, liver and renal functioning, CK, thyroid functioning, drug toxicology, computed tomography and lumbar puncture. Only after this can an emergency medicine practitioner plan the most appropriate management.

Conclusion

A good mental health assessment is vital for timely and appropriate treatment and disposition for what is an increasingly large group of patients in the ED. Formulating an accurate

assessment of a person's mental state and risk, enables appropriate provision of treatment and intervention. This may include referral to specialist mental health services for treatment planning. The mental health professional is then able to conduct a more detailed assessment to assist in determining appropriate treatment and disposition.

CONTROVERSIES

- Most hospitals now have specialized mental health teams placed within the ED. There is a trend towards the development of short-stay psychiatric beds (with varying models of care) with a purpose-designed area within or attached to the ED where mental health patients receive care after initial assessment. Increased specialization has the potential to de-skill emergency medicine personnel, both nursing and medical. On the other hand, a greater presence of mental health staff can help to build capacity and serve as a role model to ED clinicians. To date it is uncertain which particular model of care is more effective in the short-term treatment of mental health patients.
- Despite the improved presence of mental health teams within EDs, mental health patients are exposed to access block and overcrowding in EDs. This has resulted in mental health patients spending prolonged periods of time in the ED while waiting for inpatient beds to become available. This has the potential for poor quality of care and the unnecessary use of sedation and restrictive practices. ED and mental health teams must work collaboratively to ensure good outcomes for mental health patients.

20.1 MENTAL STATE ASSESSMENT

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20.2 Distinguishing medical from psychiatric causes of mental disorder presentations

David Spain

ESSENTIALS

- 1** Morbidity and health costs are reduced by distinction of medical from psychiatric causes of mental disorder presentations to emergency departments.
- 2** Always ask if any medical condition exists in addition to the psychiatric complaints. This will identify most medical causes of mental disorder.
- 3** Missed medical diagnosis is most commonly associated with failure to undertake an adequate medical history, mental state examination and physical examination.
- 4** Substance-related disorders are most easily identified on direct or collateral history.
- 5** The presence of delirium or new cognitive defects makes an organic or substance-related illness almost certain.
- 6** The diagnosis of delirium may require repeated assessments over time.

Some diagnoses and dispositions can be determined quickly after a medical and psychiatric history, with the addition of a mental state and full physical examination. This sometimes takes place without diagnostic procedures. Other presentations require extensive and intensive evaluation, repeat evaluation, observation in hospital and significant investigations before the diagnosis is clear.

Medical clearance in emergency departments (EDs) can be inaccurate due to the presence of intoxicating substances or patient factors that limit assessments. A non-judgemental approach with prudent intervention based on known or likely risks, close monitoring in a safe environment and repeated assessment of physical and mental state over time are often necessary to obtain an accurate diagnosis and optimal outcome.

Studies on medical clearance by ED staff and psychiatrists have repeatedly shown a poor ability to discover medical conditions. This failure is commonly due to one or more of the following factors: inadequate history; failure to seek collateral history; poor attention to physical examination, including vital signs; absence of a reasonable mental state examination; uncritical acceptance of medical clearance by receiving psychiatric staff; and failure to re-evaluate over time.³ Medical conditions were most easily identified in the ED by the triage nurse or medical officer when asking whether any medical conditions existed in addition to the psychiatric complaints.⁴

Introduction

Emergency physicians (EPs) often assess patients with suspected mental disorder. The critical question posed is: What is causing this? Causes broadly include psychiatric, medical, intoxication and behavioural. Identifying the likely cause and careful consideration of the capability of local facilities usually leads to correct disposition, reduced morbidity and costs.¹ EPs need a simple classification defining the principal diagnosis of the presenting mental disorder consistent with the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-V) terminology. This allows us to communicate with psychiatric colleagues and should assist diagnostic, management and disposition accuracy. Table 20.2.1 is such a suggested classification.

Medical issues are traditionally called organic. That terminology persists but is increasingly challenged by a postulated medical basis for some psychiatric disorders.

Medical clearance has been used for over 40 years, but there is still no accepted universal agreement of what that means or should entail.² As a minimum, it aims to identify medical conditions causing, aggravating or co-existing with an apparent mental disorder that require medical rather than psychiatric care. Overall, the process should be considered an imperfect risk reduction strategy.

General approach

Patients with abnormal behaviour labelled as psychiatric after routine medical and psychiatric assessment frequently have a final diagnosis of a medical cause or precipitant for the mental disorder. The incidence ranges between 19% and 80%.² Deciding whether a particular presentation of mental disorder is medical or psychiatric is often difficult, as there are very few absolutes that distinguish medical from psychiatric illness. Careful collection and weighting of appropriate information commonly only leads to a differential diagnosis.

Table 20.2.1 A simple classification of principal diagnosis of mental disorder for emergency physicians

DSM-V terminology	Broad traditional clinical grouping	Likely principal management and disposition
Axis 1		
Clinical disorder due to a general medical disorder	Organic	Medical
Delirium, dementia and amnesia and other cognitive disorders	Organic	Medical
Substance-related disorder—intoxication or withdrawal disorder	Organic	Medical
Substance-related disorder—substance induced persistent disorder	Organic	Psychiatric
Clinical disorder (not identified to above or axis II principal diagnosis)	Psychiatric	Psychiatric

20.2 DISTINGUISHING MEDICAL FROM PSYCHIATRIC CAUSES OF MENTAL DISORDER PRESENTATIONS

Box 20.2.1 Triage safety questions⁵

- Is the patient a danger to him- or herself?
- Is the patient at risk of leaving before assessment?
- Is the patient a danger to others?
- Is the area safe? Does the patient need to be searched?

(From Pollard C. *Psychiatry Reference Book – Nursing Staff*. Hobart: Department of Emergency Medicine Royal Hobart Hospital; 1994 with permission.)

Evaluation requires a thorough approach and a commitment of time and effort. Special skills are required for medical clearance and psychiatric interview. A coordinated and focused medical and psychiatric assessment has the highest yield of correct diagnoses.¹ Proformas or clinical pathways may improve compliance and documentation of important details, but have not demonstrated improved patient outcomes.

National Emergency Access Targets (NEAT) in Australia have changed the management in some situations. Approaches vary depending on institutional capabilities and local agreements. Detailed medical clearance for every patient is no longer universally practiced in ED. Many known psychiatric patients are now triaged directly for psychiatric assessment. Inpatient psychiatric services have, in response, taken the responsibility for medical assessment for those incompletely or not assessed in EDs. Triage screening still leaves a volume of complex patients requiring detailed medical assessment in the ED.

Triage

Triage is vital, as many apparent psychiatric presentations have medical conditions. Correct identification by nursing staff facilitates correct management and reduces morbidity and mortality. Many patients with psychiatric illness are also a significant risk to themselves or to others and require urgent intervention. Questions regarding safety should always be raised (Box 20.2.1).⁵

Nursing staff can use a triage checklist to identify presentations with high yield for organic illness (Box 20.2.2). These require ED medical assessment. With local service agreement these also allow streamlined psychiatric referral without ED medical clearance for those with a known mental disorder and a low medical risk. These are based on consensus guidelines previously developed by EPs and Psychiatrists.⁶ They require vigilance by the psychiatric team to consider that a low risk of medical cause remains. They have been operating for some years without obvious increase in adverse outcomes. They are yet to be validated.

If a psychiatric diagnosis is likely, then an appropriate urgency rating by the Australasian Triage Scale for psychiatric presentations should be applied. This triage categorization for

Box 20.2.2 High-yield indicators of organic illness identified at triage

Emergency department triage and referral of adult patients to psychiatry

1. Does the patient have a new psychiatric condition? Yes No

If Yes please specify:

2. Any history of active medical illness needing evaluation? Explore patient concerns re new medical issues or concerns of current medical illness or regards co-morbid medical conditions.

If Yes please specify:

3. Any abnormality of vital signs? Please document observations below.

Pulse: BP: Temp: Resp Rate: O₂ Sat:

Values considered abnormal are:

- Temp $\geq 38^{\circ}\text{C}$
- Pulse <50 or >120 beats/min
- Blood Pressure: systolic <90 or >200 mm Hg; diastolic >120 mmHg
- Respiratory Rate >22 or <10 breaths/min
- O₂ saturation $<90\%$ on room air

4. Any physical complaint or sign? (Any trauma, abnormal gait, abnormal speech, pallor, cyanosis, sweatiness, irregular pulse, unequal pupils, headache, chest pain, abdominal pain)

If Yes please specify:

5. Any acute ingestion, misuse, chronic abuse or withdrawal of any substance? (e.g. illicit drugs, alcohol, overdose.)

If Yes please specify:

6. Any features of delirium such as: lethargic, stuporose, fluctuating or altered level of consciousness, inattention or disorientation to time, place or person?

If Yes please specify:

7. Is the person aged <15 years old or >55 years old?

Outcome:

If the answer is No to all the above questions, no further evaluation is necessary and the patient can be directly referred for psychiatric assessment. If the answer is Yes to any question, the patient needs ED medical assessment before any referral is initiated.

psychiatric presentations has been developed and verified and allows reasonable waiting time standards for urgency to be applied in Triage Category 2–5 (Box 20.2.3).⁷ A Triage Category 1, when there is severe behavioural disturbance with immediate threat of serious violence, has been sensibly added to that scale by the Australasian College for Emergency Medicine.

Triage should consider privacy issues to obtain an accurate history. Collateral information, if available, should be obtained, considered and documented. This information should allow the patient to be placed in an appropriate and safe environment with continuing visual and nursing observations while further assessment occurs.

The interview environment

A climate of trust is very important, as many details of the psychiatric interview are sensitive. The psychiatric interview should take place in as quiet and private an environment as possible. The choice of the interview site may be limited in emergencies to ensure safety for both the patient and the staff.

History

A careful traditional medical history is the most common identifier of medical illness causing a mental disorder presentation. Substance-related disorders are most easily identified on history. Drug history should check compliance and detail prescribed, recreational and over-the-counter

Box 20.2.3 Guidelines for Australasian Triage Scale coding for psychiatric presentations⁷

Emergency: Category 2

Patient is violent, aggressive or suicidal, or is a danger to self or others, or requires police escort

Urgent: Category 3

Very distressed or acutely psychotic, likely to become aggressive, may be a danger to self or others. Experiencing a situation crisis

Semi-urgent: Category 4

Long-standing or semi-urgent mental health disorder and/or has a supporting agency/escort present (e.g. community psychiatric nurse^a)

Non-urgent: Category 5

Long-standing or non-acute mental disorder or problem, but the patient has no supportive agency or escort. Many require a referral to an appropriate community resource

^aIt is considered advantageous to 'up triage' mental health patients with carers present because the carers' assistance facilitates a more rapid assessment.

(From Smart D, Pollard C, Walpole B. Mental health triage in emergency medicine. *Aust NZ J Psychiatr* 1999;33:57–66 with permission.)

medications. Gradual onset and a previous psychiatric history are more commonly associated with psychiatric illness. Conversely, abrupt onset, no premorbid decline and no past psychiatric history favour a medical cause.

Family history is often a key indicator of psychiatric or medical cause. For example, a newly depressed 30-year-old man with a family history

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of Huntington disease or porphyria is more likely organic. Conversely, an 18-year-old man with a hypomanic presentation plus strong family history of bipolar disorder is more likely psychiatric. Suicidal and homicidal risk should be assessed routinely to ensure safety. The system review is a useful screen for organic illness.

HIV-related illness is the new great mimic of modern psychiatry and medicine. Risk behaviours should be explored. Positive HIV status always warrants assessment for an organic cause of any new behavioural disturbance. Clinically, these problems often initially present with symptoms of mild anxiety or depression. Many treatable medical causes are only evident after significant investigations.

Delirium, a highly specific but not absolute indicator of medical or substance-induced disorders, should always be sought. By definition, this requires a history of recent onset and of fluctuation over the course of the day. Classically, there will be subtle changes in the level of consciousness or the sleep–wake cycle. Patients may have poor recent memory or not be able to attend sufficiently to give a history if delirious. The psychiatric history, including life profile, may give evidence of the presence or absence of premorbid decline. An abrupt onset of abnormal behaviour with no premorbid decline is more suggestive of an organic cause.

Collateral history

Collateral history is important as the patient is not always capable of, or willing to give, full information. This history often crystallizes a diagnosis that would otherwise be uncertain or missed. Previous discharge summaries may provide information regarding alcohol and drug use, previous behaviour and diagnosis. The family should be asked to bring in all medications, including over-the-counter items. Family, friends and caregivers may give rapid access to collateral history. Collateral may be the only source for a history of a patient's fluctuating mental status, suggesting delirium, even when the patient appears quite lucid in the ED.

Examination

Lack of attention to important details of the examination is a frequent cause of missed medical illness. Areas that commonly yield positive findings, but are frequently omitted, are: the neurological examination; appearances of endocrine disease; toxicodromes; signs of malignancy; stigmata of drug or alcohol abuse; and vital sign examination. Poor cooperation can prevent detailed examination and should be documented so that future consulting clinicians are aware of a deficient entry examination.

Vital signs

Abnormal vital signs are frequently the only abnormality found on examination of patients with serious underlying medical disease. They must always be acknowledged and explained. Pulse oximetry should be included rapidly to exclude hypoxia. A bedside blood sugar level should be routine.

Mental state examination

This is an account of objective findings of mental state signs made at the time of interview. It is the psychiatric equivalent of the physical examination and specifically details the current status. It should be performed by the EP as part of medical clearance. Observations made by other staff, such as hallucinations, may be significant and can be included with the source identified. Careful consideration of the mental status frequently clearly distinguishes medical from psychiatric illness, guiding further investigation and management. For example, the presence of delirium or other new cognitive defects make an organic illness almost certain. Disorientation is highly suggestive of delirium. Delirium can be very subtle. Due to the fluctuating nature, the delirious patient may appear normal on a single interview. Other less obvious features, such as lability of mood, variability of motor activity or lapses in patient concentration making the interview difficult, can be the only clues and are easily overlooked. The importance of formulation using collateral history and repeated mental state examination is stressed. Documentation is important so that mental status changes on repeat assessment can be appreciated.

Examination tools

Elderly patients with delirium or cognitive defects are frequently not recognized by EPs. These patients are at high risk of morbidity and mortality. Cognitive defects may be rapidly and reliably identified by EPs during mental status examination by the use of Folstein's Mini Mental State Examination (MMSE).⁸ A score of less than 20 suggests an organic aetiology. A fall of two or more points on serial MMSE is highly suggestive of delirium. Other screens suitable for EP use are the Quick Confusion Scale,⁹ the 4AT test and the 6-Item Cognitive Impairment Test.¹⁰

Elderly patients with possible dementia or delirium may require more detailed screening with the confusion assessment method as a recognized standard. However, assessors with special training are required.

The tests above are suitable screening tools for EDs but are not intended to replace formal neuropsychological assessment.

Proformas of medical history, mental state examination and physical examination may improve the thoroughness of assessment and documentation.

Investigations

Investigations always should be guided by clinical findings and be tailored to each individual presentation.

First presentations and suspicion of a medical cause or co-morbid illness aggravating mental disorder are the major indications for emergency investigations. Baseline blood tests, such as full blood profile, blood sugar level, electrolytes, liver function tests, calcium and thyroid function tests, may at times detect clinically unsuspected problems. Examination and culture of urine and cerebrospinal fluid should be undertaken if occult infection is considered. A urine drug screen may confirm clinical suspicions of drug-related illness when collateral and patient history of misuse is absent. HIV and syphilis testing should be done on all patients with significant risk. Mandatory brain computed tomography (CT) is not indicated, but the threshold for imaging in first presentations of altered mental state without obvious cause or after head trauma should be low. Herpes encephalitis may not produce imaging changes on CT but should be considered when fever, delirium or cognitive changes are present with sudden alterations in behaviour. Magnetic resonance imaging and electroencephalogram examination will rarely be indicated in the ED for this group of patients.

Diagnostic formulation

EPs providing medical clearance of clients who do not meet low-risk criteria at triage should suspect organic disease until proved otherwise. In particular, reversible medical causes of an abnormal mental state should be sought. Proformas improve documentation and summation. Consideration of the factors in Table 20.2.2 may help to determine doubtful cases. There are few absolutes that distinguish organic from psychiatric patients. Use of the five-axis DSM-V system improves the ability to consider the patient's presentation in the context of total functioning. It also allows EPs to communicate with psychiatric peers in the recognized language.

Some patients require observation, re-examination and further investigations before a definitive answer is obtained. Intoxicated patients usually require observation until sober when valid mental health assessments can occur. Interim care and disposition vary depending on the presentation, the past history and the facilities available. A common expectation of EPs for patients referred to psychiatrists is to

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Table 20.2.2 Factors influencing the likelihood of medical or psychiatric illness as the principal diagnosis

Organic	Psychiatric
Abnormal vital signs	Family history of psychiatry disorder
Age >40 with first psychosis	Past psychiatric illness
Delirium	Fully orientated
Conscious level fluctuates	Clear sensorium
Inability to attend	
Memory impaired	
Impaired cognitive abilities	Intact cognition
Neurological signs, e.g. dysarthria	
Abnormal physical signs	
Abrupt onset	Slow onset
Dramatic change in general status (hours to days)	Premorbid slow deterioration in employment/family/socially
Recent medical problem	Recent significant life event
Medication, drugs/alcohol/withdrawal	Non-compliance psychiatric medication
Marked new personality changes	
Visual, tactile or olfactory hallucinations more common	Auditory hallucinations more common especially: Voices arguing Voices commentary Two voices discussing Audible thoughts
Agitation/irritability	
HIV/AIDS	
Failed psychiatric treatment	
Disorganized delusions	Structured delusions
Movement disorders	Somatic passivity experiences
Perseveration	
Confabulation	
Illusions or misinterpretations	
Circumstantiality	
Concreteness	Thought withdrawal, insertion or broadcasting
FH degenerative brain disease	FH psychiatric illness
FH heritable metabolic	FH: family history psychiatric illness

FH, Family History

document that the patient is 'medically cleared'. The assessment is known to be imprecise and difficult.^{1,2} Better documentation is to state that the ED assessment has revealed no evidence of an emergent medical problem that would preclude admission to psychiatric care and further medical evaluation.

Conclusion

A thorough medical history, psychiatric history, collateral history, physical examination, mental state examination and judicious specific investigation will identify most patients likely to have an underlying physical cause for a mental disorder presentation. Omission of any of these steps may lead to missed medical diagnosis and incorrect disposition.

CONTROVERSIES AND FUTURE DIRECTIONS

- Where and when the assessment of a mental disorder ideally occurs is somewhat controversial. Urgent assessment in the traditional hospital-based general ED with strict medical clearance is ideal and is the safest for abrupt onset of a new mental disorder illness. Patient volume and time demands with resource constraints are forcing alternative models for entry to care. Many EDs are triaging patients as likely medical, emergent psychiatric or non-emergent psychiatric. Depending on local service availability, early streaming based on this triage allows many psychiatric clients (most non-emergent) to be directed away from the ED to appropriate community mental health services. Addition-

ally, community-based psychiatric services are increasingly managing acute episodes of behaviour disorder in the community without the need for hospitalization or emergency department involvement. Hard outcome studies are yet to be undertaken on these new models.

- NEAT was expected to increase pressure on ED and psychiatric services to respond in a timely fashion. There is an absence of data on quality related to NEAT for mental disorder attendances. Despite the new targets, services commonly have not been able to approach or consistently meet targets for admitted psychiatric patients.
- Providing adequate resources and a safe physical environment for assessment, management and disposition of the rapidly escalating number of patients with a substance-related disorder is a major ED challenge. Assessments during intoxication are typically unhelpful. Intoxication may last hours to days and require medical therapy or brief admission. While the ED may be an appropriate resource for the initial care of severe behavioural disturbance, no universally applicable model has been found to manage patients who need a safe place to sober up from intoxications before reassessment. Larger EDs in heavily populated areas have been trialling short-stay acute behavioural units that combine emergency, psychiatric, toxicology, and alcohol and drugs services.

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20.3 Deliberate self-harm/suicide

Jennie Hutton • Grant Phillips • Peter Bosanac

ESSENTIALS

- 1** Deliberate self-harm is a frequent presentation to emergency departments and is a symptom of diverse underlying problems, be they biological, social or psychological.
- 2** Patients with deliberate self-harm form a heterogeneous group, most of whom do not have ongoing suicidal behaviour.
- 3** Assessment of suicide risk following deliberate self-harm is to inform treatment and to identify risks amenable to intervention and protective factors. It involves assessment of background demographic, psychiatric, medical and psychosocial factors as well as the presenting crisis. The patient should feel listened to and understood following the assessment.
- 4** There is no 'gold standard' for suicide risk assessment and the level of risk can change quickly.
- 5** The most consistent factors predicting fatal and non-fatal repetition following deliberate self-harm are psychiatric illness, personality disorder, substance abuse, multiple previous and types of attempts, hopelessness, social disconnectedness and intoxication.
- 6** A planned strategy to deal with these patients should address triage, restraint and observation, medical and suicide risk assessment, treatment, disposition and follow-up.
- 7** Management requires coordinated care with emergency, mental health and primary care clinicians, as well as carers.
- 8** Treatment decisions should be collaborative wherever possible and take into account any advance statement that may have been made. The next of kin should be contacted wherever practicable for both collateral information and collaboration.
- 9** The legal framework for the location in which individuals practice should be known and considered.

Introduction

Suicide is a deliberate act of intentional self-inflicted death. It is the most extreme manifestation of deliberate self-harm (DSH), where the spectrum spreads from superficial lacerations through to actions intended to end life. Although suicide is uncommon, 10% of people who complete suicide are seen in an emergency department (ED) in the month prior to death, with a substantial proportion not having psychosocial assessment, thus providing an opportunity for intervention.¹ Regardless of the presentation to ED, about 8% of patients have experienced recent suicidal ideation or behaviour, which they may not disclose unless specifically explored.² However, the major ED impact is in the identification and assessment of large numbers of patients potentially at risk of suicide, with

initial management of co-morbidities and modifiable risk factors.

DSH is a maladaptive response to internal distress and may not have suicidal intent; however, it may indicate a risk for suicide. DSH is a common ED presentation (approximately 0.4% of all ED visits) and the goals of management include treating the physical health sequelae, assessing the risk of non-fatal or fatal repetition and prevention, and diagnosing and commencing treatment of potentially reversible psychosocial causes.

Epidemiology

In Australia there were 3128 deaths from intentional self-harm in 2017, with age standardised rates of approximately 19.1 per 100,000 in males and 6.2 in females (fig. 20.3.1).³ Intentional self-harm accounted for 1.9% of all deaths in 2017. However, with a median age at death of 44.5 years,

intentional self-harm (11.4%) was responsible for the most Years of Potential Life Lost (YPLL) of all diseases and trauma. As a comparison Ischaemic Heart Disease which contributed 7.4% of YPLL in 2017 has a median age at death of 85 yrs.

Across OECD (Organisation for Economic Cooperation and Development) countries, suicide rates were lowest in South Africa, Greece, Mexico, Israel and Brazil, at less than 7 deaths per 100,000. They were highest in Lithuania, Hungary, Japan and Latvia, at more than 17 deaths per 100,000. The World Health Organization estimates that the low- and middle-income countries account for 78% of global suicides.

Hospital presentations for DSH are at least 10 times higher than suicide rates. The 2007 Australian National Survey of Mental Health reported 1.9% of males and 2.7% of females experienced suicidal ideation within 12 months.⁴ This rate may be as high as 25% in certain populations and age groups.

Risk of suicide

An episode of DSH is one historical risk factor predictive of future suicide behaviours. Approximately 1% to 2% of patients complete suicide during the year following an attempt, and in approximately 40% of suicides there is a history of a previous self-harm. A systematic review of fatal and non-fatal repetition of self-harm reported a suicide rate of 2% at 1 year and 7% after 9 years.⁵ Hospitalization and aftercare decrease the short-term risk of suicide, but have little impact on the long-term risk of suicide. However, this may be due to undertreatment of psychiatric illness.

Repeated episodes of deliberate self-harm

DSH usually invokes help from friends, family and the medical profession so the patient's social situation and psychological well-being tends to improve. This effect is prominent in younger patients, but may not occur in patients aged over 60 years. The risk of repetition is 12% to 16% in the following year, with 10% of these occurring in the first week.⁵ This is more likely in females who are unemployed, have cluster B (e.g. borderline, narcissistic and histrionic) personality traits or have substance-abuse problems. A younger age at first attempt, the presence of long-standing affective disorders, drug/alcohol misuse disorders and anxiety all correlate with repeated attempts. Some patients have chronic suicidal ideation and multiple repetitions of DSH. They often suffer from personality disorders, psychotic disorders, chronic medical conditions, alcohol or drug use, a history of childhood sexual

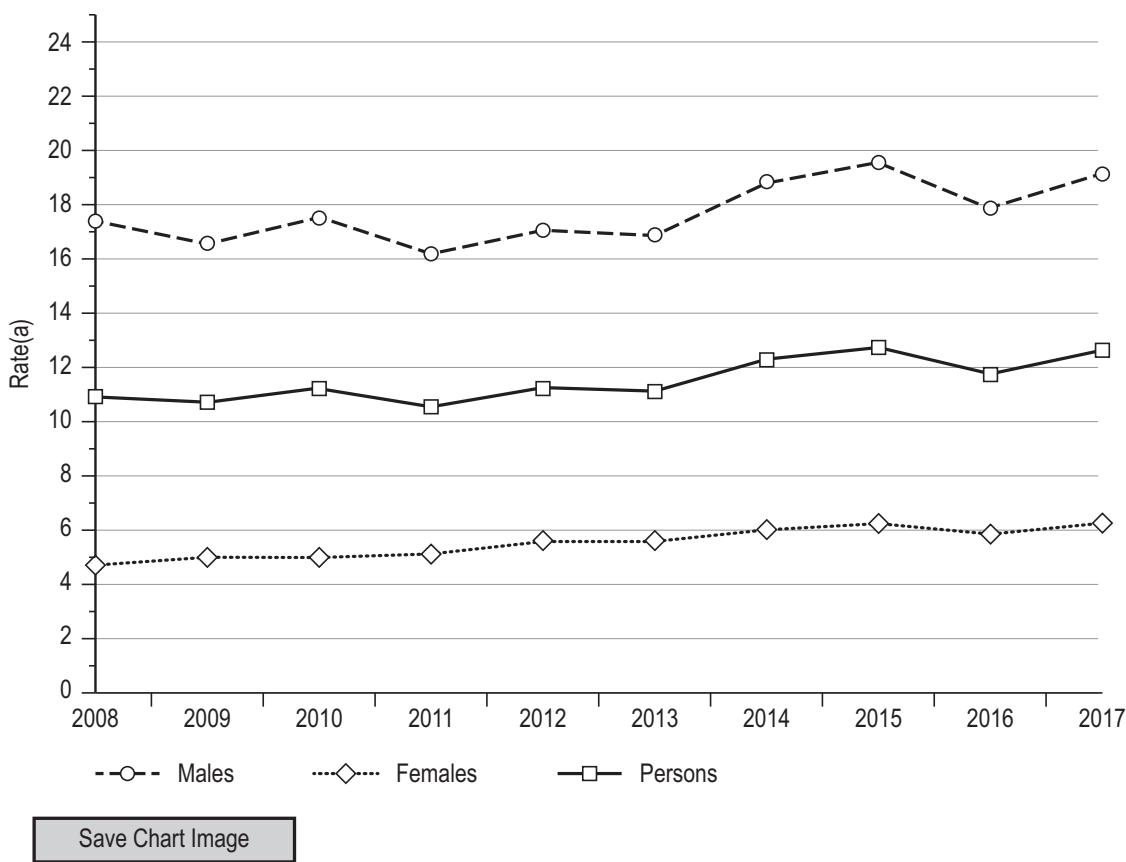


FIG. 20.3.1 Suicide rates Australia (2008–2017). (From Causes of Death, Australian Bureau of Statistics, 2017. Accessed Jan 2019)

abuse and violent behaviour. They use DSH as a means of fighting off anxiety, hopelessness, loneliness or boredom, as well as subjective experiences of emptiness or extreme distress. They may also be maladaptive ways of eliciting assistance from family, friends or health carers. These patients are at increased risk of eventual suicide. Reversible potentiating factors should be addressed where possible.

Patients with DSH who leave the ED prior to a psychosocial assessment may have a higher risk for repeat DSH, probably associated with lack of specialist follow-up and treatment of reversible factors.

Patient characteristics

Demographic factors

Age

Suicide and DSH are rare in children under 12 years of age. Australian data suggest a peak at 30 to 34 years in males (27.5 per 100,000) and 50 to 54 years in females (10.4 per 100,000).³ There is another peak in the elderly, with suicide rates increasing with age from 65 years.

The incidence of DSH increases throughout puberty, reaching a peak at 15 to 24 years of age and decreasing thereafter. The ratio of rates of DSH to suicide decreases markedly with age.

DSH is uncommon in the elderly, who have a high ratio of successful to unsuccessful attempts.

Gender

In Australia, the overall rate ratio of M:F suicide is 3.4 in 2010 compared with 2.7 in New Zealand.^{6,7} The rate for male DSH has been increasing in Western countries recently with the male to female ratio approximately 1:2. Females choose methods that are less likely to be fatal and may be more likely to present to hospital following DSH.

Social and cultural factors

Suicide rates are higher in those who live alone or are in a lower social group, especially in urban areas characterized by social deprivation and overcrowding. Being single, separated, divorced or widowed increases the risk of suicide two- to threefold in the high-income countries. In these countries, being partnered reinforced by children decreases the risk of suicidal behaviour.

Recent data in Australian aboriginal people reports substantially higher suicide rates that commence at a lower age than in the non-aboriginal population.³ The suicide rate for Aboriginal or Torres Strait Islander People in 2017 (25.5 per 100,000) is twice as high as non-indigenous people

(12.6 per 100,000). In addition, 76% of these deaths are attributed to male indigenous people.³ A higher suicide rate is seen in indigenous groups of other developed countries for example, in New Zealand, the age-standardised rate was 197.7 per 100,000 Maori in 2013 compared with a rate of 172.2 per 100,000 non-Maori.

Rural areas in Australia and New Zealand and remote areas in the UK have a higher rate than urban areas.^{3,6,7} Incarceration is a risk factor for suicide; in any form of custody the suicide rate is three times that of the general population.

Some social groups, such as doctors, dentists, musicians, lawyers and law-enforcement officers, are more prone to suicide. Most adults (75%) with DSH have relationship problems with their partners, and teenagers with their parents. A perceived or potential loss, such as a major argument or separation, often precedes the act on a background of ongoing social difficulties or substance use.

Unemployment increases the risk of DSH by 10 to 15 times, with the risk increasing with duration of unemployment. This may not be a cause or effect, but may be due to some underlying factor, such as psychiatric illness, personality disorder or substance abuse.

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Medical factors

There is an increased risk of suicidal ideation in people with chronic ill health; the majority of such patients have sought medical advice in the 6 months before suicide.

Psychiatric factors

There is a pre-existing psychiatric disorder in 90% to 100% of cases of suicide, with depression accounting for 66% to 80%, but this rate may be based on retrospective psychological autopsy and therefore be open to dispute. The lifetime rate of suicide among psychiatric inpatients is 3 to 12 times higher than in the general population and involves a greater proportion of more violent methods, such as jumping from buildings, or hanging. One-third of these episodes occur after self-discharge from hospital, with another third occurring during approved leave. The high-risk time is the first week of admission and during the first 3 months after discharge.

Psychiatric disorders are present in up to 60% of patients who complete DSH, but may be transient and secondary to acute psychosocial difficulties. Da Cruz et al. examined the cases of 286 individuals who died within 12 months of mental health contact in North West England; 43% of the sample attended the ED on at least one occasion and 12% of the sample attended an ED on more than three occasions and could be considered 'frequent attenders'. Most frequent attenders had a history of self-harm (94%), 68% had a history of alcohol abuse, 63% were unemployed at the time of death and 49% had a history of drug abuse.

The psychiatric diagnosis that carries the greatest risk of suicide is mood disorder, particularly major depressive disorder if associated with borderline personality disorder, anxiety or agitation. Fifteen percent of these high-risk patients complete suicide over a lifetime. Depression correlates well with the occurrence of suicidal ideation, but may not be as strong a predictor of planning and preparation (intense thoughts, plans and capability) and, therefore, suicide completion. Hopelessness is the most important factor associated with suicide completion and may be of greater importance than suicidal ideation or depression itself.⁸ Therefore depressed patients should have their attitudes towards the future carefully assessed. Patients with cluster B personality disorders are at a high risk of DSH and suicide, especially if associated with labile mood, impulsivity, alienation from peers and associated substance abuse.

Up to 10% of people with schizophrenia die by suicide. Young adult males are at high risk, especially if there is associated depression with feelings of hopelessness, previous DSH or suicide behaviours, unemployment or social isolation.

Individuals with alcohol use disorders have an overall approximately 7% lifetime risk of dying by suicide, with women being at greater risk than men. Fifteen percent of alcohol-dependent persons eventually complete suicide. The majority of these are also depressed. Young males

dependent on heroin have 20 times the risk of the general population.

Chronic alcohol dependence is uncommon in DSH, but alcohol intoxication is involved in 50% to 90% of suicide attempts. Acute alcohol ingestion is found in approximately 35% of people who die by suicide.

Frequent attenders

Frequent attenders to EDs (defined as more than three presentations in a year) are also at high risk. This group has seven times the risk of the general population and rates of suicide similar to clinical psychiatric populations. This risk is particularly pronounced in patients who present with panic attacks, especially if associated with depressive symptoms.

Aetiology

No specific psychological or personality structure is associated with suicide and patients who complete suicide or DSH do so for many unrelated reasons. The precipitant may be a personal crisis or life change amplified by poor social support, substance abuse or psychiatric disorder. Intoxication may decrease inhibitions enough to allow an act to proceed. A study by Wyder interviewed 112 people following a DSH. She found that 51% had considered DSH for 10 minutes or less, but of those who had been affected by alcohol that number jumped to 93%.⁹

The most frequent methods of suicide in Australia are hanging, strangulation and suffocation, with these modes being used in 56% of all suicide deaths in 2010 in Australia. Poisoning by drugs was used in 12% of suicide deaths in 2010, followed by poisoning by other methods including alcohol and motor vehicle exhaust (10%). Firearms accounted for 7% of suicide deaths in Australia in 2010, a rate which has declined from 20% a decade earlier, possibly due to firearm restriction legislation. Proportions due to each method vary according to region, residence, age and sex. In the United States, firearms accounted for 57% of male and 32% of female suicide deaths.

One-third of patients with DSH express a wish to die, but most do so to communicate distress. DSH may serve many functions for the person. At its most simple, it serves an integrative function calming the person at a time of great distress. It may also be a way of mobilizing assistance for someone who is feeling overwhelmed by circumstances. Many patients threaten suicide or magnify being at risk of suicide to increase the likelihood of admission to hospital. These patients are more likely to be substance dependent, have personality diatheses (e.g. marked borderline, antisocial or dependent traits or disorder) or homelessness, and be single and in legal difficulty. However, these instances of goal-directed behaviour should not be discounted, and the behaviour should be taken seriously. A presentation to an ED is a declaration that the person

is in a self-defined crisis for which they are using maladaptive coping measures.

Most cases of medically serious DSH are due to self-poisoning, with 90% associated with alcohol intoxication. The most common drugs are non-prescription analgesics and psychotropic drugs. Many overdoses are related to alcohol or illicit substance intoxication and may be accidental rather than deliberate, although this distinction is often difficult to ascertain. Self-injury may involve cutting of the skin in various sites about the body but may also involve self-inflicted cigarette burns, excoriation of the skin or hitting themselves or other objects. More violent forms of self-injury are less common and suggest serious suicidal intent. Bizarre self-mutilation may occur in psychotic patients who may not necessarily have an intention to die but are acting in accordance with delusional beliefs or in response to command hallucinations.

Assessment

A person who expresses suicidal ideation or engages in DSH is sending a distress signal that emergency physicians must acknowledge. Suicidality should also be assessed in patients with symptoms or signs of depression, unusual behavioural changes, substance abuse, psychiatric disorders and complainants of sexual violence. Those who present with injuries of questionable or inconsistent mechanism, such as self-inflicted lacerations and gunshot wounds or motor vehicle accidents involving one victim, should also be considered for assessment. Many would argue that assessment of self-harm should be a routine part of any ED assessment. A retrospective study by Da Cruz et al. found that 40% of persons who died by suicide had presented to the ED at least once during the year prior to their death. Assessment in the ED ideally will contain elements that provide the person with the opportunity to discuss psychosocial aspects of their life. Within this discussion, it may be that suicidal ideation or thoughts of DSH may be elicited. This may allow early referral to psychosocial support, thereby providing the person with holistic care to help address their needs.

Assessment requires a systematic, multidisciplinary approach involving prior staff education, appropriate triage, observation and restraint procedures (in the setting of imminent risk and the absence of less restrictive options), and a planned strategy for assessment followed by treatment and disposition. The priorities are to define the physical sequelae of the act, risk of further DSH behaviour, psychiatric diagnoses and acute psychosocial stressors. These aspects are those that can then be targeted for short-term interventions. However, assessment tools and scales designed to give an overall indication of the magnitude of risk (low, medium or high) are not clinically helpful in identifying patients at imminent risk of suicide, as the predictability of completion of suicide is bedevilled by the low prevalence of suicide with

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false positives in the 'high-risk' groups. Moreover, most of those who go on to completion of suicide will be categorized as 'low risk', as this group is far greater in number than the high-risk group.

Triage

In a patient who has attempted DSH, initial management involves resuscitation, treatment of immediate life threats and preventing complications. The patient should be triaged according to the physical problem as well as current suicidality, agitation, aggression and mental state. The mental health triage scale can be used for this purpose. A triage score of 2 or 3 should be applied if patients are violent, actively suicidal, psychotic, distressed or at risk of leaving before full assessment can occur. Constant observation is required at this point and nursing staff, security or police may be needed. In Australia, a number of different triage scales can be used. There is some evidence that a mental health triage scale improves outcomes; however, the accuracy of the assessment can be limited by a number of environmental, staff and patient factors.

Medical assessment

The patient's safety in the ED should be optimized by limiting the availability of drugs, removing sharp implements, removing car keys, ropes, belts or sheets, and securing nearby windows. Other concurrent and concealed methods of self-harm should be sought. This may be facilitated by changing into hospital gowns, whereby the patient is more easily identified if they abscond. In addition, other means to increase visibility, such as security cameras, high-visibility cubicles or assigning a special nurse, should be considered. Assessment of the patient may be difficult, either due to a general medical cause or being unsettled from the precipitant of the act, or from not wanting to be in hospital or allow medical intervention. This may necessitate the therapeutic utilization of anxiolytic medication; the use of physical restraint may be considered if at high risk or unable to be fully assessed and wanting to self-discharge. This may be done under a duty of care to the patient or the local mental health act may be utilized in extreme situations. Emotional support of the patient, friends and relatives is required during and after this phase, with clear explanation of the rationale and the procedures. Distinguishing medical from psychiatric causes of mental disorder presentations is discussed elsewhere in this book (see [Chapter 20.2](#)).

Suicide risk assessment

Initially, an assessment needs to be done in the ED to determine patient disposition, but a more comprehensive psychiatric assessment may need to wait until substance or anxiolytic medication effects wear off. Collateral sources

of information need to be accessed since patient history can be unreliable or incomplete. Friends, family, local doctor, ambulance officers, helping agencies already involved and previous presentations documented in the medical record can all add useful information in order to advise an assessment. A therapeutic relationship should be formed and the clinician should be non-judgemental, non-threatening and clearly willing to help. A positive attitude has been shown to improve outcomes with this group of patients. It is the responsibility of the clinician to establish rapport with the patient, and all patients benefit from feeling that they have been listened to and understood.

People presenting in crisis are hypersensitive to any negative transference. This may intensify the patient's already low self-esteem, increasing future self-harm potential and making a therapeutic relationship difficult to establish. When managing a patient who may be expressing self-harm ideation, the ideation should be discussed openly. Expressions of self-harm carry individual meaning for each person. It is important, in a therapeutic relationship, to explore the meaning that this carries for the person, and alternatives.

Risk factors may be divided into two main categories: static and dynamic. Static factors have been historically identified by Durkheim who showed that some less socially integrated groups within society were at greater risk of suicide than others. These static factors are enduring and in the context of a person's developmental history and social circumstances. Hence, being male, unemployed, single, socially isolated, poorly educated, from a lower socioeconomic group, with a history of mental disturbance and substance-use disorders would all place someone in a higher risk group.

Dynamic factors are the more fluid day-to-day factors that intensify the risk posed by the static factors. Flewett divides these factors into internal and external factors. The internal factors include current feelings of abandonment, desperation, hopelessness, co-morbid depression, current drug use or physical illness. External factors are those of increased social dislocation, including homelessness, bereavement, intoxication, and an adverse life event, such as the recent loss of a job or relationship.

The role of dynamic risk is highlighted by Rosenman when he states: 'for conditions with multiple risk factors... each factor adds a little to the risk, but only when it interacts with other factors. No single predictor or combination of predictors is present in every individual, and membership of the high-risk group changes from moment to moment. Half a bottle of whiskey may create a high suicide risk within an hour'.

Assessment of suicide risk involves assessing background demographic, psychiatric,

medical and social factors; these are the static factors that underlie any presentation and will determine the chronic suicidal risk that the person presents. Dynamic risk factors as well as the current circumstances and risk of suicidal behaviour itself are outlined in [Table 20.3.1](#). There are epidemiological differences between people who self-harm and those who complete suicide. Although the groups are different, there is an important overlap. The more an individual's characteristics resemble the profile of a suicide completer, the higher the risk of future suicide or suicide behaviours. Despite this, in long-term follow-up studies very few of these factors have been shown to be good independent predictors of suicide following DSH. The most consistent factors are psychiatric illness, personality disorder, substance abuse, multiple previous attempts and current suicidal ideation and hopelessness.

Moreover, contemporary risk assessment is focussed on prevention rather than prediction-oriented assessment and the centrality of engagement with the patient and their individual predicament and concerns. It is important to engage the patient in identifying strengths, and supports as part of the interview. In many situations the precipitating stressors are relieved with intervention or time.

Use of scales

Many screening tools have been devised to identify high-risk groups within those presenting with DSH. PATHOS, the Suicidal Intent Scale, the Sad Persons Scale and other scoring systems have been devised to complement medical assessment of suicide risk. However, many of these scales use outdated risk factors and patient populations unrepresentative of EDs. Scales need to be sensitive, but this misclassifies a large number of individuals as potentially at risk of suicide. These deficiencies need to be considered when applying suicide risk scales in the ED and these scales should not be used as an absolute assessment of suicide risk or of the need for psychiatric admission. In addition to validated questionnaire assessment, there are a number of validated interview assessment tools, such as the Suicide Attempt Self-Injury Interview. Problems that clinicians report in using these tools is that of the time taken to administer them. In any event, these tools have been shown to be as accurate as a mental health clinician's global assessment, although they predominantly utilize demographic risk factors replete in the general population and without a sound evidence base.

The problems associated with suicide-risk assessment are summarized in [Box 20.3.1](#).

An example of useful questions that can be used in assessment are given in [Box 20.3.2](#).

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Table 20.3.1 Factors associated with suicide

Variable	High risk	Low risk
Static factors		
Gender	Male	Female
Marital status	Separated, divorced, widowed	Married
Employment	Unemployed or retired	Employed
Medical factors	Chronic illness, chronic pain, epilepsy	Good health
Psychiatric factors	Depression, bipolar, schizophrenia, panic disorder, previous psychiatric inpatient, substance abuse	No psychiatric history
Social background	Unresponsive family, socially isolated or chaotic, indigenous background, refugee from conflict areas, past history of trauma, developmental trauma	Supportive family, socially stable and integrated
Dynamic factors		
Suicidal ideation	Transient, intense suicidal ideation, plan and intent, intoxication and impulsivity with impaired judgement	Infrequent, transient
Attempts	Multiple	First attempt
Lethality	Violent, lethal and available method	Low lethality, poor availability
Planning	Planned, active preparation, extensive premeditation	No realistic plan, telling others prior to act
Rescue	Act performed in isolation, event timed to avoid intervention, precautions taken to avoid discovery	Rescue inevitable, obtained help afterwards
Final acts	Wills, insurance, giving away property	
Coping skills	Unwilling to seek help, feels unable to cope with present difficulties	Can easily turn to others for help, can plan to overcome present difficulties, willing to become involved in aftercare
Current ideation	Admitting act was intended to cause death, no remorse, continued wish to die, hopelessness or helplessness	Primary wish to change, pleased to recover, suicidal ideation resolved by act, optimism
Precipitant	Similar circumstances can recur, acute precipitant not resolved	Stressful but transient life event, acute precipitant addressed

(Reproduced with permission from Salter A, Pielage P. Emergency departments have a role in the prevention of suicide. *Emerg Med.* 2000;12:198–203).

Definitive treatment and disposition

Following necessary medical treatment and suicide-risk stratification, disposition may involve compulsory or voluntary admission to a psychiatric or medical ward, short-term observation or discharge with appropriate follow-up. Restraint and compulsory admission may be necessary for the high-risk patient who wishes to self-discharge. Approximately 30% of DSH patients are admitted for psychiatric inpatient care, but the factors involved in the decision for psychiatric hospitalization following DSH involve a complex evaluation of risk, potential for treatment and social supports.

Patients who are intoxicated with alcohol can be both behaviourally disinhibited and emotionally labile and, as discussed, are at higher risk of

intentional self-harm. Short-term observation allows intoxication to resolve so that more comprehensive and longitudinal psychiatric assessment can take place. A short-term stay in hospital can also help to resolve many acute areas of conflict and make psychiatric evaluation more accurate. ED short-stay wards or psychiatric assessment and planning units are appropriate for these admissions, especially if a multidisciplinary team is available to review the patient and to initiate management and follow-up.

Important elements of management involve addressing the modifiable elements of the precipitating problem, treating psychiatric illness and environmental interventions, such as family counselling, encouraging a support network and developing coping and problem-solving skills. Adaptive solutions to the current crisis should be reinforced utilizing short-term

Box 20.3.1 Problems in assessing suicide risk

Suicide is rare, even in high-risk groups, so it cannot be predicted without a high rate of false-negative or false-positive errors.

Suicidality presents in heterogeneous ways that may not be recognized.

Suicidality is transient and affected by intoxication, stress and being in hospital.

The patient may be reluctant, oppositional or manipulative.

The patient may present in an atypical fashion, especially the elderly with physical complaints.

Suicide risk factors identify high-risk subgroups but not individuals.

The demographic factors associated with suicide have changed recently, thus changing the make-up of risk groups.

Risk factors are based on studies of long-term follow up and, therefore, long-term risk.

Subtle changes in mental status and behaviour may be missed if not assessed by the usual doctor.

Unexplained improvement in psychological status may be the result of increased motivation to die.

Patients may deny their true intentions due to embarrassment, fear of being stopped in carrying out their own wishes, fear of being institutionalized or fear of the confidentiality of the interview.

Patients may say life is not worth living or that they feel they would be better off dead, but not necessarily have an increased risk of suicide unless they have made suicidal plans or attempts, or if they have pervasive hopelessness.

Correlation between medical danger and suicidal intent is low unless the patient can accurately assess the probable outcome of their attempts if treatment has not been received.

Box 20.3.2 Useful questions

I have seen some paperwork, but I wonder if you could let me know what happened?

While you were taking the tablets, what was going through your mind?

Did you think you had any other options?

What did you think was going to happen?

How long have you been thinking about this?

If you could change a couple of things in your life, what would they be?

How are you feeling now?

What has changed that means you are no longer feeling suicidal?

How are you coping in the emergency department?

Who is important to you? Do they know what has happened?

Are you thinking you need to be in hospital?

If you went home now do you think you'd be OK?

Do you have any plans as to how to address the issues that led you to feel suicidal?

How can we help?

(From Ryan C, Large M, Gribble R, et al. Assessing and managing suicidal patients in the emergency department. *Aust Psychiatr.* 2015;23(5):513–516, with permission.)

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solutions. Factors that should be addressed while patients are in hospital include referral to services to help address the dynamic risk issues, such as problems with relationships, employment, finances, housing, legal problems, social isolation, bereavement, alcohol and drug abuse, and dependence. In this regard, social workers or mental health nurses are invaluable. For greatest effect, these should be available after hours and on weekends since the majority of DSH presentations are after hours. For repeat attenders who are often socially isolated, hospitalization should not be a substitute for social services, substance-abuse treatment and legal assistance, although admission may be necessary while appropriate supports are put in place.

Dispositional decisions need to be taken, weighing up the relative and potential iatrogenic harm generated by hospitalization and the now common legal mandate for treatment in a least restrictive environment. Discharge will be with referral to community agencies with responsibility for supporting the person in the community and, according to risk assessment, may include community mental health teams, general practitioners (GPs), non-government support agencies, etc. The aim of disposition is to minimize risk factors while empowering the person to develop more positive and capable coping styles for future crises, and for timely follow-up following discharge from hospital. The plan should be clear to each patient and includes details such as how they keep their environment safe and potentially disable any plan. Safety plans may also include identifying the warning signs for the patient, internal coping strategies or social strategies to help distract them. This is in addition to contact details for professionals and agencies available in a crisis.

A number of brief contact interventions, such as postcards and single telephone calls, have been proposed following a patient's discharge from the ED. The common mechanism of action for these is suggested to be enhanced social support and suicide prevention literacy. Currently there appears to be no clear evidence to uniformly employ these for all patients with suicidal behaviour in the ED.

Pharmacotherapy has been shown to be useful in addressing the debilitating symptoms of a major depressive disorder and, along with psychotherapy, can help the person regain their previous level of functioning. Once risk and disposition have been addressed, the pharmacotherapeutic management and ongoing assessment can be by the local medical officer, who can refer as necessary to mental health specialists. Pharmacotherapy involves the treatment of the underlying psychiatric disorder. Overall, antidepressants decrease the risk of attempting suicide, although the lethality of suicide attempts is increased if tricyclic antidepressants are

taken in overdose. Selective serotonin reuptake inhibitors and other newer classes of antidepressants (including Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs), Noradrenergic and Specific Serotonergic Antidepressant (NaSSa), Norepinephrine Reuptake Inhibitor (NRI) etc.) may have a more selective effect in decreasing suicidal behaviour and are less toxic in overdose than tricyclic antidepressants—the latter are no longer prescribed as first-line antidepressant medications by psychiatrists. These factors make the newer class of drugs an attractive choice for depressed patients who are suicidal. An increase in aggression in young patients initiating fluoxetine had been associated with a transient increase of suicidal behaviour. However, there is ongoing controversy surrounding the risks of different types of antidepressants.

Prevention

Comprehensive strategies for the prevention of suicide have been or are being developed in Finland, Norway, Sweden, Australia and New Zealand. Suicide prevention focuses on psychiatric, social and medical aspects, and usually involves public education, media restrictions on reporting of suicide, and school-based programmes with teacher education. Other prevention methods include the training of doctors in the detection and treatment of depression and other psychiatric disorders, alcohol and drug abuse information, enhanced access to the mental health system and supportive counselling after episodes of DSH. Decreasing the availability of lethal methods may involve legislative changes, such as more stringent gun control, restricting access to well-known jumping sites, or changes to the availability or packaging of tablets. Overall, studies into the effectiveness of suicide-prevention strategies have shown inconsistent reductions in suicide rates following interventions. Approaches to reduce DSH repetition have also shown disappointing results. Improved recognition and treatment of mental illness, improved social services and drug and alcohol-support services may be of greater benefit than specific suicide-prevention strategies.

Ethical and governance considerations

In assessing and managing patients with DSH and suicidality, the patient's desire for autonomy and self-determination (e.g. declining recommended or reasonable treatment options, follow-up or support) must be considered in terms of their mental state, the static and imminent dynamic risk factors, the protective factors and the available support (e.g. social, family, carer, accommodation, financial, etc.) These considerations

must also be balanced with the patient's capacity to provide informed consent and their human rights and dignity, against that of the paternalism of clinicians initiating immediate treatment or restricting immediate care to the ED or other inpatient setting (e.g. psychiatric inpatient unit).

Often, in circumstances of imminent risk to self, the patient's requests or demands for confidentiality may not be absolute, in so far as it is often necessary to obtain collateral history from others (e.g. GPs, psychiatrists, family, carers, etc.) and communicate with others about the immediate assessment and management of risk. Other aspects of confidentiality include local governance around accessing electronic mental health databases or clinical records that record service contact data about patients.

The disposition of ED patients who have presented with DSH or a suicide attempt must also be considered through the prism of the health service's key performance indices. For example, such key performance indices may cover response times for triage and target times for disposition from the department. Accordingly, the patient's disposition must also be considered in terms of balancing non-maleficence with utilitarianism (the 'greater goods' of accessibility, responsiveness and quality of healthcare for a community). Adapting services to most effectively assess and support these patients is an ongoing challenge for ED and requires ongoing evidence review.

The framework of care in which the above issues and dilemmas are considered is also informed by relevant local mental health, medical treatment and human rights legislation. ED clinicians should familiarize themselves with the relevant local legislation and the processes of invigilation. Health services require written policies with regard to care of suicidal patients in the ED, which cover clinical pathways with evidence-based content and the support of clinical action, including constant observation, scope of searches by staff and bodily restraint.

Conclusion

Assessment of suicide risk is an important skill in emergency medicine, since many patients present to EDs with suicidal thinking or behaviour. Although the risk of suicide for an individual patient is difficult to predict, emergency physicians can provide a system for assessment and identification of risk groups. Acute interventions can attempt to prevent short-term completion of suicide or repetition of DSH, since emergency physicians are predominantly involved in the care of these patients, often using short-stay wards. It is during this period in the ED that linkage to ongoing support services can be affected. A team approach involving psychiatry and social work is necessary

20.4 DEPRESSION

in most cases, with many problems resolved by a short-term hospital admission, brief crisis intervention and intensive short-term follow up.

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20.4 Depression

Evan Symons

ESSENTIALS

- 1 Clinical depression is common, affecting 2% to 5% of the population at any time.**
- 2 Depressive symptoms can be accurately assessed through a systematic interview and mental state examination.**
- 3 The diagnosis of depressive syndrome depends on the severity, pervasiveness and persistence of the symptoms.**
- 4 Commonly comorbid conditions need to be identified, including anxiety and addictive disorders.**
- 5 In the majority of cases, depressive illness can be treated appropriately in a primary health care setting. The need for specialist input and/or hospital admission reflects increasing severity and risk.**

Introduction

The need to determine the presence and severity of a depressive syndrome is a very frequent task in the emergency department (ED). Assessment of depression is necessary in relation to a variety of patient presentations. The classic ED situation is the overdose or other attempted suicide or self-harm, where the assessment of depression forms part of further evaluation after the patient has been medically stabilized.

It is also becoming more common for patients to present to the ED complaining of depression (often on the advice of family, friends or crisis help lines) without having harmed themselves. Patients with a variety of medical conditions, especially conditions that are chronic or disabling, also often develop a depressive syndrome that can form a major part of the reason behind an ED attendance. Some patients who present to EDs with personal crisis or self-harm

may have been identified as suffering from a personality disorder. They are at high risk of co-morbid depression. The evaluation of depressive symptoms is also an important aspect of the assessment of patients seen in the ED with alcohol and drug abuse problems.

In these assessments, it is very important to have a clear concept of the syndrome of 'clinical depression'. This syndrome is called 'Depressive Episode' in the *International Classification of Disease*—10th edition (ICD-10) and 'Major Depression' in the *Diagnostic and Statistical Manual of Mental Disorders*—5th edition (DSM-5).² The importance of diagnosing a depressive episode lies principally in determining the presence of a clinical syndrome, which is in need of treatment, is likely to respond to treatment and is likely to persist without treatment. The clear delineation of a depressive episode is also an essential basis for differential diagnosis from other medical and psychiatric conditions and for distinguishing

between the clinical syndrome of depression and the day-to-day fluctuations of mood and states of dejection, pessimism, frustration and disappointment, which are the lot of all human beings.

The diagnosis of a depressive episode depends on the pervasive presence of enduring mood change, marked loss of interest in usual activities or marked loss of energy and drive, as well as a number of other associated symptoms. The list of symptoms contributing to the depressive episode syndrome in ICD-10 is shown in Box 20.4.1. The DSM-5 syndrome of major depression has the same list of symptoms, with the exception of 'loss of confidence or self-esteem'. An adequate number of these symptoms must be present for at least 2 weeks before the diagnosis of depressive episode can

Box 20.4.1 Symptoms contributing to the diagnosis of a depressive episode in ICD-10

1. Depressed mood, most of the day, nearly every day, largely uninfluenced by circumstances
2. Markedly diminished interest or pleasure in all, or almost all, activities, most of the day, nearly all day
3. Loss of energy or fatigue, nearly every day
4. Loss of confidence or self-esteem
5. Unreasonable feelings of self-reproach, or excessive or inappropriate guilt, nearly every day
6. Recurrent thoughts of death or suicide or any suicidal behaviour
7. Diminished ability to think or concentrate, or indecisiveness, nearly every day
8. Psychomotor agitation or retardation, nearly every day
9. Insomnia or hypersomnia, nearly every day
10. Change in appetite (decrease or increase with corresponding weight change)

(From World Health Organization. *The ICD-10 Classification of Mental and Behavioural Disorders*. Geneva: WHO; 1993.)

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be made. The pervasiveness of the symptoms is defined principally by the specifications that they must be present 'most of the day' and for 'nearly every day'.

ICD-10 further classifies depressive episodes into mild, moderate and severe, according to the total number of symptoms present (mild = 4/10 symptoms, moderate = 6/10 symptoms and severe = 8/10 symptoms). However, it is important to note that, even in mild or moderate depression, the patient must have at least two of the first three symptoms; that is, the patient must have two of depressed mood, loss of interest or loss of energy, most of the day, nearly every day, for at least 2 weeks. The diagnosis of severe depressive episode requires the presence of all three of the first three symptoms.

The diagnosis of a depressive episode does not in any way depend on the presence or absence of a precipitating life event or situation. The ICD-10 also has a category of brief depressive reaction (one of the 'adjustment disorders'), which forms part of the differential diagnosis of a depressive episode. This syndrome is defined by the presence of a precipitating life event and depressive symptoms. However, if the depressive symptoms are of sufficient number, pervasiveness and duration to qualify for the description of a depressive episode, then this diagnosis should be made regardless of the presence of a precipitant. The notion that 'this patient's depression is understandable given the circumstances' should never detract from a proper evaluation of the severity and duration of the symptoms.

Epidemiology

Clinical depression, defined as 'Major Depression' or an ICD-10 'Depressive Episode', is a very common condition. Extensive epidemiological community surveys in many populations around the world have established that the 6-month prevalence rate of major depression is in the range of 2% to 5% in any population.³ The epidemiological research has also shown that only a minority of persons with current depressive syndromes are receiving active treatment.³

The age onset of the first depressive episode is typically in the third decade, but can be at any age. The male to female ratio is 1:2. A person who has had one episode of clinical depression has an 80% chance of recurrence, and patients with recurrent depression have an average of four episodes in their lifetime.⁴

Incomplete recovery is common. Studies of hospitalized patients have shown that, while at least 50% of patients recover from an index episode within 6 months, 30% remain symptomatic for more than 1 year and 12% for more than 5 years.⁵

There is some evidence for an increase in the prevalence of Major Depression and a younger age of onset, over the last 40 years.⁶

Aetiology

The aetiology of depression is complex, involving both genetic and environmental factors. Important environmental factors include childhood experiences of adversity or neglect and stresses in adult life. The effect of genetic factors may be mediated, in part, through inherited predispositions to excessive worry and anxiety.³

Precipitating life events, especially those involving loss, are known to play a part in triggering individual episodes of depression.⁷ This effect is greatest for the first episode of depression. Second and subsequent episodes are more likely to occur without identifiable precipitating events,⁸ suggesting that the first episode has a neurobiological priming effect.⁹

Neurobiological changes in depression are also complex. Based, in part, on the supposed mechanism of action of antidepressant medication, early work focused on evidence of depletion of amine neurotransmitters in the central nervous system.¹⁰ More recent research has suggested depression may involve alterations in neural cell populations, especially in the hippocampus.¹¹

Prevention

Depression is a major public health problem. The World Health Organization has recently estimated that 322 million people are living with depression worldwide. Depression is responsible for 7.5% of all years lived with disability, making it the 'single largest contributor to non-fatal health loss' globally.¹² Public health measures have included campaigns to raise awareness of depression both in the general public and in health care providers. ED staff can play a very significant role in case identification and in ensuring referral for effective treatment.

Clinical features

The syndrome described as a 'Depressive Episode' (or 'Major Depression') is defined principally by its symptoms and, to a lesser extent, signs. As the severity of the depressive episode is also dependent on specific characteristics of the individual symptoms and signs (as well as the total number of symptoms), it is also important to understand the varieties of their manifestations.

Symptoms

It is useful to start the history with an exploration of the problem that has brought the person to the ED. This problem may be an overdose or other attempted suicide or self-harm, a personal

or relationship crisis, a period of alcohol or other drug abuse, an exacerbation of a chronic medical condition or chronic pain or some other complaint. It is also important during the clinical assessment to begin to form some picture of who the patient is, including whether he or she lives alone or with others, the nature and quality of his or her personal relationships and his or her daily occupation, interests and activities. These inquiries not only assist in building rapport through demonstrating an interest in the patient, but also elicit information that is necessary for understanding the patient's symptoms in context.

At some point, the patient can be told that the interviewer would now like to explore the symptoms of depression in more detail. It may be helpful to group the symptoms of the depressive episode (see Box 20.4.1) into various domains of the patient's experience. The first group ('depressed mood', 'markedly diminished interest' and 'loss of energy') refers to the pervasive mood state and the quality of the patient's spirits or enthusiasm for life. The second group ('loss of self-esteem', 'unreasonable self-reproach or guilt' and 'recurrent thoughts of death or suicide') refers to the cognitive contents of the patient's thoughts. The third group ('diminished concentration' and 'psychomotor agitation or retardation') refers to the degree of agitation or lethargy associated with the patient's thought processes and physical activity. The final group ('insomnia or hypersomnia' and 'change in appetite') refers to physiological changes.

Both the pervasiveness and duration of these symptoms should be assessed. The syndrome is, by definition, one in which the symptoms have become persistent and inescapable, not the occasional or sporadic experience of these symptoms that nearly everybody endures sometimes. Duration is important because the syndrome must be present for at least 2 weeks before the diagnosis can be made, although often the patient may have been unwell much longer than this.

The timing of onset of a depressive episode can be difficult to establish because the onset is often very gradual and insidious (although it can be relatively rapid). The patient may have experienced previous episodes, which become confused with the present one, and patients often confuse long-term feelings of low self-esteem with the current episode. Hence, the question 'How long have you been feeling like this?' is often unproductive. It is more useful to ask the patient to describe the presence and pervasiveness of each of the symptoms 'during the last 2 or 3 weeks or so' and, in particular, to try to identify some recent time at which there has been a change in the clinical state or function of the patient.

The pervasiveness and duration criteria taken together imply a diminished ability to carry out normal activities and to meet responsibilities. Although many depressed patients push themselves to keep going, careful enquiry reveals that this has become more arduous. Difficulty in attending to tasks may range from diminished effectiveness at work, child care or study to, eventually, neglect of self-care and nutrition. Thus impairment in function is another indicator of the severity of the episode.

'Depressed mood, most of the day, nearly every day' is perhaps the most difficult of the symptoms to characterize. 'Mood' refers to a person's underlying emotional state, the emotional baseline that permeates each day. It is useful to ask not only 'Do you feel depressed?' but also 'What is that like for you?' Some patients describe feeling much more unhappy than usual or sad all the time or unexpectedly tearful; others report feeling more irritable with others or more inclined to worry. The severity of the mood change may be shown in a loss of mood reactivity, which can be elicited by asking 'Can you cheer yourself up, take your mind off your worries?' and 'Do you find that the things that normally make you happy don't seem to cheer you up as much as usual?'

'Markedly diminished interest or pleasure in all, or almost all, activities, most of the day, nearly every day' is somewhat easier to assess, especially if the interviewer takes the time to build up a picture of the patient's usual day. With careful inquiry, a nuanced picture can be built up of the extent of the patient's withdrawal from his or her usual activities. Included within this criterion is a lack of pleasure or interest in sexual activity.

'Loss of energy or fatigue, nearly every day' is an important symptom, which is sometimes overlooked. The emphasis should be on the loss of energy; that is, whether the patient is aware of having much less energy or drive than usual. In severe cases, the patient may describe feeling the body is heavy or thoughts are sluggish, at which point this symptom overlaps with 'psychomotor retardation'. Loss of energy is an important symptom in differential diagnosis, which may point to such conditions as anaemia, hypothyroidism, diabetes or other undiagnosed medical conditions.

The cognitive symptoms of depression ('loss of self-esteem', 'unreasonable self-reproach or guilt' and 'recurrent thoughts of death or suicide') can to some extent be observed in listening to the patient's spontaneous comments and, as such, form a part of the mental state examination. However, patients who are more introspective have some awareness of a change in thought processes and are able to describe the ways in which their thoughts have become more gloomy than usual. This insight is lost when depression

becomes more severe and the patient tends to regard the self-reproach or thoughts of suicide as entirely justified.

In assessing 'loss of confidence or self-esteem', the emphasis should be on the loss or change in the person's self-concept. It can be helpful to approach the issue with suggestive questions, such as 'Tell me about a time when you felt better about yourself', 'Did you used to feel more confident at work?' or 'Was there a time when you felt more adequate as a parent?'

'Unreasonable feelings of self-reproach or excessive or inappropriate guilt, nearly every day' is probably one of the most consistently reliable symptoms pointing to a diagnosis of depressive episode. Sometimes, a very conscientious person may habitually find fault with him- or herself without being clinically depressed. However, a person who is not depressed will usually be able to consider other points of view, to debate the sense of culpability internally and to consider whether the sense of guilt may be 'excessive', 'inappropriate' or 'unreasonable'. This capacity to rationalize about thought processes becomes progressively more impaired as the patient becomes more severely depressed, until the patient's guilt appears unquestionable.

In psychotic forms of depression, the sense of guilt may take on bizarre dimensions in which the patient can feel responsible for all the evil in the world or for distant events. A not uncommon experience is for the patient to see a report on the television of a calamity, such as an earthquake, and to feel responsible for the event.

'Recurrent thoughts of death or suicide' can arise in a depressive episode in a variety of ways. Not uncommonly, the thoughts may simply come into the patient's mind; the patient reports having thoughts of being dead, wanting to be dead or thoughts of suicide that are uncharacteristic, unbidden and unwanted, without any intention to act on these thoughts. Sometimes the suicidal thoughts are directly linked to excessive or delusional guilt, in which the patient feels his or her death to be necessary and inevitable; here the risk of suicidal action is very high.

In other cases, the suicidal thoughts are a logical consequence of a sense of hopelessness, a lack of faith in the future. This last type of suicidal ideation is less specific for the diagnosis of depressive episode, as it may also reflect an apparently realistic appraisal of life circumstances, an attitude of philosophical pessimism or poor coping skills in a person with impaired personality function. These distinctions are important because the suicidal ideation, which is a part of a depressive episode, may be expected to resolve with treatment of the depression, whereas the other forms may not.

'Diminished ability to think or concentrate or indecisiveness, nearly every day' is a relatively

straightforward symptom to assess and is useful as an indicator of the severity of the depressive episode. It can be assessed by asking about ability to focus on work or a recreational activity, such as watching television or reading a book. Some patients report that their mind is easily distracted or restlessly inattentive. Many report the intrusion of negative ruminations (concerning lack of worth, sense of failure or guilt, thoughts of suicide or other worries), which go round and round in their minds. Progressive impairment in the capacity to concentrate will demonstrate increasing severity of depression; a severely depressed patient may not even be able to focus on one newspaper story and take in the contents.

'Psychomotor agitation or retardation, nearly every day' refers to abnormalities of movement, facial expression, speech and thought processes, which are directly assessed in the mental state examination and are discussed more fully below. However, this can also to some extent be assessed through the history from the family. 'Psychomotor agitation' includes restless, fidgety behaviour, the inability to sit still or attend to a task, and anxious, repetitive speech or even perseveration. 'Psychomotor retardation' includes lack of spontaneous bodily movement, lack of facial expression, lack of verbal communication and slowness of response. Retardation is the more common and the patient or family may report progressive withdrawal and decrease in activity to the point where the patient sits for long hours apparently doing nothing. The presence of significant psychomotor agitation or retardation is usually indicative of a severe depressive episode.

Changes in sleep pattern ('insomnia or hypersomnia, nearly every day') are very common in depression, even in mild episodes. It is worth enquiring in detail about the specific changes in sleep pattern, as these relate to the severity of the depressive episode. Initial insomnia or delay in the onset of sleep is not specifically associated with depression, as it can be strongly associated with anxiety or primary insomnia. Middle insomnia (waking after 2 or 3 hours of sleep) and early morning waking are more specific to depression. The extent of difficulty the patient has in going back to sleep and the mood and thought content when awake during the night are also relevant.

Change in appetite may involve an increase or decrease with corresponding weight change. Severe loss of appetite with marked loss of weight, in the absence of medical illness or deliberate dieting, is associated with severe depression.

Signs

The most important signs are:

- signs of psychomotor agitation or retardation
- the affective state of the patient

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- the thought content
- the degree of insight.

The patient with psychomotor agitation demonstrates, in milder forms, fidgety or repetitive behaviours, such as hand wringing or sighing. This can progress to an inability to sit still and, eventually, continuous pacing. The patient may say little while looking very apprehensive and preoccupied or may impinge all the staff with repetitive, anxious questions, apparently seeking reassurance, which is never achieved. In severe cases, speech becomes perseverative.

By contrast, the psychomotor-retarded patient maintains a relative immobility, lying in bed or sitting in a chair for long periods, with infrequent changes in posture. The face may be relatively expressionless, look sad or show an anxious dread. Both the facial expression and the body language show diminished reactivity during interview. There is little spontaneous speech and, if responses to questions can be elicited, the responses lack richness, depth or elaboration. Slowness of thought processes is shown especially by a marked increase in the time taken to supply an answer to a question. In severe cases, the patient may be mute.

The affective state of the depressed patient during the interview is most often sad, but sometimes anxious or even hostile. As the depression becomes more severe, the patient tends to show a diminished range of affects and has an impaired affective reactivity (e.g. the patient does not smile in response to social cues).

During the interview it is important to observe the themes evident in the patient's spontaneous conversation. Themes of despair, failure, guilt and death are typical of a depressive episode. The degree of insight may be a marker of the severity of the depressive episode.

Variants

Melancholic depression

Some severe depressive episodes can be distinguished, which have severe mood symptoms, marked changes in physiological function and significant psychomotor agitation or retardation.

This form of the depressive syndrome is designated 'Major Depression with Melancholic Features' in DSM-5 and 'Depressive Episode with Somatic Syndrome' in ICD-10. The ICD-10 criteria for the 'somatic syndrome' are shown in **Box 20.4.2**. At least four of the eight symptoms must be present to make the diagnosis. Most 'depressive episodes with somatic syndrome' are also likely to meet the criteria for 'severe depressive episode'.

The clinical significance of making the diagnosis of melancholic depression is that this form of depression is likely to require intensive biological treatment.

Box 20.4.2 ICD-10 criteria for the 'somatic syndrome' (melancholia)

- Marked loss of interest in activities that are normally pleasurable
- Lack of emotional reactions to events or activities that normally produce an emotional response
- Waking in the morning 2 hours or more before the usual time
- Depression worse in the morning
- Objective evidence of marked psychomotor retardation or agitation
- Marked loss of appetite
- Marked loss of libido

(From World Health Organization. *The ICD-10 Classification of Mental and Behavioural Disorders*. Geneva: WHO; 1993.)

Most of the symptoms contributing to the diagnosis of the 'somatic syndrome' are more severe and are more specific forms of the symptoms of a 'depressive episode.' It is not just any sleep disturbance, but marked early morning waking which is important. Similarly, it is not just a change in appetite, but a significant (more than 5% of body weight) loss of weight, which is important. The presence and severity of the psychomotor agitation or retardation is the most important sign, since these phenomena can be objectively and systematically observed and rated.¹³

Psychotic depression

This is discussed in Chapter 20.5. The patient with a psychotic depression will usually meet the criteria for a severe depressive episode, often with the 'somatic syndrome'.

Mild and moderate depressive episodes

In clinical practice, it is usually not difficult to recognize a 'severe' depressive episode.

Greater uncertainty may be associated with making the diagnosis of 'mild' or 'moderate' depressive episode, especially in patients who have a long-term history of poor self-esteem or are temperamentally inclined to worrying, moodiness or irritability. Some research evidence¹⁴ suggests that these temperamental factors can affect the presentation of the depressive syndrome. Thus a person who is a habitual worrier who develops a depressive episode is likely to worry more and perhaps to withdraw from social contact or abuse alcohol or anxiolytic drugs. A person who tends to be moody or irritable is likely to become more so in a depressive episode and may appear demanding, complaining and unreasonable.

Nevertheless, the essential and salient characteristic of even a mild or moderate depressive episode is that the patient has a persistent mood change for at least 2 weeks. The interviewer should focus on the symptoms of depressed mood, loss of interest and loss of energy because

it is the enduring presence of these symptoms, which makes the diagnosis clear. Of the additional symptoms contributing to the diagnosis of depressive episode, probably the most common are difficulty with sleep and diminished ability to think and concentrate.

A patient with persistent depressed mood and impaired concentration almost certainly has some functional impairment. A useful approach to this question is to ask the patient about normal daily activities and then assess the extent to which these activities are disrupted by the symptoms. Can the patient do household chores? Does this require unusual effort? Can the patient go to work? Is the patient functional at work? Are even simple leisure activities like watching television disrupted by the patient's mood state? It is this evidence of change in function that permits the identification of a mild or moderate depressive episode, regardless of pre-existing temperamental vulnerabilities.

Depression in the elderly

The symptoms of depression in older people are generally very similar to those in younger age groups and should be assessed in a similar way.¹⁵ Symptoms, such as loss of energy, insomnia or change in appetite, also may be influenced by co-morbid medical illness, but a persistent mood change or loss of interest should prompt consideration of a depressive episode. Older people may tend to minimize their feelings of depression and, in these cases, a collateral history of loss of interest in usual activities may be found. Not uncommonly older people are seen in the ED following an overdose that may appear medically trivial. These patients should always be carefully assessed for the presence of a depressive syndrome.

'Pseudo-dementia' is a term used to describe patients with a depressive syndrome who present with an apparent change in cognitive function. The patient with depressive pseudo-dementia is likely to have a relatively recent and relatively abrupt change in concentration and memory. In contrast to the patient with dementia, the patient with pseudo-dementia usually shows a great awareness of having memory difficulties and will tend to demonstrate the impairment to the interviewer with considerable anxiety. In addition, the patient with depressive pseudo-dementia manifests other symptoms of a depressive episode.

Differential diagnosis

The differential diagnosis of the depressive syndrome is important because there are several other clinical disorders involving depressed mood or other symptoms of depression, which have a different prognosis and treatment.

Brief depressive reaction

A brief depressive reaction (also called 'Adjustment Disorder with Depressed Mood' in DSM-5) can be diagnosed when a person experiences some depressive symptoms without meeting the full criteria for a depressive episode, following stressful life events. Typically, the person describes a depressed mood which is not persistent; that is, there are good days and bad days and the depressed mood can be relieved by distraction or pleasant activities. Common stressful life events include relationship crises or other interpersonal conflicts.

This is often the diagnosis in patients who are seen in the ED following an overdose, although care should be taken to inquire about symptoms of a depressive episode. Treatment involves brief psychotherapy aimed at helping the person achieve some resolution of the personal crisis. If the hospital has a crisis counselling service, the patient can be referred to that service for brief therapy. Alternatively, the patient can be referred to their general practitioner (GP) or other community counselling service. Social work staff in the ED often have good knowledge of local crisis counselling services.

Grief

The symptoms of acute grief can be mood disturbance, guilt, impaired concentration, sleep and appetite disturbance, impaired function in daily activities and preoccupation with memories of the deceased.¹⁶ There is a considerable overlap with the symptoms of a depressive episode. However, it is customary to respect the feelings of the bereaved and to recognize that it is usually beneficial for the person to be supported through the natural process of grief, preferably by family, friends or other familiar persons, such as the family GP.

However, if the symptoms become more severe or more prolonged (such as beyond 6 months), it is appropriate to consider the diagnosis of a depressive episode. Symptoms suggestive of the development of a depressive episode include persistent and progressive lowering of self-esteem, persistent thoughts of death and suicide, markedly impaired concentration and psychomotor retardation.

Bipolar depression

ICD-10 specifies that in a person who has a history of bipolar disorder, a diagnosis of 'depressive episode' should not be made even if the patient meets the criteria for a depressive episode. Instead, the diagnosis of 'bipolar affective episode, current episode mild, moderate or severe depression' should be made. The distinction is important because of the treatment and prognosis. In particular, antidepressant medication should be used very cautiously in the person with

Box 20.4.3 Signs contributing to the diagnosis of a manic episode in ICD-10

1. Increased activity or physical restlessness
2. Increased talkativeness ('pressure of speech')
3. Flight of ideas or subjective experience of thoughts racing
4. Loss of normal inhibitions, resulting in behaviour that is inappropriate to the circumstances
5. Decreased need for sleep
6. Inflated self-esteem or grandiosity
7. Distractability or constantly changing activity or plans
8. Behaviour that is foolhardy or reckless
9. Marked sexual energy or sexual indiscretions

(From World Health Organization. *The ICD-10 Classification of Mental and Behavioural Disorders*. Geneva: WHO; 1993.)

bipolar disorder because of the risk of provoking a switch to mania.

The symptoms of a bipolar depressive episode are in themselves not consistently different from the symptoms of any other episode of depression. The distinction therefore rests on a previous history of treatment for bipolar disorder or a history of a manic episode that may not have been treated.

A manic episode, as defined in ICD-10,¹ involves an elevated or irritable mood sustained for at least a week and at least three (or at least four if the mood is only irritable) of the signs shown in Box 20.4.3. Mania is discussed in more detail in Chapter 20.5.

The depressed patient seen in ED who is suspected of having a bipolar disorder should usually be referred to a psychiatrist for assessment and treatment. Bipolar disorder is a life-long condition, with a high rate of recurrent episodes, which requires specialized pharmacological and psychological management.

Organic mood disorder

Many medical conditions (Box 20.4.4) are especially associated with a typical depressive syndrome. Because the medical condition is considered likely to have a pathophysiological significance in the development of the depressive syndrome, these conditions are termed 'organic mood disorders'.

Occasionally, the depressive syndrome may be the first presentation of a previously undiagnosed medical illness. Clinical or laboratory evidence of hypothyroidism was found in 5% of patients with a depressive syndrome in one series.¹⁷ Hypercalcaemia due to unsuspected hyperparathyroidism very occasionally presents with depressed mood, lethargy or cognitive change as the presenting symptoms.¹⁸ The first presentation of pancreatic cancer with a depressive syndrome is well recognized.¹⁹ A depressive syndrome may be the first presentation of Huntington disease, before the onset of the movement disorder, and the diagnosis will

Box 20.4.4 Medical conditions associated with depressive syndrome

- Hypothyroidism
- Hypercalcaemia
- Pernicious anaemia
- Pancreatic cancer
- Lung cancer
- Stroke
- Alzheimer dementia
- Vascular dementia
- Parkinson disease
- Huntington disease
- AIDS
- Central nervous system tumour
- Multiple sclerosis
- Neurosyphilis
- Brucellosis

only be suggested by the family history.²⁰ Some patients with HIV infection have been found to present with a mood disorder before manifesting other symptoms of AIDS.²¹ Because many medical conditions associated with depressive symptoms involve central nervous system disease, any neurological signs should prompt investigation for an unsuspected cerebral tumour, for example.

However, more commonly, the depressive syndrome presents in a patient with an already recognized medical illness. In these cases, it is important to evaluate carefully the severity and persistence of the depressive symptoms and not dismiss them as an understandable reaction to the illness. Symptoms, such as loss of energy, sleep disturbance and anorexia, may be difficult to evaluate as they may be related to other pathophysiological change, but the patient with persistent depressed mood, loss of pleasure in activities, marked loss of self-esteem and feelings of guilt or hopelessness is likely to be experiencing a depressive episode. If such a depressive episode is diagnosed and treated, the patient will experience relief of suffering and a greater ability to deal effectively with other medical problems.

Many drugs have been associated with depressive symptoms, often based on only a few case reports.²² Medications with a particularly strong association with depression include interferon, isotretinoin, methyldopa, benzodiazepines, digitalis, β-blockers, oral contraceptives and corticosteroids. A useful approach is to consider drugs that have recently been introduced in relation to the time course of the depressive symptoms.

Mood disorder due to psychoactive substance use

Chronic alcohol misuse is frequently associated with depressed mood, low self-esteem and feelings of guilt and hopelessness. Severe sleep disturbance can also be precipitated by rebound wakefulness as blood alcohol levels

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fall during the night. The person who regularly abuses alcohol is also likely to experience fatigue, impaired concentration, appetite disturbance and loss of sex drive. These symptoms may mimic those due to a depressive episode, such that it is not possible to make a differential diagnosis of a depressive episode while the patient continues to drink, nor is it likely that the depressive symptoms will remit without abstinence. Patients with alcohol-induced mood disorders should be encouraged to attend alcohol detoxification and rehabilitation programmes. There is some evidence that antidepressant medication may help to reduce both depressive symptoms and alcohol consumption.²³

Amphetamine withdrawal is often associated with a markedly depressed mood, which usually improves within a few days if the patient remains abstinent.

The abuse of alcohol and other drugs is sometimes an attempt to self-medicate for a pre-existing depressive syndrome. This history should be especially sought in the patient whose abuse of alcohol or other drugs is of recent onset or follows important life change, such as bereavement or divorce. However, even if a pre-existing depressive syndrome is identified, the patient should be informed that treatment of their substance use problem is an important component of recovery.

Dysthymia

Dysthymia refers to a chronic form of depression in which the patient experiences symptoms, such as lack of enjoyment in life and a gloomy or pessimistic outlook, without meeting the full criteria for a depressive episode. The depressed outlook tends to become interwoven with the personality of the patient, who tends to be sombre, self-critical and lacking in confidence and motivation. Dysthymia often has onset in early adult life and can persist for many years. The disorder has been well characterized²⁴ and found to be relatively common (about 3% of the general population) in epidemiological studies.²⁵

Sometimes, patients with a dysthymic disorder develop further symptoms indicating a superimposed depressive episode, which can be termed a 'double depression'.

Patients with dysthymia may present to EDs as a consequence of suicidal ideation or behaviour. The condition should be regarded as serious because of its chronicity. The patient should be referred to a psychiatrist or mental health service as treatment can be difficult.²⁶

Anxiety

Anxiety disorders include panic disorder (recurrent panic attacks), generalized anxiety disorder (persistent worrying associated with muscular tension and autonomic symptoms),

obsessive-compulsive disorder and phobic disorders, such as agoraphobia or social phobia. Any of the symptoms of each of these anxiety disorders may occur as part of the symptoms of a depressive episode if a person with a pre-morbid anxious temperament becomes depressed. However, primary anxiety disorders are also common. In these cases, the patient gives a history of typical anxiety symptoms usually extending over many months or even years. Many patients with primary anxiety disorder go on to also develop a depressive syndrome.

Because of both the overlap in symptoms and the frequent co-morbidity, it may be difficult to distinguish primary anxiety disorders from primary depressive disorders in the emergency setting. Probably the most important symptoms are persistent depressed mood and suicidal ideation, which may require inpatient treatment. Patients who do not have persistent depressed mood and suicidal ideation, but who have a mixture of other depressive symptoms and anxiety symptoms, can be safely directed to their GP or to an outpatient mental health service for further evaluation.

Personality disorder

The concept of personality disorder refers to enduring patterns of behaviour, including especially interpersonal behaviours, which are well outside the usually sanctioned range of behaviours in a particular culture and which are associated with substantial subjective distress or conflict with others. The diagnosis of personality disorder should only be made if the behaviour patterns are persistent, relatively inflexible and have been present since a young age, often beginning in childhood or adolescence.

Although a variety of specific personality disorders have been described, the two most common forms in the ED are antisocial personality disorder and borderline personality disorder.

Persons with antisocial personality have a long-term history of disregard for social rules, usually resulting in a chequered employment history, broken relationships and often violent or criminal behaviour. As a result of personal crisis precipitated by these behaviours, persons with antisocial personality not infrequently present to ED with acute brief depressive reactions, helplessness and suicidal ideation or behaviour. Assessment should be especially directed at clarifying if a superimposed persistent depressive episode is present and the severity of this episode.

Inpatient psychiatric treatment is problematic because the patient often has difficulty adhering to ward rules and expectations. If the depressive symptoms are not severe and seem to be reactive to recent stressors, it is preferable to try to engage the patient in a realistic discussion of the current

problems and, if possible, make a referral to crisis counselling. However, in some cases, when the depressive symptoms are more severe and the risk of suicidal behaviour is high, it may be necessary to arrange inpatient admission.

The person with borderline personality disorder displays erratic interpersonal behaviour, as well as considerable impulsivity and recklessness. The interpersonal behaviours include a strong tendency to see others in 'all good' or 'all bad' terms, and to react dramatically to perceived rejection or abandonment. Reckless and impulsive behaviours include abrupt breaches in relationships, alcohol and other drug abuse, and self-damaging acts, such as cutting. Persons with borderline personality often describe chronic feelings of emptiness and loneliness, often associated with suicidal ideation. These features are sometimes misdiagnosed as depression when they may actually represent the patient's usual way of feeling rather than a discrete depressive episode. Because borderline personality disorder is a long-term condition, intervention with the patient who presents in the ED in crisis should, if possible, be directed towards facilitating or enhancing the patient's engagement with outpatient treatment services.

As many as 50% of patients with borderline personality may also meet the criteria for a depressive episode at any one time.²⁷ Although a diagnosis of borderline personality may have been made on the basis of the longitudinal history, it is therefore also important to try to assess the severity, persistence and duration of current depressive symptoms. If the patient is already engaged with an outpatient mental health clinician, it is useful to liaise with the therapist regarding recent symptoms and function.

Assessment

The assessment of the patient for depression should cover:

- the current social circumstances of the patient
- recent stressors or precipitating events
- thorough evaluation of the symptoms of the syndrome of clinical depression and their severity
- consideration of previous depressive or manic episodes
- mental state examination
- risk assessment
- consideration of possible medical illness as a cause of symptoms
- detailed evaluation of alcohol and other drug use
- identification of treatment services already available to the patient.

It is generally a good idea to start the interview with some basic social information. Does the

patient live alone? How is he or she occupied or employed? Is there a supportive relationship or other family? This information assists in understanding the context of the symptoms and helps with treatment planning.

Exploration of precipitating events is important partly because these worries are likely to be occupying the mind of the patient, and discussion of these issues helps to build rapport in the interview.

Identification of the presence and severity of the depressive symptoms is the most important part of the assessment. Unfortunately, it is often not done systematically and the 'diagnosis' of depression is made only on the basis of a patient's statement about 'being depressed' and one or two other symptoms, such as sleep and appetite disturbance. Systematic evaluation requires detailed exploration of the symptoms described above. Particular attention should be paid to the persistence, pervasiveness and duration of the symptoms. If this systematic approach is taken it is possible to determine:

- if the syndrome of clinical depression is present or not
- the severity of the syndrome.

The proper diagnosis of a depressive syndrome and the assessment of the severity of the syndrome are of major importance in treatment planning.

There may be insufficient time in an emergency interview to explore fully the previous psychiatric history. However, it is useful to ask if the patient has been depressed before, whether or not any previous episodes were treated and what was the response to previous treatment. It is also important to identify any previous episodes of mania in case the depressive episode may be a presentation of bipolar disorder.

Mental state examination focuses on the signs described above. Persistently sad affect and noticeable psychomotor agitation or retardation are indicators of more severe depression. Similarly, if the patient's conversation is very preoccupied with themes of failure, despair, guilt or death, the depression is likely to be more severe. Inquiry about these matters should be extended to look for delusional beliefs. Useful questions may include 'Do you feel responsible for bad things happening?', 'Do you feel there is something drastically wrong with you?' or 'Do you believe you deserve punishment?' Understanding the patient's level of insight into his or her condition is also important to treatment planning, particularly if involuntary treatment should become necessary due to the risk of suicide.

Risk assessment is multifaceted. If the patient has attempted suicide through overdose or other means, inquiry should be made about the circumstances of this attempt, the patient's understanding of the lethality of the attempt

and whether or not the patient sought help afterwards or made an effort to conceal the attempt. The patient's current thoughts about suicide and his or her attitude to suicide are also relevant. Many patients admit to having thoughts of suicide but indicate that they would be deterred from suicidal action by, for example, having responsibility for dependent children. The disappearance of these 'protective factors' from a patient's considerations is an indicator of worsening risk. Patients with psychotic depression may be at higher risk because they lack such 'emotional' constraints on suicidal behaviour. Other factors associated with increased suicide risk include lack of supportive relationships, living alone, being unemployed and current alcohol abuse.

Risks of self-neglect, malnutrition and dehydration also need to be considered.

A primary medical condition causing depressive symptoms is likely to be suggested by other symptoms and signs or be pre-existing. There are no mandatory investigations for the assessment of a depressive episode, although checking haemoglobin and thyroid biochemistry is sensible.

Inquiry should be made about alcohol and other drug-use patterns and, especially, recent changes in pattern use. A person with long-standing alcohol or other drug abuse is likely to have a substance-induced mood disorder and needs to address this as the major focus of treatment. A recent marked increase in alcohol or other drug use may indicate an attempt to self-medicate for a depressive syndrome.

It is always useful to ask the patient if she or he is currently seeing a psychiatrist, psychologist or other mental health therapist or has a good relationship with a trusted GP. These existing health

care professionals can often be the natural starting point in planning treatment interventions.

Treatment

Treatment for a depressive episode involves the prescription of specific antidepressant medication or a specific course of psychotherapy or both.

Medications

Commonly used first-line antidepressant medications are shown in Table 20.4.1. Because none of these medications has been shown consistently to have superior efficacy, the choice of medication is based on the acceptability of the side-effect profile and previous treatment response.

The selective serotonin re-uptake inhibitors (SSRIs) are usually well tolerated and are a good first choice. Some patients experience agitation, nausea or gastrointestinal hyper-motility when they start SSRI medications. These symptoms usually settle in a week or two. The most troublesome long-term side effect of SSRIs is sexual dysfunction (especially delayed ejaculation or anorgasmia). These side effects sometimes require a change of medication. The side effects of serotonin-noradrenaline reuptake inhibitors (SNRIs), such as venlafaxine and duloxetine, are similar to SSRIs, with the addition of excessive sweating and itch at high doses. Abrupt discontinuation of SNRIs is associated with a range of unpleasant symptoms (including headaches, nausea and emotional lability).

Mirtazapine has useful sedating properties and can be very helpful in a patient with marked insomnia or agitation. Because it stimulates appetite, its use is limited in patients with a weight problem. Mirtazapine, reboxetine and moclobemide are useful alternatives for patients

Table 20.4.1 Commonly used antidepressant medications

Drug	Class	Usual daily oral dose range (mg)	Half-life (h)
Fluoxetine	SSRI	20–60	24–144
Citalopram	SSRI	20–40	23–45
Escitalopram	SSRI	10–20	27–32
Fluvoxamine	SSRI	100–300	9–28
Paroxetine	SSRI	10–40	3–65
Sertraline	SSRI	50–200	22–36
Venlafaxine	SNRI	75–225	3–7
Moclobemide	RIMA	450–600	1–3
Mirtazapine	–	30–60	20–40
Reboxetine	–	8–10	12–13
Duloxetine	SNRI	60–120	12

RIMA, Reversible monoamine oxidase inhibitor; SNRI, serotonin and noradrenaline re-uptake inhibitor; SSRI, selective serotonin re-uptake inhibitor.

who experience sexual dysfunction with SSRIs or SNRIs.

Tricyclic antidepressants (e.g. imipramine, amitriptyline and dothiepin) and irreversible monoamine oxidase inhibitors (MAOIs; phenelzine and tranylcypromine) continue to be prescribed for some patients, but they tend not to be first-line drugs. The use of tricyclics has decreased because of side effects (especially anticholinergic) and because of their cardiac toxicity in overdose. Irreversible MAOIs are generally inconvenient to take because of the need for dietary restrictions.

Psychotherapy

The psychotherapies commonly used for depression include supportive psychotherapy, cognitive behavioural therapy (CBT), interpersonal psychotherapy (IPT), acceptance and commitment therapy (ACT) and mindfulness-based cognitive therapy. Most psychiatrists and clinical psychologists have appropriate training and skills to offer one or more of these therapies. Many GPs and other health professionals, such as social workers, nurses and occupational therapists, also have received training in these therapies.

Supportive psychotherapy is the least well defined of the psychotherapeutic treatments. The core of the treatment is a supportive relationship, education about the nature of depression and practical advice.

CBT is a structured psychotherapy, usually involving 10 to 20 sessions. The behavioural techniques include reversing social isolation, scheduling relaxing or pleasurable activities and working with family members to provide incentives for helpful behaviours. The main part of the therapy involves 'cognitive restructuring', a systematic exploration of the patient's unhelpful thought patterns, followed by collaborative work to help the patient substitute more positive responses.²⁸

IPT is also a structured psychotherapy, typically of about 16 sessions. The therapy focuses on helping the patient to make changes in his or her interpersonal relationships, which may be contributing to the depressive syndrome.²⁹

ACT is a mindfulness-based behavioural psychotherapy, which encourages individuals to accept negative experiences that cannot be avoided and to make decisions to establish an authentic and fulfilling life.³⁰

Mindfulness-based cognitive therapy combines the principles of CBT with mindfulness-based stress reduction techniques.³¹

Evidence

All currently available antidepressants have been shown to achieve better symptom reduction than placebo, with no one antidepressant consistently demonstrating superior efficacy.³² In drug trials, up to 40% of patients in the placebo arm have shown improvement, which may include the non-specific effects of supportive interventions as well as spontaneous remissions.³³ As the natural history of depression in a community sample (which includes relatively minor, untreated cases) shows a median episode duration of 12 weeks, spontaneous remission appears to be common.³⁴ Patients with psychotic depression respond better to the combination of an antidepressant and an antipsychotic medication than to an antidepressant medication alone.³⁵

Both CBT and IPT have been shown to be effective in achieving symptom reduction compared to pill placebo control.^{36,37} CBT and IPT have been shown to be as effective as medication for mild-to-moderate depression.³⁷ The treatment of severe depression with psychotherapy alone is supported by some evidence³⁸ but remains controversial.

There are no systematic data regarding supportive psychotherapy (as it is not a standardized treatment) but substantial clinical experience attests to its efficacy.

Mild-to-moderate depressive episodes

As long as the suicide risk is containable, the great majority of these patients can be treated as outpatients. Therefore the most important part of treatment planning in the ED is to identify an appropriate referral pathway. If the patient is already in contact with a mental health professional or has a trusted GP, it is preferable to refer the patient back to these persons and, if possible, make phone contact with that doctor or therapist with advice regarding the emergency presentation. If the patient does not have their own doctor or mental health professional, it is appropriate to refer the patient to an outpatient mental health service.

Patients with mild-to-moderate depressive episodes can improve with either medication

or psychotherapy and can be advised to discuss these treatment options with the follow-up doctor. It is not essential to start the antidepressant medication in the ED; it is probably more appropriate to leave this to the follow-up doctor who can monitor for efficacy and side effects.

Some patients may only have mild-to-moderate symptoms but, nevertheless, be at significant suicidal risk, associated with recent suicidal behaviour and persistent suicidal ideation. The risk is increased if the patient lives alone. Such patients require admission to a psychiatry ward, where the options for medication and psychotherapy can be further explored.

Severe depressive episodes

Most patients with severe depressive episodes will be admitted because of significant suicide risk or substantial functional impairment. The evidence suggests that these patients require treatment with antidepressant medication and are often initially too symptomatic to engage in psychotherapy. Classical indications for electroconvulsive therapy are psychotic depression and severe retarded depression (especially if the patient has inadequate oral intake).

CONTROVERSIES AND FUTURE DIRECTIONS

- Population-based studies indicate that clinical depression is very common, possibly increasing in prevalence and significantly undertreated.
- A major challenge for all health services is to improve the rate of case identification.
- Equally important will be the further development of effective referral pathways to appropriate treatment.

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Full references are available at <http://expertconsult.inkling.com>

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20.5 Psychosis

Evan Symons

ESSENTIALS

- 1** In the age of community mental health treatment, emergency departments have become major sites for the assessment of patients with psychosis.
- 2** An important responsibility of the emergency department clinician is to exclude delirium and 'organic' causes of psychotic symptoms, including intoxication with illicit substances.
- 3** Key risks associated with acute psychosis include self-harm/suicide, aggression, misadventure and homelessness. Disposition decisions, including community referral or hospitalization, depend on the collection of information about treatment history, community supports and risk assessment, as well as assessment of the mental state and the preference of the patient.
- 4** Patients with psychosis and their carers should be involved in treatment planning wherever possible.

Introduction

Psychotic illness is a frequent cause of presentation to the emergency department (ED).^{1,2} It is estimated that in excess of 64,000 people in Australia aged 18 to 64 years have had a psychotic illness and have been in contact with public specialized mental health services each year. This equates to 5 cases per 1000 population or 0.5% of the population. Because these patients are usually severely mentally unwell, they also account for a significant share of the workload of EDs.

The tasks of the ED staff in relation to patients with psychotic illness are complex and varied. Initially, there is usually a need for containment and stabilization of an aroused and frightened patient with impaired reality testing. The patient is often in the hospital unwillingly and frequently following a major crisis in the community or at home. Patient preference should be elicited and considered in treatment and disposition planning wherever possible. There is often a need to manage behavioural disturbance, potentially involving risk of harm to the patient, staff or others, while the patient remains in the ED for significant periods of assessment and for the implementation of disposition plans. It is also important to exclude medical causes for the psychotic symptoms and to consider the presence of co-morbid medical conditions. In determining disposition, consideration must be given to the need for voluntary or involuntary admission or, alternatively, referral to an array of community-based treatment services.

Box 20.5.1 Tasks of the emergency department in relation to the patient with psychosis

1. Stabilization of the aroused or frightened patient
2. Management of behavioural disturbance in the emergency department
3. Exclusion of medical causes for the psychiatric presentation
4. Assessing the presence of co-morbid medical illness
5. Determining the need for voluntary or involuntary admission
6. Arranging referral to community services
7. Liaison with family and other carers

Finally, it is important to involve families and other carers in both the assessment phase and in treatment planning. These tasks are summarized in Box 20.5.1.

Classification

Traditionally, psychotic illnesses were classified into 'functional' (i.e. non-organic) psychoses and 'organic' psychoses. Developments in psychiatric nosology have expanded this classification and the *ICD-10 Classification of Mental and Behavioural Disorders*³ now contains at least 16 different diagnoses, many with several subtypes, which could be used to describe patients with psychotic symptoms.

However, in emergency practice, the differentiation of the specific psychiatric syndrome is

Box 20.5.2 Pragmatic classification of patients with psychotic symptoms

1. Psychotic symptoms due to general medical condition
 - Delirium
 - Dementia
 - Psychosis in clear consciousness without cognitive impairment
 - Psychosis caused by medications
2. Acute and chronic schizophrenia
3. Mania with psychosis
4. Depression with psychosis
5. Intoxication or substance-induced psychosis
6. Psychotic-like reactive states

not always possible. The pragmatic classification shown in Box 20.5.2 is based on:

- excluding medical causes for the psychotic presentation
- considering the role of alcohol and other drugs of abuse
- making a provisional psychiatric diagnosis as a guide to initial management and
- considering the possibility that the symptoms may be related primarily to psychological stress.

A description of each of these categories is given in the section on clinical features.

Epidemiology and prognosis

The two principal 'non-organic' conditions, which involve psychotic presentations are schizophrenia and bipolar disorder (type 1).

The prevalence of schizophrenia is about 1% of the adult population. It is not a rare disorder. The male:female ratio is approximately 1:1. Onset can be at any age, but mostly before the age of 30.⁴ Age of onset is slightly later on average for women than for men.

Schizophrenia is usually a chronic condition, but with a variable course. In the long term, about 20% of cases have a good recovery, 20% have recurrent episodes with good recovery between episodes, 40% have recurrent episodes with incomplete remission and 20% have a severe chronic course.⁵ The 20-year suicide rate may be as high as 14% to 22%.⁵

The prevalence of bipolar I disorder (which, by definition, means that the patient has had at least one manic episode) is about 1.0% of the population. The male:female ratio is 1:1. The onset is often in late adolescence and 95% of cases have onset before the age of 26.⁶

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A patient who has had one episode of mania has about an 80% chance of a recurrence within 5 years. Although there is usually a good recovery between episodes, there is a very high rate of recurrence, with an average of one episode of mania or depression every 2 years, although the frequency of episodes in the individual case varies greatly.⁷ The 22-year suicide rate is 13%.⁷

Aetiology and prevention

The aetiology of schizophrenia and bipolar disorder is not well understood, despite intensive research. Both disorders involve genetic and environmental factors. A person who has one parent with schizophrenia has about a 10% chance of developing the disorder; this is similar for bipolar disorder. There is insufficient knowledge about the aetiology of either disorder to suggest effective strategies for primary prevention.

There is considerable scope for secondary prevention, which is early diagnosis and prompt treatment, especially in relation to recurrent episodes. Strategies include the education of patients and families, the identification of early warning signs of relapse and the use of maintenance and prophylactic medication.⁸ ED staff can make a major contribution to this preventative work by emphasizing the importance of continuing treatment and facilitating engagement with generalist and specialist mental health services.

Clinical features

Psychotic symptoms due to a general medical condition

Delirium

Delirious patients often manifest psychotic symptoms. Visual illusions (misperception of real objects, such as mistaking an innocuous object for a malevolent figure or animal) and delusions of persecution (e.g. the patient believing he is being poisoned by the doctors and nurses) are particularly common. Other symptoms include auditory hallucinations, affective lability, apparent formal thought disorder and grandiose or religious delusions.

Delirium should always be considered in older patients and those who present with abrupt onset of psychotic symptoms. The pathognomonic features of delirium are disorientation (especially for time and place) and a fluctuating conscious state. Not uncommonly, the patient plucks at the air or the bedclothes in apparent response to visual illusions or hallucinations. The abnormalities of mental state can fluctuate widely over the course of a day from relative lucidity to marked disturbance.

The delirious patient usually has a history or symptoms of a medical disorder and manifests

abnormalities of vital signs or other abnormalities on physical examination or laboratory investigation. However, the absence of abnormal investigation results does not exclude a diagnosis of delirium.

The differentiation of medical and psychiatric causes of altered mental state is discussed in detail in Chapter 20.2.

Dementia

Psychotic symptoms in dementia can include auditory and visual hallucinations, delusions (often persecutory) and delusional misidentification (e.g. the delusion that a person closely related to the patient has been replaced by a double). These psychotic symptoms are common in dementias of all types, including Alzheimer disease and vascular dementias. A mean prevalence of 44% has been found across several cross-sectional samples.⁹ The diagnosis of dementia depends on the presence of multiple cognitive deficits and will usually be evident from other features of the history and presentation. A change in the mental state of a patient with dementia should prompt consideration of superimposed delirium.

Psychosis in clear consciousness without cognitive impairment

Occasionally, patients present with psychotic symptoms of organic cause, without features of delirium or dementia. The variety of medical conditions associated with psychotic presentations is shown in Box 20.5.3. Although these disorders are relatively rare as the cause of psychiatric presentation, they should be especially considered in relation to a patient with new-onset psychosis over the age of 40 (i.e. older than the usual age of onset of the much more common schizophrenia and bipolar disorder).

In emergency practice, the psychoses associated with epilepsy are probably those most likely to be associated with uncertainty in management. These psychoses are of two types. Some patients with established epilepsy develop chronic inter-ictal psychosis; that is, a psychosis

Box 20.5.3 Medical causes of psychotic presentations

- Epilepsy
- Hypo- or hyperthyroidism
- Huntington disease
- Wilson disease
- Porphyria
- B12 deficiency
- Cerebral neoplasm
- Stroke
- Viral or autoimmune encephalitis
- Neurosyphilis
- Human Immunodeficiency Virus (HIV)-associated neurocognitive disorders

without specific temporal relationship to seizure activity. The clinical picture is often like schizophrenia and the disorder should be treated in its own right with antipsychotic medication.¹⁰ The second presentation is of a post-ictal psychosis, usually following a cluster of seizures and sometimes with a lucid interval of 1 or 2 days. The patient can present with both schizophrenia-like and mood symptoms. The mental state spontaneously returns to normal within a few days, as in the more common post-ictal delirium.¹¹

Psychoses caused by prescribed medications

A long list of medications, many based on sporadic case reports, can sometimes be associated with psychotic symptoms.¹² The two most common are corticosteroids and dopamine agonists.

Steroid psychosis usually presents a manic-like picture and can show florid psychosis. It is most often associated with doses greater than 40 mg equivalents of prednisolone per day.¹³

Dopamine agonists used in the treatment of Parkinson disease (e.g. levodopa and bromocriptine) are associated with auditory and visual hallucinations, persecutory delusions and hypomania. The psychotic symptoms are dose-related but dose reductions may be associated with severe exacerbation of parkinsonian symptoms.¹⁴

Acute and chronic schizophrenia

The symptoms of schizophrenia include the 'positive' symptoms of acute psychosis and the 'negative' symptoms, such as apathy and social withdrawal.

Positive symptoms involve delusions, hallucinations and formal thought disorder. The content of delusions may include beliefs that the patient is an important person (grandiose), that the patient has special communication with deities or spirits (religious) or that there is something awry with the patient's body or the world (hypochondriacal and nihilistic). The most common delusions are beliefs that other persons or the TV or radio are making special reference to the person (delusions of reference) and beliefs that certain persons or agencies are engaged in conspiracies to harm the patient (delusions of persecution).

Hallucinations are usually auditory but can be in any sensory modality. The specific types of auditory hallucinations first described by Schneider,¹⁵ although not specific to schizophrenia, are strongly supportive of the diagnosis. These include a voice making a running commentary on the patient's actions, two or more voices discussing or arguing about the patient and a voice repeating the patient's thoughts aloud.

Sometimes the most obvious positive symptom of psychosis is formal thought disorder. This usually takes the form of loosening of associations (lack of logical connection between

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statements) and tangential (off the point) replies to questions. The effect of these symptoms is to make it difficult or impossible to take a sequential history. In more severe cases, the language itself becomes incoherent as grammatical conventions are abandoned and invented words ('neologisms') are used. In the emergency setting, the less severe forms of formal thought disorder may also be shown by highly anxious, delirious or intoxicated patients.

The negative symptoms include blunting of affect (lack of emotional response), apathy (loss of volition), poverty of speech (severely diminished verbal communication) and autistic withdrawal from social interaction. These symptoms can be difficult to distinguish in the acute setting from the effects of co-morbid depression or from the bradykinesia caused by antipsychotic medications.

In emergency practice, the three most common types of presentation of schizophrenia are the first psychotic episode, acute psychotic relapse of an established illness and a social crisis in a patient with chronic schizophrenia. It is useful to distinguish these types of presentation because of the management implications.

The patient with a first episode of psychosis is typically a young adult who has been brought to the ED by family or police often following months of concern about deterioration in the patient's mental state or behaviour. Sometimes there will have been an acute episode of bizarre, suicidal or aggressive behaviour. Exclusion of medical causes of psychosis is important in the first episode, especially in the older patient. It may be difficult to be certain whether the syndrome is one of mania (see below) or schizophrenia, but this distinction is not crucial in emergency assessment. More important is the fact that the patient is likely to be frightened and confused, as is the family also. The patient may require involuntary hospitalization.

The acute relapse of an established illness can also involve considerable distress to the patient and family. In these cases, it is useful to look for changes in medication, problems in compliance, changes in the treatment system (e.g. the absence of the treating doctor), alcohol and other drug abuse, and recent stressful events. It may be possible to avoid hospitalization.

Patients with chronic schizophrenia are now treated most frequently through community mental health services. They may present with an exacerbation of the psychosis for the reasons outlined above. However, the presentation is often related to social problems, such as conflict with family or difficulties with accommodation or finances. In these cases, it can be very useful to communicate with the community mental health services to clarify the patient's baseline level of function and current problems. Some patients

with chronic illness are effectively homeless and have poor engagement with community services, irregular medication use and ongoing drug abuse. Although it is difficult in a busy ED, these patients ideally need some work towards establishment of continuity of care and long-term treatment plans.

The term 'schizoaffective disorder' has been used to describe an illness in which patients show typical symptoms of schizophrenia as well as having definite manic or depressive episodes. In practice, in the ED, such patients can be assessed and managed in a similar way to patients with schizophrenia.

Mania with psychotic symptoms

The manic syndrome is one form of presentation of bipolar disorder, the others being a depressive episode and mixed affective state.

The typical manic syndrome is very distinctive. The patient presents with euphoric or irritable affect, pressure of speech (rapid, continuous speech which is difficult to interrupt), distractibility and disinhibited or overfamiliar behaviour. If delusions are present, they are typically grandiose (that the patient has an important mission) or persecutory (e.g. that other persons are engaged in a conspiracy to prevent the patient fulfilling his or her destiny). Collateral history will usually show that the patient has been well until the last few days when the patient has become overactive and disorganized with a markedly decreased need for sleep.

In mixed affective psychosis, the patient often shows typically manic arousal and irritability, but may have a depressive theme evident in the content of speech. Depressive psychosis is discussed below.

Sometimes a delirious patient with affective lability, irritability, disinhibition and distractibility may be misdiagnosed as manic. The diagnosis should be considered in the older patient without a previous history of bipolar disorder. The distinction can be made on the basis of the impairment of cognitive function (disorientation, fluctuating conscious state and memory impairment) in delirium and clinical or laboratory evidence of medical illness.

It may be difficult to distinguish acute mania from acute schizophrenia in the emergency setting, especially in first episode cases. Being certain of the diagnosis is not crucial, as the short-term management is similar (see below).

Major depression with psychotic features

Patients who exhibit psychotic features during a depressive syndrome are severely depressed. The content of delusions and hallucinations relates to the patient's feelings of worthlessness or guilt and may include the conviction that the patient should die. Because the patient is unable to evaluate these beliefs rationally, the risk of

suicidal actions is high and these patients should be closely supervised.

The patient with a depressive psychosis will show the other typical features of a depressive syndrome. Most often, the mental state assessment will show a patient who lacks spontaneity and is withdrawn and sad. Occasionally, however, the patient may be agitated and irritable.

The differential diagnosis and management of depressive syndromes are discussed in Chapter 20.4.

Substance-induced psychosis

Drugs of abuse are associated with psychotic presentations in several ways: psychosis as a manifestation of acute intoxication, psychosis during withdrawal reactions, chronic psychosis following prolonged use and the exacerbation of pre-existing psychotic illness due to drug abuse. Drugs of abuse that may contribute to psychosis are listed in Box 20.5.4.

The psychosis associated with intoxication may include auditory and visual hallucinations and persecutory or grandiose delusions. The patient is usually agitated, highly anxious and incoherent, and often shows autonomic signs, such as dilated pupils. Some drugs, such as phencyclidine, are particularly associated with disinhibited rage. Management is focused on ensuring safety and maintaining vital functions in the expectation that the psychosis will clear when the intoxication resolves.

Alcohol and benzodiazepines can lead to psychotic symptoms (most commonly visual hallucinations) in the context of withdrawal delirium. The psychotic symptoms resolve through management of the withdrawal with benzodiazepines.

Amphetamine (and amphetamine derivatives), phencyclidine and lysergic acid diethylamide (LSD) have all been associated with chronic psychosis, which can persist for weeks or months after cessation of drug use.^{16–18} Whether or not the patients who develop these chronic psychoses may have been predisposed to psychotic illness is controversial but, nevertheless, the psychosis should not be regarded purely as an intoxication effect but treated in its own right. Amphetamine

Box 20.5.4 Drugs of abuse associated with psychosis

- Amphetamine and methamphetamine
- Methylenedioxymethamphetamine (MDMA, ecstasy)
- Cocaine
- Phencyclidine
- Ketamine
- Lysergic acid diethylamide
- Cannabis
- Alcohol
- Benzodiazepines

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drugs are most frequently associated with this chronic psychosis, usually following prolonged heavy amphetamine abuse. The clinical picture can be quite distinctive, including beliefs that the patient is being watched or followed or that thoughts may be monitored with an implanted device. 'Running commentary' auditory hallucinations may occur as well as tactile hallucinations, which may lead the patient to excoriate the skin in pursuit of a supposed infestation with insects.

The role of cannabis as a cause of chronic schizophrenia-like psychosis is uncertain, although cannabis frequently exacerbates psychotic symptoms in patients with an existing illness.¹⁹

Alcoholic hallucinosis is a relatively uncommon condition found in some patients with long-term alcohol abuse histories. The patient experiences auditory hallucinations of a derogatory or 'running commentary' type in clear consciousness, without being in a withdrawal state. This disorder may persist for weeks or months and the symptoms may respond to antipsychotic medications.

Because alcohol and drug abuse can exacerbate psychosis in patients with an established schizophrenic or bipolar disorder, inquiry should be made into their use with every patient.

Psychotic-like reactive states

Patients with histories of severe personality disorder, post-traumatic stress disorder and dissociative disorder sometimes present with quasi-psychotic states.^{20,21} These episodes usually follow acute stress, such as a relationship or other social crisis, or events that trigger recall of traumatic experiences. The patient is usually extremely anxious and may have impaired verbal communication, further complicating assessment. Psychotic-like experiences can include intense subjective experiences of a derogatory internal monologue, which can seem like auditory hallucinations or intense fears of being harmed, which mimic persecutory delusions. Some patients' recall of traumatic experiences is so persistent and vivid that it seems as if it is actually happening again.

When such patients are seen in emergency settings, they often need containment and assessment in a similar manner to patients with true psychoses. Benzodiazepines and sedative antipsychotic medications (see below) are often useful in reducing the high level of arousal.

Assessment

Objectives and sources of information

The assessment of the psychotic patient in ED has several objectives. The basic questions are:

- Is the altered mental state primarily due to a medical condition?
- To what extent are drugs or alcohol contributory?

- Can a primary psychiatric diagnosis be made?
- Can the patient be treated at home or is hospitalization necessary?
- Should the patient be detained involuntarily under the Mental Health Act?

These questions cannot be answered by considering only the clinical state of the patient. Decisions about risk assessment and disposition depend on a careful consideration of the social circumstances of the patient, recent events that have led to the emergency presentation and past and current engagement with community mental health treatment services. Diagnostic clarification is often greatly assisted by previous treatment records.

Information should be sought from family and community mental health teams about recent function, symptoms, dangerous behaviours, and alcohol and other drug use. The police who sometimes bring patients with psychosis to ED can often give important information about the circumstances that led to the presentation.

The assessment process is not a single one-off review of the patient's mental state, nor is it a linear process in which the various objectives of assessment can be serially addressed. It tends rather to be a back and forth process as multiple lines of inquiry are simultaneously pursued and the clinical data re-evaluated in the light of new information.

At the end of the assessment process, it should be possible to record a summary of the various parameters of assessment as outlined in **Box 20.5.5**, which can then form the basis for management planning.

Initial stabilization of the patient

In order that conditions can be created for an adequate assessment, there is an immediate need to stabilize the patient. The acutely psychotic patient has distorted understanding and may be an unwilling participant in the process. It is preferable to try to engage the patient in a calm manner with straightforward and clear explanation of the need for assessment. The patient's own concerns and perceptions of the problem

should be listened to, without initially trying to seek answers to specific questions. This attention is reassuring to the patient and provides an opportunity for observation of the mental state, even if the patient's account lacks coherence.

Patients who are aroused and agitated, intoxicated, or have persecutory delusions may pose a risk of violent or aggressive behaviour. In these cases, it is important to monitor safety by having security staff present, by not assessing the patient in a confined space, and by remaining out of striking distance and not turning one's back on the patient. Sometimes the patient may have to be sedated before much assessment can be made. Sedating the aroused patient is discussed in **Chapter 20.6**.

Moderate use of benzodiazepines need not significantly complicate the mental state assessment, although these drugs may exacerbate delirium. High doses of benzodiazepines (especially diazepam, which has active metabolites with long half-lives) can produce a prolonged delirium, which will delay the assessment process.

Mental state assessment

Especially in the aroused patient, it is often difficult to carry out a formal mental state examination. Nevertheless, it is possible to collect a lot of information by simple observation. The general appearance can give clues to the patient's level of self-care. The rate and mode of speech can suggest the presence of formal thought disorder. Hostile or euphoric affects may suggest a manic syndrome or intoxication. Patients may spontaneously reveal delusional ideas or auditory hallucinations, or may admit to these on specific questioning. Orientation to time and place and recent events should always be assessed because of the strong association of disorientation with delirium. Although detailed cognitive assessment is usually not possible, an attempt should be made to assess short-term memory function and attention and concentration.

As with all aspects of assessment, the assessment of mental state should not be based on a single evaluation but on serial assessments by medical staff and the observations of the nursing staff throughout the time the patient is in the ED.

Risk assessment

It is important to inquire directly about suicidal and homicidal ideation and to record the patient's statements. However, risk assessment depends on an evaluation of the whole situation. A patient with persistent persecutory beliefs may be at significant risk of behaving aggressively towards perceived persecutors, even though he or she may deny hostile intent. Conversely, a patient's expression of suicidal ideation may reflect long-standing frustration and dissatisfaction (which

Box 20.5.5 The psychotic patient—brief assessment schedule

1. Circumstances of referral
2. Presenting problem
3. Social circumstances
4. Previous treatment
5. Current mental health services
6. Current medication
7. Alcohol and other drug use
8. Mental state examination
9. Medical assessment and investigations
10. Provisional diagnosis
11. Risk assessment
12. Treatment and disposition plan

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may be alleviated by receiving help) rather than intent to act in a suicidal manner. The degree to which the patient can exercise judgement is also important. A floridly psychotic or grossly disorganized patient is at greater risk than a patient with chronic symptoms who presents with a social crisis. The home situation and the views of family should also be considered and taken very seriously. Inquiry also should be made into the provision of care for dependent children.

Decisions about hospital admission and involuntary detention usually focus appropriately on danger to self and others. Uncertainty may sometimes arise regarding the use of Mental Health Act detention powers in relation to patients who clearly deny any intent to harm themselves or others, but who are clearly in need of treatment, lack insight and are very unlikely to receive treatment unless compulsorily detained. However, most jurisdictions make some provision in their mental health legislation for such patients to be detained in the interests of their health or to prevent other 'harms', such as harm to reputation. The decision to detain involves balancing the patient's right to autonomy against the probable risks of not receiving treatment. In general, such a patient has only been brought to the ED because family, friends or other carers have been concerned about the behaviour or mental state of the patient; therefore it is wise to consult with these concerned others if there is doubt about the decision to detain.

Medical evaluation and investigation

Medical evaluation has three goals: excluding delirium (or dementia), considering other organic causes of psychosis and assessing for the presence of co-morbid medical illness.

The practice of 'medical clearance' prior to psychiatric evaluation may detract from a comprehensive evaluation of the patient. A more satisfactory process is to compile an adequate history of the presenting illness, assess the mental state, review the medications and alcohol and other drug use, consider previous medical history, check vital signs and carry out as comprehensive a physical examination as possible, with particular attention to signs of injury, poisoning or intoxication.²² In services where both emergency physicians and psychiatrists are available, direct discussion about cases of uncertain diagnosis is useful.

Medical causes for an altered mental state will usually be suggested by the history, mental state assessment, abnormal vital signs and physical examination. As noted above, particular consideration should be given to medical causes in a first presentation of psychosis, especially in an older patient.

Investigations should be driven by history and examination findings, such as neurological

signs or signs of infection. Nevertheless, because of the difficulties in compiling comprehensive medical histories, it is often appropriate to do a number of 'screening' investigations as indicators of unsuspected medical illness. The range of suggested tests varies, but usually includes urea and electrolytes, full blood count, liver function tests, random blood sugar, blood alcohol level, thyroid function tests and B12 and folate levels.²³

The availability of computed tomography (CT) scanning in more centres has facilitated the use of neuroimaging as an aid to diagnosis. This investigation is likely to be indicated in patients where stroke, neoplasm, haemorrhage or central nervous system infection may be suspected. It is also appropriate to consider a CT scan of the brain in first episode psychosis cases to assess further the possibility of neurological disease presenting with only psychotic or affective symptoms. However, the yield of positive results with this investigation is low,²⁴ especially in the younger patient²⁵; therefore neuroimaging is generally not required as an emergency investigation if the patient is otherwise medically well.

It is well established that patients with chronic psychotic illness tend to have poorer physical health than the general population.²⁶ Common conditions include obesity, late onset diabetes, hypertension, arteriosclerotic disorders, smoking-related disorders and alcohol and other drug-related disorders. The prevalence of these problems can be related to lifestyle factors, the side effects of medication and the difficulties in making effective use of primary medical care. It is worth considering the possible presence of these common conditions as they sometimes need acute treatment or contribute to an exacerbation of the mental state.

Treatment

Management in the emergency department

Once medical causes have been excluded, the primary psychiatric diagnosis is likely to fall into one of the following groups:

- drug-induced psychosis
- acute schizophrenia
- mania
- chronic schizophrenia
- psychosis-like reactive state
- depressive psychosis.

Patients with psychotic illness often stay in the ED for prolonged periods. Sometimes this is due to delays in the assessment process, but it is also significantly a result of access block; that is, the lack of ready availability of beds in psychiatric wards. In some hospitals, these circumstances have resulted in the establishment of specific psychiatric 'holding beds', within or closely related to the ED, where patients may be observed and

treated for up to 48 hours while further management and disposition plans are being made.^{27,28} The availability of such specialized psychiatric observation units is likely to reduce the need for reliance on sedative medications to manage behavioural disturbance. The patient can move around more freely, preferably with access to an outside secure area, and specialized mental health staff can provide assessment, supervision, explanation and reality orientation.

In the more conventional ED setting, behavioural management is more difficult as a balance must be achieved between imposing restrictions on the patient and maintaining the safety of all patients and staff. Psychotic patients should be in areas that can be easily observed, and often one-to-one supervision will be necessary, preferably with trained mental health nurses. If possible, this should be in a quiet area without too much coming and going. Engagement of the patient in reality-based conversations (explanation of what is happening, attention to personal concerns) is often useful. It may be possible to enlist the help of family members in providing reassurance and comfort.

The use of specific medications will depend in part on the diagnostic picture. Patients with drug-induced psychosis are usually quite aroused and require significant levels of sedation. Benzodiazepines, such as midazolam and diazepam, are usually preferred as they are less likely to lead to medical complications (especially arrhythmias) in a person who has already taken other drugs and has a high sympathetic drive. The period of sedation may become prolonged for several hours (or even days if high doses of diazepam are used). The mental state needs to be reassessed for the presence of persistent psychosis when the sedation abates.

Patients with acute schizophrenia, mania or persistent psychosis following drug use all have similar management in the short term. These patients tend to be aroused and agitated and to have considerable difficulty in coping with the restrictions and the stimulation of the ED environment. If the patient will take oral medications, sedative antipsychotics (e.g. olanzapine) or benzodiazepines (e.g. lorazepam) can be used. These are better prescribed as regular doses (e.g. olanzapine 5 mg tds or lorazepam 1 mg qid) than on a pro re nata (PRN) basis to ensure consistency in dosing. Repeated divided doses to maintain a more constant level of sedation are preferable to infrequent large doses. Estimates of the probable appropriate dose can be made on the basis of the size of the patient and the degree of arousal, and then titrated upward or downward on the basis of response in the first 24 hours.

If the patient refuses oral medication, lorazepam (if available) or clonazepam can be used

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intramuscularly or intravenously. Olanzapine also can be used effectively intramuscularly. Patients who are likely to stay in the ED or short-stay unit for more than 24 hours can be given zuclopentixol acetate 50 to 150 mg IM (dose dependent on the size of the patient). This is a medium-acting depot antipsychotic preparation that will last for 3 to 4 days. However, the onset of action is delayed for 6 to 8 hours, and this medication should be avoided in neuroleptic-naïve patients because of the risk of prolonged dystonia.

The patient who presents with acute schizophrenia who is not aroused may benefit from explanation and only small doses of medication, such as olanzapine 5 mg at night. Similarly, the patient with chronic schizophrenia should be maintained on usual medications, possibly with the addition of a PRN benzodiazepine if very anxious.

Patients with psychotic depression can be quite agitated, but also may be quiet and withdrawn. They should be considered at high risk of suicidal behaviour and need close supervision. Their mental anguish may be helped in the short term with the use of benzodiazepines or sedative antipsychotics (olanzapine or quetiapine). Regular doses are better than PRN, although smaller doses are needed than in the treatment of the acutely schizophrenic or manic patient. It is not essential to commence an antidepressant medication during the time the patient is in the ED.

The patient with severe personality disorder or a history of severe trauma who presents with a psychosis-like reactive state often requires similar treatment to a patient with acute schizophrenia. The patient may require containment in a place of safety and will benefit from explanation and reassurance. Benzodiazepines and sedative antipsychotics can be very useful in lowering arousal.

Admission to inpatient care

The decision to admit the patient for inpatient psychiatric care depends on the acuity of the presentation, the supports available at home, the degree of risk and the availability of community mental health services.

Patients with an acute episode of schizophrenia, especially a first episode, often require admission because they are often very disorganized, lack insight and are likely to be non-compliant with medication; they also may be at risk of suicide or aggressive behaviour. However, the increasing availability of mobile crisis teams (community mental health teams with the capacity for rapid and intensive follow-up in the home) has made it more possible to treat even these acutely unwell patients at home. This is usually preferred by the patient and sometimes by the family, especially where the patient is an adolescent or young adult still living with their family. In these cases, careful assessment of potential risks to the patient or others and a frank discussion of these issues with the family is advisable.

The acutely manic patient who has been brought to the ED almost certainly requires admission. Once established, the manic syndrome is likely to persist for several weeks if untreated. In some cases, especially those involving recurrence of a previous bipolar disorder, the patient presents relatively early in the relapse and with sufficient insight to accept advice about increasing or changing medications. If such a patient is discharged to outpatient care, specific arrangements should be made with the family and the community mental health services for monitoring and follow-up.

The patient with an acute psychotic depression almost always requires admission because of the high risk of suicidal behaviour.

On the other hand, patients with chronic schizophrenia who present with a mild exacerbation of symptoms or family or social crisis should generally be managed in the community if possible. These are chronic conditions analogous to diabetes or asthma and quality of life can be enhanced if the patient can be helped to engage with community treatment services, achieve stability of accommodation and daytime activity, and learn to self-manage the condition.²⁹

For patients with reactive psychoses in the context of personality disorder or trauma history, the individual circumstances vary widely and the decision to admit depends on careful assessment of the risk factors. Every effort should be made to return the patient as quickly as possible to reality-based perceptions of the world and to restore a sense of autonomy and personal responsibility. It is sometimes not possible to achieve this during the course of an ED stay and a brief crisis admission to a psychiatric unit may be necessary.

Criteria for involuntary treatment

When inpatient admission is considered desirable but refused by the patient, consideration should be given to the use of Mental Health Act powers for referral and detention. Contemporary mental health legislation requires the person considering this option (which may be a doctor or other authorized mental health practitioner) to review options for less restrictive treatment before making this decision.

Mental health acts generally stipulate that persons can only be referred under the act if they suffer from a 'mental disorder' and are also at some 'risk'. Risks involving danger to self through suicidal intent or behaviour, and danger to others as a result of aggression or persecutory delusions, are usually straightforward grounds for referral and detention. The decision may be more difficult in relation to the patient with partial insight. The need for detention involves weighing up the potential consequences of not receiving treatment, the possibility of access to community services and the availability of family or other social supports.

Where mental health specialists are not readily available to the ED, ED doctors may appropriately

refer a patient under the Mental Health Act so that assessment by a psychiatrist can take place at another location. Especially in cases where the need for involuntary treatment is uncertain, it is good practice for the ED doctor to make this referral to ensure that the decision to detain or release can be made by a psychiatrist, who is in a clearer position to take medico-legal responsibility.

Community referral

The range of potential community treatment options is now wide. Patients may receive outpatient treatment through general practitioners, private psychiatrists and psychologists, community mental health clinics, public and private drug and alcohol services, relationship counselling agencies and various other specialized services (e.g. non-government community support services, services for indigenous persons and services for victims of trauma). In planning outpatient care, a good approach is to determine initially which service providers may be already involved in helping the patient and the strength of the patient's relationship with those services. Direct communication between the ED staff and the community service providers is very desirable, especially if the patient is a new referral to those services.

Some of the more effective psychiatric emergency services work in close liaison with mobile crisis teams or acute care teams, who actively and intensively follow up discharged patients in their own homes or in crisis accommodation.^{28,30}

CONTROVERSIES AND FUTURE DIRECTIONS

- As a result of the contemporary mental health community focus, EDs will continue to have a major role in the assessment and stabilization of patients with psychosis.
- Should this assessment occur within traditional EDs or should EDs facilitate the development of co-located psychiatric emergency services?
- The models of care that will achieve the best integration of emergency mental health assessments with community services require better definition.

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Full references are available at <http://expertconsult.inkling.com>

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20.6 Pharmacological management of the aroused patient

John C. Spencer

ESSENTIALS

- 1** Benzodiazepines and antipsychotics, often used most effectively in combination, are the first-line drugs for sedation of the aroused patient.
- 2** As much information as possible should be collected before the patient is sedated.
- 3** The risks involved in administering sedative drugs need to be considered, particularly at higher doses.
- 4** Dose adjustments are necessary in the older or medically compromised patient.

Introduction

Aroused patients who present to the emergency department (ED) of their own accord can generally be best assisted by verbal reassurance and prompt mental health evaluation. Reducing the waiting time and arriving quickly at an action plan will provide the best response to the patient's anxiety and agitation.

For highly aroused patients who have been brought to the hospital reluctantly, the immediate need is to gain control of the situation to permit further evaluation, while ensuring the safety of the patient, the staff and the public.

Where possible, it is desirable to collect some information about the patient before sedation. The patient should be approached in a calm manner in a safe, observed area of the ED, with security staff in the background if necessary. The patient should be asked about his or her understanding of the problems and listened to attentively, even if the account is incoherent. This attention will be reassuring to the patient and helps in building rapport. During this process observations can be made about the mental state. If possible, vital signs should be recorded and a brief physical examination carried out, with particular attention to signs of injury, intoxication or overdose.

In the hostile or frightened uncooperative patient, it will often be necessary to proceed to rapid tranquilization. This is a familiar procedure to the emergency physician and the practice can be enhanced by attention to the basic principles of care, an awareness of the risks and knowledge of the characteristics of the available drugs.

Pharmacological management should always be tailored to the particular patient. The medically compromised patient will be at greater

risk of the complications of sedation. In elderly patients, decreased and delayed metabolism and elimination can result in prolonged therapeutic and adverse effects. Dose adjustments and agents with shorter half-lives and more favourable side-effect profiles must be considered for these patients.

General principles of rapid tranquillization

The general principles of care are:

- Use sedative benzodiazepines and/or antipsychotics as the first-line agents.
- Should the situation allow, oral dosing is the least distressing approach for patients and staff.
- Treating physicians should use agents with which they are familiar. In particular, they should be aware of maximal safe dosing and expected adverse effects.
- The endpoint should be a calm cooperative patient. Sedation to the point of loss of airway protection is dangerous.
- The patient should be nursed in a quiet, calm and gently lit environment if possible.
- Sedated patients should be monitored with basic observations; a 12-lead electrocardiogram (ECG) should be performed on any patient being administered repeat doses of antipsychotics.
- Supportive care, such as hydration, indwelling catheterization, pressure care and deep vein thrombosis prophylaxis, are essential for patients requiring ongoing sedation. This is particularly relevant in overcrowded EDs and if patients are detained in the ED for prolonged periods.

- Maintenance of patient dignity by using single rooms and limiting visual exposure of the patient to the public is often forgotten but should be a basic standard of care.

Risks of rapid tranquillization

There are inherent risks in attempting to gain control of the aroused patient, including risks of injury to the staff and patient. If physical restraint is necessary to administer parenteral medication, adequate staff, trained in restraint procedures should be on hand. Sometimes mechanical (padded strap) restraint may be necessary in the early stages or to limit the dose of medication if the patient is developing toxic effects. Mechanical restraint should not be maintained in the absence of chemical sedation due to the risks of physical injury and rhabdomyolysis, as well as for ethical reasons.

The risks of adverse events from medication administration are well recognized.

Over-sedation and resultant respiratory depression and pulmonary aspiration are relatively common and for the most part avoidable with proper care.

Sudden cardiac death, particularly with agents that prolong the QT interval and precipitate torsade des pointes and ventricular tachycardia (VT), is a rare but catastrophic complication of rapid tranquilization. This risk is heightened in the aroused patient with increased circulating catecholamines and in patients with pre-existing heart disease or conduction disturbance. Antipsychotics combined with other medications that prolong the QT interval pose an increased risk. The agents most associated with risk of sudden death are thioridazine and clozapine. Droperidol and haloperidol are associated with QT prolongation but rarely with the risk of torsade des pointes. Quetiapine and chlorpromazine are associated with QT prolongation but this is probably less clinically significant than with the above agents. The atypical agent olanzapine appears to be relatively safe from this perspective.

Hypotension can occur with administration of any agent with alpha blockade effects, but is especially associated with chlorpromazine (particularly when given intravenously). Dyskinetic reactions are seen with all antipsychotics, most frequently with the butyrophenones, such as haloperidol, and less commonly with atypical agents, such as olanzapine. Neuroleptic

malignant syndrome is a risk with any antipsychotic agent, even following a single dose.

Anticholinergic effects, such as delirium and urinary retention, are risks with virtually all antipsychotics and are generally seen at high doses. Delirium is also caused by high doses of benzodiazepines, particularly diazepam, which accumulates with recurrent dosing. All antipsychotics have the potential to lower the seizure threshold.

Elderly patients are at significantly greater risk of drug accumulation and adverse effects. They are also at far greater risk of delirium, particularly with the combination of possible underlying cognitive impairment and environment change. Age-related reductions in hepatic metabolism and renal function make it reasonable to assume that all agents will have prolonged elimination half-lives in these patients. Even small doses of benzodiazepines can produce significant and prolonged respiratory depression in the elderly. Standard doses of antipsychotics, such as haloperidol, may result in prolonged extrapyramidal effects that impair mobility for days to weeks post-administration.

Specific agents

Benzodiazepines

Midazolam This water-soluble benzodiazepine has major benefits over diazepam in that it produces fewer site reactions and can be given intramuscularly. It has a rapid effect by intramuscular (IM) or IV injection (2 to 5 minutes), with a half-life of 1 to 3 hours. The active metabolite has a similar half-life. The elimination half-life is significantly prolonged in the elderly. The major adverse effect is respiratory depression. It is available in ampoules (5 mg/mL, 15 mg/3 mL, 5 mg/mL and 50 mg/10 mL).

Diazepam Diazepam can be used orally or intravenously. It is not recommended for IM use due to unpredictable absorption. Diazepam demonstrates biphasic elimination with rapid redistribution of 1 to 3 hours, followed by a prolonged terminal elimination phase of up to 20 hours. Hepatic metabolism produces active metabolites and excretion is renal. Elimination is significantly prolonged in the elderly. Major adverse effects are respiratory depression and accumulation causing delirium. It is available in ampoules (10 mg/2 mL), tablets (2 mg and 5 mg) and elixir (10 mg/10 mL).

Clonazepam Clonazepam can be used by oral, IV or IM routes. Clonazepam has a prolonged elimination half-life (20 to 50 hours) with hepatic metabolism and renal excretion. The major adverse effects are excessive sedation and risk of accumulation. It is available in ampoules (1 mg/mL), tablets (0.5 mg and 2 mg) and oral liquid (2.5 mg/mL).

Lorazepam In Australia, lorazepam is readily available in oral preparation in 0.5/1/2 mg tablets. However, in other countries, it is widely used intramuscularly in the sedation of psychotically aroused patients. It is available in a parenteral 2 mg ampoule in Australia but only on a hospital's application under the Special Access Scheme. Thus it is only used in a small number of hospitals due to the prohibitive nature of this application. It is well absorbed orally and intramuscularly with an elimination half-life of 12 to 15 hours. The hepatic metabolites are non-active. The major adverse effect is excessive sedation, but it is less likely to accumulate than diazepam or clonazepam.

Antipsychotics

Droperidol Droperidol can be administered intramuscularly or intravenously. Clinical effects are seen within 3 to 10 minutes, maximum at 30 minutes and the elimination half-life is approximately 2 hours. It is significantly more sedating than haloperidol, which makes it an attractive choice for the aroused patient. It is also a potent antiemetic. The black box labelling of droperidol is highly controversial as there appears to be little evidence that there is greater cardiovascular risk with this agent than with haloperidol. QT prolongation is seen with greater frequency at higher dose, but deterioration to torsade de pointes is rare. The risk is greater when combined with agents that prolong the QT interval or in patients with pre-existent QT prolongation. As with haloperidol, there is a risk of dystonic reactions and neuroleptic malignant syndrome (ampoules 2.5 mg/mL).

Haloperidol Haloperidol can be given by oral, IM or IV routes. Peak plasma levels occur 20 minutes after IM injection and 2 to 6 hours post-oral dose. Mean elimination half-life is 20 hours, but this includes initial rapid elimination followed by a prolonged elimination over days. Hepatic metabolites are renally excreted. Major adverse effects are extrapyramidal effects that may persist for days (particularly in the elderly), prolongation of QT interval with risk of torsade and neuroleptic malignant syndrome (NMS). It is available in tablets (0.5 mg, 1.5 mg and 5 mg), liquid (2 mg/mL) and ampoules (5 mg/mL).

Olanzapine Olanzapine is licensed for oral, sublingual (SL) and IM use. Also, there are common reports in the literature of IV use. It is an atypical antipsychotic that is well absorbed orally with peak plasma levels 2 to 5 hours post-oral dose and 30 minutes post-IM injection. It has a half-life of approximately 33 hours and is hepatically metabolized to inactive metabolites that are renally and faecally excreted. There is also now a long-acting preparation with a half-life of 30 days. Major adverse effects include excessive

sedation, mild anticholinergic effects and NMS. Extrapyramidal side effects (EPSEs), including dystonias, are rare. Cardiotoxicity is also rare. It is available in tablets (2.5 mg, 5 mg, 7.5 mg and 10 mg), dissolvable tablets, wafers (5 mg and 10 mg) and ampoules (10 mg).

Risperidone Risperidone is for oral and SL use. It is an atypical antipsychotic that is well absorbed orally with a peak effect in 1 to 2 hours. It is hepatically metabolized to an active metabolite that is renally excreted. The half-life of the parent compound is 3 hours in extensive metabolizers and 17 hours in poor metabolizers; the active metabolite elimination half-life is 24 hours. Risperidone's adverse effect profile is benefited by the absence of anticholinergic effects, but includes postural hypotension with initial dosing, extrapyramidal effects and NMS. Extrapyramidal reactions, including dystonias, are less frequent with risperidone than with haloperidol. There has been an increased mortality associated with risperidone and elderly patients on frusemide, so caution should be taken to ensure adequate hydration in these patients. It is available in tablets and SL 'quicklets' (0.5 mg, 1 mg, 2 mg, 3 mg and 4 mg) and solution (1 mg/mL).

Chlorpromazine Chlorpromazine is for oral, IM or IV use. It has variable and incomplete absorption and a large first-pass metabolism, with peak plasma levels 1 to 4 hours after oral and 30 minutes after IM administration. Metabolism is hepatic with many metabolites that are renally excreted. Elimination is complicated with early (2 to 3 hours), intermediate (15 hours) and late (60 days) elimination phases. Major adverse effects are postural hypotension, strong anticholinergic effects, excessive sedation and the risk of NMS. Extrapyramidal effects are relatively uncommon. It is available in tablets (10 mg, 25 mg and 100 mg), syrup (5 mg/mL) and ampoules (50 mg/2 mL).

Zuclopentixol acetate ('Acuphase')

This is given intramuscularly. Zuclopentixol acetate is a medium-acting depot preparation of a typical thioxanthene antipsychotic. Maximal plasma levels are achieved 24 to 36 hours post-IM injection, declining to 30% of maximum levels by day 3. It is hepatically metabolized to inactive metabolites and is faecally excreted. Zuclopentixol acetate should be avoided in neurolept-naïve patients and those with organic brain disorders, cardiac disease and lowered seizure threshold. This is because any adverse effects, including NMS, will be prolonged because of the slow absorption and elimination. The usual dose is 50 to 100 mg.

Dexmedetomidine and clonidine

These central α-agonists have a significant sedative effect. Dexmedetomidine is used as

an infusion, primarily in the intensive care unit setting. Clonidine has a recognized role in opiate and, to a lesser extent, alcohol withdrawal. It may be administered by the oral, subcutaneous, IM or IV route. It has a rapid onset of action when given parenterally and a half-life of greater than 12 hours. There is the potential for both these agents to have an increasing role in the ED for the management of hyperaroused patients. Both have a risk of bradycardia and hypotension and should be avoided in patients with pre-existent cardiac conduction abnormalities and be used with caution in patients on rate-lowering agents.

Anaesthetic agents

Ketamine Ketamine is an N-methyl-D-aspartate (NMDA) receptor antagonist that has widespread anaesthetic, sedative and pain-relieving properties with the usual maintenance of airway and breathing in correct dosages. There are increasing reports of its safe usage both in the prehospital and ED environments, and it has been written into ambulance protocols.^{1,2} It is given parenterally usually IM to dose up to 4 mg/kg with rapid onset of sedation. It is presented in a 200 mg/2 mL ampoule.

A rapid tranquillization algorithm

There are a variety of published algorithms for rapid tranquillization.^{3–15} The following is a reasonable approach in terms of effectiveness, the risk of adverse effects and availability. This algorithm applies to the management of a previously well adult patient. It must be remembered that, in general, the risk of adverse events is increased the greater the doses used. Elderly patients as a general rule should have lower initial doses and smaller daily doses.

First-line treatment

Try to develop rapport with the patient, use verbal de-escalation techniques and oral/sub-lingual medications if possible. Oral agents of choice include:

- benzodiazepines: diazepam 10 mg, clonazepam 2 mg or lorazepam 2.5 mg (elderly: lorazepam 0.5 to 1 mg)
- and/or:
- antipsychotic: olanzapine 5 to 10 mg oral/SL (elderly: olanzapine 2.5 mg oral/SL or risperidone 0.25 to 0.5 mg oral/SL).

Second-line treatment

If oral therapy is not achievable or is not effective, parenteral medications must be given. Agents of choice include:

- Droperidol or haloperidol IM 5 to 10 mg, every 1 to 2 hours up to maximum 20 mg/24 hours (ensure that an ECG is done within 15 minutes of administration where possible) **OR**
- Olanzapine IM 5 to 10 mg, repeated 2 to 4 hourly up to a maximum of 30 mg/24 hours **and/or**
- Lorazepam IM 1 to 2 mg, every 60 minutes up to a maximum of 8 mg in 24 hours.
- The use of IM olanzapine within 60 minutes of an IM/IV benzodiazepine has been associated with additive respiratory depression and hypotension. The combination should only be used where adequate resuscitation facilities are present and the benefits outweigh the risks.
- The side effects include hypotension, arrhythmia and EPSEs. Treatment of EPSE can be initiated with benztrapine oral/IM/IV 1 to 2 mg as a single dose, but prophylactic use is not indicated.

There is evidence of more rapid onset of sedation and less adverse events when a combination of midazolam and antipsychotics is used rather than midazolam alone.¹²

Or

- ketamine 2 to 4 mg IM 1 mg/kg IV. Risks include hallucinations and imagery—especially care in the already psychotic patient. Other side effects include hypertension and raised intracranial and intraocular pressure.

IV sedation may be considered if it is safe to insert an IV canula, when IM medications ARE not effective, AND there is serious risk of harm to PATIENT AND STAFF and for immediate treatment of extreme agitation. Antipsychotics (droperidol or haloperidol IV 5 to 10 mg every 60 minutes until sedated) with a maximum dose of 20 mg in 24 hours, or lorazepam IV 1 to 2 mg every 60 minutes up to 8 mg in 24 hours may be used. Short-acting anaesthetic agents may be considered in the presence of adequate facilities and expertise, and include midazolam IV 5 to 10 mg stat and then titrated at 3- to 5-minute intervals until sedated; propofol IV 50 to 100 mg stat, then titrated at 3- to 5-minute intervals until sedated; and/or ketamine 1 mg/kg as a single dose.

Third-line treatment

If the maximal doses of the above agents have been reached with the first- or second-line drugs without adequate effect, it is necessary to try other options. Sometimes the first- or second-line drugs may have to be avoided because of previous adverse effects. The maximum doses described here are based on the likelihood of very limited greater benefit (and the probability of greater adverse effects) of exceeding these doses.

Third-line agents include:

- diazepam 2.5 to 5 mg IV, up to a maximum of around 100 to 150 mg (risks include accumulation, delirium and respiratory depression; should not be given intramuscularly)
- clonazepam 1 to 2 mg IM/IV up to a maximum of 8 mg/day. Clonazepam can also be given as an infusion at a rate of 4 to 6 mg/24 hours; the rate of the infusion can be varied according to the arousal level of the patient (risks include accumulation, delirium and respiratory depression)
- haloperidol 2.5 to 5 mg IM/IV, up to a maximum of around 30 to 50 mg/24 hours (risks are similar to droperidol)
- chlorpromazine can also be given as an IV infusion, with an initial rate of 6.25 to 12.5 mg/h to gain initial control and then reduced to a maximum of around 200 mg/24 hours (risks include anticholinergic effects, hypotension, delirium, accumulation, QT prolongation and NMS.)

Aroused patients with amphetamine intoxication should be managed with benzodiazepines and supportive care, sometimes requiring large doses for initial control. Both IV midazolam and oral/IV diazepam are reasonable first choices. Severe intoxication with hyperthermia and rigidity requires paralysis and intubation. In patients who present with paranoid psychosis associated with amphetamine abuse, the addition of an antipsychotic, such as olanzapine (oral or IM), is appropriate.

Maintenance therapy

Following initial rapid tranquillization, the patient will remain sedated for several hours, during which collateral history may be obtained. When the patient awakes, a further psychiatric assessment should be made, especially with a view to deciding whether the patient needs to be admitted to a psychiatric unit.

20.6 PHARMACOLOGICAL MANAGEMENT OF THE AROUSED PATIENT

If the patient does need to remain in hospital, consideration must be given to further appropriate medication. A general approach is to use lorazepam (1 or 2 mg three times a day) or sedative antipsychotics (olanzapine 5 or 10 mg three times a day). It is better to prescribe regular medication (rather than 'pro re nata' [PRN]) to ensure consistency of dosing. The appropriateness of the prescribed medication and the side effects should be reviewed at least daily.

If the patient remains uncooperative, IV benzodiazepines or IM olanzapine can be used on a PRN basis. If adequate facilities are available for monitoring respiratory function, the use of an infusion of clonazepam or chlorpromazine can help to achieve control. Alternatively, some patients who are likely to remain in the ED for more than 24 hours may benefit from a one-off dose of zuclopentixol acetate.

CONTROVERSIES AND FUTURE DIRECTIONS

- The role of butyrophenones versus atypical antipsychotics is controversial from a drug safety perspective.
- There is debate about the appropriateness of prolonged restraint and sedation of patients 'stranded' in emergency departments.
- The role of the central alpha-2 agonists in the management of hyperaroused patients in the emergency department is yet to be determined.
- Increased experience and usage of ketamine.

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Full references are available at <http://expertconsult.inkling.com>

20.6 PHARMACOLOGICAL MANAGEMENT OF THE AROUSED PATIENT

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SECTION
21

CHALLENGING SITUATIONS

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21.1 Death and dying

William Lukin • Carol Douglas

ESSENTIALS

- 1** Death and management of the dying process is core business for emergency medicine.
- 2** Death in the emergency department can be either sudden and unexpected or the natural and expected evolution of a disease process.
- 3** Emergency physicians have a responsibility to understand the principles of a 'good death' and to manage departmental deaths in alignment with these principles.
- 4** Communication skills for discussing death and dying are part of the skill set of an emergency physician.
- 5** Persons undertake advance care planning to support best care at the end of life. Personal wishes and values supporting such decisions may be available for viewing at the time of admission to the emergency department. Such considerations may support a 'good death' or may complicate clinical decision making and resuscitation.
- 6** How a death is managed in the emergency department has a profound impact on the next of kin and their grieving process. Emergency physicians should understand and be able to manage their role in establishing a normal grieving process for bereaved families.
- 7** Organ donation should be considered for all patients where death is expected. Suitability for donation should be discussed with an organ donation specialist.
- 8** Local statutory obligations for coronial reporting must be well understood and observed.
- 9** The emotional health of emergency medicine practitioners should be monitored and external assistance sought when appropriate.

is the unexpected death of a loved one at an emergency department (ED), where sudden unexpected and violent death is not uncommon.

Death and dying patients are an inevitable part of emergency medicine practice. In 2014 to 2015 a total of 4916 people died in Australian EDs before they could be admitted.¹ These deaths can be either sudden and unexpected or the natural evolution of a dying process. Sudden unexpected death from trauma or rapid, overwhelming disease processes is somewhat unique to emergency medicine; the management of patients and families in this situation is something with which all emergency physicians must be familiar. The management of the patient dying from a life-limiting illness in the ED calls for a skill set different from that needed to deal with an unexpected death, but it is just as important. For some, facing a surviving family or counselling a dying patient may symbolize failure in the battle against disease; however, it is a privilege and, done correctly, can be an extremely fulfilling part of emergency medicine practice. In such situations, one does not have the benefit of a long-standing doctor-patient relationship. The support and mutual understanding that are the cornerstones of family practice are missing; therefore rapport must be forged in the heat of the moment. Families need space and time to come to grips with a death, but both are limited in the ED. Access block and overcrowding should not preclude sensitive, empathetic grief management.

To follow the strain and pace of a difficult resuscitation with the grace and emotional energy required to care for a family requires considerable effort. Emergency physicians also have a duty of

Introduction

For most people, the normal expectations are that they will live a full life, that parents will predecease their children and that the dying person

will be able to deal with any unfinished business and die surrounded by loved ones, as portrayed in the media. There is an expectation that death will be natural, peaceful and, for the majority, free of pain. In marked contrast to such expectations

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care to the survivors, who deserve compassion as much as the recently deceased.

Similarly, management of the patient dying at the end of a life-limiting illness can be a complex and challenging task. Patients and their families in this setting attend the ED for many reasons, including fear, unrelieved symptoms and the inability to access appropriate services. This does not always represent a failure of the health system but is determined by clinical complexity, as an ED is sometimes the only place that can deliver the level of care required. An understanding of the concepts of advance care planning is required. Clinicians must be familiar with local processes, as these may vary from state to state (see [Chapter 21.6](#)). ED clinicians should have sufficient knowledge of local palliative resources to enable advocacy roles for patients with special needs and foster partnerships with local care providers to facilitate transition into other services.

The concept of a good death is recognized widely and based on key themes ([Box 21.1.1](#)).² These apply equally to unexpected and expected deaths. Death in an ED may violate some or all of these principles. Emergency physicians should apply these concepts to practice as best they can within the constraints of a busy, crowded ED.

The better the memory of the death, the more likely the bereavement will be normal. The quality of care provided may prevent significant morbidity, as pathological or unresolved grief can lead to later problems with physical and mental health.³

The process of dying

Diagnosing dying

Death does not occur at a finite moment. Cardiac death, cerebral death, brain-stem death and

cellular death form a continuum over minutes or hours. Considerable effort has been directed to the core recognition of diagnosing death. Legal definitions for diagnosing brain death, circulatory death and the staff involved are outlined in the relevant transplantation and organ donation acts in various jurisdictions. This has been done largely to facilitate organ transplantation.

There has been little research in the area of diagnosis of the dying process and the part that emergency physicians may play in this. The diagnosis of dying is a skill best exemplified by palliative medicine specialists. The timing of the death can be hard to estimate and comes with experience. A diagnosis of the likelihood of dying sets appropriate goals of care and so enables the emergency physician to engage families in preparation and allows patients to be supported with appropriate systems of care. Where possible, the patient should be enabled to maintain some control and may be able to plan for the time he or she has remaining (see [Chapter 21.6](#)).

Managing the dying process

When the point of dying is reached, the practitioner must be acutely aware of the dying person's needs. Although physical needs, such as analgesia, are relatively easily met, other domains can easily be ignored.

For patients whose death is inevitable or not unexpected, guidance documents published by the International Collaborative for Best Care of the Dying Person can be tailored to local conditions and can help to support clinicians.⁴ These care documents can be instituted in the ED. This tool focuses team care on the optimal relief of the dying patient's symptoms and the avoidance of unnecessary interventions. The intent is to provide hospice-level care in other clinical settings.

At this point, the principles of a good death previously described can act as an aspirational target as emergency clinicians attempt to rationalize the care they provide.

A large family may need significant space, which can interfere with the routine work of the ED; ideally a private room should be available. The clinicians' role then includes focusing on physical comfort, symptom management, and the privacy of the patient and family.

Death

Family members should be encouraged to be present during resuscitation efforts. A senior support person should be available for the family if at all possible during this time. As survival becomes increasingly unlikely, family members can be encouraged to be involved in decision making around resuscitative efforts and whether or not they should continue. After death, families should be encouraged to view, touch and talk to the deceased. It is well recognized that this facilitates the grieving process. They will remember these moments for the rest of their lives. Participation in the resuscitation process and in the decision to end it can be helpful.

Initiation of the grieving process

Quality management of grief states can prevent significant morbidity, as pathological or unresolved grief can lead to later problems with physical and mental health. Emergency physicians have a duty of care to the survivors and to playing their part in the initiation of family grief.

Grief is not like an illness, to be fought and cured, as so often is the case in Western medicine. Generalizations can be made about human behavioural tendencies and time lines can be drawn for predicted recovery, but each person's grieving process is unique. Some people never get better and nobody survives grief unchanged.

All relatives need time to receive the clear message of death, which they may have to be given again and again. Some need to make meaning of the event, and the clinical art of managing perceptions is paramount. For the families of the deceased, this time will be recalled with unrivalled clarity. It is a great privilege to be part of those memories and it carries the responsibility to assist the family in keeping with best-practice principles for the initiation of grieving.

Breaking bad news

The interview with the family of the recently deceased can be more difficult than the resuscitation. Handled with sensitivity, however, it can be a positive start to successful grieving and recovery.

Box 21.1.1 Ten key elements of best care for the dying

1. The fact that the patient is in the last hours or days of life should be acknowledged by the multidisciplinary team and documented by the senior doctor responsible for the patient's care.
2. Where possible and deemed appropriate by the relative, carer or advocate, recognition of the imminence of death should be shared with the patient.
3. The patient and relative, carer or advocate should have the opportunity to discuss the patient's wishes, feelings, faith, beliefs and values.
4. Anticipatory prescribing for symptoms of pain, excessive respiratory secretions, agitation, nausea and vomiting and/or dyspnoea should be in place.
5. All clinical interventions should be reviewed in the best interest of the patient.
6. There should be a review of hydration needs, including the commencement, continuation or cessation of clinically assisted (artificial) hydration.
7. There should be a review of nutritional needs, including the continuation or cessation of clinically assisted (artificial) nutrition.
8. There should be a full discussion of the plan of care with the patient where possible and deemed appropriate and with the relative, carer or advocate.
9. There should be regular reassessments of the patient at least every 4 h.
10. Care of the patient and relative, carer or advocate immediately after death should be dignified and respectful.

(From Ellershaw J, Lakhani M. Best care for the dying patient. *BMJ* 2013;347:f4428, with permission.)

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The room in which such information is given should be private and comfortable and contain a telephone. Tea, coffee, iced water and simple food should be readily available. If refreshments arrive soon after the news has been broken, this can help to diffuse tension. The offering of food is a time-honoured expression of warmth and comfort and facilitates communication and the grieving process.

The emergency physician should greet the family by name, confirm the relationship with the patient of each and shake hands or touch them gently. All parties should be seated, and a helpful way to start is to ask the family members what they know. A simple unambiguous summary of events should be given. This must often be repeated and the family members given time to ask questions.

It is important to use the word 'dead' or 'died'; euphemisms such as 'passed away', 'she's gone' and 'departed this life' are unclear messages that can mislead. The grieving process cannot start until there is acknowledgement of death. A truthful explanation can be comforting. There is no curriculum for teaching this type of interaction. Junior staff should be able to be present when a more senior staff member is conducting these discussions, thus facilitating role modelling. Over time, junior staff should be encouraged to facilitate these discussions in the presence of more senior mentors.

Sedatives

Requests for sedatives can come from survivors or a third party, who may ask that the bereaved be given medication. It is now recognized that the use of anxiolytic medication is contraindicated in early grieving. This must be carefully explained to families making such a request. Anxiety, sadness and insomnia can be a natural part of early grief.

Reactions

There is a range of responses to the information that a close relative has died. The mode of death can be a guide. Homicide can lead to great distress, along with suicide and unintended injury. Some common reactions are as follows:

- Disbelief: Some will immediately deny the event, claiming that it must be somebody else or that they are dreaming. Reinforcement is required.
- Numbness: Some sit mute, appearing not to take in the information. They need time to absorb it.
- Expressive: A sudden flood of tears or loud cries with upsetting or disturbing noises should be allowed to run its course. Such acknowledgement can be a positive response.
- Guilt: Particularly with homicide and suicide, such news is often followed by 'if only' or 'why couldn't I have?' Here, gentle repeated reassurance and discussion can be

important. These people are at risk of pathological grief reactions and can be helped by seeing the body and talking to it.

- Displacement activity: An immediate call to inform relatives, organize the funeral and discuss family matters is a poor prognostic sign. These people are often seen as mature, rational and born organizers, but they are at risk of pathological grief reactions months later.

Offers of follow-up can be made at this time. If the family members have unresolved questions, they need to have a contact in the ED to arrange further meetings if required.

Viewing the body

Relatives and their invited friends should be encouraged to view the body. By seeing the body, by feeling and touching it, the grieving process, separation and rebuilding can start. People should be encouraged to speak, touch, kiss, stroke, caress—even to argue, negotiate and cajole in private for as long as they wish. This facilitates natural grieving. The presence of a bereavement or viewing room can make this process much easier as, particularly with children, visiting can go on for several hours. A hospital morgue may be used; some have a purpose-built facility and appropriate staff support.

Cultural issues

Various ethnic and religious groups have differing practices for the handling and disposal of bodies. Emergency physicians should be able to manage different family requests in a sensitive manner while bearing in mind local statutory obligations.

In the case of Australians of aboriginal or Torres Strait Island descent, cultural practices and beliefs vary from region to region and families will guide practitioners. Aboriginal and Torres Strait Islander liaison services should be accessed.

Death certificates

Doctors managing deaths in the ED must understand and have a sound knowledge of reporting requirements for the coroner's court (see [Chapter 28.2, The coroner](#)).

Organ donation

A thorough knowledge of local definitions is crucial for the emergency physician expected to participate in efforts to improve the rates of organ transplantation (see [Chapter 21.7](#)).

Bereavement counselling

Most hospitals have qualified practitioners to support the recently bereaved. Referral should be

arranged prior to the family's departure if counsellors have not already made contact. Ministers of religion are trained in grief counselling and are usually available after hours. The general practitioner should always be promptly informed of the death of a patient. Social workers are expert in grief counselling and many funeral companies and coroner's offices now provide counselling services.

Subsequent issues

Permission to leave

Recently bereaved people are sometimes confused, frightened, stunned and at a loss as to what to do next. When forensic issues (identification and statements) and viewing have been completed, they can be given the dead person's possessions and politely given permission to leave the hospital. 'There is nothing more you can do' or 'Can I phone someone or get a taxi to take you home?' may be usefully offered.

Information about contacting a funeral office to arrange for collection of the death certificate and the body and to discuss burial rites should be given in a readily available explanatory leaflet.

Professional issues

One of the important aspects of looking after survivors is caring for the carers, who are often overlooked. That is, patient death has been reported to lead to physical and emotional symptoms in emergency medicine practitioners.⁵ Often, after an unsuccessful resuscitation, the professional may choose to talk about the events within the team environment. It is uncertain whether this improves psychological outcome. There is, however, a distinct propensity for those who spend their lives among the dying and their suffering to become cynical and full of black humour. The cultural norms of emergency medicine can become so integrated into personal values that the physician may not even recognize their presence. We should regularly assess our own emotional fatigue and, if there is a significant divergence between our personal values and career activities, we may want to seek support from a trusted source.

CONTROVERSIES AND FUTURE DIRECTIONS

- Partnering with palliative care colleagues will improve the skill mix of emergency clinicians. Local documentation to support the dying patient may be tailored for use in the ED or short-stay unit.
- Increasingly, attention will be paid to ensuring the well-being of staff who are constantly exposed to death and dying in the course of their duties.

21.2 SEXUAL ASSAULT

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21.2 Sexual assault

Jeremy Stevens

ESSENTIALS

- 1** Sexual assault is defined as an act of a sexual nature carried out against a person's will.
- 2** There is widespread under-reporting of this criminal offence.
- 3** The complex medical, legal and psychological sequelae mandate a team-based approach for victims involving doctors, police and counsellors in a collaborative effort.
- 4** Management by a sympathetic non-judgemental physician can help the victim to regain control.
- 5** Medical evaluation is specifically directed at the issues of injury assessment and management, infection risk and emergency contraception.
- 6** The forensic aspects of the examination require vigilant examination and documentation by the physician to assist the court in legal proceedings.

Introduction

Sexual assault is defined as an act of a sexual nature carried out against a person's will. Following sexual assault, a patient presenting should first be evaluated for acute traumatic physical injuries and drug or alcohol exposure. The victim should be offered prophylaxis for sexually transmitted infections (STIs) and pregnancy as appropriate. If the clinician is required to collect forensic evidence to assist in any police investigation, consent must be obtained for recording the victim's account of the assault, the findings on physical examination and the collection of forensic material. Follow-up medical care and psychological support should be arranged prior to safe discharge.

Definitions

Every jurisdiction has its own legislation and definitions used to describe all types of sexual offences with a lack of consent being the crucial issue. Sexual assault is an act of a sexual nature

where the victim does not give consent and includes attempts to force the victim into sexual activity. Types of sexual assault include rape (sexual penetration), sexual assault (intentional touching of a sexual nature) and attempted or threatened rape or sexual assault (assault with intent to commit a sexual offence). Penetration is not an essential element to sexual assault.

The absence of physical resistance by the victim is not regarded as consent. Consent means free agreement of a persons' free will. Consent is not given when a person is physically forced or intimidated or if he or she is incapable of giving consent due to being asleep or so affected by drugs or alcohol that free agreement is not possible.

Sexual assault by a carer upon a child or dependent person (such as a disabled person) is termed sexual abuse. In this case consent is not at issue as it involves the child in sexual activity that is either beyond the child's understanding or contrary to accepted community standards. Legal definitions regarding age vary depending on the jurisdiction.

Epidemiology

It is estimated that 0.4% of Australians aged 18 years and over experience sexual assault.¹ Crime statistics are limited; it is estimated, for example, in the Australian Bureau of Statistics Personal Safety Survey 2005, that only 19% of women who were sexually assaulted reported the incident to police.² Victims hesitate to report because of humiliation, fear of retribution, fear that they will not be believed, self-blame and lack of understanding of the criminal justice system.

Males experience sexual assault less frequently; for females, it is estimated that less than a quarter were assaulted by a stranger. Stranger assaults are more common among males.

Sexual assault is more common in vulnerable populations. Individuals in psychiatric facilities may be targeted and their reports may not be believed, as may occur with intellectually or physically disabled persons with diminished ability to detect or escape from such danger. Homeless women with serious mental illness have a very high lifetime risk for this violent victimization. Young adult male prisoners are also at risk.³

Barriers to care

The ABS study⁴ found that once an incident of sexual assault has been reported to the police, one in four cases results in the perpetrator being charged, but the conviction rate is low, with less than 50% of defendants found guilty. The study showed that 12.5% of women also did not report the assault to the police because of shame and embarrassment. Emergency physicians and nurses must be aware of these attitudes that the victim and they themselves may have when approaching the sexual assault victim. A non-judgmental, accepting stance by care providers is essential. It is not the health professional's role to make a judgement as to whether a criminal

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offence occurred; the courts will decide this. False allegations of rape are made, but such a person is likely to be in need of help in any event.

The role of the doctor in attending to victims of sexual assault who have consented to forensic examination and evidence collection is not the usual model of a therapeutic relationship. There is a dual obligation, as it is recognized that the physician has both a therapeutic role and a duty to the court to provide completely objective expertise in collecting evidence and interpreting the findings on examination to a court of law, where the impartiality of experts is key to their duty.

Consent

Victims who experience sexual assault frequently experience a loss of control and may feel in danger. For the person to regain control, every step of the process must be explained and consent gained. Consent must be obtained for the forensic examination and evidence collection and for the release of the information to the police. Consent must be informed, specific and freely given. The consent must be witnessed. The capacity of the victim to give consent has to be carefully assessed. The mental competence to understand the information can be impaired, for example, by the ingestion of drugs or alcohol, and the victim's mental state should be first tested. Certain patients are bound by formal legal requirements, which vary in each jurisdiction, for consent or responsibility for medical treatment. These include intellectually disabled persons, psychiatric patients under involuntary admission and children under custody orders or under the care of the state.

The evidence collected under this consent must be accurately labelled and secured.

Chain of evidence

Once a forensic specimen has been collected from its origin, all aspects of its existence must be recorded. All persons coming into custody of the specimen must be identified and the details of all transfers of custody and maintained security of the material must be recorded. A forensic register must be maintained for all items in a dedicated and secure storage facility.

Medical evaluation of the victim (MCQ 1)

The medical, forensic and psychological needs of a complainant depend on the nature and timing of the assault. The immediate medical needs are paramount. Medical care for victims of sexual assault includes consideration of physical injury, toxicological issues and the risks of acquiring an infection or becoming pregnant.

Evaluation of acute traumatic injuries is the first priority. The literature typically reports that about half the victims have some sort of physical injury,⁵ although less than 5% of victims require admission to hospital for treatment. An analysis of over 1000 cases in the United States⁶ revealed that physical examination showed evidence of general body trauma in 64% of victims. Genital trauma was noted in 52%, whereas 20% had no injuries documented. An Australian study confirmed non-genital injuries in 46% of women and genital injuries in only 22%.⁷ These findings indicate that many sexual assault victims may not have either general or genital trauma on examination, and this absence does not mean that an assault did not occur.

A study from Florida found that 1 in 1500 sexual assaults resulted in the death of the victim, with asphyxiation being the most common cause of death. Although there has been no comparable Australian study, the Australian Institute of Criminology reports that 288 homicides were committed in Australia in 2003 and that a sexual assault was the precipitating factor in 9.⁸

Survivors of strangulation may have no visible markings in up to 50% of cases.⁹ Although external injury may appear trivial, it may indicate potentially significant sequelae, both acute and delayed. Airway compromise from laryngeal injury, mucosal oedema or soft tissue swelling may occur, as may aspiration. Hypoxic brain damage depends on the duration of hypoxia and, if present, is usually obvious. Vascular injury, such as carotid artery dissection, has been reported and may present as a delayed focal deficit from subsequent stroke up to 2 weeks after the incident.¹⁰ Attempted strangulation warrants a high index of suspicion to rule out injuries, and a period of observation may be required.

Examination findings, where present, can include ligature abrasions, fingertip bruising from the assailant's grasp and curvilinear abrasions caused by fingernail markings, occurring singly or in sets, caused by the victim's struggle to pry the assailant's fingers from her neck. In addition subconjunctival haemorrhage and petechial haemorrhages of the skin may be present.

Penetration with foreign bodies can cause overt or occult pelvic injury. Further investigation or operative intervention may be necessary.

Forensic history, examination and evidence collection (MCQ 3)

The forensic history and examination is carried out for the purpose of obtaining evidence of the rape or assault that could be used in a prosecution. The aim is to record the victim's report of the assault and collect and record evidence related to this report as well as to collect DNA. Specific consent should be sought before this

examination is undertaken, as therapeutic benefit is not intended. Specific consent must be additionally obtained to turn over the specimens to the police. Police services produce kits that give a comprehensive guide to the history and examination, including body charts required for various aspects of the prosecution. Each emergency department (ED) should have access to a multidisciplinary team including a clinician trained in such collection. In many jurisdictions there may be a specified forensic medical service.

Physical examination recorded for the forensic record must include every wound detected on meticulous forensic examination. Injury could have been inflicted by the assailant or in the victim's attempted defence or escape; in the interpretation of the injury, even minor wounds that may not require treatment take on key forensic significance. Physical examination requires a sympathetic but professional and methodical approach of every body surface, as with the collection of relevant forensic samples. Every injury must be carefully recorded on a body chart. Height and weight are required for the interpretation of toxicological results.

Standard nomenclature including lacerations, abrasions and bruises should be used in wound description (Table 21.2.1). Correct anatomical sites must be recorded and labelled, including in genital examination.

A wound is a disruption in the continuity of tissues produced by physical injury. Description of the physical characteristics of a wound includes the site, size, shape and depth of the wound as well as the appearance of the wound edges and adjacent tissue, the contents of the wound and whether there is evidence of healing. Bruises may not occur at the site of the trauma and their size does not always correlate with the applied force; they may be altered by coincident conditions, such as anticoagulant therapy. The term *laceration* is often misused to describe an incised wound. The correct classification of injuries can assist in determining the mechanism of injury or the object or weapon that caused the injury.

Patterns of injury may be observed. Blows to the head, face and neck may cause bruising, lacerations and fractures and include hyphaemas, dental trauma and tympanic membrane perforation. Fingertip bruising and imprint bruising may be evident. Attempts at self-defence may result in injuries to the hands—for example, incised wounds to the palm or bruising on extensor surfaces of the arms. Fingertip bruising can be present on the medial thighs. Bite marks may be seen on breast or buttocks. Abrasions from contact with unshaven skin may be detected. Postmenopausal women are significantly more likely to need surgical management and repair of genital injuries than are younger women.¹²

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Table 21.2.1 Standard wound nomenclature and specific considerations

Wound type	Definition	Important descriptors	Considerations
Bruise	An area of haemorrhage within or beneath skin due to blunt trauma Also called haematoma, contusion or haemorrhage	Colour and pattern of multiple bruises	The age of a bruise cannot be determined by colour Yellow discolouration indicates bruise is at least 18 hours old ¹⁴
Abrasions	Superficial injury of skin caused by pressure and movement applied simultaneously	Shape and depth	May indicate direction May contain trace materials
Laceration	Ragged or irregular tear in skin, subcutaneous tissues or organs from blunt force	Size and depth	Irregular or crushed margins, bridges of intact tissue Intact structures within wound (e.g. tendons)
Incised wound	Injury produced by a sharp-edged object	Length, depth	Sharply defined edges

Examination of the genitalia includes the inner thighs, buttocks and anus. Common locations for genital injuries include tears or abrasions of the posterior fourchette (where the two labia meet posteriorly), abrasion or bruising of the labia minora and fossa navicularis (directly anterior to the fourchette) and bruising or tears of the hymen. After relevant forensic specimens have been collected, it may be necessary to use a Foley catheter to tease out any folds in hymenal tissue to facilitate the inspection of hymenal injury. An examination of the vagina and cervix can then be completed using a speculum. In the course of this any evidence of injury is recorded, as is any bleeding or discharge, with the source identified. Perianal injury may need a moistened swab to tease out folds for inspection and proctoscopy may be required for inspection as appropriate.

Despite the relatively low frequency of obvious injury, the documentation of such injuries increases the chance of successful prosecution.¹³ Photography must have the specific consent of the victim and is best performed by an experienced practitioner, and the secure storage of images must be ensured.

Collection of forensic specimens

The perpetrator may have left evidence on the victim. Sampling from sites of contact between the victim and assailant is the basis of evidence collection. Specimens collected are guided by the circumstances. Standardized evidence collection kits used in each jurisdiction contain both forms of swabs and slides appropriate to obtain trace evidence of saliva, semen, blood and skin-to-skin contact. Samples should be collected, allowed to dry, sealed and packaged with all contents carefully labelled and the chain of evidence maintained. Slides should be made where the presence of semen is suspected.

Any sample collected from the victim that contains cellular material from the victim's assailant

can be used for DNA testing. This includes spermatozoa, semen if it contains cells or blood or tissue from under fingernails, which should be clipped. DNA evidence left on or in the body of a victim, particularly in moist areas, degrades quickly over 2 to 10 days. The forensic assessment should thus be made as soon as possible. Underpants and panty liners worn during or after the assault may be contaminated with forensic material and should be retained. DNA, if moist, degrades quickly; therefore underclothes with overgrowth of organisms should be stored in paper and not plastic bags.

Proof of sexual contact is established by the detection of spermatozoa or semen either on or within the victim or on the victim's clothes. The likelihood of detecting spermatozoa or semen from the vagina is generally very low by 72 hours. However, under some circumstances, spermatozoa may persist for days longer and can be obtained from the endocervical os or cervix. The detection of sperm or semen from the rectum or mouth is possible but very dependent on the actions of the victim after the assault, which should be recorded. The presence of DNA in deposited saliva may give a positive result for up to 2 days. Skin swabs for epithelial cells are generally unhelpful after 12 hours.

Care must be taken when the victim undresses for the examination. Hair or clothing fibres from the offender or other traces from the crime scene may have adhered to the body or clothes of the victim. The victim should undress standing over a drop sheet, which should then be included in a bag into which the clothes are placed. This becomes part of the physical evidence.

The most accurate laboratory method currently available to identify the assailant is DNA testing. The chance of incorrectly identifying an alleged assailant as the source of DNA material is very small. However, the risk of contamination of the evidence samples with that of DNA belonging

to other individuals is significant and has resulted in wrongful incarceration.¹⁴ Accordingly, forensic collection and analysis techniques are under increasing scrutiny by the legal system and sources of contamination must be excluded. All measures to minimize DNA cross-contamination in the clinical setting—including the consistent use of gloves, gowns, mask and drapes—and in the techniques of collection must be taken and recorded.

Toxicological issues

Drugs may be administered to the victim in order to facilitate sexual assault. The commonest drug is alcohol, but large numbers of drugs, including flunitrazepam and gamma hydroxybutyrate (GHB), have been implicated and the victim may be unaware or have no memory of events surrounding the assault. Self-reported alcohol consumption immediately prior to assaults is very common, including up to 77% of those reporting drug-facilitated sexual assault, and alcohol is the most commonly detected substance on toxicological testing.¹⁵ This is likely to have had a significant impact on conscious state and the ability to consent at the time of assault and may impair the victim's subsequent recall of events. The victim is at additional risk, particularly where there is a combination with prescription or recreational drugs. The interpretation of drug levels and their possible effects is difficult. In general, urine is the preferred specimen, although blood samples should be collected within 24 hours of the assault, and these must be refrigerated prior to laboratory analysis.

Medical aftercare

The risk of genital infection after sexual assault (MCQ 4)

The risk of acquiring a STI following rape is reported to be 4% to 56%, with infection reflecting those organisms that are locally prevalent. One study showed that with baseline testing, 43% of victims had evidence of pre-existing infection.¹⁶ The finding of pre-existing infection is not admissible in court under Australian law. Most experts discourage testing for STIs in the ED unless the victim is symptomatic.

Baseline screening for the following infections is recommended in follow up:

- HIV: HIV antibody
- Hepatitis B: Hepatitis B surface antigen (HbsAg), hepatitis B core antibody (anti-HBc) and hepatitis B surface antibody (anti-HBs)
- Syphilis: Rapid plasma reagin (RPR) and *Treponema pallidum* haemagglutination assay (TPHA)
- Chlamydia: Polymerase chain reaction (PCR) endocervical swab, first void urine

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- Gonorrhoea: Endocervical swab, PCR and microscopy culture and sensitivity
- Trichomonas*: High vaginal swab, microscopy culture and sensitivity

Although the risk of acquiring an infection is difficult to define, antibiotic prophylaxis is not generally recommended for the victim unless the person committing the assault is known to be suffering from an STI, is at high risk for having an STI or is thought unlikely to return for follow-up. Poor follow-up rates are the norm and all patients should be offered prophylaxis in the ED if urgent follow-up cannot be ensured. If antibiotic prophylaxis is considered necessary, the regimens recommended for the treatment of gonococcal infection (which will also treat chlamydial infection) and trichomoniasis should be used. Prophylaxis for syphilis should also be considered (use the regimen for early syphilis).

Hepatitis B virus (HBV) can be transmitted by sexual intercourse but the risk of transmission is undefined. HBV vaccination and hepatitis B immune globulin (HBIG), 400 IU IM, should be available where the assailant is either known to be HBV-positive or the victim is considered to be particularly at risk of infection (refer to Chapter 9.6).

It is likely that the victim will be concerned about HIV or will become concerned at a later date. The offer of HIV testing should be made, accompanied by the usual full explanation. Written consent must be obtained before the test is done. HIV seroconversion has occurred in persons whose only known risk factor was sexual assault, although the frequency of this occurrence is thought to be low.¹⁷ In consensual sex, the risk for HIV transmission from vaginal intercourse is 0.1% to 0.2% and for receptive anal intercourse 0.5% to 3.0%. The risk of transmission from oral intercourse is much lower. Specific circumstances of an assault that might increase the risk for HIV transmission include the site of penetration, site of exposure to ejaculate and the presence of mucosal trauma, genital lesions or another STI.

Other factors that should be considered in the recommendation for post-exposure prophylaxis (PEP) include multiple assailants, the likelihood of an assailant having HIV (given the local epidemiology for HIV) and whether the assailant is from a high-risk group, including men who have sex with men or who use drugs by injection.

HIV PEP should be offered as soon as possible after the assault up to 72 hours post-exposure. Local and regional guidelines should be consulted (refer to Chapter 9.7)

Tetanus prophylaxis must be considered as part of the management of any injury.

Pregnancy prophylaxis

The risk of pregnancy following a single unprotected episode of coitus has proven difficult to define. However, a large prospective study from North America rated the risk of pregnancy from rape as 5%.¹⁸ Emergency contraception is readily available in Australian pharmacies and it is the responsibility of the medical practitioner to make sure that the patient knows of its availability and has immediate access to the medication.

Progestagen levonorgestrel is used alone for emergency contraception in a dose of 1.5 mg and can be given up to 5 days from the time of unprotected intercourse. If this single dose is given within 72 hours, the proportion of pregnancies prevented was 85% in the World Health Organisation's multicentre study.¹⁹ The earlier it is given, the more effective it will be.

The literature demonstrates that there is poor compliance with follow-up instructions in this setting. Arrangements for follow-up testing for pregnancy, STIs, HIV and hepatitis B vaccination should be supplied as written instructions, as victims may subsequently remember little of their interview.

Crisis intervention

Acute reactions to rape range from emotional numbing to shame, self-blame and severe emotional distress. The predominant reaction is a devastating sense of loss based on the fear for survival and the gross invasion of bodily boundaries, thus removing the victim's control over that which she finds most personal to her. Longitudinal data suggest that sexual assault survivors are at increased lifetime risk of post-traumatic stress disorder (30%) and major depression (30%). The input of sexual assault counsellors in evaluating the patient's immediate and ongoing emotional and safety needs must be in place prior to discharge. The role of various psychological therapies in decreasing long-term sequelae is not yet clear.

It has been found that the greater support the doctor provides the victim, the better the outcome. However, this study found doctors were the least supportive health professionals in this setting.

Children

Child sexual assault is ideally managed by a team with specific paediatric expertise. The circumstances regarding children who are the victims of sexual assault differ from those relating to adults. First, the child is likely to have been the victim of chronic abuse rather than an attack by a stranger. Second, almost always the offender will

be a man known to the child, often in a position of authority and trust. This introduces the issue of protecting the child from further molestation. The injury pattern is highly variable. Chronic sexual abuse tends to develop as a pattern of behaviour between the victim and the offender, beginning with touching and possibly leading to penetrative intercourse. This escalation of activity may evolve over a lengthy period and physical trauma may not be a feature. If the child has been the victim of a stranger assault, the risk of physical injury is greater than that for an adult victim.

Conclusion

A patient presenting for care after sexual assault should first be evaluated for acute traumatic injury and any intoxication issues. The victim should be assessed in order to offer appropriate PEP to pregnancy and sexually transmitted diseases including gonorrhoea, chlamydia, trichomoniasis, hepatitis B and HIV, plus routine tetanus prophylaxis. Specific informed consent must be obtained prior to forensic evaluation. The involvement of a multidisciplinary team with an experienced forensic examiner and sexual assault counsellor is of value. Discharge must not occur until the immediate safety of the victim has been ensured. Follow-up for medical issues and ongoing psychological support should be arranged prior to discharge. A sympathetic, non-judgemental approach on the part of the physician can help to improve the victim's outcome.

CONTROVERSIES AND FUTURE DIRECTIONS

- The incidence of sexual assault has previously been under-recognized among the disabled, mental health inpatients, military and police recruits in academies and a range of other institutional and educational settings.
- One of the most challenging areas is the endemic problem of violence, including sexual violence inflicted on indigenous women. Some groups of Aboriginal girls and women report that half of them have been the victims of incest or sexual assault.
- Every precaution must be taken to reduce possible cross-contamination of DNA during the collection and storage of forensic specimens.²⁰

Full references are available at <http://expertconsult.inkling.com>

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21.3 Family violence

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ESSENTIALS

- 1** Family violence encompasses physical, sexual, financial and psychological abuse.
- 2** All forms of family violence are inter-related in a complex way. Victims of violence may suffer many forms of abuse over their lives.
- 3** Between 30% and 50% of women and approximately 15% of men experience family violence over their lifetimes.
- 4** Family violence occurs across all socioeconomic, religious and cultural groups.
- 5** There is a range of barriers to disclosure and reporting to authorities.
- 6** Effectively responding to family violence requires a multidisciplinary and co-ordinated approach involving health practitioners, social services and justice agencies.

Definition

Family violence involves all types of violence within intimate or family relationships. It includes physical and sexual abuse, threats and intimidation, psychological, emotional and social abuse and financial deprivation; it can occur across the life span.

Physical violence is defined as intentionally inflicted harm using bodily force or a weapon. It encompasses sexual violence—such as non-consensual or coercive sexual activity using physical force—sexual harassment, stalking, forced or deceptive sexual exploitation, threats or intimidation and non-personal violence, such as intentional property damage. Psychological abuse, which frequently precedes physical abuse, may take the form of threats, verbal harassment, ridicule or behaviours designed to intimidate, humiliate, control and isolate the victim.

Family violence most often occurs within current or former intimate relationships and is described as a gendered phenomenon, as it is largely perpetrated by men against women. However, although women account for the larger proportion of victims, males can also be affected, and this form of violence may also occur in same-sex relationships. Family violence may involve any family member related by blood or law. Children may be directly victimized or suffer harmful consequences when they see, hear, witness or are otherwise exposed to the effects of family violence.

The subjective experience and definition of family violence are strongly influenced by

cultural beliefs and previous life experiences; the individual's perceptions of his or her experience may vary greatly depending on these differences.

Family violence is also referred to as *domestic violence* or *intimate partner violence*. The more inclusive term of family violence accounts for violence within a range of intimate and family relationships.

Incidence

The prevalence of family violence varies according to definition (whether sexual and emotional abuse are included), timing of the abuse (current, during adult life or cumulative lifetime prevalence) and whether the violence is actual or threatened. In Australia, 1 in 6 women and 1 in 16 men from 15 years of age onwards have been reported to have been victims of physical and/or sexual violence by a current or previous cohabiting partner.¹

Australia's National Research Organisation for Women's Safety (ANROWS) reports that one in four Australian women had experienced emotional abuse by an intimate partner since the age of 15 years.⁹ In contrast, one in seven Australian men had experienced emotional abuse by an intimate partner since the age of 15 years.⁹ It is reported that 6% of women who had experienced violence from an ex partner had children in their care when the violence occurred.⁹ Women are at greater risk of experiencing family violence during pregnancy and the early years of motherhood. Women will often experience family violence for the first time during pregnancy or experience an increase in the type or intensity of violence.²

Vulnerable groups

Certain groups within the population may be more vulnerable to the effects of family violence. Among these are indigenous communities, culturally and linguistically diverse (CALD) communities, people with disabilities and the elderly. They may experience distinct forms of abuse specific to their particular group or community.

Indigenous communities

Members of indigenous communities may be exposed to heightened levels of family violence. Indigenous women are five times more likely to be the victims of family violence and homicide than non-indigenous women.³

Culturally and linguistically diverse communities

CALD communities experience additional complexities with respect to family violence. Although it is important to avoid generalizations and stereotypes, cultural values and beliefs can have implications for the way in which the individual experiences and responds to violence. CALD victims may encounter greater difficulty obtaining assistance and support from mainstream service providers for reasons including discrimination and marginalization, lack of awareness of their legal rights and protections, immigration issues, concerns regarding bringing dishonour to the family, fear of authority figures and communication barriers.

Disability

Women with disabilities can be disproportionately affected by family violence. Victims with cognitive and physical disabilities experience greater difficulty in accessing mainstream services due to communication barriers, lack of appropriate transport and accommodation, reliance on the perpetrator of violence and limited recognition of their victimization status.

Elderly

The elderly are at risk of abuse from people on whom they depend. Physical or cognitive impairments add to their vulnerability. Older persons can become socially isolated due to a decline in social contacts and supports, thus increasing the risk that abuse will go undetected.

Risk factor identification

The identification of risk and factors contributory to family violence within intimate relationships has allowed for improved understanding of the nature, form and degree of danger to victims as well as the conditions under which incidents of family violence are more likely to occur.

Although the growing evidence base about risk factors has informed the development of a variety of tools and measures designed to improve and detect those at risk, the presence of these factors is not an infallible predictor of violence. For example, some victims with multiple risk factors will not experience escalating or severe violence, whereas fatal family violence can occur in the absence of clearly defined risk and contributory factors.

Despite this caveat, understanding these factors is an important step toward improved identification and intervention in violent behaviour. To this end, risk factors are generally classified at the level of the individual, relationship and social environment.

Individual-level risk factors have been identified for both victims and perpetrators of violence. Individual characteristics associated with men having an increased risk of perpetrating violence are alcohol abuse, drug use, low education standards, unemployment and being a former rather than current partner. There is some association between perpetrator mental health and violence, particularly conditions such as depression and psychosis. Problem gambling is also a risk factor for both the perpetration of family violence and victimization.

For victims, pregnancy and new birth have been associated with both emerging and escalating violence. There are other risk factors for both victim and perpetrator, and family violence specialists are best placed to determine this risk.

At the level of the relationship, a history of abusive and violent behaviour is among the strongest predictors of further violence. Separation or the announcement of an intention to end an intimate relationship is associated with an increased risk of violence.

Social environment factors affecting family violence include gender inequality supported by societal norms and economic or social policies that create or sustain inequalities.

Family violence has now been identified as a health issue that affects health outcomes in a multitude of physical and psychological ways. Most presentations to health professionals and emergency departments (EDs) by victims of violence are a complex mix of indirectly related physical and psychological problems and are not trauma related.

Physical injury and illness

Physical injuries resulting from family violence may have patterns similar to those of other forms of non-accidental injury, such as a history inconsistent with the injury, injuries of varying temporal stages or unreasonable delay in presentation. Non-accidental injuries are often in central rather than peripheral areas of the body. Injuries to defensive areas of the body or to the back, legs, buttocks, back of the head and soles of the feet reflect attempts at self-protection. Injuries inflicted on females are likely to be contusions, abrasions, lacerations, fractures and dislocations. The head, face and trunk have been identified as primary targets in intimate partner violence; therefore further research into intimate partner violence and traumatic brain injury has been recommended. Women are more likely to be choked, beaten or sexually abused. Men have a greater risk of having objects thrown at them or weapons used against them. Although family violence-related injuries may follow certain patterns, injury pattern is of low positive predictive value in the identification of family violence.

Abuse before, during and after pregnancy represents a threat to the well-being of both mother and baby. Approximately 40% of women who are physically abused are forced into non-consensual sex at some stage. This results in high rates of sexually transmitted disease, unintended and adolescent pregnancy and termination of pregnancy. There is also an established complex link between family violence and preterm labour, low-birth-weight babies and postnatal depression.

Prevention of access to or interference with general health care or antenatal care may occur, with up to 17% of abused women reporting partner interference with accessing health care.

In Australia, homicide among intimate partners and other family members forms a substantial proportion of annual homicide incidents. Between 2002 and 2012, approximately 41% of all homicide incidents were categorized as domestic/family homicides.⁴ Many homicide victims had presented to an ED in the 2 years preceding their death. Documentation of violence and intervention are often uncommon.

Psychological impact

Family violence is an independent risk factor for mental illness. Women who have experienced family violence have an approximately 11-fold increase in dissociative disorders, 6-fold increase in somatization disorders, 5-fold higher incidence of anxiety and are three times more likely to suffer depression, phobias and drug dependence.^{5,6} Exposure to family violence has also been shown to be associated with the onset of post-traumatic stress disorder. Abused women have twice the rates of hazardous alcohol consumption and

dependence.⁶ Abuse occurring both in childhood and adulthood causes a further significant increase in the incidence of mental illness. The experience of psychological abuse, especially ridicule and humiliation, is particularly responsible for causing low self-esteem.

Impact on children

The impact of family violence on children includes potential victimization, witnessing violence, separations from family, foster care, risks of future mental illness and an increased potential to perpetrate violence in the future.

Children living in a home where violence is perpetrated against a parent are 15 times more likely to be victims of abuse or neglect themselves. Family violence is a risk factor for becoming a perpetrator of homicide in the pre-teenage group.

Sustained exposure to family violence contributes to cumulative harm for children, affecting their development, behaviour and well-being. Overall, approximately one-third of the population risk for all mental illness is attributable to family violence.⁵

Social

A perpetrator's controlling behaviour towards a victim can lead to the victim's social isolation, failure to acquire paid employment and lack of contact with medical practitioners.

Financial dependence and the responsibility for children increase isolation; there is also a loss of choices and the difficulty of separating from the perpetrator. Poverty among such victims is prevalent and multifactorial. Separation from or incarceration of the perpetrator may lead to further loss of income.

Homelessness may be relative, where there is no sense of safety or security in the home, or absolute, where there is a need for interim or emergency accommodation or where families are forced to live on the streets. Children or elderly people living in violent circumstances may be institutionalized by authorities or carers.

Outcomes for male victims differ from those for female victims in several significant ways. Male victims typically express fewer feelings of fear and terror and less frequently feel trapped and controlled. Men are also generally less constrained by financial dependence. As fear, control, dependence and isolation contribute greatly to the psychological outcomes of family violence, women still suffer approximately 95% of the serious physical and psychological consequences of family violence.⁶

Economic cost

The costs of family violence are vast. Costs include pain, suffering and premature mortality, health costs (victim, perpetrator and children),

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CHALLENGING SITUATIONS

production-related costs (lost productivity), consumption-related costs (property replacement), second-generation costs (child care, child protection), administrative (legal and forensic) and transfer costs (income support, lost taxes). The cost of intimate partner violence against women in Australia is estimated to be \$12.6 billion per year.⁷ If no further action is taken to prevent violence against women, it is estimated costs will accumulate to \$323.4 billion over the 30-year period from 2014 to 2044.⁷

Barriers to the detection and reporting of family violence

Detection rates of family violence in EDs are low. Only 10% of those who present with acute family violence-related injuries or issues will be asked by the attending nurse or physician to volunteer information about the violence issue. Documentation of violence in the medical record is rare. Barriers to detection may include system factors, such as inadequate privacy; cultural, social and gender issues; and/or the health practitioner's lack of time and education as well as his or her personal attitudes. The Victorian Royal Commission into Family Violence identified health professionals as being in a unique position to identify and respond to family violence and recommended that they receive targeted training to improve their awareness and responses.

Crime statistics in Australia show a general increase in the reporting of family violence. A range of barriers can inhibit victims' disclosures, including feelings of fear and shame, concerns about not being believed or about further victimization, anxiety about possible medical or legal processes, as well as familial, cultural or religious pressures. In some cases, individuals do not recognize themselves as victims of violence or may not yet have considered seeking assistance in respect to their violent partners.

Indigenous women in Australia rarely report violence. Historical interactions with police, such as forcible removal of children and high rates of Aboriginal death in custody, contribute to indigenous women fearing for the safety of themselves and their families when police or social services are involved. Moreover, the lack of accessible and culturally appropriate legal processes creates further barriers to reporting. The elderly may be prevented from reporting by fear of further abuse, neglect or the threat of institutionalization.

The Royal Commission into Family Violence highlighted that the following groups; indigenous, CALD, disabled, elderly, Lesbian, Gay, Bisexual, Transgender, Intersex, Queer/Questioning and Allied (LGBTIQA), rural, faith community, male victims, women in prison, women in the sex industry. These individuals face unique barriers to reporting their experiences of family violence and to accessing appropriate services.

Screening

The high prevalence of family violence, low positive predictive values of demographic factors and clinical presentations, low detection rates and high incidence of subsequent physical and psychological illness have supported the argument for universal screening. Opportunistic screening may increase detection rates of family violence. The use of a single screening question may be as effective as asking several questions. The use of sensitive inquiry is recommended.⁸ Screening questions should be simple and direct, such as 'Do you feel safe at home?' or 'Are you afraid of your partner?' Explanation that these questions are routine may improve patient comfort. Such questions must always be asked in a safe environment (with no family member present aged over 2 years).⁸

Screening may indicate to the victim that channels of communication are open and that help will be available. It educates women about violence, its nature and prevalence. Screening may also be important in detection of perpetrators.

Most women find screening an acceptable practice; however, most medical practitioners and nurses are not in favour of it. Reported barriers include a lack of education on how to ask questions about abuse, language barriers, a personal or family history of abuse and time constraints.

Screening may improve detection rates and referral rates to external agencies. However, no evidence currently exists to show that screening leads to improved health outcomes for victims.

Management

The management of family violence is complex. Leaving a violent relationship is no guarantee of safety and may precipitate increased levels of violence. Leaving a violent relationship is a process rather than an event and requires support through all phases. Help may best be offered by a collaborative team approach; validating the disclosure, expressing concern, listening, providing support, ensuring safety and offering a bridge to services.

Understanding

Interviews with survivors of family violence provide a framework for understanding the stages through which a victim must work before leaving a violent relationship. The pre-contemplative phase is where the victim is not consciously aware of or is in denial about the abuse. A contemplation phase follows, where the abuse is acknowledged but the victim is unable to decide to leave. A preparatory stage follows, where steps are taken in preparation for leaving and taking action. The action phase involves leaving

the relationship but is typically characterized by episodes of return to the relationship. A maintenance phase occurs when a period of 6 months without return to the relationship has occurred. However this is not a sequential process.

Listening and understanding where the victim is in terms of progress through these phases assists in assessing readiness for change and guides intervention. The aim is to validate the person's experience, emphasize that they did not deserve or cause the abuse and empower the making of independent decisions that lead to improvements in safety and well-being.

Referral

There are multiple services to assist victims of family violence. If available, consult internal specialists for more information and advice (e.g. social work, mental health). Relevant external services to consult include a family violence crisis line, family violence outreach and men's referral service.

Safety

Safety is paramount and emergency accommodation or hospital admission may be required to ensure immediate safety. Safety is an ongoing issue as the greatest risk of injury occurs while leaving the relationship and for the 6 to 12 months after separation. Most cases of family violence homicides occur as the woman is leaving or has left the home. Continued contact with the perpetrator due to custody issues makes the risk of abuse a continuing one. Internal and external specialist services can assist with safety planning for the victim/survivor.

Reporting

Most Australian states and territories have not implemented mandatory reporting of family violence for adults. The exception is the Northern Territory, where mandatory reporting provisions were introduced in 2009. In contrast to adult victims of family violence, all Australian states and territories have some type of mandatory reporting of suspected cases of child abuse and neglect. Variations exist regarding which professionals are legally required to report; however, these generally include doctors, nurses and midwives. Most jurisdictions protect the identity of persons making a notification whether mandated or not.

Documentation

Documentation in the medical record may provide vital evidence and should be objective and accurate. Direct quotes and descriptions of behaviours and appearances increase objectivity. Body maps and photographs assist documentation of physical injury. Sexual assault examinations ideally should be performed by specially trained staff to ensure legal admissibility of evidence.

21.4 ALCOHOL-RELATED ILLNESS

Careful consideration must be given to ensure the security/safety of patient information so as to avoid placing the victim at further risk of violence.

The management of family violence requires a co-ordinated response from all practitioners and service providers involved from when the victim first discloses the violence. This may include the health system, social services and the police and judicial system. At all times, the victim's wishes must be paramount and the service providers should do their utmost to support these wishes.

Conclusion

Family violence is a pervasive social problem that does not discriminate across age, cultural background, religion or socioeconomic status. The implications of family violence are substantial, including physical injury, mental illness, economic and social costs and fatal outcomes. Despite the high prevalence of family violence, it frequently remains undetected and unreported. Identification of risk factors for violence and interventions aimed at increased identification and referral can be considered in the ED

environment. When violence is disclosed, the expression of concern and a willingness to listen, risk assessment, safety planning, support and stage-appropriate referral are the mainstays of management.

CONTROVERSIES AND FUTURE DIRECTIONS

- Although there has been considerable research on screening for family violence in emergency departments, further research regarding the outcomes after screening interventions is required to ensure the efficacy and safety of screening.
- Mandatory reporting of violence among adults remains controversial.
- Management strategies should not be aimed at encouraging a woman immediately to leave the violent relationship. Risk assessment, safety planning, support and stage-appropriate referral are the mainstays of management.

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21.4 Alcohol-related illness

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ESSENTIALS

- 1 Acute alcohol intoxication and withdrawal are responsible for many emergency department attendances and carry significant morbidity and mortality.
- 2 Chronic gastrointestinal and hepatic disease, mental illness, central nervous system disease and immunosuppression are common in alcohol-dependent persons, with complications that increase the morbidity and mortality further.
- 3 Wernicke encephalopathy is an uncommon but serious illness related to vitamin B₁ deficiency. Treatment requires high-dose parenteral thiamine.
- 4 Many serious illnesses mimic alcohol intoxication or are masked by it. Maintain a high index of suspicion in the intoxicated patient with an altered state of consciousness.
- 5 Emergency physicians are uniquely placed to screen for high-risk drinking and other drug use as well as to offer brief advice or intervention to this group to reduce the burden of recurrent alcohol abuse.

interpersonal violence and self-harm. Chronic alcohol use contributes to many hospitalizations and deaths due to alcohol-related medical conditions and injuries, resulting in both physical and psychosocial impairment.

Many acutely intoxicated patients have significant co-morbidities masked by alcohol.

Patient with alcohol use disorders may present in states of acute alcohol intoxication or withdrawal. Emergency physicians should not only recognize and treat alcohol-related emergencies but also intervene in patients at high risk from their alcohol intake who present with other conditions. Early opportunistic screening using recognized alcohol screening tools and standardized brief interventions reduce 'at-risk' drinking and the morbidity and mortality from alcohol-related illness.

Epidemiology

Australia was ranked second of 34 Organisation for Economic Co-operation and Development (OECD) countries in alcohol consumption per capita in 2015. Australian alcohol consumption per capita is estimated at 11.2 L of pure ethanol per person per annum.¹ A study in five rural EDs

Introduction

Alcohol use disorders, which include alcohol abuse and alcohol dependence, are common across the world and have a high prevalence in emergency department (ED) presentations.

Alcohol misuse not only places the individual at risk of acute intoxication and injury but also poses significant long-term health issues.

Acute alcohol intoxication causes much morbidity and mortality from all forms of trauma, including falls, motor vehicle and other accidents,

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in New South Wales found that the percentage of patients engaging in risky drinking ranged from 4% to 32%.² A point prevalence survey of ED patients showed that 1 in 5 Australians and New Zealanders drank at levels that increased their lifetime risk of alcohol-related disease or injury and also that 17% to 35% of injury presentations to EDs involved alcohol consumption.³ One in seven of all patients presented for reasons related to alcohol consumption, and in certain departments the prevalence was as high as one in three. There are more alcohol-related presentations due to injury during weekends, but patients with alcohol-related conditions present to ED at all times throughout the week. The patients tend to be younger (age groups 18 to 29 and 30 to 39 years), male and brought to the ED either by ambulance or police.^{3,4}

Six percent of young persons (aged 12 to 19 years) attending city hospital EDs are there for alcohol-related reasons, with injury significantly more likely among alcohol users than among illicit drug users.⁵ Among young people attending the ED, nearly 38% may be drinking harmfully, 18% may have consumed alcohol in the previous 6 hours and 15% consider their attendance to be alcohol-related. Up to 45% of injured patients attending EDs may have consumed alcohol within the previous 24 hours and almost 30% in the previous 6 hours.⁶

The natural history of alcohol dependence is to remit and relapse, with a relentless progression to early death. Risk factors for alcoholism include a family history of alcohol dependence or total abstention, parental divorce, youngest child, other substance misuse, availability of alcohol and extremes of income.

Pharmacology

Pharmacokinetics

Ethanol is passively absorbed from the entire gastrointestinal tract (GIT), with about 25% from the stomach. Absorption is rapid, within 60 to 120 minutes of intake, and may be slowed by food. Ethanol is distributed throughout the body water; females and obese people with lower ratios of body water to fat reach higher blood alcohol concentrations (BACs) sooner than their leaner counterparts. Hepatic oxidative metabolism occurs via alcohol dehydrogenase. Alcohol-tolerant people also utilize the hepatic microsomal ethanol oxidizing system, which is upregulated with increasing drinking. First-order elimination kinetics becomes saturated as the BAC increases, changing to zero-order kinetics and slower sobering at higher BACs.

Pharmacodynamics

Alcohol is thought to act on γ -aminobutyric acid A (GABA_A) inhibitory neuroreceptors in the brain,

causing central nervous system (CNS) depression. The characteristic euphoria is thought to be related to the release of endogenous opioids (endorphins). A rapidly rising BAC causes quicker and more pronounced behavioural changes than the same level achieved over hours. A steady state of absorption to metabolism and excretion can be achieved at about one standard drink per hour. A standard drink is defined as containing 10 g or 12.5 mL of pure alcohol. Acute intoxication depends on factors such as habituation, food co-ingestion, body habitus and the concentration of alcohol in the drink.

Measurement of blood alcohol concentration

The blood alcohol concentration may be estimated using a Breathalyser that estimates BAC after measuring alcohol concentration in alveolar air. This is a useful non-invasive screening tool but relies on a cooperative and awake patient being able to exhale adequately for the reading. There is an approximate difference of 15% to 20% between breath alcohol readings and serum BAC. Readings are influenced by many factors, including temperature, hyper- or hypoventilation prior to exhalation, haematocrit level, other substances such as ketones, time since ingestion and machine error. A directly measured serum blood alcohol concentration is more reliable. The Australian legal limit for driving is 0.05%; in New Zealand it is 0.04%, whereas in the United States and the United Kingdom it is 0.08%.

Chronic alcohol-related illness

Gastrointestinal

Chronic alcohol use results in disease of the GIT, liver and pancreas. Morbidity most frequently arises from GIT bleeding, liver disease and pancreatopathy.

Gastrointestinal bleeding

The most common causes of alcohol-related GIT haemorrhage are peptic ulcer disease (PUD) and the consequences of portal hypertension, such as oesophagogastric varices or subepithelial gastropathy. Mallory-Weiss tears, oesophagitis and alcoholic gastropathy are less frequent causes of alcohol-related GIT haemorrhage. Heavy alcohol use may be a risk factor for the development of PUD, although the exact pathogenesis is poorly understood and the role of alcohol may be additive to the effects of *Helicobacter pylori*, non-steroidal anti-inflammatory drugs (NSAIDs) and tobacco.

Although Mallory-Weiss tears are less common, up to 44% are associated with alcohol use and may account for significant morbidity due to blood loss.

Alcoholic liver disease

Alcoholic liver disease (ALD) comprises a spectrum of disorders from alcoholic fatty liver (steatosis) and inflammation (hepatitis) to progressive fibrosis (cirrhosis) and hepatoma. These occur from chronic insult to the liver due to oxidative stress, damage from free radicals and the immunogenicity of alcohol metabolites. Many factors are involved in the aetiology of ALD, including genetic predisposition, gender, ethnicity, nutrition, ingestion of other hepatotoxic agents (i.e. drugs of abuse, weight-loss supplements, paracetamol), obesity and co-existent chronic viral hepatitis, non-alcoholic fatty liver and other liver diseases, such as autoimmune conditions.

The duration and amount of alcohol consumed play important roles; drinking at levels above the National Health & Medical Research Council (NHMRC), Australia recommendations (more than two standard drinks a day, both in men and women) is a defined risk for the development of alcohol-related injuries, ALD and eventual cirrhosis. The NHMRC also recommend drinking less than four standard drinks per occasion so as to reduce the short-term adverse effects of alcohol use, in particular alcohol-related injuries. Alcohol dependence does not inevitably lead to cirrhosis, which occurs in only 10% to 20% of heavy drinkers.⁷ Alcoholic fatty liver is a common finding among alcohol-dependent patients but is not a frequent cause for presentation to an ED.

Alcoholic hepatitis and cirrhosis Alcoholic hepatitis may present as acute anorexia, nausea, vomiting, right-upper-quadrant pain and jaundice. Treatment is supportive and abstinence from alcohol is essential (see Chapter 9.6).

Cirrhosis typically presents late, with subtle malaise, anorexia, weight loss, weakness and fatigue along with a combination of liver cell failure and the development of portal hypertension. Acute decompensation usually manifests as symptomatic ascites, jaundice, pruritus, spontaneous bacterial peritonitis (SBP), hepatic encephalopathy, variceal bleeding and/or coagulopathy.

Ascites Ascites due to hypoalbuminaemia, secondary hyperaldosteronism and portal hypertension is usually recurrent. Sudden exacerbations may be caused by SBP, portal vein thrombosis, a hepatoma or medication non-compliance. Symptoms include abdominal discomfort, girth increase and anorexia. Fever, chills and abdominal pain occur with SBP or, conversely, signs of sepsis may be minimal but there is a sudden worsening of jaundice or encephalopathy.

Coagulopathy and encephalopathy Coagulopathy results from the failure of hepatic synthesis of coagulation factors, thus parenteral

administration of vitamin K and factor concentrate or fresh frozen plasma is required in the bleeding cirrhotic patient. GIT bleeding may also precipitate hepatic encephalopathy, with confusion and characteristic asterixis. This potentially reversible decrease in neuropsychiatric function must be distinguished from other causes of an altered level of consciousness in the cirrhotic patient.

Hepatic encephalopathy is associated with an increased nitrogenous GIT load (as from a gastrointestinal bleed), dehydration, sepsis, certain drugs, hyponatraemia or hypokalaemia, worsening liver function and increasing jaundice.⁷

Thrombocytopaenia Thrombocytopaenia is a common finding in. The aetiology is multifactorial: direct toxicity of the alcohol on the bone marrow, portal hypertension and platelet sequestration in the enlarged spleen, decreased thrombopoietin (TPO) synthesis in the liver, with a subsequent reduction in the proliferation and differentiation of megakaryocytes and platelet formation.

Alcoholic pancreatitis

The term *alcoholic pancreatitis* describes a group of pancreatic diseases caused by chronic heavy alcohol intake. It includes acute alcoholic pancreatitis, recurrent abdominal pain or GIT symptoms induced by alcohol, high serum levels of pancreatic enzymes or an abnormal pancreatic ultrasound. Recurrent bouts of acute alcoholic pancreatitis precede the development of pancreatic pseudocysts, chronic pancreatitis and pancreatic malignancies.

Alcohol is the most common aetiology of chronic pancreatitis (70% to 80%), although as few as 10% of heavy drinkers will develop it. Like cirrhosis, its aetiology is multifactorial; other risk factors include tobacco smoking and hyperlipidaemia, which should be addressed if early signs of pancreatitis are recognized. Alcoholic pancreatitis, both acute and chronic, is managed conservatively with abstinence from alcohol as well as the administration of intravenous fluids, parenteral analgesia and, if pancreatic necrosis or an abscess is suspected, antibiotics (see Chapter 7.9).

Chronic pancreatitis can be debilitating, with recurrent cycles of pain and admissions to hospital. Progressive pancreatic calcification, failure of exocrine and endocrine function and chronic pain can all be mitigated if alcohol is avoided. Recurrent pancreatic insults and chronic pancreatitis increase the risk of pancreatic carcinoma by up to 16 times.

Mental health and mental state issues

Depression and suicidal intent

Alcohol is a recognized risk factor for suicide. Mood expression and intent of self-harm are

often underestimated when intoxicated patients are seen in the ED. A Scandinavian study showed that 62% of 1207 'parasuicides' who presented to an ED involved alcohol use, with even higher rates in young males. Psychiatric referral was less likely if alcohol was involved; yet, after 5.6 years, 3.3% of these individuals had completed suicide. This represented a 51-fold increased risk compared with the general population, with the risk of completed suicide being greatest in the first year.⁸

Alcoholic hallucinosis

Alcohol misuse causes psychotic symptoms by several mechanisms, including direct intoxication, alcohol withdrawal, delirium tremens (DTs), Wernicke encephalopathy, Korsakoff psychosis and alcoholic dementia. Alcohol dependence doubles the risk of psychotic symptoms.

Alcoholic hallucinosis is a schizophrenia-like syndrome that differs from the other causes in that it occurs at a younger age, in a setting of clear consciousness and unrelated to acute withdrawal. There are no associated physical symptoms of autonomic dysfunction, as in the DTs, and its duration is longer, with predominantly auditory hallucinations as opposed to visual ones. Its chronicity and the derogatory auditory hallucinations are similar to those occurring in schizophrenia, but thought disorder is not a feature.

Alcohol withdrawal states

The alcohol withdrawal syndrome follows prior alcohol dependence. Its clinical importance lies in the potential severity of the symptoms and signs, the need to consider alternative or comitant pathology and the likelihood of seizures occurring. The principal symptoms are tremor, agitation, nausea and vomiting, sweating, anxiety and autonomic nervous system overactivity with tachycardia, tachypnoea and fever. Sleep disturbance, hallucinations and generalized tonic-clonic seizures often begin within 10 hours of reduced alcohol intake, with peak intensity by day 2; it may last up to 5 days.

Alcohol withdrawal scales A number of scales measure alcohol withdrawal. One simple one is to rate symptoms as mild (tremulousness), moderate (agitation) and severe (confusion). Most EDs use an alcohol withdrawal scale (AWS) to measure symptoms, predict the likelihood of seizure and direct preventative management. The most commonly used AWS is the Clinical Institute Withdrawal Assessment—Alcohol, Revised (CIWA-R) scale. This scale measures 10 items and was primarily developed for planned detoxification or for use on general medical and psychiatric wards. Surprisingly, blood pressure and pulse, although often abnormal, are not included in the

scale. A modified version that includes seizures in the AWS is also used.⁹ Patients with high scores have an increased risk of seizure if they remain untreated. The higher the score, the greater the relative risk.

Pharmacological therapy Benzodiazepine (BZD) therapy reduces signs and symptoms of alcohol withdrawal and prevents complications.¹⁰ All BZDs appear to have similar efficacy, but diazepam, lorazepam and chlordiazepoxide have been studied most. Longer-acting agents, such as diazepam used with symptom-triggered dosing (as opposed to regular), decrease the total of drugs given and both shorten and smooth the clinical course. Early treatment is preferred to waiting for advanced withdrawal.

Published data on ideal doses are lacking. High-dose oral diazepam 20 mg q1–2h may be needed for symptom control and up to 160 mg/day may be required to allow for BZD tolerance, which is common in alcohol-dependent patients. Under-dosing for fear of over-sedation is common.

Antipsychotics such as droperidol, haloperidol and olanzapine are commonly used to manage the agitation and other behavioural disturbances induced by severe alcohol withdrawal. However, they lower the seizure threshold and can cause anticholinergic syndrome if given in excessive doses. They can also cause prolongation of the QT interval and increase the risk of torsade de pointes in alcoholic patients, who are often hypokalaemic, hypocalcaemic and hypomagnesaemic. Ethanol, of course, would 'treat' the symptoms of withdrawal; however, it has been shown to be inferior to BZDs.¹¹

Baclofen, a GABA_A agonist, is increasingly used in the management of alcohol withdrawal, with various studies showing efficacy in decreasing withdrawal symptoms.¹¹

Alcohol withdrawal seizures Around 3% to 5% of those with severe alcohol use disorder experience withdrawal seizures within 48 hours of stopping drinking, and 15% will have a seizure within their lifetimes. Previous withdrawal seizure is the strongest predictor of recurrent seizure. Most alcohol withdrawal seizures are short-lived and self-terminating. They occur early (usually 7 to 24 hours after the last drink), are grand mal in type (i.e. generalised, not focal); they usually (though not always) occur as a single episode. Localizing signs or prolonged seizures should prompt a search for alternate pathology. Intravenous BZD are the first line treatment for seizures secondary to alcohol withdrawal using the same doses as for seizures of any other cause (see Chapter 8.5). Phenytoin is not recommended for alcohol withdrawal seizures unless there is a coexistent epileptic disorder.

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Delirium tremens 'DTs' are characterized by confusion, altered conscious state and autonomic hyperactivity. They usually develop 2 to 5 days after stopping or significantly reducing alcohol consumption. It usually lasts between 1 and 3 days, but in severe cases it can last up to 14 days. The incidence of DTs is reduced by effective early management of withdrawal and the exclusion of intercurrent illness. DTs occur in less than 1% of cases during any single withdrawal episode. The diagnosis is important, as the mortality from DTs approaches 15% if left untreated. As symptoms usually manifest within 48 hours, DTs may be encountered in EDs experiencing access block or in short-stay observation units.¹²

Risk factors associated with the development of DTs are older age, intercurrent illnesses, tachycardia greater than 120 beats/min, signs of alcohol withdrawal at BAC of more than 0.1%, seizure history and history of delirious episodes.¹¹ DTs are rare in the absence of these factors. The treatment includes management in an intensive care unit (ICU) with regular intravenous BZD, such as midazolam 0.1 to 0.2 mg/kg, and treatment of any underlying conditions, such as sepsis.^{13,14} If treatment is required for hallucinations, the drug of first choice is diazepam. If hallucinations do not respond to diazepam alone or the patient has an underlying thought disorder, an antipsychotic such as olanzapine, haloperidol or droperidol may be added.

Wernicke encephalopathy

The classic features of Wernicke encephalopathy are ataxia, confusion and ophthalmoplegia, usually lateral rectus palsy. This is caused by thiamine deficiency, but severe deficiency may be present without these signs.¹⁵ In alcohol-dependent persons, oral thiamine absorption is poor. Malabsorption, reduced storage and impaired utilization of thiamine increase the risk of Wernicke encephalopathy.

Post-mortem studies suggest that thiamine deficiency sufficient to cause irreversible brain damage remains undiagnosed ante-mortem in 80% to 90% of alcohol-dependent persons. Wernicke encephalopathy should be considered in all patients in coma, as replacement of depleted brain thiamine is necessary. The mortality from this condition approaches 20% if it is left untreated.

Treatment of Wernicke's encephalopathy is parenteral thiamine 500 mg IV tds for at least 5 days. The recommended prophylactic thiamine dosage has been increased to 200 mg parenterally tds. Ophthalmoplegia is the first sign to respond, with complete recovery after a few hours except for a residual fine horizontal nystagmus in 60% of patients. Recovery from ataxia takes a few days and can be incomplete, with persistent ataxia over the medium and long-term. Improvement in mental status may take several weeks. It is important to correct any magnesium deficiency simultaneously, because magnesium is a

cofactor required for normal functioning of several thiamine-dependent enzymes. Supplementation of other water-soluble vitamins, especially niacin and pyridoxine, is advised, because patients suffering from Wernicke encephalopathy are often deficient in these vitamins. Unless the patient is acutely symptomatic from hypoglycaemia, glucose-containing intravenous fluids should be avoided before administering thiamine so as to avoid precipitating Wernicke encephalopathy.

Other alcohol-related neurological problems

Alcohol is a neurotoxin; its chronic heavy use causes CNS damage, peripheral neuropathy, myopathy and movement disorders such as tremor, parkinsonism, dyskinesias, cerebellar ataxia and asterixis.

Peripheral neuropathy

Peripheral neuropathy is common in alcohol misuse and has multiple aetiologies, including direct toxic effect of ethanol and malnutrition with thiamine deficiency. The prevalence among chronic drinkers is unclear but is estimated at between 9% and 50%. Other contributing factors are increased age, total lifetime dose of alcohol, nutritional status (malnutrition and thiamine deficiency) and family history of alcohol misuse. Alcoholic peripheral neuropathy is most commonly sensory in the lower limbs.

Alcoholic autonomic neuropathy

Alcoholic autonomic neuropathy is uncommon. It is often asymptomatic or causes erectile dysfunction in males, postural hypotension and/or diarrhoea. It is related to different pathological processes than sensory peripheral neuropathy.

Ataxia

Ataxia is a common presenting symptom and sign and may be due to peripheral neuropathy affecting proprioception, cerebellar degeneration or a combination of both. Cerebellar ataxia is possibly an extension of the insult from thiamine deficiency, as in Wernicke encephalopathy. Full recovery is rare and permanent damage occurs, affecting the superior cerebellar vermis, contrary to what occurs in Wernicke encephalopathy, where the ataxia may be reversible by thiamine administration.

Syncope

Neuronal failure resulting in syncope and amnesia is due to the direct toxic effect of alcohol on the CNS. This is especially common in binge drinkers. Orthostatic hypotension from autonomic failure is differentiated on the clear relationship to posture.

Respiratory illness in alcohol-dependent persons

Alcohol dependence increases the risk of community-acquired pneumonia owing to

immunosuppression as well as general lifestyle factors, such as hygiene and smoking. Typical organisms include *Streptococcus pneumoniae* and *Haemophilus influenzae*. There is also a higher frequency of cavitating disease, empyema and unusual pathogens. Anaerobic and gram-negative organisms are frequent colonizers of the oropharynx and GIT, and aspiration pneumonia is common. Opportunistic disease, such as tuberculosis, *Pneumocystis jirovecii* pneumonia and Legionnaires' disease are also more frequent in alcohol-dependent persons.

Metabolic problems with alcohol use

Acute alcohol intoxication and chronic alcohol abuse can be associated with a variety of metabolic and electrolyte disturbances.

Alcoholic ketoacidosis

There is contention about the existence and frequency of alcoholic ketoacidosis. This refers to high-anion-gap metabolic acidosis associated with the acute cessation of alcohol on a background of chronic alcohol abuse and relative starvation. Clinical features include nausea, vomiting, abdominal pain, tachycardia, tachypnoea and hypotension, all of which may occur in other alcohol-related emergency presentations.

Chronic alcohol intake can lead to depletion of the body's carbohydrate and protein stores due to relative starvation. Reduced hepatic gluconeogenesis from substrates—such as lactic acid, glycerol and amino acids—can cause hypoglycaemia. In dehydrated states, the combination of hypotension and hypoglycaemia results in reduced insulin production and raised catecholamines, cortisol, glucagon and growth hormone. These hormones promote the utilization of fatty acids for energy, resulting in ketogenesis.

Alcoholic ketoacidosis has been described as 'a common reason for investigation and admission of alcohol-dependent patients', although research data appear limited. There may be an increased frequency of sudden death among patients who present in this fashion.¹⁶

Diabetic ketoacidosis

Acute alcohol intoxication can precipitate ketoacidosis in persons with known insulin-dependent diabetes.

Acute alcohol ingestion can cause a state of acute insulin resistance. Alcohol-induced post-prandial hyperinsulinaemia occurs without a significant decrease in blood glucose levels, consistent with impaired insulin sensitivity. Relative starvation may result in hypoglycaemia and reduced insulin release. Alcohol-induced insulin resistance is important in these patients to recover from hypoglycaemia.

Light or moderate ethanol drinkers have a decreased risk of diabetes mellitus, while this risk is increased in heavy drinkers.¹⁷

Other metabolic acidosis

Metabolic acidosis in alcohol intoxication can be due to lactic acidosis, acetic acidosis or ketoacidosis.¹⁸ One study of 60 ED patients with BAC greater than 0.1% described 7 with a raised serum lactate, all of whom had alternative reasons for this, such as seizure, hypoxia and sepsis. The treatment of an alcohol-dependent patient with metabolic acidosis is symptomatic, with intravenous crystalloid fluid resuscitation and rehydration, parenteral thiamine, 5% or 10% dextrose for hypoglycaemia, electrolyte replacement and a search for and treatment of another underlying cause, such as sepsis.

Electrolyte disturbance

Chronic alcohol abuse is often associated with various electrolyte disturbances, such as hypokalaemia, hyponatraemia, hypomagnesaemia, hypophosphataemia and hypocalcaemia. The causes include poor intake, malabsorption, excessive losses from vomiting, reduced renal tubular reabsorption and dilutional changes due to polydipsia.

Electrolyte imbalances result in the disturbance of other endocrine systems. Thus hypomagnesaemia suppresses parathyroid hormone release, resulting in hypocalcaemia. Electrolyte disturbances are also related to alcohol-induced illness, such as pancreatitis or pneumonia.

Hypoglycaemia There is little evidence that hypoglycaemia occurs in adults with simple alcohol intoxication alone; one large study of ED patients screened for alcohol use and serum blood glucose found no linear relation between blood alcohol and glucose levels. The incidence of hypoglycaemia is not increased in alcohol-related ED attendees compared with sober patients. Intravenous glucose administration has not been shown to be useful in changing rates of alcohol elimination or decreasing periods of intoxication. However, it is essential in each patient with an altered mental state to measure the blood glucose and treat if it is low.

Children and malnourished chronic alcoholics have limited hepatic glycogen stores, so glucagon is not effective in treating hypoglycaemia, as it cannot initiate gluconeogenesis. In the intoxicated or alcohol-dependent adult patient, an alternative cause for hypoglycaemia should still be sought.

Cardiovascular

Coronary heart disease

There is a reduced mortality from coronary heart disease in diabetic moderate drinkers. However, alcohol use in diabetes increases the risk of retinopathy, peripheral neuropathy and foot ulcers. Coronary protective effects of alcohol

are due to influences on increased high-density lipoprotein (HDL) cholesterol, platelet function and fibrinogen.

Hypertension

Acute alcohol intake is a vasodilator, whereas drinking alcohol over the longer term causes systolic hypertension and increased aortic stiffness. An assessment by the World Health Organization Global Burden of Disease 2000 Comparative Risk Analysis attributed 16% of all hypertensive disease to alcohol intake. These findings may be confounded by other lifestyle factors, and there are many contrasting effects of alcohol at various intakes, depending on gender and body mass index (BMI). Thus raising HDL cholesterol is cardioprotective, but developing central obesity, or a 'beer gut,' is not. Overall, any benefits of moderate alcohol consumption on coronary disease are likely to be outweighed by harmful effects.

Cardiac arrhythmias

Heavy alcohol use is associated with an increased risk of sudden cardiac death, most commonly due to ventricular arrhythmias. Atrial arrhythmias including atrial fibrillation, or 'holiday heart', occur commonly after heavy binge drinking in both acute and chronic drinkers. They are not necessarily associated with cardiomyopathy. The risk of a cardiac arrhythmia is increased by electrolyte abnormalities, such as hypokalaemia, hypomagnesaemia and hypocalcaemia.

The treatment of arrhythmias is as recommended by the current Advanced Cardiovascular Life Support guidelines.

Cardiomyopathy

Concentric left ventricular hypertrophy is common in chronic alcohol users. Dilated cardiomyopathy may ensue, with progressive dilatation and fibrosis leading to congestive cardiac failure. This myotoxic process has a worse prognosis than idiopathic dilated cardiomyopathy, particularly if drinking continues. Myocyte function can improve with total abstention.

Aggressive anti-failure therapy should be implemented with dietary measures, such as reduced sodium intake, an angiotensin converting-enzyme inhibitor and other pharmacotherapy, even if total abstention cannot be achieved.

'Wet beri-beri' cardiomyopathy is caused by severe thiamine deficiency, which leads to myocardial dysfunction and peripheral vasodilation. Thiamine absorption is impaired by alcohol, and long-term use of furosemide depletes the body of water-soluble vitamins, including thiamine. Changes in myocardial function occur within 1 hour of starting parenteral thiamine therapy and function is back to normal within 1 week of treatment.¹⁹

Malignancy

Alcohol has been causally linked with many types of neoplasia, most commonly those of the GIT. Oropharyngeal and other head and neck cancers have a direct link to alcohol. Drinking more than 1.5 bottles of wine daily elevates the risk of oesophageal cancer 100 times. Hepatocellular carcinoma (HCC) is usually preceded by alcoholic cirrhosis in the Western world, although other causes include hepatitis B and C viruses. Progression of cirrhosis to HCC is more rapid if drinking continues. Chronic alcohol consumption is also related to laryngeal, breast, pancreatic and colorectal carcinomas.

Important illnesses to be excluded that mimic alcohol intoxication

It is hard to know when to look for another cause for altered conscious state in the habitual drinker or intoxicated person, as many alternative conditions must be considered that mimic apparent alcohol intoxication (Box 21.4.1). Close observation looking for trends in autonomic responses and neurological signs and detailed

Box 21.4.1 Illnesses not to be missed in the person presumed to be intoxicated

Metabolic and encephalopathic

- Hypoglycaemia
- Hyperglycaemia
- Wernicke encephalopathy (thiamine deficiency)
- Hyponatraemia
- Liver failure
- Renal failure

Head injury

- Skull fracture
- Cerebral contusion
- Subdural and extradural haematoma

Other intracranial pathology

- Infection
- Cerebrovascular accident
- Seizure and post-ictal state
- Space-occupying lesion

Toxicological: illicit drugs

- Opioids, gamma-hydroxybutyrate, ecstasy and related drugs (e.g. ketamine, amphetamines and cocaine)

Toxicological: prescription medications

- Opioids, baclofen, benzodiazepines, antidepressants and anticonvulsants

Toxicological: other alcohols

- Methanol, ethylene glycol and isopropyl alcohol

Other sepsis

- Central nervous system infections, urinary tract infection, pneumonia and aspiration

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examination looking for other pathology are more appropriate than waiting for, or intervening after, a certain period of time. Occult head injuries, unusual cerebral infection—such as cryptococcal meningitis, cerebral abscess or herpes encephalitis—are potential diagnoses that may require exclusion. Bias against treating an inebriated patient who is uncooperative and disruptive may lead to flawed early disposition in order to free up time for more 'deserving' patients, and significant injuries or other associated complications may be missed.

Alcohol-related trauma

In 2015, approximately 22% of road deaths involved young people aged 18 to 25 years despite the fact that these accounted for only 13% of licensed drivers. Of individuals, 67% were killed during times of high alcohol exposure. Alcohol users increase their risk in two ways: likelihood of injury and seriousness of injury. Alcohol abusers are more likely than sober persons to be involved in a trauma event; in addition, heavy drinkers have a higher risk for injury incidents than non-drinkers. Given similar traumatic circumstances, a drinker is likely to be hurt more seriously than a non-drinker. Although there are some exceptions, most research findings support this positive relationship between alcohol use and severity of injury. The exact mechanisms of the alcohol-severity relationship are not known, but it could be related to its disinhibitory effects as well as altered perception of risk. In addition, alcohol can complicate the initial assessment and management of the injured patient, masking physiological signs of serious injury and posing as a risk for regurgitation and aspiration of the stomach contents.

Other toxicological states in the alcohol-dependent patient

Multiple drug ingestion

Multiple drug ingestion, whether prescription or illicit, is common in regular drinkers for recreational reasons, due to dependence, to 'come down' from other drug effects, accidentally or in deliberate self-harm. The most common and important ingested drugs to consider include BZDs, opiates and paracetamol, antidepressants including tricyclics and selective serotonin reuptake inhibitors, γ -hydroxybutyrate, ecstasy and other sympathomimetics, such as cocaine and ketamine. Baclofen is increasingly prescribed to treat alcohol dependence and can cause altered mental state in deliberate overdose or if a high treatment dose is restarted after a period of non-compliance.

Other alcohols

Other alcohols—such as methanol, ethylene glycol and isopropyl alcohol—although rare, should

be considered in the significantly intoxicated, self-harm patient. 'Methylated spirits' bought over the counter in Australia contains only 95% ethanol v/w with no methanol at all and, in New Zealand, the methanol content has been reduced to 2% or less, due to deaths attributed to chronic misuse and methanol poisoning there.

Serum drug levels

The only clinically useful screening serum drug levels are paracetamol and ethanol. Other drug levels take hours to days to perform (institution-dependent); thus they are not of use at the time and should be requested only if there are specific indications. The only safe antidotes to consider are naloxone, thiamine and glucose. Flumazenil is not recommended owing to the risk of inducing seizures secondary to BZD withdrawal and then not being able to manage them effectively.

Sepsis

Sepsis must be considered in any person with an altered conscious state potentially masked by alcohol intoxication; a directed septic workup should be carried out.

Treatment of alcohol-related illness

Alcohol intoxication

Intoxication starts with a feeling of well-being and an increasing sense of relaxation, followed by impairment of judgement and incoordination. At a BAC of 0.1%, dysarthria, ataxia and disinhibition are common. At a BAC of 0.2%, confusion occurs and new memories are not formed. At a BAC of 0.25%, cortical depression is seen, with the onset of stupor. At a BAC of 0.4%, most patients are unconscious and at risk of respiratory depression and death. The mean BAC found in fatal alcohol intoxication is 0.45%.

'Pathological intoxication'

Some people have idiosyncratic responses to alcohol, the 'pathological intoxication', which is more common among certain ethnic groups. A clear indicator of alcohol tolerance and neuroadaptation is the recording of high BAC in a person functioning at an otherwise reasonable level—for example the patient capable of normal conversation and gait with a BAC 0.3%. This may follow a continuous prolonged drinking binge.

Treatment of the acutely intoxicated person

The treatment of an acutely intoxicated person is supportive, protecting the airway and placing the individual in the semi-prone position to reduce the risk of gastric aspiration. Gastric emptying procedures are not recommended under any circumstances. Intravenous fluids in simple alcohol intoxication do not increase

the elimination or decrease the BAC. Likewise, intravenous administration of 5% dextrose has not been shown to be useful in changing the rates of alcohol elimination or decreasing periods of intoxication.

There remains no antidote to alcohol intoxication. As alcohol affects endogenous opiate GABA receptors, both naloxone and flumazenil have been tried with no effect. Flumazenil use in the alcohol-intoxicated patient is dangerous, as it renders BZDs ineffective in the treatment of seizures for about 45 minutes after its use. It can also precipitate seizures if the patient is a chronic BZD user. Various substances have been tried in animals, but none so far is safe and/or effective. There has been interest in pyridoxine and, more recently, its analogue metadoxine in hastening alcohol metabolism and reversing both the biochemical and clinical symptoms of intoxication, but studies are small.

'Hangover'

In the United Kingdom in 2003, it was estimated that £2 billion in lost work value was due to post-alcohol-related headache and malaise 'hangover', making this a greater economic problem than habitual intoxication. Paradoxically, light or binge drinkers' hangovers cause the most lost work time, as the hangover is more common and the sufferer is more commonly in regular employment than the heavy drinker.

Hangover is distinguished from the alcohol withdrawal syndrome as it follows a defined single episode of intoxication. Symptoms include headache, feeling generally unwell, diarrhoea, anorexia, nausea, tremulousness and fatigue. The presence of two or more of these symptoms following alcohol intake has been used to define a hangover. Acetaldehyde, the dehydrogenated metabolite of alcohol, has been implicated. Alcohol alters cytokine production and thromboxane B₂ is increased, an effect blocked by prostaglandin inhibitors. This may explain why prostaglandin inhibitors, such as NSAIDs, including aspirin, may have some limited prophylactic effect on hangover development.

Hangover is not solely dose-related. Hangovers are worse with dehydration, poor food intake, decreased sleep, increased physical activity while intoxicated and poor general physical condition. Congener by-products of some alcohols including aldehydes, esters, histamine, phenols, tannins, iron, lead and cobalt are found, especially in darker liquors, which are associated with an increased severity and incidence of hangover. The ingestion of clear liquors, such as gin, vodka and rum, may be associated with fewer hangovers. The evidence for hangover treatment and prevention is minimal.²⁰

The habitual alcohol-dependent emergency attendee

Most EDs, particularly in metropolitan areas, have a group of recurrent ED attendees who keep presenting with alcohol intoxication and chronic alcohol-related disease. Such people are usually male, aged 30 to 40 years and often have no fixed place of abode. They are usually well known to neighbouring EDs, community services and police. They tend to attend in cycles, and an absence of attendance may indicate a prison term, a medical illness and/or hospital admission, an attempt at sobriety, use of an adjacent ED or sudden death. Over a year they may accumulate multiple investigations, especially computed tomography (CT) scans of the head. This group has an increased mortality over time from assault and other trauma as well as alcohol-related illness associated with neglect.

The emergency department as a temporary refuge

For the alcoholic individual, the ED provides a temporary refuge in an otherwise chaotic lifestyle and an opportunity for a health assessment and intervention. It is important to realize that providing care for this group of people is core business for every ED, despite any frustrations felt. Interventions to alter lifestyle and prevent recurrent attendances can be successful. ED-initiated case management involving community linkages, and assistance with accommodation improves health outcomes but may increase ED utilization. Serial inebriate programmes may target this group, often commencing with socialization skills, such as personal hygiene and nutrition management. Acceptance to such programmes is often precipitated by the threat of imprisonment. Such programmes have been demonstrated to be cost-effective.

Assessment of alcohol misuse

Alcohol screening tools

Emergency physicians witness daily the effects of lifestyle abuse on ED presentations and thus may find many opportunities to intervene opportunistically to affect the long-term health of the patient as well as treating the immediate presentation. This is particularly valuable for patients with irregular contact with other medical services, such as the itinerant and the homeless.

Screening for chronic alcohol abuse or dependence

Any screening tool to be of value must have adequate sensitivity and specificity for detecting the illness involved, and there should be an effective, cost-effective intervention available.

Box 21.4.2 CAGE screening questionnaire for alcohol abuse

C = 'Have you ever felt you should Cut down on your drinking?'
 A = 'Have people Annoyed you by criticizing your drinking?'
 G = 'Have you ever felt bad or Guilty about your drinking?'
 E = 'Have you ever had a drink as an Eye-opener first thing in the morning to steady your nerves or help get rid of a hangover?'

Yes to two or more indicates probable chronic alcohol abuse or dependence.

Many screening tools for chronic alcohol abuse or dependence have been developed for primary care, with the best known being the CAGE questionnaire (Box 21.4.2).²¹ This poses four questions on behaviour and a positive answer to two or more indicates probable chronic alcohol abuse.

Paddington alcohol test

An effective and quick alternative in the time-pressed setting of an ED is the Paddington alcohol test (PAT), which includes 'routine' focused selective screening combined with education, audit and feedback.¹⁵ PAT has reduced screening time to 1 minute by simply quantifying the amount of alcohol consumed, how often and whether in the opinion of the patient the reason for ED attendance is excessive alcohol consumption.

Opportunistic screening and brief intervention

Brief intervention, usually consisting of a counselling session lasting 10 to 15 minutes and a pamphlet on safe levels of regular alcohol consumption, can reduce the frequency of dangerous drinking by 30%. After ED-initiated PAT screening and trained alcohol health worker follow-up, it can also reduce recurrent ED attendances by as much as 50%.

Focused PAT screening of high-risk patients (Box 21.4.3) followed by brief advice and referral for trained alcohol health worker intervention appear to be the most time- and cost-effective methods of reducing alcohol-related harm and ED attendances.²² Brief advice consists of informing the patient during the ED 'teachable moment' that he or she has a drinking problem. This advice increases compliance to attend brief intervention later by 20%. Using PAT to screen all ED attendances as opposed to only those presentations considered at 'high risk' may increase the incidental pick-up of at-risk drinkers but may also decrease the enthusiasm of ED staff to provide screening because of the time required and the many negative

Box 21.4.3 The top 10 ED presenting conditions associated with alcohol use

Fall
 Collapse
 Head injury
 Assault
 Accident
 Unwell
 Unspecific gastrointestinal problems
 Psychiatric-behavioural symptoms
 Cardiac symptoms
 Repeat attendee

To be used with the Paddington alcohol test (PAT).
 (From Crawford MJ, Patton R, Touquet R, et al. Screening and referral for brief intervention of alcohol misusing patients in an emergency department: a pragmatic randomised controlled trial. *Lancet*. 2004;364:1334–1339 with permission.)

screens. Although it has been demonstrated that ED doctors and nurses with empathy and volition can be trained to provide ED-based brief intervention on the spot, the long-term benefit of this type of brief intervention is uncertain.

Pharmacotherapy for alcohol use disorder

A variety of pharmacological agents are available for the treatment of alcohol use disorders. These are rarely started in the ED, as patients need ongoing monitoring and support, and they must be referred for counselling and/or rehabilitation by their general practitioners. Agents that can be considered for use during treatment include acamprosate, naltrexone, disulfiram, topiramate or baclofen.

Acamprosate acts on GABA receptors in the CNS to reduce the craving for alcohol after detoxification. It is safe and well tolerated, suitable for use in the treatment of alcohol-use disorder and aimed at maintaining abstinence. Mild gastrointestinal side effects may occur and therapeutic levels take 5 to 7 days to become established.

Naltrexone is a partial opioid agonist that is useful in reducing the effects of endogenous opioids. It has had success in opioid addiction treatment as well as in alcohol-use disorder.

Disulfiram is an acetaldehyde dehydrogenase inhibitor. If alcohol is consumed while the patient is on disulfiram treatment, even in small amounts, unpleasant effects (flushing, throbbing headache, shortness of breath, nausea, vomiting, palpitations, hypotension, syncope) are felt immediately. It is contraindicated in patients with known ischaemic heart disease or history of psychotic episodes and in pregnancy.

Topiramate has been shown in several randomised controlled trials to be beneficial

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in increasing the percentage days abstinent, decreasing the number of drinks per day, and improving levels of plasma gamma glutamyl transferase. Unfortunately it is associated with many significant adverse effects (cognitive impairment, paresthesias, weight loss, headache, fatigue, dizziness, depression), thus limiting its use. Baclofen is a GABA agonist that is increasingly prescribed to treat alcohol dependence. There are still only limited data regarding its benefits. Tolerance develops with therapeutic use, and if patients restart a high treatment dose

after a period of abstinence, they can develop significant CNS and respiratory depression. Sudden cessation of chronic baclofen treatment can also be associated with a withdrawal syndrome characterized by hallucinations, delirium, seizures and fever.²³

These agents may be used safely in combination, although this has not been shown to have a superior effect. Pharmacotherapy produces better results when used in combination with cognitive behavioural therapy and motivational sessions.

CONTROVERSIES

- The true prevalence and incidence of alcoholic ketoacidosis is uncertain.
- The dose of parenteral thiamine to prevent Wernicke encephalopathy is somewhat controversial.
- There is a question about whom to target for brief intervention by emergency clinicians: high-risk attendances or unselected patients.

Full references are available at <http://expertconsult.inkling.com>

21.5 The challenging patient

Georgina Phillips • Kirsten Cassidy

ESSENTIALS

- Many patients characterized as 'challenging' share common characteristics, including complex and chronic medical disease, mental illness, marginalization, poverty, high levels of drug and alcohol use and lack of social supports, safety and security.
- An understanding of the issues that contribute to the challenging nature of some patients may help the practitioner to develop a management approach characterized by sound knowledge, clear and achievable goals and compassion.
- Management strategies and practiced communication techniques may help to alleviate the dissatisfaction and frustration frequently experienced by the clinician.
- Allied health and psychiatric services in the emergency department facilitate multidisciplinary and holistic care for the patient with complex needs.
- Safety and security for all patients and staff must be assured. Physician self-awareness and self-care will help guard against burn-out in these situations.

Introduction

The emergency department (ED) may be the only easily accessible health care for patients with multiple and challenging needs. For those impaired due to chronic illness, drugs and alcohol, mental illness or social circumstances, the ED is an environment where services are available 24 hours a day or during crisis. The challenges posed by complex patients are compounded by system factors, such as decreased after-hours services, ED overcrowding and access block. Some patients require urgent management for reasons other than medical issues—for example, a behaviourally disturbed patient who causes disruption and threatens violence within the ED, a very important person (VIP) who may distract the attention of staff or someone who poses a security risk. This chapter describes and discusses several types of patients

with the aim of understanding the circumstances that contribute to these presentations and helping the practitioner to develop an approach to management.

The management of a complex patient in a difficult environment represents a common challenge for emergency physicians. As approximately 1 in 20 patient interactions are likely to be challenging, clinicians can accept, train and prepare for these situations as they should for any complex resuscitation. All emergency staff may find dealing with challenging patients tiring and frustrating and experience feelings of dissatisfaction. Physician characteristics such as younger age, longer working hours, depression and anxiety can contribute to increased feelings of frustration.¹ Self-awareness and the maintenance of physician well-being is an essential platform for the successful and satisfying management of these complex situations.

THE HOMELESS PATIENT

ESSENTIALS

- Multidisciplinary management of the homeless person is required.
- Discharge planning is difficult and short-stay admission is frequently required.

Definition and epidemiology

Definitions of homelessness vary. A homeless person is often considered to be someone living on the streets without shelter. A broader definition includes any person without a conventional home who lacks most of the economic and social supports that a home normally affords. These persons are often cut off from the support of relatives and friends, have few independent resources and often no immediate means; in some cases they have little prospect of self-support.

The most widely accepted definition in Australia, and the one used by government and other specialist agencies to gather data, describes three kinds of homelessness:

- Primary homelessness, such as sleeping rough or living in an improvised dwelling.
- Secondary homelessness, including staying with friends or relatives and with no other usual address, including people in specialist homelessness services.
- Tertiary homelessness, including people living in boarding houses or caravan parks, over both the short and long term, with no secure lease and no private facilities.²

Concepts of homelessness vary with culture. People from Aboriginal and Torres Strait Islander

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cultures may experience homelessness when they are separated from their spiritual home, despite adequate shelter; conversely, they may feel a spiritual connection to the land on which they live independent of the presence of shelter. Three broad categories of indigenous homelessness are identified in Australia: those living in public places, those at risk of losing their house and those who are spiritually homeless.³

Estimates of the prevalence of homelessness are difficult to arrive at owing to variations in definition and methodologies of identification. Every night in Australia, around 105,000 people are homeless.⁴ More than 160,000 Australians experience homelessness each year, one-third of them children, and resources allocated in response to homelessness are grossly inadequate. Homelessness is more prevalent among women and is closely related to the experience of domestic violence and inequity in general. Homelessness among children, families and older people is increasing. The Australian indigenous population comprises 3.3% of the Australian population but accounts for 25% of those accessing homeless services, primarily as a result of domestic and family violence, overcrowded dwellings and evictions.⁵ Ex-prisoners, war veterans, the mentally and physically ill, people leaving health care facilities and protective services, youths and people in rural communities experience an increased incidence of homelessness.

Clinical features

Homeless patients presenting to the ED exhibit high rates of complex physical and mental illness and substance dependence. Due to poverty and social isolation, access to health care is impeded, with a subsequent cycle of deterioration in health. Lack of housing stability, social supports and points of reference within the local community lead to a high rate of utilization and re-presentation to the ED despite the development of outreach programmes and case management strategies.⁶ Homeless patients may present to the ED up to 10 times more frequently than the rest of the population.⁷

Re-presentation rates within 28 days of discharge are high and may account for up to 48% of all re-presentation episodes and 23% of all patients who re-present to the ED.⁷ Certain features, such as sociodemographics (age <65 years, receiving government pension), service utilization history (case management and discharge at own risk) and clinical features (primary psychiatric presentation, complex medical history and high numbers of prescribed medications) are highly predictive of re-presentation.^{7,8} Presentations by homeless people are often of low acuity. Triage categories are non-urgent in up to 91% of attendances.⁷

Presentations with infectious diseases (e.g. TB and HIV), penetrating trauma, depression, schizophrenia and ethanol and drug abuse are common. Deliberate self-harm presentations are more frequent and are followed by a higher rate of re-presentation with recurrent self-harm and approximately double the rate of death from successful completion of suicide than in the domiciled population.⁹ Homeless patients presenting with deliberate self-harm are more likely to be recent victims or perpetrators of violence or to have criminal records or a personality disorder, thus highlighting the complex links between these variables.

Management

The management of the homeless patient requires a multidisciplinary approach and an understanding of the social and financial constraints the patient faces. Allied health services may be able to provide background information or links to established community services, assist with discharge planning or with emergency accommodation or other social services. Discharge planning may be especially difficult and short-stay admission for the management of simple conditions normally treatable at home or admission to low-acuity facilities may assist with improvements in health and other social parameters. A compassionate approach to the homeless patient, where patients were assigned a volunteer who offered food and conversation, was found to decrease significantly rates of re-presentation, dispelling the myth that increasing patient satisfaction encourages homeless patients to re-attend.¹⁰

THE PRISONER

ESSENTIALS

- 1** The prison population is disadvantaged and vulnerable.
- 2** Prisoners' health needs differ from those of the general public.
- 3** Presentations are often injury-related and are generally of high acuity.
- 4** Security events are uncommon.

Definition and epidemiology

In all states and territories except Queensland, prisoners are defined as persons greater than 18 years of age remanded or sentenced to adult custody (age 17 in Queensland).¹¹ The patient brought to the ED by police from the community under arrest differs from the patient who is

Table 21.5.1 Challenges involving the prisoner in the emergency department

Security issues	Patient care issues
Perceived threat to safety of staff and other patients	Clinical management of complex illness
Potential for violent incidents	Medical, psychiatric and addiction co-morbidities
Presence of non-hospital security staff	Maintenance of confidentiality
Weapons in the emergency department	Discharge planning

residing in prison. Both types of patients may pose security issues, but their health needs and demographics differ.

The prisoner poses several challenges when seen in the ED (Table 21.5.1).

The prison population in general has low educational achievements, poor records of employment, high reliance on social welfare, poor nutrition and more complex physical and mental health needs when compared with the general population; from a health perspective, these represent a cohort of patients distinct from the wider community.¹²

Prisoners have a high rate of pre-existing mental and physical illness, substance use and dependence and high rates of hospitalization. They also have a high rate of risk-taking behaviours that increase the likelihood of poor health, such as tattooing and heavy alcohol and substance use. They display behaviours with addictive or compulsive orientations and low impulse control. These factors contribute to the illnesses experienced, modes of presentation and responses to the health staff and treatments offered.

Clinical features

Prisoners are commonly younger men and frequently indigenous (Australian, Maori and Pacific Islander). Presentations are most commonly injury related and are overall more severe as compared with those in the general male population, with a higher frequency of fractures, blunt head injuries, greater rates of hospital admission and death.¹³

Mental health issues and high suicide risk are common among prisoners and incarceration is more common in those with mental illness. Risk factors for incarceration for those with mental illness include prior incarcerations, substance-related diagnoses, homelessness, schizophrenia, bipolar or other psychotic disorder diagnoses and male gender.¹⁴

Substance withdrawal is implicated in approximately 9% of presentations and 6% of admissions.¹⁵ Due to the increased risk of overdose following periods of abstinence, recently

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released inmates who use opiates are at particularly high risk of overdose, and overdose deaths are eight times more likely in the 2 weeks following release than in a comparable non-incarcerated group of men.¹⁶

Prisoners have a high rate of admission to hospital (range 36% to 49%), which may be due to a higher acuity of illness, with approximately 80% of prisoners triaged as category 3 or above, thus exacerbating the practical and logistical difficulties encountered in managing unwell people in custody. Prisoners have a decreased length of stay in the ED compared with the non-prisoner population.¹⁵

Violence and security issues

Episodes of violence are uncommon. The rate of security incidents may be lower than for the non-prisoner population.¹⁵ Perceived threat and the accompanying stress caused to staff are yet to be quantified.

The presence of weapons provides the potential for serious injury to the patient if escape is attempted or to staff if the patient removes a weapon from security staff. Fatalities have been documented.¹⁵

Management

The urgency with which a prisoner is assessed depends on a combination of medical issues and security considerations; prioritization, in order to expedite management and decrease length of stay in the ED, is reasonable.

Prisoners may perceive the ED as a threatening, embarrassing environment that lacks privacy, where they can be seen by members of the public to be under guard and restrained. Most express feelings of distress when removed from their familiar environment. Prisoners are unable to have the normal reassurance and support of family while in hospital. The presence of guards during medical assessment raises confidentiality concerns for the patient. These concerns need to be weighed against security issues. Guidance from custodial staff as to whether it is safe for them leave the cubicle or remove restraints may be helpful. If the clinician feels insecure, custodial staff should remain within the room. The history obtained in the presence of guards may be inaccurate. Patients may be fearful of disclosing the mechanism of injuries due to fears of reprisal or prison guards in attendance overhearing the circumstances of injury.

In many Australian states, psychiatric services are not resourced or mandated to care for prisoners, and mental health acts do not cover those incarcerated under separate forensic laws. This may render the ED care of the mentally unwell prisoner even more difficult, as psychiatric illness

may be undiagnosed or undertreated and access to normal mental health clinicians to aid in assessment and treatment may not be available.

Opportunities for following up of medical conditions are limited. There may be little possibility for observation of the person's condition upon return to detention. Outpatient follow-up is time- and resource-intensive and logically difficult for the prison staff. There is therefore often a need for more extensive investigation while the prisoner is in the ED. A low threshold for ruling out potential illnesses and for admission to hospital is generally required.

If the patient is returning to prison, clear written discharge instructions should be formally communicated and discharge medication with dispensing instructions provided. Liaison with the prison nurse or forensic medical officer should establish whether their facilities and staffing can provide the expected management.

THE BEHAVIOURALLY DISTURBED AND VIOLENT PATIENT

ESSENTIALS

- 1 Complex co-morbidities of organic illness, psychosocial issues and substance misuse can manifest as acute behavioural disturbance.**
- 2 An understanding of legal and ethical considerations can inform rapid decisions and humane treatment in behavioural emergencies.**
- 3 A safe environment and team approach can maximize containment of disturbed and violent behaviour while respecting the privacy and dignity of patients.**
- 4 A strategic approach to understanding and managing violence in the ED may minimize the harmful effects of violence to staff, patients and carers.**

Aetiology and epidemiology

A behavioural emergency can be defined as an unarmed threat by a patient or others characterized by agitation, aggression, violence and irrational or altered behaviour. Violent and unarmed threats involving patients in the ED have been described with an incidence of between 0.3%¹⁷

and 2%.¹⁸ Accurate information on the incidence and subsequent management of acute behavioural disturbance is limited by the lack of clarity around what constitutes a behavioural emergency and significant differences in treatment response both within and between EDs. Heavy recreational drug use and alcohol binge drinking in the community have contributed to the public perception that behavioural disturbance requiring urgent medical care has increased. It has also been argued that psychiatric deinstitutionalization and limited community supports have led to an influx of unstable, mentally ill patients to the ED.

The aetiology of acute behavioural disturbance in the ED is largely mental illness or substance intoxication and often a combination of the two.¹⁷ A smaller number have an organic illness, including dementia, manifesting as a behavioural emergency.¹⁹ Most patients are male (approximately 65%) and under the age of 40,^{17,20} and around 20% are brought to the ED in police custody.^{17,21} The majority of unarmed threats occur in the late afternoon, evening and overnight, with a weekly peak on Saturdays.¹⁷ Between 58% and 80% of these require some form of chemical or physical restraint as part of management.^{17,18,20}

Prevention

Experienced clinicians are able to recognize environmental and individual factors that can lead to unstable and dangerous behaviour. Crowded, noisy and brightly lit departments are the antithesis of the calm and stable surrounds that promote controlled behaviour and de-escalate aggression. Fear, confusion and inadequate communication can trigger anger and aggressive behaviour in both patients and carers; also, long waiting times and negative waiting room environmental factors have been suggested as contributors to violence in the ED.

In order to prevent anger or illness from escalating to a behavioural emergency, recognition of verbal and non-verbal cues is required, as well as an ability to utilize environmental and clinical resources to ensure a calm, controlled situation. EDs are now incorporating separate rooms or areas that are quiet, private and secure as sites for the assessment and containment of behavioural disturbance.²² This model has become the recommended standard in Australia for assessing and containing aggressive and agitated patients both at a national²³ and state level.²⁴ Physical separation from the main ED and the removal of stimulation may be enough to reverse the trend to increased aggression. Respectful and clear communication with lowered voice level, eye contact and non-threatening body language may establish a rapport that enhances a therapeutic bond between clinician and patient. Explanation of

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treatment decisions and the reasons for them may alleviate confusion, while bargaining and rewarding compliance can diffuse tension. It is recommended that, while also setting clear behavioural limits, the patient should be allowed a semblance of autonomy and control.

A 'security response' is utilized in the ED to contain behaviour when disturbance and aggression can be anticipated.²⁵ This is aided by prior police and ambulance notification of the imminent arrival of a patient who represents a behavioural emergency. A team comprising hospital security service, nursing and medical staff can in itself be a disincentive for increased aggression when an aroused patient is being confronted. In the event of violence, the team response carried out in a separate area of the ED can quickly control behaviour safely and thus prevent further episodes or prolongation of aggression.

Clinical features

Clinical assessment comprises three components: diagnosis, evaluation of risk and assessment of arousal (Table 21.5.2).

Signs of acute intoxication or withdrawal may follow recognized patterns or drug toxicomes, whereas psychiatric instability may manifest with features of psychosis. Differentiating between organic illness, delirium and substance intoxication or psychosis can be extremely difficult in the initial assessment and may be clarified only after immediate management and behavioural containment. A breath alcohol determination is useful, and intravenous puncture sites may suggest substance misuse. In an agitated and aroused patient, the act of taking a blood pressure or putting a stethoscope on the chest may be recognized as a familiar and non-threatening action and thus be better tolerated than attempting to get a detailed history or expecting a rational response to verbal requests.

The role of investigations in the behaviourally disturbed patient is dictated by the clinical presentation. Routine laboratory blood testing is of

Table 21.5.2 Aims of clinical assessment in the face of acute behavioural issues

Diagnosis	What is the aetiology of the behaviour: psychiatric, substance related, organic, personality?
Risk assessment	Can the patient's autonomy be over-ridden? Can he or she be kept in the emergency department against his or her will?
Arousal assessment	Does the patient require containment or sedation, and how rapidly?

low yield. Urine drug screens have no role in the acute assessment or management. Cognitive abilities should guide the readiness for psychiatric assessment, rather than the suspected presence of drugs or alcohol. A positive breath alcohol should not preclude mental health assessment in the patient who is alert and orientated.²⁶

Risk assessments are often made rapidly and intuitively in the highly agitated and aggressive patient. The decision to contain and restrain an aroused patient with extreme behaviour is primarily based around the perceived threat of harm to self or others. If patient competence cannot be assessed, then the assumption of risk of harm and the doctor's duty of care override patient autonomy. Clinical features that are suggestive of high risk include threats or actual self-harm, suicidal behaviour or ideation, threats or actual violence to others, altered conscious state due to illness, injury or substance intoxication and incompetence. Risk assessments and restraint can be made only within an acute framework (i.e. pertaining to hours rather than weeks or months), as this is the length of time a person can humanely be contained within an ED setting. Patients with longer-term high-risk behaviours are not suitable for physical or chemical restraint in the ED and may be managed more appropriately in a mental health or forensic setting.

Assessment of arousal requires utilization of collaborative and clinical tools and informs decisions about urgency and methods of restraint. Information about behaviour immediately prior to ED presentation can be gathered from police and ambulance officers. Physical struggle and violence requiring restraint during transport to the ED is an indication of the need for ongoing restraint. Physical intimidation, threats or acts of violence to self, people or property, attempts to escape, uncontrollable verbal abuse and aggressive acts such as spitting, all indicate extreme arousal and the need for immediate containment and restraint. Signs that a patient is increasingly aroused and that violence may be imminent, include physical agitation and restlessness, pacing, sweating, loss of rational thinking, increased voice tone, swearing or foul language, eye widening and pupil dilation. Early recognition of these prodromal features may prevent the escalation of aggression and ensure the safety of both staff and patient.

Legal and ethical considerations

Sedation and restraint for behaviour containment represent significant deprivations of personal liberty. Australasian law strongly upholds the fundamental principle of individual autonomy and mental health legislation mandates a 'least restrictive' approach to involuntary care. Emergency physicians must also respect patient autonomy and be mindful of employing the least restrictive

practices in making decisions to restrain aroused and aggressive patients (see Chapter 28.1).

The ability to detain and treat people without their consent is lawfully recognized in emergency situations, committal under legislation (e.g. mental health acts), suicide prevention, to protect others from harm, self-defence, 'necessity' or 'in best interests' and for incompetent patients.²⁷ Thus ED staff are comprehensively protected under the law if they act in good faith and with integrity when managing acute behavioural disturbance. Doctors are also legally required to maintain confidentiality, to take reasonable care, not to take advantage of a patient and to meet professional standards. Containment and restraint often take place in highly visible sites within the ED, where the patient is exposed to the scrutiny of other staff, patients and visitors, which can undermine personal privacy and confidentiality. Similarly, abusive and aggressive patients may provoke anger and frustration in ED staff. Competent patients are responsible for their actions and are expected to behave within a reasonable and legal framework. Damage to property and assault to person are crimes that are subject to prosecution if they occur in an ED and toward ED staff. There are occupational health and safety requirements that mandate a safe working environment and can inform structural changes and clinical practices in the management of violence in the ED.

Medical ethics and the law complement each other in recognizing personal autonomy and human rights. A compassionate approach that respects the human dignity of all patients and recognizes the medical duty to provide care is likely to result in both a lawful and an ethical framework for managing patients with behavioural emergencies.

Management

Once the decision to contain and restrain a patient with behavioural disturbance has been made and preventative de-escalation measures have been unsuccessful, it is worth determining the desired end point of management. Containment methods differ significantly according to the desired outcome, which may range from a calmed, awake patient through to one who is fully tranquillized and physically restrained. In an ED setting, containing and restraining a patient is not therapeutic and should be viewed as a transient departure from the normal physician-patient collaboration.

Containing a highly aroused and aggressive patient requires a team of trained staff: a minimum of six people comprising hospital security staff and orderlies, with medical and nursing staff to assist with team leadership, documentation, drug administration and subsequent monitoring.²⁸ Smaller hospitals may have to utilize police in their initial team response, but this is not recommended,

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given the differing training and aims of hospital- and police-based restraint practices. Police should be involved when a weapon is present or the violent person is not a patient receiving treatment. The importance of prior planning, regular aggression management training and good communication cannot be overemphasized.

Chemical restraint

The pharmacological management of the acutely aroused patient is discussed in detail elsewhere (see Chapter 20.6), but the principles should be emphasized. The least traumatic measures are advocated, depending on the desired end point of chemical restraint and the risks to staff and patient in administration.

Oral benzodiazepines are preferred where possible and may allow patients a small sense of control if they are able to choose this option ahead of parenteral sedation. Choice between intramuscular or intravenous administration of sedation depends on perceived risks to staff, ease of obtaining intravenous access, need for blood tests or other intravenous therapy and desired rapidity of sedative effect. A standardized intramuscular sedation protocol can be effective and safe.²⁹ Where rapid tranquillization is desired, the intravenous route of administration is required, as the onset of action is within the first 5 minutes rather than the approximate 15 to 20 minutes of intramuscular drugs.³⁰ Commonly used drugs for rapid tranquillization include benzodiazepines (diazepam and midazolam), neuroleptics (droperidol and haloperidol) and antipsychotics (olanzapine). Increasingly, ketamine is used in patients who are difficult to sedate and in transport situations.³¹ A combination of intravenous midazolam with droperidol or olanzapine has been shown to be more effective than midazolam alone or than high-dose droperidol or olanzapine alone with respect to time to adequate sedation and need for re-sedation.^{32,33} Intravenous midazolam alone may cause more adverse events relating to airway obstruction and over-sedation and is more likely to require re-sedation within an hour. High-dose parenteral midazolam is not supported due to concerns about effect and safety.³⁴ Careful monitoring in a high-acuity area of the ED is required when parenteral chemical restraint is used.

Physical restraint

Physical restraint can initially proceed on the floor and move to a trolley as soon as practical. A five-point hold is recommended, involving securing the head as well as the upper and lower limbs in firm grasp. Personal protective gear of gown, safety goggles and gloves should be worn by all involved and an oxygen mask or loosely applied towel over the face can be used if the patient is spitting. Although it is paramount not to inflict

harm on the patient, the safety of staff is also a priority and may justify the use of moderate physical force. Using staff physically to restrain a patient is a temporary measure only and should be followed by more definitive restraint in the form of sedating drugs, physical shackles or both.

Physical restraint with shackles provokes emotional distaste in many clinicians, but it can be used safely and humanely in an ED setting. There have been reported deaths in restrained, agitated patients, described largely in the United States, where 'hobble' restraints including prone positioning with hands and feet secured together behind the back are used.³⁵ Where supine positioning is used, physical shackles have been shown to be safe.³⁶ Soft-edged, strong, fabric shackles securing the wrists and ankles of a supine patient to the trolley are recommended. Concomitant chemical sedation is advised, with appropriate monitoring. Prolonged shackling is inhumane and carries risks of musculoskeletal injury, respiratory compromise and psychological trauma. All Australian states have laws that mandate careful and close observation of physically restrained patients as well as regular review of the need for such ongoing, extreme restraint.

Although few EDs have appropriate resources, it may be possible to contain patients with behavioural disturbance in a less restrictive manner by using seclusion rooms. Such areas must be visible to ED staff, be easily accessible to a security response team and have no dangerous furniture or fittings with which patients could potentially harm themselves or others.

Patient perspective

Emergency clinicians rarely consider patient preferences when faced with the need urgently to control aggressive or threatening behaviour, and there is limited evidence to inform this issue. The majority of patients prefer chemical restraint rather than physical interventions, and seclusion is preferred over physical shackles. Benzodiazepines are the preferred drug for chemical sedation rather than neuroleptics.³⁷

Disposition

Behaviourally disturbed patients commonly spend many hours in the ED, both for accurate assessment and for diagnostic purposes. Increasingly, the lack of access to general medical, psychiatric and detoxification inpatient beds means that timely transfer for definitive care is delayed. The result is prolonged, inhumane containment of behaviourally disturbed patients, which is likely to lead to worse therapeutic outcomes. For this reason, ED doctors must be strong advocates on behalf of their patients as well as maintaining vigilant clinical review of the patients' physical and mental state and the need for ongoing

restraint. Patients who are transferred to inpatient wards for ongoing care must be alert, have stable vital signs, not require further monitoring and be declared safe for transfer by the most senior available ED clinician. Respiratory depression and death have occurred in patients transferred to psychiatric wards after receiving chemical sedation from the ED; therefore the time, nature and route of drug administration must be taken into account in considering safety for transfer.

The decision to admit a patient depends on the result of clinical and investigative findings, ongoing mental health and risk assessment and the progress of the patient over time. It may be appropriate to keep behaviourally disturbed patients under ED observation for up to 24 hours in order to clarify the aetiology of the altered behaviour and determine a safe disposition. Patients with aggression and arousal due to substance intoxication often wake up several hours later with normal behaviour and no recollection of their earlier violence. This presents a preventive health opportunity to counsel, educate and refer the patient for ongoing drug and alcohol review. Patients should be informed that their substance misuse has resulted in dangerous behaviour both for themselves and others, but many will already be socially marginalized and vulnerable as a result of homelessness, substance addiction and psychosocial stressors. A multidisciplinary care-coordination approach optimizes a safe discharge for these patients.

Normal clinical and investigative findings, the absence of substance intoxication and exclusion of acute mental illness mean that the patients do not require further ED care. Such patients may still present a behavioural challenge and, if ongoing risk to self or others exists, they should be discharged to the care of the police. Collaborative decision making with mental health clinicians is often required in such situations, as these patients often suffer antisocial or other personality disorders that are difficult to manage in both forensic and health settings. For those discharged to the community, mental health and social work follow-up is recommended.

At all stages in the assessment, containment, restraint and disposition of patients with acute behavioural disturbance, clear documentation is mandatory. The importance of recording management events and the reasons behind containment or discharge decisions protects staff from clinical and legal criticism as well as aiding care in potential future ED presentations.

Violence

The impact of occupational violence and aggression is under-recognized in Australasian EDs, although it has been increasingly documented.³⁸ Violence severity appears to

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have increased, with some recent fatal consequences.³⁹ Aggression and violence most often stem from acutely disturbed patients, although violence in the ED can also come from visitors and carers as well as hospital staff. Internationally recognized as a growing problem, ED violence is also generally poorly documented and under-reported, with limited formal hospital support for those exposed and rare conviction for the perpetrators.^{40,41} Although conventional definitions of violence centre around the act of intent to cause physical or psychological harm, in an ED setting, aggression and violence are commonly manifestations of underlying illness or substance intoxication. The absence of a malicious intent to cause harm may be a reason why violence has been under-recognized in the hospital environment and has led to an alternative workplace definition: any episode in which staff experience either implicit or explicit challenges to their personal safety, health or sense of well-being.⁴²

Other reasons for under-reporting of ED violence stem from hospital systems that act as barriers by burdening staff with excessive and time-consuming paperwork, confusing policies, inadequate confidentiality and lack of peer support. Although most episodes of violence in the ED do not result in serious physical injury, staff who experience violence may be traumatized, which can lead to feelings of stress and anger. The cumulative effect of violence may result in clinician 'burnout' and staff attrition.

The concept of 'zero tolerance', which has been adopted from the justice system in some hospitals, is unworkable in the health care setting, where clinical aggression is conjoined with a duty of care between the clinician and the patient. As a principle, zero tolerance fails to recognize that aggression and violence may be manifestations of a clinical illness that requires remediation and care. Three core components comprise a strategic approach to managing violence in the ED: environment (appropriateness, safety); staff (education, training, teamwork); and systems (reporting, follow up, peer support, policies).⁴³ Prevention and early intervention within a safety and patient-care framework is emphasized. Principles of training should be applied to all health care providers and include training programs tailored to staff groups, stratified risk levels within the organization and included within a culture of continuous quality improvement underlies prevention of occupational violence and aggression training and responses.

Generally a comfortable environment with clear visibility that facilitates good communication will have a greater effect on behaviour modification than the increasing fortification of waiting rooms, triage and clinical areas in the ED. Violence minimization is assisted

by security cameras and televisions at triage so potential aggressors can see that they are being monitored, the visible proximity of security staff, high visibility within the clinical work space, restricted access areas, minimizing access to potential weapons as well as widely dispersed and simple-to-use duress alarm devices. Introducing armed security personnel into EDs increases risk to staff and patients and is not recommended.²⁴ Staff training and support are paramount in managing ED violence. Physician can learn and practice communication techniques to de-escalate aggressive interactions.⁴⁴ Interdisciplinary programmes that involve role play and real scenario discussions can enhance cooperation between all ED staff while also clarifying roles and responsibilities during actual security responses. Peer education sessions can serve to change culture towards a preventative and proactive approach, based on good communication skills and sound knowledge about behavioural emergencies. Hospital security staff are experts in the containment of aggressive and violent patients within a healthcare framework and can lead team-based prevention and safety training for ED staff.

In general, ED doctors are required to take a leadership role when managing a violent episode, although collaboration with experienced nursing colleagues improves care. Awareness of personal factors that may affect the escalation of violence and the subsequent outcomes is therefore essential. Anger, fear and personal insult can lead to interactions with aroused patients that may escalate aggression rather than diffuse tension. The role of peer support and follow up in such situations is vital. Similarly, issues of gender, language and culture are often under-recognized as factors influencing the escalation and management of a behavioural emergency. Male staff may experience higher levels of physical violence than women. Self-awareness and consideration of these issues can optimize management of the violent episode, as well as minimize the potential negative outcomes for staff and others.

The final component of the structured approach to ED violence management is ensuring adequate documentation and follow-up systems, which include debriefing and support. Reporting should be incorporated into the standard documentation of any security incident within the ED, rather than the onus of staff who have been victims of violence. As the issue of workplace violence is one of occupational health and safety, follow-up of violent incidents should fall within this framework, thus depersonalizing the impact of aggression and owning violence as an organizational responsibility rather than one belonging to the individual.

THE FREQUENT ATTENDER

ESSENTIALS

- 1** Frequent attenders to the ED have increased morbidity and mortality.
- 2** Assumptions about inappropriate use of the ED have been shown to be false.
- 3** ED-based multidisciplinary care coordination can lead to improved psychosocial status for frequent attenders.

Definition and epidemiology

Patients who present to hospital EDs more than three times a year can be defined as 'frequent attenders'⁴⁵ and represent a particularly vulnerable population.⁴⁶ Both internationally and within Australasia, the frequent attender population has consistent characteristics that include poverty, homelessness, chronic and complex medical illness, psychiatric illness and drug and alcohol abuse.^{47–49} Frequent attenders also suffer a high mortality, with an increased risk of death from violent causes such as suicide and substance misuse.⁵⁰ They are known to use health services in a frequent, chaotic and episodic way; they often attend multiple EDs and are difficult to engage in any long-term care. Importantly, availability and engagement with primary health care providers does not alter ED use by frequent attenders.⁵¹

Although they represent only a small number of people, frequent attenders can be responsible for up to 8% or more of annual ED attendances.⁵² Demographic details vary according to how the frequent attender population is defined and analysed in the literature; however, they are consistently more likely to be male, older and socially isolated.^{6,46} A range of 27% to 55% have chronic and complex medical illnesses as the key reason underlying their frequent ED use, whereas the remainder suffer primarily psychiatric, social or drug- and alcohol-related illness.^{6,53} Commonly, heavy ED users display a combination of all of these co-morbidities. Patterns of attendance generally fall into two categories, with those suffering primarily psychosocial illness or substance abuse sustaining consistently frequent ED use over many years, whereas those with primarily chronic medical illness showing peak ED attendance over 1 to 2 years.⁵³ Recent research from New Zealand demonstrates the natural attrition of frequent ED attenders over time⁵⁴; however, the principal finding in studies around the world is the high mortality rates in this population.

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Clinical features

There is great variability in the clinical presentation of frequent attenders. Acute exacerbations of underlying chronic medical illness are common as are traumatic injuries or injuries and illness sustained through violence or substance misuse, including acute substance intoxication. Infections in the respiratory, gastrointestinal and dermatological systems are frequent. Deterioration in mental state or self-harm and suicide attempts are also common reasons for ED attendance.⁵² Compared with the whole population, frequent attenders are more likely to present out of hours,⁵³ have more serious and urgent illness and more often require inpatient services.⁴⁶ Frequent attenders are more likely to discharge themselves from the ED prior to completing their ED care or to self-discharge before assessment after the initial triage process.⁵²

There is a pervasive assumption that frequent attenders present to the ED excessively and unnecessarily and are therefore suitable for diversion to general practitioners. Evidence suggests that this belief is false and that the majority of patients presenting frequently for ED care do so appropriately and are unsuitable for diversion to primary care providers.⁵² Patients may be adversely affected if their symptoms are belittled and their attendance classified as 'inappropriate'.⁵⁶

Management

Understanding the vulnerability of frequent attenders and their complex co-morbidities while adopting a humane approach is fundamental. Medical care follows standard procedures. Access to past history and information from all health care and community services involved in the care of the frequent attender provides an essential context enabling timely, focused and relevant care, without unnecessary duplication of services and investigations. The development and wide dissemination of individualized acute care plans can assist in streamlining assessment and management when frequent attenders re-present to the ED after hours. Utilization of ED-based multidisciplinary services for care coordination has been shown to be of benefit when caring for the frequent attender.⁶

Attempts to reduce perceived unnecessary ED attendance have met with varying results. Neither the education of patients nor management care plans has reduced the frequency of their ED attendance. The most successful international diversion strategies have adopted multidisciplinary approaches, including social worker support.^{57,58} ED-based multidisciplinary case management has been shown to increase ED utilization but also to lead to improvement in psychosocial factors, such as housing status and engagement with primary and community care providers.⁶ If psychosocial improvements are desired, ED use may have to

increase for frequent attenders. Frequent attenders are a complex, unwell and chaotic population. Diversion away from the ED has no proven patient benefit; therefore it may be that the ED is the best site of care for such vulnerable patients and can have a role in improving their overall well-being.

THE PATIENT WITH DRUG-SEEKING BEHAVIOUR

ESSENTIALS

- 1 Drug addiction can be viewed as a chronic, organic disease.**
- 2 Drug-seeking behaviour is problematic for the patient and the clinician.**
- 3 Physicians managing these patients may experience dissatisfaction, frustration and feelings of manipulation.**

Definition and aetiology

Drug abuse is defined as a maladaptive pattern of drug use indicated by continued use despite knowledge of its being a social, occupational, psychological or physical problem that is caused or exacerbated by the use.⁵⁹ Addiction is defined as a primary, chronic neurobiological disease that develops as a result of genetic, psychosocial and environmental factors and manifests as use of a substance to the extent that the user is periodically or chronically intoxicated, exhibits compulsive use, has great difficulty in voluntarily ceasing or modifying his or her substance use and exhibits determination to obtain psychoactive substances by almost any means. Typically, tolerance is prominent and a withdrawal syndrome frequently occurs when substance use is interrupted.⁵⁹ Drug-seeking behaviour can be defined as behaviour aimed at obtaining controlled substance prescriptions for reasons of dependence, abuse or illicit use in a manner that is problematic to the prescriber.⁶⁰ Patients may have a range of underlying disorders, such as psychiatric illness, substance misuse, chronic pain and complex medical conditions, which have resulted in drug dependence and institutionalized behaviour on many levels.

The concept of addiction as a disease is useful in modifying the clinician's approach to patients with addiction issues. The illness model has countered the widely held view of addiction as a wilful behaviour with moral implications. Likening addiction to other chronic illnesses, such as hypertension and diabetes, helps to understand the chronicity of the problem and the vulnerability to relapse. The rehabilitation of patients with

substance-abuse problems has, however, been handled largely by non-physicians who work closely with their patients, therefore rendering effective intervention in the ED challenging.

Clinical features

Identification of the patient seeking drugs may be difficult. Features raising suspicion of drug seeking include previously documented drug-seeking behaviours, inconsistent history or examination findings, requests for specific narcotic or other drugs of dependence, unwillingness to try simple analgesia, higher than expected analgesia requirements and demanding or aggressive behaviour. Other features that may raise suspicion include complaints of lost or stolen prescriptions or medications, letters from remote medical practices supporting the provision of medications and presentations that are possible to feign, such as migraine or ureteric calculus. Drug-seeking patients commonly have a past history of mental illness, drug dependence and self-harm.⁶¹

The possibility of missing organic illness is considerable in patients suspected of drug seeking, as nearly 20% require hospital admission and 17% self-discharge against medical advice. Missed, too, is the opportunity to acknowledge drug dependence and refer appropriately. Of drug-seeking patients seen in the ED, only 11% have a documented discussion around this issue in the medical record and only 23% are referred to addiction, psychiatric or chronic pain services.⁶¹

Management

There is considerable individual variation in the management of patients who are drug seeking. Clinicians often find these interactions frustrating and unsatisfying and may feel abused or manipulated. The development of a general approach may assist (Box 21.5.1).

Limit setting requires confidence, experience and familiarity with local laws that limit the

Box 21.5.1 General approach to the drug-seeking patient

- Attempt to develop rapport with the patient.
- Ensure that new organic pathology does not exist.
- Determine that genuine pain has been adequately treated.
- Once you have some degree of certainty that problematic drug-seeking behaviour exists, set clear limits regarding medications requested.
- Consider the possibility of open discussion with the patient regarding the behaviour.
- Consider referral to appropriate services for ongoing care.
- Develop management protocols for particular patients if frequent attendance or threatening behaviours develop.

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prescribing of controlled drugs. A departmental policy regarding the drugs within the ED that are available for dispensing after hours and may be prescribed on an outpatient basis can give guidance. Approaches vary, but a factual and dispassionate explanation about the inability to prescribe controlled substances due to departmental policy or legal requirements may be of assistance.

The physician must determine the appropriateness and utility of an open discussion surrounding the perceived problem behaviour. If open discussion is possible, referral for assistance may be more successful. Opportunities for interdisciplinary discussion of particular patients and an approach to their management with the development of an easily accessible electronically available protocol may assist those in front-line management.

THE VERY IMPORTANT PERSON

ESSENTIALS

1 Management of the VIP should be based on the maintenance of standard clinical procedures.

2 Management may be aided by the establishment of a plan resembling a disaster plan aimed at co-ordination of clinical and administrative issues.

3 Specific issues include security, confidentiality and management of the media.

Definition

A VIP in the ED can be defined as anyone whose presence in the ED may, by virtue of fame or public position, disrupt normal ED functioning.⁶² The VIP may be a person of worldwide repute or may also be someone of local fame or importance, such as a prominent staff member. A 'VIP syndrome' can occur where the treating staff become so overwhelmed by the person's presence that they cease to operate in their normal way and the patient's care is compromised. Disaster plans are formulated in hospitals to deal with situations that overwhelm normal ED operations. In a similar manner, the formulation of a plan to deal with VIPs to ensure optimal management of the patient may help to prevent poor outcomes.

Management

Medical issues

The key goals of management should be the maintenance of standard clinical procedures.

The clinician should perform a standard clinical evaluation without omitting questioning, examinations or procedures that would normally occur due to other considerations, such as embarrassment. Consultation with inpatient specialists should proceed as appropriate and the frequency and timing should reflect standard practice. Deviation from normal procedures—whether in assessment, referral or disposition, invites errors and lack of clarity in management decisions. Health care providers function most efficiently in performing their normal roles; nursing staff, junior medical staff and allied health should be involved as appropriate.

Access to the ED should be restricted after the arrival of the patient. Heads of state may be accompanied by their own teams of physicians. The treating clinician should liaise and consult with these physicians when immediate concerns, such as resuscitation, have been addressed.

EDs are accustomed to managing multiple complex patients at once. However, the presence of a VIP may consume the attention of many staff. The senior medical and nursing clinicians must ensure that adequate staff is assigned to the management of other patients in the ED and that other patients do not suffer adverse outcomes due to the presence of the VIP.

Different issues arise in treating medical colleagues or their families, other staff members or friends and relatives who are 'relative' VIPs. In aiming to expedite the management and ensure the comfort of someone who is known to the treating clinician, as with the VIP, the safest pathway for the patients is not to deviate from standard medical care.

Administrative issues

The essential administrative issues are security for the VIP and the hospital staff, protection of privacy and confidentiality, containment of the press, timely release of appropriate information and a co-ordinated response to the VIP's needs. If the patient is of national importance, the response may resemble a disaster response and require the appointment of a central co-ordinator to manage the initial crisis, security control and media liaison.⁶²

Liaison with hospital security is essential to minimize entry of unnecessary people to the ED and to ensure the safety of the VIP. Assistance from clinical staff may be required to identify those required to enter the ED. Internal security may need to liaise and cooperate with external security teams. The VIP's security team must not impede medical management.

Confidentiality should be respected and consent to release information should be obtained as with any other patient. Release of information to the media should occur in a graded and accurate manner. Disclosure should occur on two levels:

the first is the acknowledgement that the VIP is present and seeking medical attention and the second level involves the graded release of medical information.⁶² One senior clinician should be appointed to convey this information. Ideally, a centre for the media should be set up on a site remote from the ED.

Although the presence of a VIP in the ED may not overwhelm services in the same way as a disaster, a similar approach with a pre-formulated plan of management may assist with the management of these rare and unexpected events and assist in attaining positive outcomes for the VIP and all other patients in the ED.

CONTROVERSIES AND FUTURE DIRECTIONS

- Refugees and asylum seekers held in detention facilities are increasingly requiring emergency care. They differ substantially to the standard prisoner population, are extremely vulnerable and have complex health needs that require a well-informed and deeply compassionate approach.
- The development of acute behavioural centres similar to trauma centres may assist in streamlining the management of acute behavioural disturbance.
- Given the significant deprivations of rights and liberty that are applied in containing those with behavioural disturbance, there is a need to learn more from patients about their experiences.
- The increasing prominence of violence as a critical issue in EDs requires careful policies and practices that protect staff safety and well-being without compromising effective emergency care.
- The perception of inappropriate ED use by frequent attenders remains controversial; some health care workers and health policy makers continue to assume that frequent attenders can and should be diverted to primary care providers.
- Understanding of drug dependence as a chronic, organic brain disease may reduce stigma and lead to the development of better medical models of treatment that can enhance the behavioural and social therapies currently practised.

Full references are available at <http://expertconsult.inkling.com>

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21.6 End-of-life decision making and palliative care

William Lukin • Ben White • Carol Douglas

ESSENTIALS

- 1** An emergency department attendance represents an opportunity to set goals for care during the attendance and beyond.
- 2** End-of-life discussions and advance care planning assist early decision making about treatment goals and end-of-life care.
- 3** Knowledge of the law assists decision making at the end of life.
- 4** Not all dying patients require the skill set of a palliative care specialist, but every dying patient will benefit from a palliative approach.
- 5** Palliative care does not preclude active treatment where the intent is understood by patient and family.
- 6** Failure to diagnose dying can compromise patient care.
- 7** The emergency department should foster close relationships with local specialist palliative care providers to improve and ensure timely access for patients and families and also to ensure that emergency staff have access to the knowledge and skills available.

Introduction

Improved socioeconomic conditions and advances in medicine, including improved management of chronic disease, have resulted in extended life expectancy. Prior to death, many people now experience a period of progressive deterioration in health and loss of independence due to complex multi-system disease and possible cognitive impairment. It is estimated that up to 40,000 adult deaths occur in Australia annually in the setting of a medical decision to withhold, limit or withdraw treatment.¹ End-of-life decision making, such as decisions not to provide, to limit or to discontinue life-sustaining treatments and the decision to transition care to a palliative approach are now a common part of the practice of emergency medicine.

End-of-life discussions and decision making can be challenging owing to the complexity of balancing family wishes with the best interests of the patient and dealing with families in times of great stress. End-of-life decisions require an understanding of the law and ethical positions of peak medical bodies and are greatly assisted by patients and their families having considered, discussed and documented their wishes. These discussions and decisions may be communicated informally or formally in advance care plans and directives supported by common law and legislation.

Palliative care is the provision of care to those facing life-limiting or life-threatening illness and

focuses on the needs of the patient as a whole across various domains, not just the physical. In addition, it looks at the family as a unit also requiring care. For patients for whom the palliative approach should be adopted, palliative care skills enable the emergency physician to engage patients on a dying trajectory and allow them to take control of this process and plan for the time they have remaining, be it hours, days or months. This enables planning for the non-physical aspects of the dying process and reduces time lost to futile medical endeavours.

The most important aims of end-of-life discussions and palliative care are the identification of what the patient sees as an acceptable outcome from any proposed treatment, enabling early and wise decisions about the appropriateness of treatment and improving communication with patients and families to facilitate the provision of patient-centred care.²

Definitions

Definitions are given in [Table 21.6.1](#).

General legal principles in end-of-life decision making

Patients have the right to decide whether to accept or refuse medical treatment. This right is underpinned by Western liberal concepts of

self-determination and individual autonomy.³ Although the state has an interest in preserving the life and health of citizens, this interest is subject to an individual's right to self-determination.

Therefore a patient's informed consent must be obtained before treatment commences. To perform a medical procedure against the wishes of a patient can amount to trespass and battery in common law and can also contravene guardianship and medical treatment legislation.⁴ A legitimate refusal of treatment must be respected, even if it is contrary to medical opinion. Where a person lacks capacity and so cannot give consent, he or she may have an advance directive (AD), or consent should be obtained from a legally authorized decision maker, such as a substitute decision maker or parent if the patient is a child.

There are exceptions to the need for consent to treat. One is cases of emergency where both the common law and various types of legislation (including guardianship legislation) permit the provision of lifesaving or other urgent treatment. Another exception is where mental health legislation authorizes treatment.⁵

A patient generally has no legally enforceable right to demand a particular treatment. Medical practitioners are not obliged to offer treatment that is not in a patient's best interests, such as treatments that are futile and where the burdens exceed the benefits of treatment. In Australia, an exception exists under Queensland's guardianship legislation for adults who lack decision-making capacity; in such cases consent is required to withhold or withdraw life-sustaining treatment.⁶

Although the vast majority of disagreements about end-of-life care are resolved informally, recourse may also be had to the courts and, for adults who lack capacity, to guardianship tribunals and the statutory office of public advocate or guardian.

Expected legal knowledge of medical practitioners

Despite attempts to harmonize the law regulating end-of-life decision making, it varies across Australian states and territories⁷ and the rest of the world. Medical practitioners play significant legal roles at the end of life, including assessing a patient's capacity to understand and make decisions, determining the scope of any consent or refusal and whether it applies to current circumstances and understanding the operation of guardianship laws to find a patient's substitute decision maker when the individual is not competent.^{1,8}

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Table 21.6.1 Definitions of terms

Term	Definition
Advance care planning (ACP)	A process that allows competent individuals to express their views regarding future health care decisions if the capacity to express those views is lost.
Advance directive (AD)	A statement that allows competent individuals to state in advance how they wish to be treated if they lack decision-making capacity in the future. Making an AD can be part of ACP. Different terms are used for ADs in different jurisdictions.
Futile treatment	The definition of futile treatment is contested, but treatment may be considered futile when it is no longer providing a benefit to a patient or the burdens of providing the treatment outweigh the benefits.
Good medical practice	Practice that is consistent with currently recognized medical standards, practices and procedures and currently recognized ethical standards of the medical profession.
Life-limiting illness	An illness where it is expected that death will be a direct consequence of the specified illness.
Life-sustaining treatment	Medical treatment that supplants or maintains the operation of vital bodily functions that are temporarily or permanently incapable of independent operation. This includes assisted ventilation, artificial nutrition and hydration and cardiopulmonary resuscitation but excludes measures of palliative care.
Palliative care	An approach that improves the quality of life for patients and their families facing life-threatening illness through the prevention and relief of suffering by means of early identification and rigorous assessment and treatment of pain and other problems, physical, psychosocial and spiritual.
Substitute (surrogate) decision maker ('person responsible' in some jurisdictions)	The person legally responsible for making decisions about health care, including its limitations, on behalf of an adult patient who lacks decision-making capacity. State guardianship or medical treatment legislation determines a patient's substitute decision maker.
Enduring guardian, attorney or medical treatment decision maker (terms vary depending on jurisdiction)	A substitute decision maker who is given authority by a patient to make health care decisions on behalf of that patient if capacity is lost.

Medical practitioners (including emergency physicians) have significant knowledge gaps regarding the law about end-of-life decision making.⁹ Because doctors play important *legal* roles in these decisions, training on the law in this area across all stages of medical education (including continuing professional development) would support doctors in improving their legal knowledge while also avoiding possible risks to them and harms to patients.⁹

Advance care planning and advance directives

Advance care planning (ACP) is planning and expressing wishes for future health and personal care for a time in the future when the individual cannot make or communicate decisions. ACP provides a means for people to ensure that their wishes and preferences are known. Most doctors, nurses and members of the community support ACP, but rates of formal planning are low despite evidence that ACP leads to improvement in end-of-life care, patient and family satisfaction and reduction of anxiety and depression in surviving relatives.¹⁰

ADs are generally a form of written advance care plan made by a competent person recognized by common law and/or legislation depending on the jurisdiction. An AD can be written at any time of life and may relate to periods of temporary or permanent incapacity. Content may vary from an expression of personal values and wishes to specific medical directions by a person with a life-limiting illness.

ADs are recognized in many parts of the world, including all Australian jurisdictions; six Australian states and territories now have specific legislation relating to ADs. All jurisdictions also have legislative provisions that allow patients to appoint a substitute decision maker, designated variously as an *enduring guardian, enduring attorney or medical treatment decision maker*, depending on the jurisdiction. The guardianship legislation of all states and territories allows for the appointment of a guardian by a court or tribunal, but this occurs only where less formal mechanisms are inadequate.⁶

A National Framework for Advance Care Directives authored by the Clinical, Technical and Ethical Principal Committee of the Australian Health

Minister's Advisory Council aims to provide a practical and ethical basis to the development of a national framework for advanced directives.⁷

Limitation or withdrawal of treatment

Emergency medicine practitioners may be confronted with circumstances where the patient and family have not considered the desired outcomes of their ongoing treatment or that death may be a possible outcome of their current condition. Up to 35% of deaths in EDs involve patients in the terminal phases of existing chronic illness who attend the ED for conditions that represent the natural evolution of the illness.¹¹ The ED has become a place where terminally ill patients frequently die and where decisions regarding the limitation or withdrawal of care are often made.

Although doctors generally must not cause or hasten a patient's death, there are circumstances where limiting or withdrawing treatment is lawful. These include when a competent adult refuses treatment, when another person (such as a substitute decision maker or parent) has lawfully refused treatment on behalf of the patient and when the treatment is not in the patient's best interests, either because it is considered futile or the burdens are not justified by the potential benefits.⁴

The Australian Medical Association states that if a medical practitioner acts in accordance with good medical practice, the following forms of management at the end of life do not constitute euthanasia or physician-assisted suicide: (1) not initiating life-prolonging measures and (2) not continuing life-prolonging measures and the administration of treatment or other action intended to relieve symptoms that may have a secondary consequence of hastening death.^{12,13}

Despite growing community interest in ADs and an increasing burden of chronic disease, the majority of patients presenting to EDs have not discussed their end-of-life wishes with family or expressed their wishes in an AD.¹⁴ In these situations, discussions should focus on the desired outcomes of treatment and the delivery of treatments consistent with those desires that offer some comfort and assistance to the patient.

Resuscitation and not-for-resuscitation orders

When first described in the 1960s, cardiopulmonary resuscitation (CPR) involved simple resuscitative measures to reverse physiological instability. Although CPR can 'stay' death on occasion, it is frequently applied in circumstances that will not result in a return to previous health and is applied in patients who are actually dying.¹⁵ American health care culture has been described as one of medical optimism, characterized by an unwillingness to give up hope for a miracle, which has led patients to choose distressing and

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burdensome treatment options that eventually end in death, whether or not these treatments had been instituted.¹⁶ Unrealistic expectations of outcomes from CPR are common.¹⁷

The combination of knowledge deficits, unrealistic expectations of outcomes and medical optimism have left patients and doctors with a sense that there is a presumed consent to CPR unless otherwise indicated.¹⁵ Not-for-resuscitation (NFR) orders have developed in response to CPR being universally applied and the presumed consent to its use. The absence of an NFR order has come to be considered as an order to perform CPR unless otherwise instructed.¹⁵ CPR is no longer seen as a medical intervention with specific indications but one of many patient choices.

The American Heart Association defines the goals of resuscitation as follows: to preserve life, restore health, relieve suffering, limit disability and respect the individual's decisions, rights and privacy.¹⁸ Decisions to commence, continue or terminate resuscitation are based on the difficult balance between the benefits, risks and cost these interventions to the patient, family members and health care system.¹⁹ Ethical reasons for withholding attempted resuscitation include respecting the patient's autonomy and choices, weighing maleficence against beneficence (avoiding treatment that may cause more harm than benefit), trying to provide a good 'quality of death' and the consideration of resources.¹⁹

Some peak medical bodies provide ethical guidance on these issues.^{18,20–22} The United Kingdom's General Medical Council (GMC) advises that 'in cases where you assess that such treatment is unlikely to be clinically appropriate, you may conclude that CPR should not be attempted'.²³ The Medical Board of Australia recognizes that 'doctors have a vital role in assisting the community to deal with the reality of death and its consequences', and good medical practice involves both 'understanding the limits of medicine in prolonging life and recognizing when efforts to prolong life may not benefit the patient'. The medical board also states that there is no duty to prolong life at all costs but that there is a duty exists to know when not to initiate and when to cease attempts at prolonging life.²⁴

The ability to 'refuse' an NFR order perpetuates the paradigm that CPR is solely a patient choice and that all deaths can potentially be prevented. The performance of CPR, under the guidance of the bodies such as the GMC and the Medical Board of Australia, is a medical decision that the patient can refuse but on which the patient cannot insist (although the situation under Queensland's guardianship legislation discussed earlier should be noted).

Palliative care

The World Health Organization defines palliative care as an approach that improves the quality of life of patients who are living with a life-limiting illness and their families through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems—physical, psychosocial and spiritual.²⁵

Palliative care is an emerging area in emergency medicine, with international evidence suggesting that the care of the patient who is imminently dying is not done well in EDs. In addition, the care of the patient who is on a dying trajectory and presents to the ED needs further research. Palliative care focuses on the needs of the patient as a whole across various domains, not just the physical. In addition, it looks at the family as a unit also requiring care. Emergency physicians should adhere to the principles of a good death for all of the patients who die in EDs.²⁶ For patients for whom the palliative approach should be adopted, skills in palliative care enable the emergency physician to engage patients on a dying trajectory and support them in taking control of this process and putting in place a plan for the end of life. This allows for choice of place of death outside of the acute setting, which requires appropriate social and clinical supports. The discussions surrounding such planning include the non-physical aspects of the dying process and may reduce time lost to futile medical endeavours that are likely to ensue in the acute setting.

Specialist palliative care versus a palliative approach

Not all dying patients need the skill set of a specialist palliative care provider. However, all patients living with a life-limiting disease and those dying in the ED can benefit from a palliative approach to care. This approach focuses on the quality of life remaining for those with life-limiting disease. This approach can be adopted by all clinicians who deal with dying patients. The complexity (in respect to palliation) of a patient fluctuates as the patient approaches the end of life. For patients whose needs are complex, timely referral to specialist palliative care providers may be helpful.

Palliative care skills for the emergency physician

Communication skills in the palliative domains (physical, spiritual and psychosocial)

Appropriate discussion around these domains enables patients to regain some control of the dying process and improves the experience for patients and families. Although there is often no time for in-depth exploration of all these themes

in a given patient encounter, simple acknowledgement of their existence by the clinician can help shape priorities for the presentation. Conversations that begin in the ED can be a stimulus for further discussions with treating teams and can also encourage and prompt families to have these discussions. While traditionally viewed as difficult, such discussions are generally welcomed by patients and families. To walk away from a dying patient without this engagement is a failure of care and a loss of opportunity for the patient.

Impeccable assessment skills

The needs of these patients for comprehensive evaluation are the same as those for any other patient coming into the ED. To deal with physical symptoms appropriately, a diagnosis is required and appropriate investigations may be undertaken if there is likely to be a benefit. For example, delirium in an older person may be relatively simply resolved through appropriate investigation and treatment of the underlying cause and should not be ignored or generically treated with sedation.

Pain relief and symptom control

Uncontrolled pain or other distressing symptoms may prevent engagement in appropriate end-of-life discussions and planning. It is imperative that these needs be met promptly in the ED. Where these needs are complex, early referral to specialist palliative care providers may assist. No patient should have uncontrolled pain in an ED and processes should address this with pain score assessments, protocol-driven analgesia and the fostering of a culture where patients and families can speak up and voice concern. For patients using opioids other than morphine relative potencies must be taken into account. This is crucial when providing rescue analgesia and for titration of adequate pain relief. If there is doubt seek specialist advice.

Management of common symptoms including nausea and dyspnoea is required to minimize the suffering experienced at the end of life. Patients who are distressed by dyspnoea may require palliation with an opioid. There is an evidence base for this approach to care, and concerns by clinicians in palliating dyspnoea with an opioid are unwarranted.²⁷

Developing a local protocol for managing pain and other symptoms in the ED is recommended.

Anticipating the end of life and diagnosing the dying

The concept of identifying patients who are at the end of life implies a recognition of the fact that they will not recover from their illness. The need for this emphasis stems from a societal view that denies death and an acute care system that views death as the enemy. Failure to diagnose dying in

a timely manner can result in over-investigation, initiation of inappropriate treatments and false perceptions of hope for the patient and family. Such lack of recognition results in patients and families being denied the opportunity to plan for what is to come and to make choices. The well-recognized 'surprise question'²⁸ is 'Would you be surprised if your patient were to die in the next 12 months?' A response of 'no' indicates a sensitive measure for commencing ACP and having the 'difficult conversation' around poor prognosis and life-limiting illness.

For emergency clinicians the question could be posed as 'Would you be surprised if this patient died during this admission?' If the answer is no, there is an opportunity to engage the patient and family in discussions about the goals of this admission. Referral to palliative care providers from the ED can shorten the length of stay in hospital by facilitating transfer home with support; this will increase the likelihood that goals of care around the end of life are established and reduces the burden on the medical emergency response teams within the hospital.

The dying

For patients whose death is imminent (hours), it may not be appropriate to transfer them out of the ED. In this case, compassionate comfort-based care is necessary and has been shown to be supported

by the use of a clinical framework such as that developed by the International Collaborative for Best Care of the Dying.²⁹ Such an approach enables hospice-level care to be delivered in all care settings, such as a short-stay unit. Best care of the dying is supported by the application of clear communication of the dying process, seeking to deal with the spiritual and cultural needs of the patient and family, ensuring anticipatory prescribing and de-prescribing of non-essential medicines and the rationalization of inappropriate interventions. Medications to control symptoms are provided by the subcutaneous route and via a continuous infusion mechanism where warranted.

The provision of high-quality end-of-life care requires early discussions and planning with the patient and family so that all concerned with the patient's care are clear about the goals of treatment. Silvester identifies three opportunities to ensure that patient-centred care is delivered at the end of life.³⁰ First, a competent person may consider and express his or her wishes via ACP. Second, when a person is no longer competent, health care professionals should determine whether ADs exist and have discussions with substitute decision makers about what outcome the patient would have wished. Third, the delivery of care at the end of life should provide a 'good death': avoiding suffering and the prolongation of dying, achieving a sense of control, relieving

burdens placed on the family and strengthening relationships with loved ones.

CONTROVERSIES AND FUTURE DIRECTIONS

- Close partnering between emergency providers and palliative care providers will provide timely intervention in emergency departments so that opportunities to establish goals of care are not lost.
- Short-stay units should be able to provide hospice-level care to the dying with support as required from specialist palliative care services or the use of locally tailored care plans for the dying person.
- End-of-life and palliative care may become subspecialty areas for emergency physicians.
- Assisted dying legislation is in place in Victoria and more states may follow. Patients seeking access to physician-assisted dying will come to emergency departments. Clinicians will need to know how to respond to these patients.¹⁹

Full references are available at <http://expertconsult.inkling.com>

21.7 Organ and tissue donation

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ESSENTIALS

- 1** Organ donation should be considered for all patients where death is expected. Suitability for donation should be discussed with an organ donation specialist.
- 2** A substantial numbers of missed potential organ and tissue donors can be identified in emergency departments (EDs) and intensive care units (ICUs).
- 3** Clinical triggers have been introduced in Australian EDs to assist with the early identification of potential donors.
- 4** Knowledge of pathways to donation and the skills required to commence donation discussions may decrease the numbers of missed potential donors and improve the numbers of organ and tissue donors.
- 5** Admission to an ICU should be considered for any intubated patient in the ED in whom end-of-life care is considered. This can facilitate early family discussions, timely prognostication and consideration of organ and tissue donation if appropriate.

Introduction

Transplantation has become the therapy of choice for patients with end-stage organ failure.

However, worldwide, there are not enough organs available to meet the demand for those on transplantation waiting lists. In Australia at any one time, there are approximately 1400 people

awaiting organ transplantation. In 2017, there were 519 deceased organ donors in Australia and 1675 transplant recipients.¹ Between 2007 and 2016, over 1000 patients were admitted to Australian and New Zealand intensive care units (ICUs) primarily to assess their suitability for organ donation; of these, almost two-thirds came directly from the emergency department (ED).²

In Australia there is a relatively small pool of potential donors, as less than 2% of patients who die in hospital are eligible to donate their organs.^{1,3} Despite this scarcity there is potential to increase the number of organ donors through higher consent rates, improved identification, increased resources for education, coordination, surgical retrieval and transplantation services. Despite high rates of community support for donation, consent rates for donation (approximately 60%) have changed little.⁴ Identification of missed opportunities for organ donation may have the greatest impact on donor numbers. Missed opportunities include situations where life-sustaining therapies are withdrawn in patients

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with imminent or potential brain death, particularly in the ED; patients who may be suitable but with whom donation is never raised owing to clinicians' unwillingness to discuss donation; resource pressures; and an incorrect perception that a patient may not be medically suitable.⁵

Although the donation of solid organs is a rare opportunity, eye and tissue (e.g. skin, bone, heart valves and connective tissues) donation can occur up to 24 hours after death and may be applicable to a larger population of patients, especially those in the ED. Few absolute contraindications to donation exist. Liver donation has occurred from patients over 80 years of age. HIV is no longer an absolute contraindication and organs are commonly donated from patients with a history of hepatitis C. Corneal donation may even be possible in patients with metastatic and hematological malignancies in whom the donation of other organs and tissue is not possible.

Emergency practitioners play an important role in the donation process. Within Australia, there is strong support for organ donation amongst ED staff, particularly amongst those who have had specific training and experience with organ donation. Lack of education, resources and time are commonly identified by ED staff as barriers to donation.⁶ However, donors identified in the ED have a greater rate of proceeding to successful donation than those referred from other inpatient critical care settings.⁷ Emergency clinicians are ideally placed to exhibit positive attitudes toward donation, support donation, identify and support potential donors and help families to make informed decisions about donation.

Donation pathways

The initial critical step in making organ donation a reality is to recognize the potential donor. These are usually ventilated patients in the ED or ICU who are expected to die often of neurological injuries but also potentially from non-neurological conditions.

Donation after brain death

The majority of deceased organ donations in Australia (70%) occur following brain death. Criteria to diagnose brain death vary slightly in different countries^{8,9} but essentially depend on the loss of capacity for consciousness and the ability to breathe. If preconditions are met (e.g. no effects of sedating drugs and a diagnosis consistent with producing severe brain injury), brain death may be diagnosed clinically by demonstrating loss of all brain-stem reflexes. A clinical diagnosis of brain death cannot be made until a period of observation has elapsed (minimum 4 hours in Australia). Thus brain death is rarely diagnosed in the ED, but patients who might become brain dead are commonly identified

there.² When clinical testing is not possible, imaging tests (e.g. cerebral angiogram, nuclear medicine scan and computed tomography [CT] angiography) may be performed. The donation of heart, lungs, liver, pancreas, bowel and kidneys from one brain-dead donor can lead to up to eight organ transplants.

Donation after circulatory death

Although donation after brain death has remained the most common route for organ donation, the 2000s saw renewed interest in donation from patients in whom death was diagnosed after cessation of circulation. Unlike brain-dead donation, the practices and processes for donation after circulatory death (DCD) vary widely across countries and reflect differing social, medical and legal environments. Patients considered for DCD in Spain and France are commonly those who present following cardiac arrest (with or without failed attempts at resuscitation)—so-called uncontrolled DCD. In contrast, in Australia, the United Kingdom and the United States, DCD is usually performed in patients who undergo elective withdrawal of cardiorespiratory support in the ICU after determining that he or she will not recover—so-called controlled DCD.¹⁰ DCD currently accounts for 30% of donations throughout Australia but has the capacity to increase overall donor numbers even further with improved recognition of potential donors.¹¹ Kidney, lung and liver donations commonly occur through the DCD route. Although possible, heart, pancreas and bowel donations are less common.

Uncontrolled donation after circulatory death in the emergency department

The recognition that patients who died following out-of-hospital cardiac arrest might still be suitable donors has led to the creation of 'rapid response teams' or 'mobile donor units' to facilitate organ donation. Although these have resulted in successful donations in Spain, France, Japan and the United States, some programs have closed down due to a failure to identify more than a handful of patients.¹² In addition, concerns over the use of vascular cannulation techniques for organ perfusion—which are similar to extra-corporeal membrane oxygenation—cardiopulmonary resuscitation (ECMO-CPR), lack of consistency over an appropriate 'hands-off' observation (varying from 2 minutes in some US states to 20 minutes in Italy) and the large resources required for small numbers of suitable patients¹³ have limited uptake of these techniques worldwide. Within Australia, a more socially acceptable, cost-effective and productive method is to identify intubated patients in the ED considered likely to die and to continue cardio-respiratory supports until its elective withdrawal later in the ICU (if appropriate).^{11,14}

Initiatives to improve organ donation rates

There is wide variation in rates of organ donation throughout the world, with Spain's more than 30 donors per million population often highlighted as a target for others. Many factors influence these numbers, including the number of road traffic fatalities, attitudes toward ongoing treatment of patients who are going to die but in whom wishes about donation are not known, access to intensive care beds (lower in the UK than in Spain and Australia), end-of-life practices in general and public support for organ donation among others. However, countries that have successfully increased donation rates have concerted approaches towards the identification of potential donors, support for clinicians involved in donation, public promotion about the benefits of organ donation and transplantation, clear legislation, infrastructure and funding.

For many years, Australia's donation rate lagged a long way behind that of similar developed countries. In the late 2000s, building on experiences from abroad, federal funding led to the formation of the Australian Organ and Tissue Authority. A co-ordinated national approach to increasing organ donation was undertaken with increased publicity, provision of dedicated organ donation staff to hospitals, improved education (notably through 'Family Donation Conversation [FDC]' workshops) and initiatives to improve the identification of potential organ donors. This has led to a progressive increase in donor numbers to 20.7 per million population in 2017 from below 10 per million in 2000.¹⁵

Identification of potential organ donors

The emergency clinician has a central role in the early identification and support of potentially suitable organ donors, with the majority of all potential donors being initially admitted through an ED. Emergency clinicians are almost always involved in decisions to withdraw life-sustaining treatments in EDs, and one study showed that almost half of all missed donors have their life-sustaining treatment withdrawn within the ED.³

As with all high impact–low frequency events, it is important that clinicians be familiar with their typical clinical presentations and that departments implement aides and processes that enhance identification.

Most potential donors present with severe neurological insults from a limited range of primary pathologies. Severe intracranial haemorrhage is the most common pathology, with other causes including traumatic brain injury, hypoxic-ischaemic insult (e.g. from prolonged cardiac arrest), and large-territory thrombotic

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Box 21.7.1 GIVE clinical trigger

G	Glasgow Coma Scale score ≤5
I	Intubated
V	Ventilated
E	End-of-life care

stroke.³ However, patients dying from single organ chronic disease (e.g. chronic respiratory failure) are also increasingly being recognized as potential donors via a controlled DCD pathway.¹¹

Clinical triggers have been developed worldwide and aim to minimize the number of missed potential donors.³ The Australian GIVE clinical trigger was introduced in 2010 (Box 21.7.1). Although it has performed well in identifying potential brain-dead donors, it has lower sensitivity for identifying DCD pathway patients. This has led to the promotion of routine referral for all patients in critical care environments who are undergoing end-of-life care.¹⁶

The identification and facilitation of organ donation is a whole-of-hospital responsibility. Many hospitals now consider routine admission from ED to ICU of

(A) patients with catastrophic brain injuries.^{17,18,19}

(B) intubated patients considered for withdrawal of life-sustaining treatment.

(C) patients in whom organ donation is being considered.

The rationale for this approach includes improved prognostication,⁴ an unrushed approach to end-of-life care, allowing time to have discussions with family members and the provision of care by teams with high-frequency experience of end of life in a critical care environment. In addition, admission to an ICU is a cost-effective use of health care dollars.²⁰

Management of devastating brain injuries and support of the potential donor within the emergency department

Given that the majority of potential organ donors are admitted through EDs, the management of these patients in this early phase has important implications. Although for some patients there is a high degree of prognostic certainty about futility, it is increasingly appreciated that early prognostication is fraught with difficulty.^{17,21,22} Many centres now routinely support these patients in the ED to facilitate admission to the ICU.

In the ED, clinicians should aim for normal physiological parameters.²³ Early urinary catheterization as well as arterial and central venous access should be achieved to facilitate these aims. Restoration of normal physiology benefits both patients with prognostic uncertainty and patients who proceed to organ donation. It is associated

Table 21.7.1 Common sequelae of devastating brain injury and treatment

Clinical signs	Practice tips
Hypertension and tachyarrhythmias (Autonomic storm)	Often transient, no intervention may be required. Consider short-acting agents if persistent (esmolol, glyceryl trinitrate). Anticipate hypotension and later need for central access and vasopressors.
Bradycardia	Usually resistant to atropine. Consider adrenaline, isoprenaline or pacing.
Hypotension	May be rapid in onset and can occur during autonomic storm; 90% of patients require vasopressor support (e.g. noradrenaline). If persistent, consider vasopressin infusion and intravenous corticosteroid. Consider and treat diabetes insipidus (see later). Consider myocardial dysfunction: treat with adrenaline and intravenous (Tri-iodothyronine) T ₃ .
Polyuria (>3–4mL/kg/h)	Consider diabetes insipidus if Na is rising >145 or high plasma/low urine osmolarity exists: treat with desmopressin (DDAVP) given as an intravenous bolus of 1–4 µg (paediatric dose: 0.25–2 µg) q2–6h or vasopressin: intravenous infusion at a dose of 0.5–2.0 U/h (paediatric dose: 0.002–0.04 U/kg/h). Replace losses with equivalent volume of 5% dextrose. Consider other causes (e.g. mannitol).
Coagulopathy	Commonly a consequence of anticoagulants, direct brain injury or multi-trauma. Correct early with blood products.
Hypoxia	Consider neurogenic pulmonary oedema or aspiration. Treat with positive end-expiratory pressure (PEEP) and mandatory positive-pressure ventilation. Consider antibiotics and need for bronchoscopy.

(Adapted with permission from Opdam HI, Silvester W. Potential for organ donation in Victoria: an audit of hospital deaths. *Med J Aust.* 2006;185:250–254.)

with higher numbers of organs transplanted per donor and a reduction in delayed graft function in recipients.^{18,23}

The progression of pathophysiology that results in eventual brain death is associated with common, predictable sequelae (Table 21.7.1). The emergency clinician should both actively seek and treat these states to maintain the opportunity for donation until it can be appropriately raised with family.

Conversations with families in the emergency department

Although initial information about diagnosis and prognosis may be conveyed to family, in most practice settings FDCs rarely need to occur within the ED. At all times FDCs are best conducted by senior staff with significant experience with donation who have undergone training in specialist donation communication.¹⁶

In hospitals with a co-located ICU, patients with devastating brain injury should be ideally admitted to the unit. Admission allows time for improved prognostication, time for family to gather and, when appropriate, an unhurried approach to end-of-life care. A comprehensive approach to end-of-life care routinely includes determination of medical suitability for organ donation and ensuing exploration.

The aim of communication in the ED is to explain the gravity of the situation, the expected

outcome and, if appropriate, to convey that the patient is dying. Admission to the ICU facilitates an unhurried approach to end-of-life care by experienced practitioners. Should a family raise the issue of donation in the ED, it can be gratefully acknowledged and the family referred to the intensive care staff to continue the conversation.

However, a number of less common scenarios can sometimes compel an earlier discussion within the ED. These include situations where there is universal agreement of futility and haemodynamic instability, thus necessitating a rapid exploration of organ donation, or where there is no co-located ICU and transfer to another hospital would be only for the purpose of exploring donation. In these scenarios, it is important that the emergency clinicians be familiar with the hallmarks of best practice in raising donation, as outlined further on.

Best practice in raising organ donation

The aim of a FDC is to assist families with making an informed and enduring decision regarding organ donation. The decision should sit comfortably with the known wishes of the patient and family. The principles listed here have a growing evidence base and they apply regardless of the location of the conversation. They have been endorsed by the Australasian College for Emergency Medicine.¹

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- Medical futility should have been established by a multidisciplinary team.
 - Before they are asked to consider organ and tissue donation, the family must understand that the patient has died (if brain dead) or that death is expected following the withdrawal of treatment.
- Prior to a FDC,
- The state's donation agency should be contacted and the Organ Donor Register checked.
 - A clinician who is not the treating clinician and who has specific donation communication training should be recruited to attend the meeting (donation specialist).
 - A pre-meeting should be held with clinicians to determine clinical facts and allocate roles.
- During the FDC,
- Discuss patient care and prognosis with family.
 - Confirm family understanding of death, or expected death following the withdrawal of treatment, before donation is offered to the family.
 - Separate conversations about death and donation to create time and space for family.
 - The opportunity for donation is offered to the family in a team-based approach, including the provision of accurate information about donation and transplantation.
- Following the FDC,
- Team review occurs after each FDC process to provide an opportunity to reflect upon and improve practice.

Eye and tissue donation

Donated human tissue has the capacity to reduce morbidity and in some cases, save lives. Tissue that can be donated includes corneas, sclerae, whole eye preparations, heart valves, pericardium, bone, skin and other musculoskeletal tissues. Amongst many indications, donated tissue is used to patch ventricular septal defects, reconstruct joints, restore sight and reduce mortality in severe burns.

Every year more than 4700 patients die in Australian EDs. The potential pool of eye and

tissue donors is significantly larger than that of organ donors, as eye and tissue donors do not have to die within a critical care environment. Within hospitals, EDs are an important source of potential donors. A recent study showed that one in three ED deaths were medically suitable to be eye donors and one in seven were medically suitable to be tissue donors.^{24,25}

The most common contraindications to donation include maximal age (which varies by jurisdiction and tissue type), neuro-degenerative conditions (e.g. Alzheimer or Parkinson disease), risk factors for blood-borne virus transmission, non-haematological malignancies (for eye donation), and any malignancy (for non-ophthalmic tissue donation).

Most eye and tissue procurement organizations have collaborative relationships with coronial services that facilitate eye and tissue donation, even in coronial cases. Eye donation can frequently occur on the hospital premises. Tissue retrieval must often occur in a controlled environment within 24 hours of death, so the identification of potential donors, discussion with families, and notification of eye and tissue donation agencies must occur in a timely fashion but can occur after the death of the donor.

Studies of bereaved families report comfort with either a direct approach by treating clinicians or a delayed telephone approach.²⁶ Despite having a high level of professional and community support, the opportunity of eye or tissue donation is rarely offered to bereaved families.

Despite the total number of patients who die within EDs each year, managing the death of a patient within the ED is a rare event for the individual clinician. Timely identification of a potential eye or tissue donor is complicated by the rarity of death as well as the complexity of age, medical and social exclusion criteria.

The routine consideration of eye and tissue donation as part of a comprehensive approach to bereavement is best facilitated by integration into a specific process or pathway. In some international jurisdictions, this is mandated by law.²⁷ The implementation of an eye and tissue donation pathway within ED can promote a broader awareness of donation.

CONTROVERSIES AND FUTURE DIRECTIONS

- With the increasing frequency of DCD, clinical triggers for the identification of potential donors may have to be extended to include all those in whom withdrawal of life-sustaining therapies is being considered.
- Although the number of donors from patients presenting to EDs in cardiac arrest is low, the growing use of extracorporeal membrane oxygenation (ECMO) may potentially result in more donations from patients who subsequently die despite initial successful resuscitation.
- Rates of eye and tissue donation could be increased by the identification of potential tissue donors in the ED.

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Full references are available at <http://expertconsult.inkling.com>

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SECTION 22

PAIN RELIEF

Edited by *Conor Deasy*

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22.1 General pain management

Adrian Murphy

ESSENTIALS

- 1 Acute pain is the most common symptom in the emergency setting.**
- 2 Pain is a complex, multidimensional, subjective phenomenon.**
- 3 Effective pain management involves both accurate assessment and timely treatment.**
- 4 Patient self-reporting is the most reliable indicator of the presence and intensity of pain.**
- 5 Both pharmacological and non-pharmacological techniques should be employed for the treatment of acute pain. Effective pain relief should always be achievable.**
- 6 In acute abdominal pain, titrated opioid analgesia should never be withheld, pending surgical review; the effect of analgesia on physical signs should not be used as a diagnostic test.¹⁻³**

Introduction

Pain is defined by the International Association for the Study of Pain as: 'An unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage'.⁴ Acute pain is defined as: 'Pain of recent onset and probable limited duration. It usually has an identifiable temporal and causal relationship to injury or disease'.⁵ Whereas in some conditions the nature and progression of the pain may be helpful in making the diagnosis of the underlying pathology, too great a reliance has been placed upon this feature, thereby allowing the patient to suffer needlessly for prolonged periods. For example, the notion that analgesia masks clinical signs in the context of abdominal pain is a fallacy; provision of pain relief often enhances a clinician's diagnostic ability.^{5,6}

It is recognized that failure to adequately treat acute severe pain, in the emergency setting, is

associated with adverse biochemical, physiological, metabolic, and psychological sequelae, and in some patients may alter responses to future painful episodes.⁷ Thus the timely management of acute pain is a fundamental pillar of good emergency medicine practice to reduce the avoidable suffering to our patients.

Physiology

Pain is one of the most complex aspects of an already intricate nervous system.⁵ A number of theories have been developed to explain the physiology of pain, but none is proven or complete.

'Gate Control Theory'

In 1965, the Melzack–Wall 'Gate Control Theory' emphasized mechanisms in the central nervous system that control the perception of a noxious stimulus and thus integrated afferent, upstream processes with downstream modulation from

the brain.⁸ However, this theory did not incorporate long-term changes in the central nervous system to the noxious input and to other external factors that impinge upon the individual.⁸

Nociceptor function

Most pain originates when specific nerve endings (nociceptors) are stimulated, producing nerve impulses that are transmitted to the brain. Nociception is the detection of tissue damage by specialized transducers.⁸ It is now recognized that nociceptor function is altered by the 'inflammatory soup' that characterizes a region of tissue injury.⁸ The final pain experience is subject to a complex series of facilitatory and inhibitory events that precedes pain awareness, such as past experience, anxiety or expectation.⁹ There are two types of nociceptors¹⁰:

- I. Mechanoreceptors, which are present mainly in the skin (also muscle, joints, viscera, meninges) and respond rapidly to pinprick or heat via A δ , myelinated afferent neurons.
- II. Polymodal, which are widely distributed throughout most tissues and are the nerve endings of unmyelinated C-type afferent neurons. These respond to tissue damage caused by mechanical, thermal or chemical insults and are responsible for the slow onset, prolonged, poorly localized, aching pain following an injury.

Once transduced into electrical stimuli, conduction of neuronal action potentials is dependent on voltage-gated sodium channels.⁵ A number of chemicals are involved in the transmission of pain to the ascending pathways in the spinothalamic tract. These include substance P and calcitonin gene-related peptide, but many others have been identified.^{5,11,12} Opioid receptors are present in the dorsal horn and it is

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thought that encephalins (endogenous opioid peptides) are neurotransmitters in the inhibitory interneurons.¹⁰

Phospholipids released from damaged cell membranes trigger a cascade of reactions, culminating in the production of prostaglandins that sensitize nociceptors to other inflammatory mediators, such as histamine, serotonin and bradykinin.¹⁰

The threshold for the perception of a painful stimulus is similar in everyone and may be lowered by certain chemicals, such as the mediators of inflammation. The discrete cognitive processes and pathways involved in the interpretation of painful stimuli remain a mystery. The cognitive and emotional reactions to a given painful stimulus are variable among individuals and may be affected by culture, personality, past experiences and underlying emotional state.^{5,8,13} In addition, intense and ongoing stimuli further increase the excitability of dorsal horn neurons, leading to central sensitization.⁵ With increased excitability of central nociceptive neurons, the threshold for activation is reduced and pain can occur in response to low intensity, previously non-painful stimuli known as allodynia.⁵ Pain is therefore a complex, multidimensional, subjective phenomenon.¹³

Assessment of pain and pain scales

Pain intensity may be assessed subjectively (i.e. as reported by the patient) or by some objective measures. In daily clinical practice, health care providers employ a combination of tools to estimate the degree of physical patient distress including subjective assessment, for example, not only by asking the patient to rate the intensity of their pain, but also by the nature of the illness or injury, the patient's appearance, behaviour and physiological concomitants. No single method has proved to be 100% reliable.

Pain scales have been developed because there are no reliable physiological or clinical signs to measure pain objectively. Ultimately the perception of pain is an individual experience. Three scales have become popular tools to quantify pain intensity^{14,15} as follows:

Visual analogue scale (VAS),

Numeric rating scale and

Verbal rating scale.

Visual analogue scale

The VAS usually consists of a 100-mm line with one end indicating 'no pain' and the other end indicating the 'worst pain imaginable'. The patient simply indicates a point on the line that best indicates the amount of pain experienced. The minimum clinically significant change in patient pain severity measured with a 100-mm VAS is 13 mm.¹⁶ Studies of pain experience

suggest that less than a 13 mm change in pain severity, although statistically significant, is not clinically significant.¹⁶

Numeric rating scale

The patient is asked in the numeric rating scale to choose a number from a range (usually 0 to 10) that best describes the amount of pain experienced, with zero being 'no pain' and 10 being the 'worst pain imaginable'.

Verbal rating scale

The verbal rating scale simply asks a patient to choose a phrase that best describes the pain, usually 'mild', 'moderate' or 'severe'.

Pain intensity is generally accepted to fall into one of three categories, as follows: mild pain (1–3/10), moderate pain (4–6/10), and severe pain (7 or greater/10).

In the clinical setting, anxiety, sleep disruption and illness burden also contribute to the burden of pain.¹² It is difficult to use a unidimensional pain scale to measure a multidimensional process. Using pain intensity alone will often fail to capture the many other qualities of pain and the overall pain experience. The best illustration of this problem is that the same pain stimulus can be applied to two different people with dramatically different pain scores and analgesic requirements.¹⁷ At best, the use of pain scales is an indirect reflection of 'real' pain, with patient self-reporting still being the most reliable indicator of the existence and intensity of pain.¹⁸ Indeed some authorities have suggested that simply asking the patient 'Do you require medication to relieve your pain?' may be all that is required to trigger initiation of analgesic therapy.

Nevertheless, pain scales are simple and easy to use. They are now routine in many emergency departments (EDs), often being a standard part of the triage process, which leads to substantially faster provision of initial analgesia.⁷

General principles

Patients in pain should receive timely, effective and appropriate analgesia, titrated according to response.⁵ The following points should be stressed:

- The correct analgesic dose is 'enough'; that is, whatever amount is needed to achieve appropriate pain relief.
- A patient's analgesic requirements should be reviewed frequently. Do not wait for pain to return to its previous level before re-dosing with analgesia. Larger early doses and more frequent doses of analgesia are associated with lower total doses and shorter duration of analgesic use. Some patients have been misled into believing that pain medicine is dangerous, so it is important to explain the safety and efficacy of this approach.

- EDs should have specific policies relating to pain and analgesia.
- Senior clinicians should lead by example.

Routes of administration

Analgesic agents may be administered by many routes including oral, intranasal, subcutaneous, intramuscularly, intravenous, epidural, nebulized, intra-pleural, intra-articular and transdermal. All may have a role in a specific clinical situation.⁷ There is a good rationale for the use of the intravenous route in moderate-to-severe pain⁷ and titration of intravenous opioids remains the standard of care for acute severe pain. However, in the presence of severe pain, and in patients where immediate vascular access is problematic, the intramuscular (e.g. morphine or ketamine), oral transmucosal (e.g. fentanyl citrate), or intranasal routes may provide a useful alternative in delivering timely and effective analgesia (e.g. intranasal diamorphine/fentanyl/ketamine).

Specific agents

Opioids

The term 'opioid' refers to all naturally occurring and synthetic drugs producing morphine-like effects. Morphine is the standard opioid agonist against which others are judged.¹⁹ These drugs are the most powerful agents available in the treatment of acute pain. Unfortunately, many health care providers are responsible for oligoanalgesia, citing concerns regarding the risks of respiratory depression and inducing iatrogenic addiction. Less than 1% of patients who receive opioids for pain develop respiratory depression.²⁰ Tolerance to this side effect develops simultaneously with tolerance to the analgesic effect.²¹

Opioid receptor effects

Opioids are responsible for a variety of effects via a number of receptors including analgesia, euphoria, respiratory depression and meiosis (μ receptor); cough suppression and sedation (κ receptor); dysphoria and hallucinations (σ receptor); nausea and vomiting, and pruritus (δ receptor).¹⁰ Opioids act on injured tissue to reduce inflammation in the dorsal horn to impede transmission of nociception and supraspinally to activate inhibitory pathways that descend to the spinal segment.¹²

Use of intravenous opioids

From a clinical practice point of view, many patients who require intravenous opioid may also require admission to hospital, as there will be ongoing opioid requirements that can only be administered in hospital. There have been occasions where patients have received opioid

analgesia that has relieved their pain and they have then been discharged without a final diagnosis. This is an unacceptable practice. A patient may present with abdominal pain with vomiting and, for instance, a provisional diagnosis of gastroenteritis is made. After opioid analgesia is given the patient may feel better and be discharged. A diagnosis, such as appendicitis or bowel obstruction, may not have been excluded. It is therefore necessary for patients to have an appropriate diagnostic evaluation to confirm a benign cause and to reassess the patient after the opioid effects have waned. For patients in whom the final diagnosis is certain, such as in anterior shoulder dislocation for example, discharge is appropriate after a suitable period of observation until the patient is deemed clinically fit for discharge. This is a different scenario from that described previously, as it is a single system problem in which there is no doubt about the diagnosis. In summary, pain that is considered severe enough to warrant intravenous opioid analgesia requires a high index of suspicion for significant pathology.

Side effects

All potent opioid analgesics have the potential to depress the level of consciousness, protective reflexes and vital functions. It is mandatory that these are closely monitored during and after administration.¹⁰ Specific side effects include:

- respiratory depression: rare <1%
- nausea and vomiting: nausea occurs in approximately 40% and vomiting in 15%¹⁰
- hypotension: opioids may provoke histamine release
- constipation
- spasm of the sphincter of Oddi; therefore patients with biliary colic may initially experience more pain. There is no good evidence to suggest that pethidine has any clinically significant advantage at equi-analgesic doses over other opioids for biliary or renal colic¹⁹
- meiosis.

Morphine

The standard intravenous morphine dose is 0.1 to 0.2 mg/kg or more, and a duration of action of 2 to 3 hours. This should be initiated as a loading dose of opioid to provide rapid initial pain relief aiming for an optimal balance between effective pain relief and minimal side effects. This means tailoring the approach to each individual patient. Thus a young fit healthy man with renal colic may require an initial bolus of 0.1 mg/kg morphine, followed by further increments of 0.05 mg/kg. Conversely, a frail elderly patient may only tolerate 1.0 to 2.5 mg morphine total to begin with. There may also be considerable inter-individual variation in response to analgesia. Procedural pain may require higher-dose opioid analgesia,

which has been found to be well tolerated and safe.²² Appropriate monitoring and resuscitation equipment should be available to maximize safety. Rapid pain relief and titration to effect are obvious advantages. Intramuscular administration is unreliable with variable absorption and older routine practices, such as prescribing '5 to 10 mg morphine IM', take no account of an individual's requirements.¹⁰

Fentanyl

Allergic reactions are extremely rare with opioids. Fentanyl does not release histamine, making it ideal for treating patients with reactive airways disease. There are advantages in using fentanyl for brief procedures in the ED because of its short half-life. The intravenous dose of fentanyl is 1 to 2 µg/kg or more, with a duration of action of 30 to 60 minutes. High doses of fentanyl may produce muscular rigidity, which may be so severe as to make ventilation difficult, but which responds to naloxone or muscle relaxants. Intranasal fentanyl is an effective analgesic in the ED and in the pre-hospital setting.⁵ The intranasal route of drug delivery is fast and painless, and confers an onset of action time similar to the intravenous route given it avoids first-pass metabolism and crosses the blood-brain barrier.

Pethidine

Pethidine use in the emergency setting has largely been superseded by other, more attractive, analgesic alternatives.^{19,23}

Oral opioids

Oral opioids tend to be underused in the ED, but are effective for all levels of pain and are associated with improved patient satisfaction. Their side effect profile may be better than paracetamol/codeine combinations. Oxycodone (immediate release) reaches peak levels at 45 minutes to 1 hour but the dose should be reduced and dosing interval increased in the elderly and in those with hepatic or renal dysfunction. The main contraindication is acute respiratory depression. The initial dose is 5 to 10 mg. However, it is important to be aware that global opiate-related deaths have soared both for men and women, across the entire socioeconomic spectrum. The increased prescribing of oral opioids has been implicated with increased deaths. Acute health care providers should ideally initiate analgesic therapy using simple analgesia (i.e. paracetamol, non-steroidal anti-inflammatory drugs [NSAIDs] etc.), in the first instance. Failure to adequately treat pain intensity following this invariably requires a step-wise approach, escalating to opiate analgesia.

Codeine Codeine is the most commonly used oral opioid prodrug. Unfortunately, up to 6% to 10% of the Caucasian population, 2% of Asians

and 1% of Arabs have poorly functional cytochrome P450 2D6 (CYP2D6), which may render codeine largely ineffective for analgesia in these patients, although some analgesic efficacy may occur via alternate cytochrome P450 pathways.

Prescribed alone in doses as high as 120 mg, codeine has been demonstrated to be no more effective than placebo in both the adult and geriatric populations, while causing increasing gastrointestinal side effects, such as nausea, vomiting and constipation, with increasing doses.⁷ It is frequently given in combination with paracetamol or aspirin.

Tramadol Tramadol is a new opioid, with novel non-opioid properties.²⁴ Its efficacy lies between codeine and morphine. It has a relative lack of serious side effects, such as respiratory depression, and the potential for abuse and psychological dependence is low.²⁴ However, other side effects, such as nausea, vomiting, dizziness and somnolence, may be troublesome and there is a risk of seizures.^{24,25} Thus it should be avoided or used with caution in patients who are taking drugs that reduce the seizure threshold, such as tricyclic antidepressants and Selective serotonin re-uptake inhibitor (SSRIs). Also, the concomitant administration of tramadol with monoamine oxidase inhibitors, or within 2 weeks of their withdrawal, is contraindicated.²⁴ The role of tramadol in emergency medicine is ill defined. One review concluded that tramadol does not offer any particular benefits over existing analgesics for the majority of emergency pain relief situations,²⁵ with oral doses having equivalent analgesic effects in mild-to-moderate severity acute pain compared with currently available analgesics.²⁵ Intravenous tramadol is less effective than intravenous morphine.²⁵

However, tramadol may be useful in certain situations²⁵:

- for patients in whom codeine is not effective
- where NSAIDs are contraindicated
- for the treatment of chronic pain.

Tapentadol Tapentadol is a centrally acting **opioid analgesic** with a dual mode of action as an **agonist** of the **μ -opioid receptor** and as a **norepinephrine reuptake inhibitor**. Analgesia occurs within 32 minutes of oral administration, and lasts for 4 to 6 hours.

It is similar to **tramadol** in its dual mechanism of action in terms of its ability to activate the mu opioid receptor and inhibit the reuptake of norepinephrine. The general potency of tapentadol is considered to be somewhere between that of tramadol and **morphine**, with an analgesic efficacy comparable to that of **oxycodone** despite a lower incidence of side effects. It is generally considered a weak-moderate strength opioid, similar in efficacy to the better-known opioids

such as **hydrocodone** and **pethidine**. The initial dose is 50 to 100 mg orally administered every 4 to 6 hours, and titrated to response. The maximum dose over 24 hours is 600 mg.

Non-opioid analgesics

Simple analgesics

Non-steroidal anti-inflammatory drugs NSAIDs are either non-selective cyclo-oxygenase (COX) inhibitors or selective inhibitors of COX-2 (COX-2 inhibitors). NSAIDs are effective analgesic agents for moderate pain, specifically when there is associated inflammation.⁷ As with opioids, there are multiple routes of administration available. Unfortunately, their use in acute severe pain is limited by the length of onset time of 20 to 30 minutes. There is no clear superiority of one agent over another. There is up to a 30% incidence of upper gastrointestinal bleeding when NSAIDs are used for over 1 to 2 weeks. The risk of bleeding in the elderly for short (3 to 5 days) acute therapy appears to be minimal.⁷ NSAID use in pregnancy (especially late) is not recommended. Ibuprofen is considered the NSAID of choice in lactation.

NSAIDs have a spectrum of analgesic, anti-inflammatory and antipyretic effects and are effective analgesics in a variety of pain states.⁵ Unfortunately, significant contraindications and adverse effects limit the use of NSAIDs, many of these being regulated by COX-1.⁵ NSAIDs are useful analgesic adjuncts and hence NSAIDs are therefore integral components of multimodal analgesia.⁵ NSAID side effects are more common with long-term use. The main concerns are renal impairment, interference with platelet function, peptic ulceration and bronchospasm in individuals who have aspirin-exacerbated respiratory disease.⁵ In general, the risk and severity of NSAID-associated side effects is increased in elderly people.⁵

Caution is therefore needed in the elderly and in patients with renal disease, hypertension and heart failure, or with asthma. NSAIDs reduce renal cortical blood flow and may induce renal impairment, especially when used in patients already on diuretics. In patients with asthma, 2% to 20% are aspirin sensitive and there is a 50% to 100% cross-sensitivity with NSAIDs.

Ketorolac is a parenteral NSAID that is equipotent to opioids, with ketorolac and morphine equivalent in reducing pain. There is a benefit favouring ketorolac in terms of side effects when ketorolac is titrated intravenously for isolated limb injuries.^{26,27} However, the utility of ketorolac in acute pain is limited due to a prolonged onset of action and a significant number of patients (25%) who exhibit little or no response.²⁸ There is also benefit to using ketorolac for acute renal colic.^{26,29} A combination of morphine and ketorolac offered pain relief superior to either drug alone and was

associated with a decreased requirement for rescue analgesia in patients with renal colic.³⁰ Rectal NSAIDs (e.g. indomethacin 100 mg) are an effective alternative to parenteral NSAIDs in the treatment of renal colic.

Paracetamol Paracetamol is an effective analgesic for acute pain⁵ and has useful antipyretic activity.³¹ The addition of an NSAID further improves efficacy.⁵ Paracetamol inhibits prostaglandin synthetase in the hypothalamus, prevents release of spinal prostaglandin and inhibits inducible nitric oxide synthesis in macrophages.³¹ Indications for paracetamol include mild pain, particularly of soft tissue and musculoskeletal origin, mild procedural pain, supplementation of opioids in the management of more severe pain allowing a reduction in opioid dosage and as an alternative to aspirin.³¹ Paracetamol has no gastrointestinal side effects of note and may be prescribed safely in patients with peptic ulcer disease or gastritis.⁷ Aspirin has the risk of gastrointestinal side effects, such as ulceration and bleeding. It also has an antiplatelet effect, which lasts for the life of the platelet.

Paracetamol is rapidly absorbed with a peak concentration reached in 30 to 90 minutes.³¹ The recommended adult dose is 1 g every 4 to 6 hours to a generally accepted maximum of 4 g/day.³¹ Paracetamol has a low adverse event profile and is an excellent analgesic, especially when used in adequate doses. Parenteral paracetamol is now available and may have additional utility (e.g. in the vomiting patient). Chronic use of paracetamol alone does not seem to cause analgesic nephropathy.³¹ It can be used safely in alcoholics and patients with liver metastases.^{31,32}

Combination drugs Non-opioid agents (e.g. paracetamol, NSAIDs and paracetamol/codeine combinations) are all useful analgesics for mild-to-moderate pain. A systematic review found that paracetamol–codeine combinations in single dose studies produce a slightly increased analgesic effect (5%) compared with paracetamol alone.³³ However, none of the studies reviewed were based in the ED. In multidose, paracetamol–codeine preparations have significantly increased side effects.³³ However, other reports state that the combination of paracetamol 1000 mg plus codeine 60 mg has a number needed to treat of 2.2.⁵ NSAIDs have a higher rate of serious adverse effects.

Other analgesic agents

Nitrous oxide

Nitrous oxide is an inhalational analgesic and sedative which, in a 50% mixture with oxygen (Entonox), has equivalent potency to 10 mg morphine in an adult.¹⁰ The Entonox delivery system uses a preferential inhalational demand

arrangement for self-administration, which requires an airtight fit between the mask/mouthpiece and face. As the patient holds the mask/mouthpiece, their grip will relax if drowsiness occurs, the airtight seal will be lost and the gas flow stops, thereby avoiding overdosage.

This system requires a degree of patient involvement and cooperation and is useful for patients who have difficult intravenous access or are needle-phobic. Patients who are elderly, young, confused or uncooperative will not find the technique effective. Nitrous oxide increases the volume of a pneumothorax or any other gas-filled cavity, so is contraindicated in patients with pneumothorax or pneumoperitoneum.

Ketamine

Ketamine is an *N*-methyl-D-aspartate (NMDA) antagonist. It may be employed in anaesthetic, analgesic, or procedural sedation doses. It is a unique anaesthetic that induces a state of dissociation between the cortical and limbic systems to produce a state of dissociative anaesthesia, with analgesia, amnesia, mild sedation and immobilization. It does not impair protective airway reflexes, and random or purposeful movements are frequently observed in patients after administration. Side effects include hypersalivation, vomiting, emergence reactions, nightmares, laryngospasm, hypertension, tachycardia and increased intracranial pressure.^{34,35}

There are many potential contraindications to ketamine use including upper or lower respiratory infection, procedures involving the posterior pharynx, cystic fibrosis, age younger than 3 months, acute glaucoma or globe penetration, uncontrolled hypertension, congestive cardiac failure, arterial aneurysm, acute intermittent porphyria and thyrotoxicosis.³⁵ Despite this, ketamine is used increasingly in the EDs as part of the procedural sedation (see Chapter 22.3). It is also an effective analgesic at sub-dissociative doses especially for opioid resistant pain (e.g. 0.2 to 0.3 mg/kg bolus plus infusion at 0.2 mg/kg/h).

Pain relief in pregnancy

Non-pharmacological treatment options should be considered where possible for pain management in pregnancy, because most drugs cross the placenta.⁵ Use of medications for pain in pregnancy should be guided by published recommendations.⁵ Paracetamol is regarded as the analgesic of choice.⁵ NSAIDs are used with caution in the last trimester of pregnancy and should be avoided after the 32nd week.⁵ The use of NSAIDs is associated with increased risk of miscarriage.⁵ Overall, the use of opioids to treat pain in pregnancy appears safe.⁵

Non-pharmacological therapies

Although pain perception involves neuroanatomical processes, the other interrelated component of pain reaction is psychophysiological. The use of non-pharmacological techniques is therefore important. These include empathy, a compassionate approach, a calm manner, patient distraction and verbal reassurance. Immobilization of fractures with splinting is effective, as is the application of ice to a wound. Other techniques, such as hypnosis, transcutaneous nerve stimulation, acupuncture and manipulation, have not been widely studied in the ED setting.

Special pain situations and non-analgesic agents

This chapter has focused on specific analgesic agents, but there are many miscellaneous agents that are effective in providing disease-specific analgesia.

- Examples of these include:
- triptans for migraine
- glyceryl trinitrate and β-blockers for acute cardiac ischaemia pain
- antiviral agents for herpes zoster
- antidepressants (e.g. nortriptyline), anticonvulsants (e.g. carbamazepine) or gabapentin for neuropathic pain
- oxygen therapy for cluster headache
- calcium gluconate for hydrofluoric acid burns
- hot water (43°C) for venomous marine stings.

In addition, adjuvant therapy with anxiolytics, such as midazolam, contributes to pain relief. Obtaining a definitive diagnosis allows directed therapy that contributes to pain relief. If specific treatments appear to be ineffective, then the diagnosis should be reconsidered.

Acute neuropathic pain

Acute neuropathic pain is an important issue in the ED. This may be due to conditions such as sciatica and cervical radiculopathy. In addition to agents such as the antidepressants (e.g. nortriptyline) or anticonvulsants (e.g. carbamazepine), another option includes the use of antihyperalgesic drugs, such as gabapentin 100 to 300 mg/dose, repeated as necessary, titrating up to a maximum of 3600 mg/day over time. The main side effects are dizziness, somnolence and ataxia. However, there have been no ED studies of gabapentin or pregabalin and there is wide variability of response.

Chronic pain

Chronic pain 'commonly persists beyond the time of healing of an injury and frequently there may not be any clearly identifiable cause'.⁵ Patients with chronic pain attend the ED with exacerbations of their chronic pain and are often taking multimodal therapies prescribed by a pain specialist. The main difference between acute and chronic pain is that, in chronic pain, central sensitization is the main underlying pathophysiology.³⁶ It is important to avoid a judgemental attitude to these patients as there is a risk of overlooking serious pathology.

Antihyperalgesic drugs in the setting of chronic pain, especially ketamine, are of particular value in those with poor opioid responsiveness.⁵ Other antihyperalgesics may be useful for neuropathic pain, such as gabapentin and pregabalin.

Another issue with chronic pain is to be aware of adjuvant therapies for decreasing the likelihood of chronic pain developing. For example, early management of acute zoster infection may reduce the incidence of post-herpetic neuralgia.⁵ Aciclovir given within 72 hours of onset of the rash accelerates the resolution of pain and reduces the risk of post-herpetic neuralgia.⁵ Amitriptyline 25 mg daily in patients over 60

years for 90 days, started at the onset of acute zoster, reduces pain prevalence at 6 months post-zoster infection.³⁷

Likely developments over the next 5 to 10 years

- Further study on the role and utility of various oral analgesics for commonly treated conditions in the ED, including new agents or formulations
- Use of patient-controlled analgesia
- Alternative administration techniques, including needless systems and micro-needle technology
- Use of non-pharmacological techniques, such as acupuncture³⁸
- Better understanding of the pathophysiology of pain.

CONTROVERSIES

- Development of a uniform approach to pain research in order to make meaningful comparisons between studies
- Development of an objective measure of pain
- The effectiveness of codeine combinations in ED patients.

Full references are available at <http://expertconsult.inkling.com>

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22.1 GENERAL PAIN MANAGEMENT

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22.2 Local anaesthesia

Anthony F.T. Brown

ESSENTIALS

- 1** Local anaesthetic infiltration and nerve blocks may be used as a supplement to oral, inhaled or parenteral analgesia.
- 2** Also, they may be the primary method of achieving analgesia, particularly where pain is localized to a digit or within a peripheral nerve distribution region.
- 3** Local anaesthetic toxicity may occur with inadvertent bolus intravenous injection or by exceeding the recommended maximum safe dose. Neurological and cardiovascular effects predominate and may be fatal.
- 4** Resuscitation equipment should always be available when using these agents. Refractory local anaesthetic systemic toxicity with cardiovascular collapse or arrest may respond to 20% lipid emulsion therapy.
- 5** Intravenous regional anaesthesia with prilocaine for a Bier block is a simple, safe technique commonly used for reduction of forearm fractures, but requires two medical practitioners and specialized equipment.
- 6** Formal training and accreditation should occur prior to independent practice, particularly with more complex blocks, such as Bier and the femoral nerve.

Local anaesthesia

Local anaesthetic infiltration and nerve blocks should be used for patients presenting to the emergency department (ED) with pain, either to supplement other analgesia or for definitive pain relief. Nerve blocks are most appropriate when the pain is localized, as in certain fractures and wounds to a digit, or within a peripheral nerve distribution region. Local anaesthesia may also be used topically, particularly in children, and prior to arterial blood gas puncture and insertion of large intravenous cannulae where, contrary to popular perception, it does not increase the likelihood of failure.^{1,2}

Pharmacology

Local anaesthetic agents are all weak organic bases that inactivate plasma membrane voltage-gated fast sodium channels, temporarily blocking membrane depolarization and preventing nerve impulse transmission. All are vasodilators, with the exception of ropivacaine and cocaine, hence the use of adrenaline to prolong their duration of activity and to improve safety by delaying absorption and/or by administering lower effective doses.

Amino ester and amino amide local anaesthetics

Amino esters

Local anaesthetic agents that contain an ester bond between the intermediate chain and

lipophilic aromatic end (amino esters) include cocaine, procaine and amethocaine. They are poorly protein bound and undergo hydrolysis by plasma pseudocholinesterase to para-amino benzoic acid.

Amino amides

Amide-type agents that contain an amide bond between the intermediate chain and aromatic end (amino amides) include lignocaine, prilocaine, bupivacaine and ropivacaine. They are highly protein bound, much more stable and undergo hepatic metabolism.

Local anaesthetics are available in single or multidose vials, with or without dilute adrenaline at 1:200,000 (containing 5 µg adrenaline per millilitre) to prolong their duration of action.

Local anaesthetic reactions

Antioxidants, such as sodium bisulphite or metabisulphite, are added to adrenaline-containing solutions and preservative, such as methylparaben, to multidose vials and are implicated in some apparent 'allergic' reactions to the local anaesthetic. Other reaction mimics include vasovagal episodes, adrenergic sympathetic stimulation and anxiety-related responses.

True allergy to local anaesthetics is extremely rare at <1.0% reactions, when verified by progressive challenge testing, and is usually to the amino amides.³ More common are contact dermatitis or delayed local swelling (discussed later).

Duration of action

The duration of action of local anaesthetics is related to the degree of protein binding, vasoactivity, concentration and possibly pH, although the addition of adrenaline is the most practical way to prolong their effect. Table 22.2.1 gives standard maximum safe doses and duration of action of commonly used agents. Solutions containing adrenaline should not be injected near end arteries, such as in the fingers, toes, nose or penis, even though surprisingly this well-established dogma is not supported by the literature. Normal blood flow is restored to the digit within 60 to 90 minutes of inadvertent injection of local anaesthesia with adrenaline (epinephrine) at standard commercial dilutions, without any evidence of harm.⁴

Adverse effects

Systemic toxicity

Systemic toxicity occurs after unrecognized rapid intravenous or intra-arterial injection or by exceeding the recommended safe maximum dose. Symptoms and signs of toxicity are related to plasma drug levels and progress from circumoral tingling, dizziness, tinnitus and visual disturbance to muscular twitching, confusion, convulsions, coma and apnoea. Cardiovascular effects are also seen with high plasma levels, including bradycardia, hypotension and cardiovascular collapse ultimately with ventricular fibrillation or asystole, which are all exacerbated by associated hypoxia. See Box 22.2.1 for the features of local anaesthetic toxicity related to increasing plasma levels.

Management of systemic toxicity

The management of systemic toxicity includes immediate cessation of the drug, summoning

Box 22.2.1 Features of systemic local anaesthetic toxicity (in order of increasing plasma levels)

Circumoral tingling
Dizziness
Tinnitus
Visual disturbance
Muscular twitching
Confusion
Convulsions
Coma
Apnoea
Cardiovascular collapse (highest plasma levels)

22.2 LOCAL ANAESTHESIA

help, airway maintenance, supplemental oxygen and incremental doses of an intravenous benzodiazepine, such as midazolam 0.05 to 0.1 mg/kg, for seizures. Major reactions may require endotracheal intubation, fluids and cautious use of vasopressors and inotropes, as high doses can impede resuscitation in toxic cardiomyopathy. Refractory arrhythmias with cardiovascular collapse from local anaesthetic systemic toxicity (LAST) may respond best to intravenous 20% lipid emulsion 1.5 mL/kg bolus followed by 0.25 mL/kg/min for roughly 10 minutes following the recovery of vital signs.⁵

As adverse reactions occur immediately or within minutes after local anaesthetic use, medical expertise, resuscitation equipment and monitoring facilities must always be readily available.

Other reactions

Other adverse reactions to local anaesthetics involve allergy, including contact dermatitis, and rarely anaphylaxis predominantly to the amino amides, catecholamine effects from added adrenaline, vasovagal reactions when the patient is upright (such as during a dental procedure), cytotoxic delayed wound healing, malignant hyperthermia from amino amide use and methaemoglobinemia due to prilocaine or benzocaine (Box 22.2.2).

Topical anaesthesia

Some agents such as EMLA (eutectic mixture of local anaesthetics including 2.5% lignocaine and 2.5% prilocaine) are used topically, particularly to decrease the pain of insertion of cannulae or for lumbar puncture and suprapubic catheter insertion in children. EMLA takes up to 1 hour for maximal effect and, paradoxically, is a vasoconstrictor making vessel puncture harder. A potentially superior alternative for cannula insertion is 4% amethocaine (AnGel), as this has a quicker onset and is a vasodilator, although operator experience in cannulation is likely to be of more relevance.⁶

Box 22.2.2 Adverse reactions to local anaesthetics (other than systemic toxicity)

- Allergy:
 - Amides >> esters
 - Additives, such as methylparaben, sodium metabisulphite
- Catecholamine effects from added adrenaline
- Vasovagal
- Delayed wound healing
- Malignant hyperthermia
- Methaemoglobinemia—prilocaine, benzocaine

Likewise, a mixture of 1:1000 adrenaline, 4% lignocaine and 0.5% amethocaine, with the acronym ALA (or known as LET in North America standing for lidocaine, epinephrine and tetracaine) up to 0.1 mL/kg, may be used inside small wounds instead of, or to reduce the pain of, injecting local anaesthetic prior to closure, again in children or adolescents.

Specific nerve blocks

The following nerve blocks are contraindicated in uncooperative patients, those with local sepsis in the injection zone and in the rare patient with true local anaesthetic allergy. Care must be taken not to exceed the recommended maximum local anaesthetic doses (see Table 22.2.1), and monitoring facilities, resuscitation equipment and medical expertise must be available at all times.

Formal training and accreditation should occur prior to independent practice, particularly with the more complex blocks, such as Bier and femoral nerve.

Table 22.2.1 Maximum recommended safe dose and duration of action of common local anaesthetics

Drug	Dose (mg/kg) ^a	Duration (h)
Lignocaine	3	0.5–1
Lignocaine with adrenaline	7	2–5
Bupivacaine	2	2–4
Prilocaine	6	0.5–1.5

^aA 1% solution contains 10 mg/mL.

Digital nerve block ('ring block')

Indications

Wound debridement, suturing, drainage of infection, fracture or dislocation reduction around the nail, fingertip and distal finger or toe.

Contraindications

Local sepsis, Raynaud phenomenon and peripheral vascular disease.

Technique

Use 2% plain lignocaine. Inject 1 to 1.5 mL using a 25-gauge needle into the palmar aspect of the base of the finger or toe, approaching vertically from the dorsum. Withdraw the needle until subcutaneous and rotate slightly until pointing to the extensor surface of the digit and inject a further 0.5 mL (Fig. 22.2.1). Perform the same procedure on the other side of the digit. Allow at least 5 minutes for the block to work.

Complications

Avoid intravascular injection by aspirating prior to injection. Do not use a tourniquet or more than 4 mL total volume, to avoid impairing the circulation due to high local tissue pressures.

Nerve blocks at the wrist

These provide anaesthesia to the hand, particularly for diffuse lesions hard to infiltrate directly, such as 'gravel rash', or when the hand is swollen or burned.

Ulnar nerve wrist block (lateral approach)

Indications Procedures on the medial border of the hand and medial 1.5 digits or combined

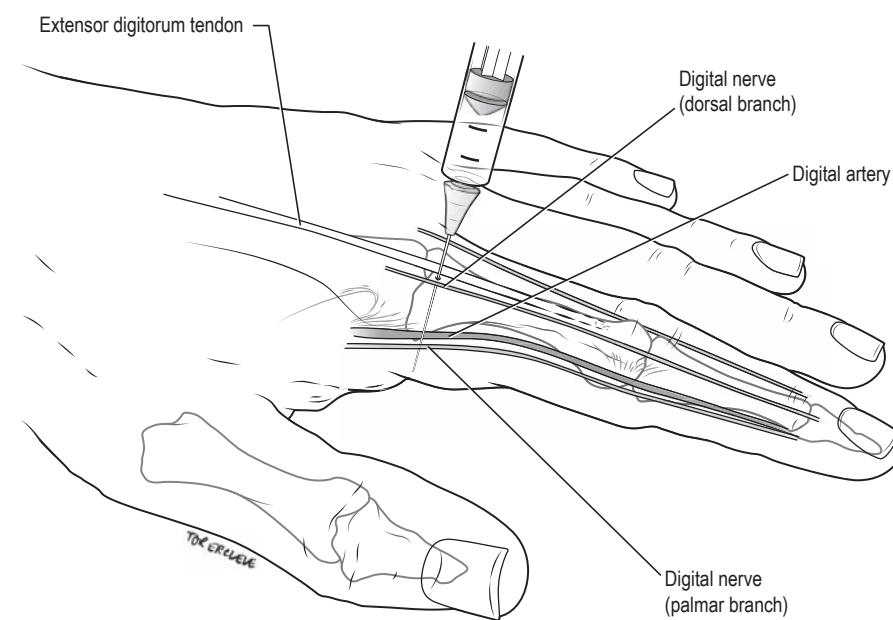


FIG. 22.2.1 Digital nerve block.

22.2 LOCAL ANAESTHESIA

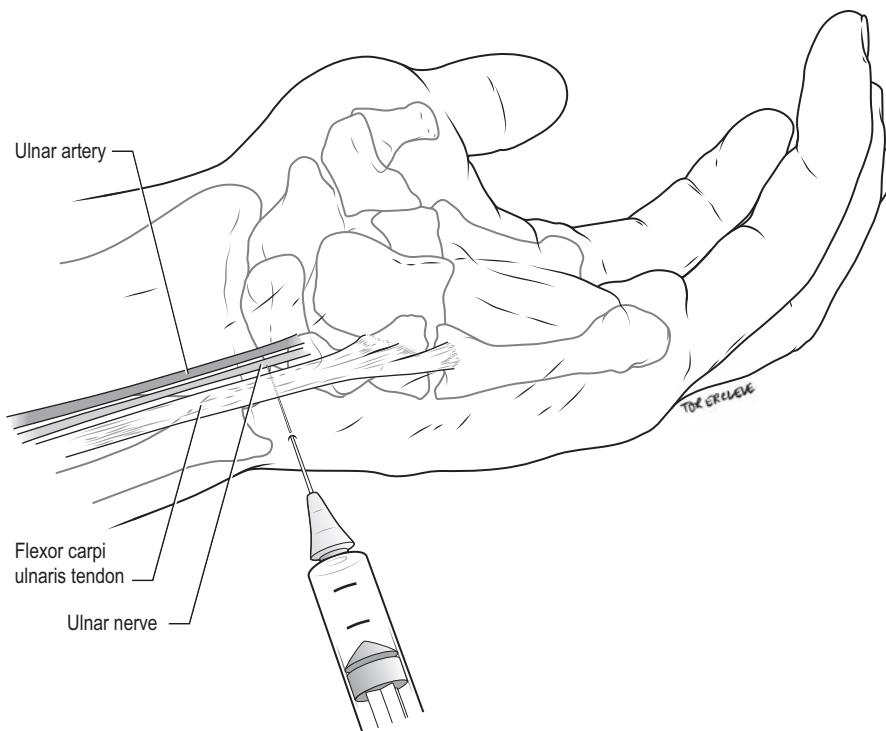


FIG. 22.2.2 Ulnar nerve wrist block (lateral approach).

with median and radial nerve blocks for hand anaesthesia.

Contraindications Local sepsis, neuritis.

Technique Identify the flexor carpi ulnaris tendon at the proximal palmar crease. Introduce a 25-gauge needle on the ulnar aspect of the tendon, directed horizontally and laterally for 1 to 1.5 cm under the tendon. Inject 4 mL of 1% lignocaine. Withdraw the needle until subcutaneous, then inject 5 mL of 1% lignocaine fanwise to the dorsal midline, to block superficial cutaneous branches (Fig. 22.2.2).

Median nerve wrist block

Indications Procedures on the lateral border of the hand in the territory supplied by the median nerve, excluding the medial 1.5 digits or combined with ulnar and radial nerve blocks for hand anaesthesia.

Contraindications Local sepsis, carpal tunnel syndrome or neuritis.

Technique Identify the tendons of the flexor carpi radialis and palmaris longus at the proximal wrist crease. Introduce a 25-gauge needle vertically 0.5 to 1 cm lateral to the palmaris longus (or 0.5 cm medial to the flexor carpi radialis in the 10% of individuals lacking a palmaris longus). Inject 5 mL of 1% lignocaine when the needle gives as it penetrates the flexor retinaculum or

paraesthesiae are elicited, at a depth usually of no more than 1 cm to the skin (Fig. 22.2.3). Avoid injecting into the nerve itself, as it may lie more superficial than this.

Radial nerve wrist block

Indications Procedures on the dorsal radial aspect of the hand or combined with ulnar and median nerve blocks for hand anaesthesia.

Contraindications Local sepsis, neuritis.

Technique Identify the tendon of the extensor carpi radialis and infiltrate 5 to 10 mL of 1% lignocaine subcutaneously in a ring around the radial border of the wrist to the area overlying the radial pulse, at the level of the proximal palmar crease (Fig. 22.2.4).

Nerve blocks of the leg

Femoral nerve block

Indications Analgesia for fractured shaft of femur, especially prior to applying dynamic splintage.

Contraindications Local sepsis, bleeding tendency.

Technique Preferably use ultrasound guidance; the goal is to place the needle tip immediately adjacent to the lateral aspect of the femoral nerve, below the fascia iliaca or between the two layers of the fascia iliaca, that surround the femoral

nerve. Proper deposition of local anaesthetic is confirmed either by observation of the femoral nerve being displaced by the injectate or by the spread of the local anaesthetic above or below the nerve, surrounding and separating it from the fascia iliaca layers. If ultrasound is not available, palpate the femoral artery below the midpoint of the inguinal ligament, which extends from the pubic tubercle to the anterior superior iliac spine. Insert a 21-gauge needle 1 cm lateral to this point, perpendicular to the skin. Advance until paraesthesiae are elicited down the leg and withdraw slightly, aspirate to exclude intravascular placement and inject 10 mL of 0.5% bupivacaine (50 mg). Alternatively, feel for a give as the needle punctures the fascia lata, aspirate, then inject 10 mL of 0.5% bupivacaine fanwise laterally away from the artery (Fig. 22.2.5).

Complications Puncture of femoral artery.

Foot blocks at the ankle

Indications Where local anaesthetic infiltration of the foot is awkward or difficult because of thick sole skin or pain, or when excessive amounts of anaesthetic would otherwise be required.

Contraindications Local sepsis, peripheral vascular disease.

Technique Three superficial nerves, the sural, superficial peroneal and saphenous, are blocked by subcutaneous infiltration in a band around 75% of the ankle circumference. Two deeper nerves—the posterior tibial by the posterior tibial artery and the deep peroneal (anterior tibial) nerve by the dorsalis pedis artery—are blocked, usually in combinations with the superficial ones, according to the area of anaesthesia required.

Sural nerve The sural nerve is blocked by injecting 3 to 5 mL of 1% lignocaine subcutaneously in a band between the Achilles tendon and the lateral malleolus, 1 cm above and posterior to the malleolus (Fig. 22.2.6). It anaesthetizes a small strip on the lateral dorsum of the foot at the base of the little toe to the lateral malleolus and the posterolateral aspect of the ankle and heel.

Superficial peroneal nerves Superficial peroneal nerves are blocked by injecting 4 to 6 mL of 1% lignocaine subcutaneously in a band between the extensor hallucis longus tendon and the lateral malleolus, on the anterior aspect of the ankle (see Fig. 22.2.6). This block anaesthetizes the dorsum of the foot, save for the lateral aspect (see the previous discussion of the sural nerve) and interdigital web between the hallux and second toe (see the later discussion of the deep peroneal nerve).

Saphenous nerve The saphenous nerve is blocked by injecting 3 to 5 mL of 1% lignocaine subcutaneously above the medial malleolus,

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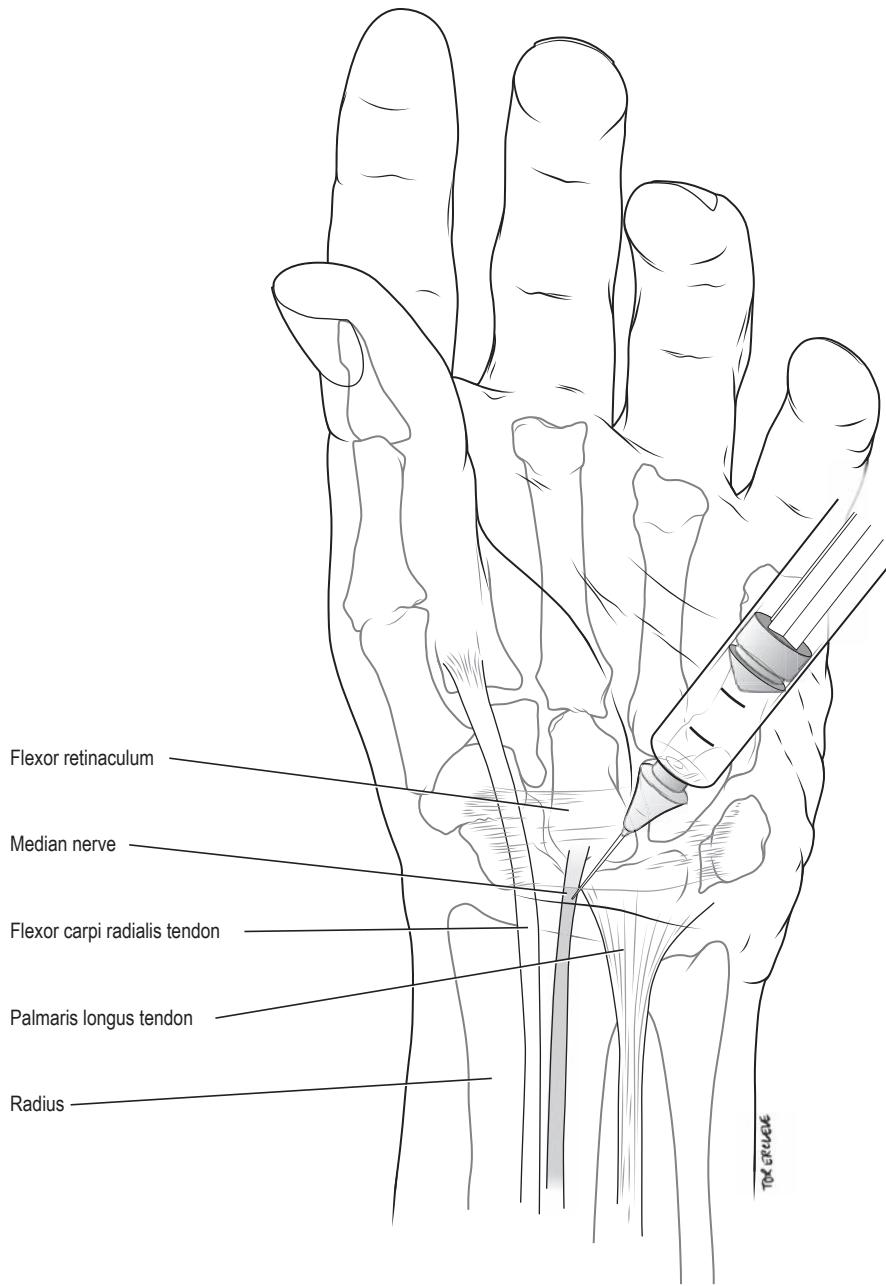


FIG. 22.2.3 Median nerve wrist block.

laterally until over the tibialis anterior tendon (Fig. 22.2.7). It anaesthetizes the area around the medial malleolus anteriorly and, to a lesser degree, posteriorly.

Posterior tibial nerve The posterior tibial nerve is blocked by infiltrating 3 to 5 mL of 1% lignocaine immediately lateral to the posterior tibial artery as it passes behind the medial malleolus, at a depth of 0.5 to 1 cm to the skin (see Fig. 22.2.7). It anaesthetizes the sole of the foot, excluding the posterolateral heel (see the previous discussion of the sural nerve), via its medial and lateral plantar branches.

Deep peroneal (anterior tibial) nerve The deep peroneal (anterior tibial) nerve is blocked by infiltrating 1 to 2 mL of 1% lignocaine just above the base of the medial malleolus, lateral and behind the extensor hallucis longus by the dorsalis pedis pulse at a depth of 0.5 cm (see Fig. 22.2.7). It anaesthetizes the interdigital web between the hallux and second toe.

Complications Exceeding a total volume of 20 mL of 1% lignocaine local anaesthetic (i.e. 3 mg/kg) risks systemic toxicity or poor peripheral perfusion due to raised tissue pressures.

Intravenous regional anaesthesia or Bier block

Indications

Operative procedures, such as debridement, tendon repair and foreign body removal in the forearm and hand. Reduction of fractures and dislocations, typically Colles fracture of the wrist.

Contraindications

Local anaesthetic sensitivity; peripheral vascular disease, including Raynaud phenomenon; sickle cell disease; cellulitis; uncooperative patients, including children; hypertension with systolic blood pressure over 200 mm Hg; severe liver disease; and unstable epilepsy.

Technique

Two doctors are required, allowing one to perform the manipulation and the other, with training in the procedure and resuscitation skills, to perform the block. Explain the procedure to the patient and obtain informed consent. Assemble and check all equipment and apply standard monitoring, including ECG, non-invasive blood pressure and pulse oximetry.

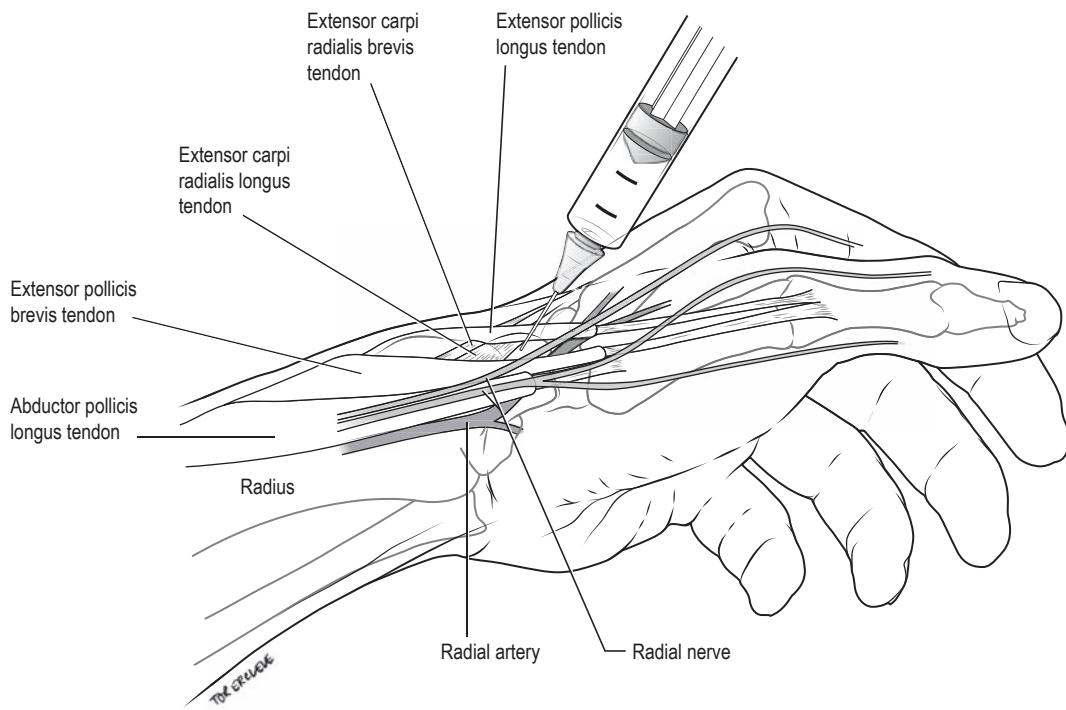
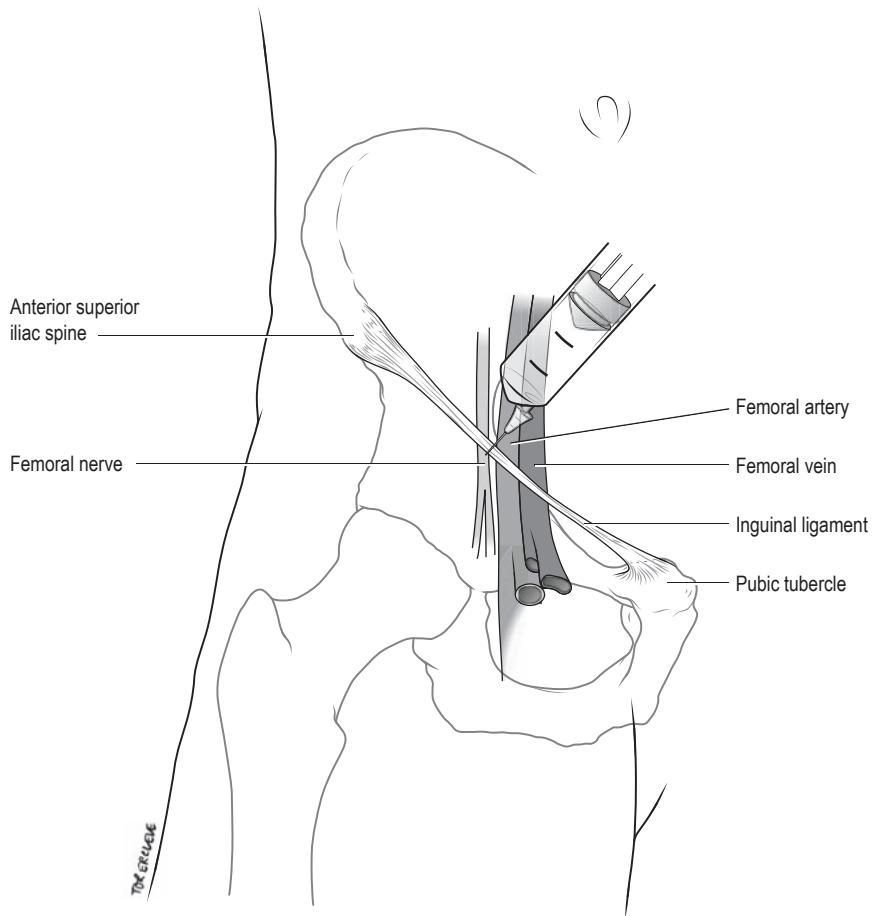
Use a specifically designed and maintained single 15 cm adult cuff, placed over cotton wool padding to the upper arm. Double-cuff tourniquets require higher inflation pressures, as they are narrower. The upper cuff is inflated first, followed by the lower cuff later, after the injection of the local anaesthetic has had time to take effect, thereby reducing tourniquet discomfort. The upper cuff is then released. The use of a double cuff does not always reduce the ischaemia pain and predisposes to accidental wrong cuff release, so this requires additional expertise and understanding.

Insert a small intravenous cannula into the dorsum of the hand of the injured limb and a second cannula in the other hand or wrist as emergency access to the central circulation. Exsanguinate the injured limb by simple elevation and direct brachial artery compression for 2 to 3 minutes, carefully supporting the limb at the site of any fracture. An Esmarch bandage may be used instead, in the absence of a painful wrist fracture.

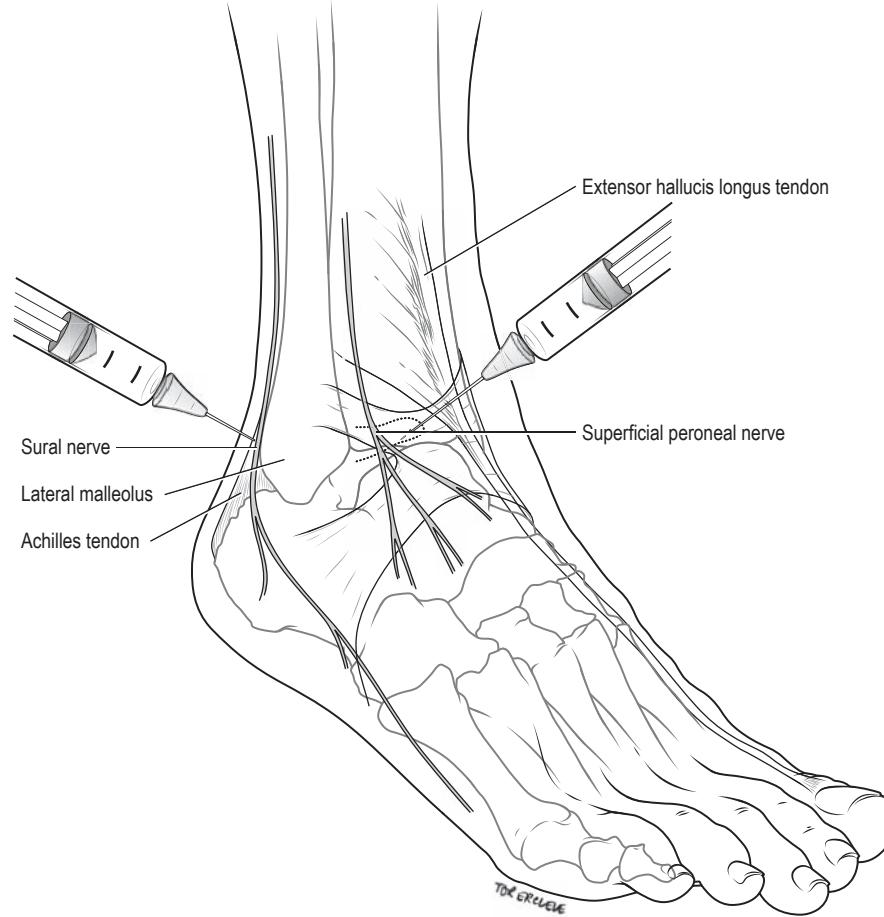
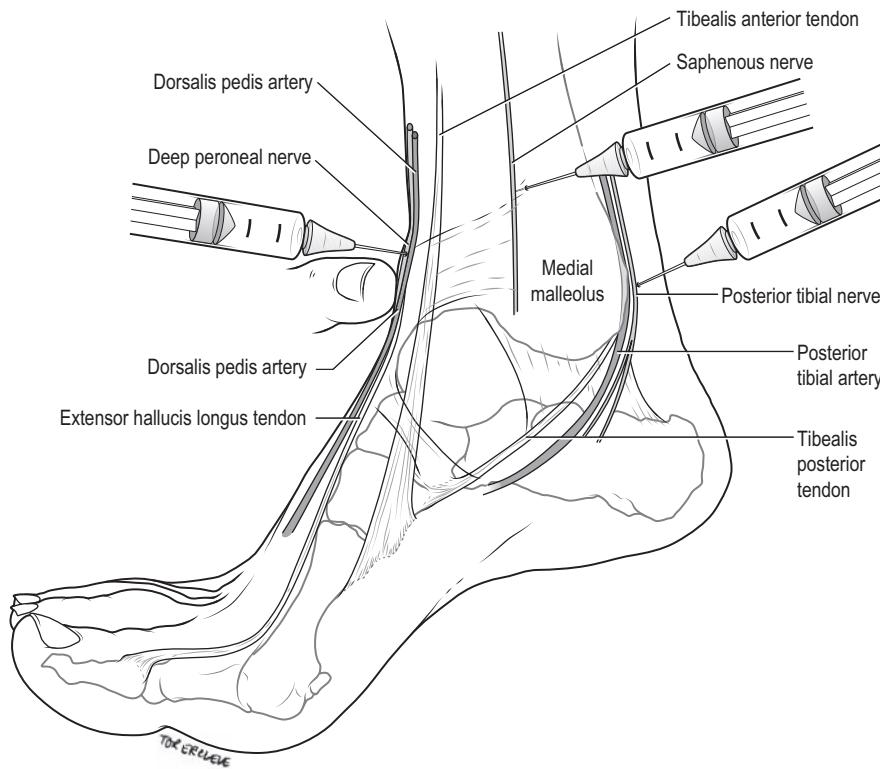
Keep the arm elevated and inflate the cuff to 100 mm Hg above systolic blood pressure. The radial artery pulse should now be absent and the veins remain empty. If this is not the case, do not inject anaesthetic but repeat the exsanguination procedure and cuff inflation.

Lower the arm once the radial artery pulse is absent and the veins are empty, and inject 2.5 mg/kg (0.5 mL/kg) of 0.5% prilocaine slowly over 90 seconds and record the time. Alternatively, 1% plain lignocaine (1.5- to 3-mg/kg total lignocaine dose) diluted to a concentration of 0.5% can be used.

22.2 LOCAL ANAESTHESIA

**FIG. 22.2.4** Radial nerve wrist block.**FIG. 22.2.5** Femoral nerve block.

22.2 LOCAL ANAESTHESIA

**FIG. 22.2.6** Sural and superficial nerve blocks.**FIG. 22.2.7** Saphenous, posterior tibial and deep peroneal nerve blocks.

22.3 EMERGENCY DEPARTMENT PROCEDURAL SEDATION

Continuously monitor the cuff pressure and wait at least 5 to 10 min to confirm the adequacy of analgesia before removing the cannula on the injured limb. Perform the surgical procedure. Keep the tourniquet inflated for a minimum of 20 minutes and a maximum of 60 minutes.

Monitor the patient carefully for any signs of anaesthetic toxicity (Box 22.2.1) over the next 15 minutes following cuff release, while organizing discharge from the monitored area.

Complications

No severe cardiac complications, deaths or methaemoglobinemia have been reported using 0.5% prilocaine at the maximum dose of 2.5 mg/kg (0.5 mL/kg).⁷ Discomfort from the cuff is possible, but rarely significant.

CONTROVERSIES AND FUTURE DIRECTIONS

- There is no evidence that injecting a standard commercial preparation of local anaesthetic with adrenaline (epinephrine) into a digit is harmful.
- Lipid emulsion therapy for LAST appears well established and has been used in other life-threatening lipophilic drug toxicity, such as with propranolol, verapamil and tricyclic antidepressant poisoning.
- Need for fasting prior to a Bier block.

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22.3 Emergency department procedural sedation

Anthony J. Bell • Greg Treston • Adam Michael

ESSENTIALS

- Emergency physicians and nurses should all be trained to provide effective procedural sedation in the emergency department (ED).
- Plan and prepare yourself, and assess the risk-benefit of each individual procedure.
- Assess the timing and nature of recent oral intake, medications, available staff to assist, other simultaneous activity in the ED and patient comorbidities.
- Determine the safe limit of targeted depth and duration of the sedation.
- Sedation is a continuum. It is not always possible to predict how an individual will respond or at which point airway reflexes may be jeopardized.
- Sedative agents should be titrated to clinical end points, rather than delivered in a cookbook fashion using generic mg/kg doses.
- Each procedural situation should be based on its individual merits, balanced against the available resources of both the ED and the health service at that moment in time.

Introduction and rationale

Procedural sedation is a core competency for the emergency physician, for the performance of brief, but painful procedures, and has become standard emergency medicine practice. Emergency department procedural sedation (EDPS) refers to the technique of administering sedatives or dissociative agents, with or without analgesics, to induce a state that allows the patient to tolerate unpleasant or anxiety-provoking therapeutic or diagnostic procedures, while maintaining cardio-respiratory function.^{1,2}

However, significant variation exists in the practice of EDPS in relation to the approach,

choice and combination of agent/s given.³ Paediatric patients in particular represent a significant challenge; children are often frightened when in pain, and their presentation to the hospital disrupts the family's functioning.^{4,5} Medical staff underestimate and undertreat pain in children.⁶ Painful procedures in the ED are remembered vividly by children, their parents and adult patients. Denial of relief from pain that is proportionate to the expressed need for such relief must be judged as an unjustified harm and amounts to substandard and unethical medical practice.⁷

Underlying principles

Guidelines

The Australasian College for Emergency Medicine (ACEM),⁸ the Royal College of Emergency Medicine, American College of Emergency Physicians (ACEP)² and the Canadian Association of Emergency Physicians (CAEP)⁹ have all published on the underlying principles for successful procedural sedation and analgesia. All guidelines cover presedation preparation and assessment, presedation fasting, physician skills, staffing, equipment and environment, patient monitoring, documentation and postsedation care. There has been a gradual change in the perception accorded to EDPS being performed in EDs over the past decade, and the use of intravenous 'anaesthetic agents' for EDPS is widely accepted and is now part of mainstream emergency medicine specialist training.

Best practice guidelines require that two medical attendants, one of whom should be a specialist or advanced trainee with sedation competency, be present. Nursing staff are also required, and the procedure must be performed in a resuscitation-capable area of the ED. Physiological monitoring is mandated during the procedure and extending into the recovery phase. The practitioner must understand the agents available and choose based on the procedure being performed (e.g. the potential for pain, the likely duration of sedation and pain relief required and staff familiarity with the agent and its effects).¹⁰

22.3 EMERGENCY DEPARTMENT PROCEDURAL SEDATION

Depth and duration of sedation

The optimal end point of any sedation episode depends on the procedure being performed and patient's characteristics. Sedation state classification ranging from minimal sedation (anxiolysis) through moderate sedation (formerly conscious sedation), deep sedation and general anaesthesia. Dissociative sedation is a separate state induced by ketamine.¹¹ The exact characteristics of respiratory and/or airway reflex depression in relation to depth of sedation are not well defined and can be quite variable.¹

Titration of drug and constant verbal and tactile reassessment of the patient reduce the risk of oversedation.² Some degree of responsiveness to painful stimuli should indicate preservation of airway reflexes, decreasing the risk of aspiration if vomiting occurs.¹²

The duration of sedation is largely determined by the choice and dose of agent used and the procedure itself, as to whether this will be brief (e.g. shoulder reduction) or longer (e.g. compound scrub, or manipulation of fractures), with most ED procedures taking less than 20 minutes. The longer the sedation, the greater the risk of an adverse event.

Indications

Indications include, but are not limited to, fracture and dislocation reduction, incision and drainage of abscesses and cardioversion.¹³ Less painful but anxiety-provoking procedures in children will also be facilitated by the use of dissociative sedation (e.g. lumbar puncture, suturing, ocular or auditory canal foreign body (FB) removal or intravenous (IV) cannulation in an uncooperative and anxious child).^{3,11}

Departmental procedures and logistics

All departments that perform EDPS should have written guidelines, standardized data collection and suitably trained staff. Patient selection is informed by the pre-procedural risk assessment, by available departmental resources to successfully and safely perform the procedure and the sedation without jeopardizing patient care elsewhere in the department and by the ability to monitor and safely discharge the patient.¹⁴

Preprocedural risk assessment

Preprocedural assessment is of critical importance before embarking on EDPS. Adverse outcomes are associated with advanced age of patient, deep sedation, high body mass index (BMI) and intra-procedural use of fentanyl in combination with either propofol or midazolam. Procedure type and fasting status do not appear associated with adverse intra-procedural adverse respiratory events.¹⁵ However, procedural *failure* is related to

patient weight greater than 100 kg and to certain procedure types, notably prosthetic hip reductions and digit and temporomandibular joint (TMJ) relocations. In terms of agents used, ketamine has a lower rate of respiratory adverse events but has the overall highest procedural success rate.¹⁶

Each procedural sedation situation should be critically assessed by the treating ED physician, with particular consideration given to:

Age

A young patient's level of anxiety and cooperation will depend upon past medical experiences, anxiety of the parent/s and the reassurance given by medical staff.¹¹

Children often present the challenge of initial lack of cooperation with the sedation process. Elderly patients, whilst mostly cooperative, may have underlying impairment of cardiorespiratory reserve and are at greater risk of respiratory depression or hypotension.

American Society of Anesthesiologists classification

The American Society of Anesthesiologists (ASA) classification system¹⁵ is a global score used to classify the physical status of patients before planned surgery (Box 22.3.1). ASA class I and ASA II patients are usually preferred as candidates for procedural sedation in the ED. If an ASA class III patient requires sedation out of necessity, this should not preclude performance of the procedure. The management of respiratory depression becomes a more active issue with increasing ASA in all age groups.^{16,17}

Airway

An adverse past anaesthetic history or a focussed airway assessment with attention to mouth opening, pharyngeal visualization (Mallampati score), neck movement, thyromental distance and dentition may signal potential difficulty should active airway intervention be required. An airway assessment checklist can be found in Box 22.3.2 and Fig. 22.3.1.

Past medical history

Some conditions predispose to gastro-oesophageal reflux (such as pregnancy or hiatus hernia), raising the theoretical risk of aspiration events during deep sedation. Unstable acute medical/neurological conditions (with the exception of arrhythmia requiring cardioversion) may carry too high a risk to justify proceeding with EDPS. Allergies to any agent in the past precludes use of that agent, and egg and/or soy allergy¹⁸ will preclude the use of propofol in particular.

Occasionally a patient with significant comorbidities will present for a procedure requiring sedation. A careful assessment of the patient,

Box 22.3.1 American Society of Anesthesiologists classification

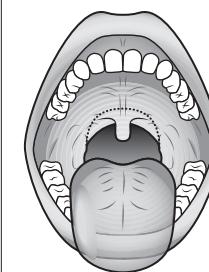
Class

1	Healthy patient, no medical problems
2	Mild systemic disease (e.g. hypertension)
3	Severe systemic disease but is not incapacitating
4	Severe systemic disease that is a constant threat to life
5	Moribund, expected to live <24 h irrespective of operation

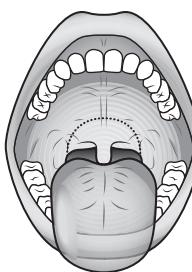
Box 22.3.2 Airway assessment for patient-controlled sedation

Predictors of difficult airway

1	Mallampati score III & IV
2	Inability to open mouth >4 cm
3	Thyromental distances <6 cm
4	Limitation of neck movement
5	Difficulty in protruding lower jaw
6	History of difficult intubation

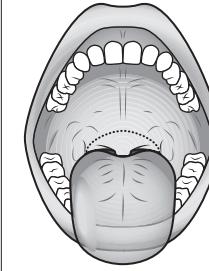


Class I: soft palate, uvula, fauces, pillars visible



Class II: soft palate, uvula, fauces visible

No difficulty



Class III: soft palate, base of uvula visible



Class IV: hard palate only visible

Moderate difficulty

Severe difficulty

FIG. 22.3.1 Mallampati score.

the urgency of the procedure and the available alternatives, in consultation with anaesthetic or intensive care unit (ICU) colleagues, would be appropriate. Often only very small doses or sedation are required in the elderly to safely perform procedures in a painless fashion.

22.3 EMERGENCY DEPARTMENT PROCEDURAL SEDATION

Fasting status

Fasting guidelines

ED patients, particularly children,³ undergoing urgent EDPS are commonly not fasted on presentation, nor at the time of the procedure. Furthermore, holding a patient for 6 hours in an overcrowded ED to achieve a goal of fasting time is impractical if an urgent procedure needs to be performed. Fasting guidelines are consensus based, not evidence based. The ASA recommends, by extrapolation, at least 2 hours and 6 hours from last intake of fluid and food, respectively,¹⁵ prior to an ED sedation, despite a lack of evidence.^{15,19} In fact, prolonged preprocedural fasting has been shown to increase the rate of vomiting in the recovery period.^{20,21}

Aspiration risk

The risk of aspiration is low. Fasting status is just one consideration when individualizing decisions about choice of agent, approach to dosing, desired depth of sedation or even referral to the operating theatre.^{12,22} EDPS does not use volatile inhalational anaesthetics or involve pharyngeal instrumentation which can induce emesis; however, there is a risk. There is no association between fasting status and adverse events during procedural sedation in the ED for a range of agents, including ketamine, midazolam/fentanyl, chloral hydrate, pentobarbital^{20,23,24} or nitrous oxide.^{12,18,25,26} A recent large retrospective observational study of paediatric propofol sedation outside of the operating theatre environment revealed only four cases of aspiration pneumonitis in almost 50,000 cases, all of whom recovered with conservative measures.²⁷

Those patients at high risk of aspiration may benefit from an alternative approach or different technique.^{28,29}

Postprocedure vomiting

This usually occurs well into the recovery period. Postprocedure vomiting is more common with ketamine or narcotics than it is with propofol or benzodiazepines.^{12,30}

Procedural urgency

The end point of sedation in the ED should be tailored to the urgency of procedure and availability of appropriate staff.^{1,9} Procedures may thus be considered:

- Emergency (e.g. cardioversion, fractures with neurovascular compromise needing reduction, intractable pain)
- Urgent (e.g. care of dirty wounds or lacerations, dislocation reductions, lumbar puncture (LP), facilitate neuroimaging in trauma)
- Semi-urgent (e.g. FB removal, care of clean wounds and laceration repairs)
- Elective procedures.

Table 22.3.1 Choice of agent and dosing recommendations

<i>Drug</i>	<i>Suggested IV drug dosages (Adult, 70 kg, normal BMI)</i>		
	<i>Initial bolus</i>	<i>Subsequent titrated IV boluses</i>	<i>Cumulative maximum dose</i>
Morphine	2.5 mg	2.5 mg	10–15 mg
Fentanyl	25–50 µg	25 µg	150–200 µg
Midazolam	2 mg	1 mg	10 mg
Diazepam	5 mg	2.5 mg	10 mg
Propofol	30 mg	20 mg	300 mg
Ketamine	20 mg	10–20 mg	150 mg
Ketafol ('10/10 mg/mL')	3 mL	1–2 mL	10 mL
Etomidate	7 mg	3 mg	20 mg

NB: These are conservative estimates and dose modification is advised where appropriate.

Parental involvement

ED survey data show the vast majority of parents want to be present for invasive procedures performed on their child in the ED.^{31,32} Despite this, many parents are asked to leave the room.³³ Parental presence should be welcomed, but ultimately their decision to stay or go should be supported.^{31,34} Should they decide to stay, provide them a preprocedural briefing as to what to expect and what they can do to support their child that includes encouraging the parent to be reassuring and to avoid transmitting anxiety to their child. The pre-brief is of particular importance when using ketamine, where the dissociative features and nystagmus may cause anxiety to the uninitiated. Provide the parent, where possible, a seated position face-to-face holding their child's hand. Regular positive updates as to progress of the procedure is good practice.

Informed consent

Informed consent must be obtained after explanation of specific risks of EDPS and the procedure itself. When using ketamine for procedural sedation, inform parents or family members who may be present in the sedation area to expect a staring sedated patient with nystagmus, possible salivation, probable lacrimation, possible myoclonic jerking and vomiting occurring in 10%–15% of patients at the end of the procedure. This is important to the family member's overall acceptance and experience of their relative's procedure. Likewise, although rare, the possibility of airway intervention beyond transient support should be raised when using propofol.

Documentation

Specific procedural sedation forms or records are recommended. When designed in accordance with current best practice, they improve documentation and may be the focus for educational initiatives and assist in audit, research and Quality Assurance (QA).^{35–37} They can also act

as a de facto protocol to ensure safe care during procedural sedation. They increase the chance of compliance with guidelines and ensure essential presedation checks and monitoring is performed. They should include provision for recording adverse events, including vomiting, aspiration or respiratory depression, as well as any interventions required.¹² Continual audit of ED sedation records should form part of the quality cycle in the ED to identify factors associated with both success and complications.

Choice of agent

The 'ideal' agent for EDPS in the ED should have rapid onset, short duration of action, rapid recovery profile, minimal side effects and an amnestic effect. The different classes of drugs used in EDPS include sedative-hypnotics, analgesics, dissociative sedatives, inhalation agents and antagonists (flumazenil and naloxone), used alone or in combination (Table 22.3.1).

Sedative hypnotics

Benzodiazepines

Midazolam Midazolam is one of the most commonly used benzodiazepines with amnestic,³⁸ anxiolytic and sedative properties. Side effects are dose dependant. Intravenous dosing for EDPS ranges from 0.025 to 0.05 mg/kg in older children and adults, up to 0.1 mg/kg in younger children. Other routes of administration include intramuscular (IM), oral, and intranasal, although onset of action is slower³¹ and many experienced clinicians have abandoned the use of intranasal midazolam, in favour of more reliable sedative agents such as ketamine. There is additive respiratory depression with opiate and midazolam containing combinations for EDPS with prolonged recovery times when compared with propofol.^{39,40–42} Furthermore, patients receiving midazolam have been reported to have more procedural recall and higher pain scores.⁴³

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Diazepam Diazepam is less potent than midazolam, but there is little or no difference in the propensity of the two drugs to produce respiratory depression.⁴⁴ Dosing should start at 0.1 to 0.2 mg/kg, with lesser subsequent doses. The anterograde amnestic effect of diazepam is significantly less than that of midazolam.^{43,45} Diazepam causes more pain on injection and a lesser degree of early sedation.⁴⁶ The elimination half-lives of benzodiazepines do not necessarily correspond with their sedative pharmacodynamic effects, and there are no clinically important sedative recovery rate differences between midazolam and diazepam.^{47,48}

Ultrashort-acting agents

Propofol Propofol is a nonopioid, nonbarbiturate sedative-hypnotic that acts at gamma-aminobutyric acid (GABA) receptors within the central nervous system (CNS), providing an amnestic effect, rapid onset (in <1 min) and short duration of action (5 to 15 minute), facilitating rapid recovery times. It is easily titratable and has some antiemetic properties.²¹ Hypotension is transient if propofol is titrated in euvolemic patients with normal cardiac function. Propofol has been shown to be safe in a wide range of settings, including procedural sedation in the ED.^{2,49,50}

The optimum dosing regimen for propofol in procedural sedation has yet to be defined. Options vary from single bolus,^{44,51,52} titration,^{19,53–56} bolus and infusion^{42,57} or infusion alone.^{58–60} Doses recommended include 1 mg/kg initial bolus and 0.5 mg/kg subsequent boluses for EDPS.^{44,61,62} In children, initial doses of 2 mg/kg initial bolus have been used.^{63,64} In adult sedation, an alternative is to reduce the dose to 0.3 to 0.5 mg/kg initial bolus followed by 20 mg boluses.⁶⁵ Dose reduction is also essential in those older than 65 years of age or those with decreased physiological reserve.⁵⁷ Higher total mg/kg doses are used in children compared with adults.^{65,66}

Propofol sedation times are shorter, respiratory complication rates equivalent to midazolam alone,⁴² etomidate⁵¹ and midazolam/fentanyl⁴⁴ and discharge times are earlier than with midazolam.⁶⁷ At higher doses, propofol is associated with greater likelihood of oxygen desaturation.⁵²

Respiratory depression is seen in up to 50% of ASA class 1 and 2 patients^{54,68,69} and 61% in the critically ill.¹⁸ Apnoea may occur but is transient.^{12,18,19,42,51,52–54,56–58,61,66,68,69} It is important to note that the combination of opiate and propofol results in higher levels of respiratory depression than propofol alone.^{70,71} Pre-oxygenation prior to sedation with supplemental oxygen used during the sedation is safe practice.

Etomidate Etomidate is a nonbarbiturate hypnotic; however, it is not globally available and propofol has become favoured. It has a

rapid onset of less than 30 seconds, with 5 to 15 minutes duration of action. Starting dose for patient-controlled sedation (PSA) is up to 0.1 mg/kg with subsequent boluses of 0.05 mg/kg. It has a similar profile to propofol in terms of respiratory depression and duration of sedation but is more cardiovascularly stable. Propofol is generally preferred above etomidate because etomidate has a 20% rate of myoclonus plus the theoretical risk of adrenal suppression, emergence phenomena and higher vomiting rates post procedure.^{72–75}

Opiates

Opiates are the most commonly used analgesics before, during and after sedation; however, they do not provide amnesia.³ Morphine is most commonly used pre-procedure and fentanyl intra-procedurally.³ Use of opiates intra-procedurally when using propofol sedation is associated with greater rate of adverse airway effects.²⁷

Fentanyl

Fentanyl has been the opiate of choice for EDPS. It should be titrated up to 1 µg/kg IV, to avoid respiratory depression from a rapid push, and should be combined with a pure sedative agent. It may also be delivered intranasally, particularly in children, although higher doses are required. Fentanyl has a rapid onset, a lack of histamine release and has a more stable cardiovascular profile when compared with morphine. Its duration of action is 30 to 45 minutes. Fentanyl has a higher in-sedation respiratory depression event rate and should be anticipated and managed.⁷⁴ Ketamine is an alternative analgesic to fentanyl for EDPS.^{15,76}

Morphine

Morphine will provide a longer duration of analgesia, extending to hours, and is very useful after the procedure for ongoing analgesia. It may have been administered pre-hospital or pre-procedure, and, if so, titrate dose accordingly.

Ultrashort-acting opiates

Newer ultrashort-acting opiates (e.g. remifentanil, alfentanil) are occasionally combined with propofol to provide sedation and analgesia, and enable rapid recovery.⁷⁷ Like fentanyl, respiratory depression is to be expected and may even occur at lower levels of sedation. Post-procedural analgesia may be required, limiting the role of ultrashort-acting narcotics in EDPS.^{78,79}

Inhalational agents

Nitrous oxide

N₂O provides anxiolysis and mild analgesia. It has rapid onset and offset and is safe but has little sedative effect. It may be useful as an anxiolytic in needle-phobic individuals to facilitate IV access before definitive IV sedation can be provided.

Despite its popularity and its convenience for the practitioner, N₂O use results in poor sedation conditions and unreliable pain reduction. This, coupled with the high rate of intraprocedural emesis when using N₂O, leaves nitrous oxide as a 'possibly useful' adjunctive agent when performing a procedure under an alternative technique (such as local anaesthetic or Bier block). Common side effects include vomiting and dizziness. Airway reflexes are preserved. Nitrous oxide can leave the bloodstream and enter air-filled cavities; therefore nitrous is contraindicated in patients in whom expansion of these air-filled cavities could compromise patient safety (e.g. pneumothorax, pulmonary blebs, air embolism and bowel obstruction).

Dissociative sedative

Ketamine

In ED procedural sedation, ketamine is used with two distinct principal aims:

1. As the primary sedative and analgesic agent, or
2. In a sub-dissociative dose as an analgesic adjunct when using an alternative sedative agent (e.g. propofol).

As a dissociative anaesthetic agent, ketamine has wide use in third world and military applications.⁸⁰ Ketamine is associated with the lowest procedural failure rate of any sedative in common use for EDPS,¹⁶ high levels of satisfaction and no procedural recall.⁸¹ At sub-dissociative doses less than 0.3 mg/kg, ketamine acts as an analgesic. With progressively larger doses, ketamine produces a dose-related 'dissociative anaesthesia' between deep sedation and general anaesthesia, generally when the dose exceeds 0.5 mg/kg. It has a rapid onset and offset of action, with preservation of airway reflexes, but it can cause laryngospasm, more notably when given intramuscularly in higher doses. It is relatively contraindicated as a sole sedative agent in patients with severe ischaemic heart disease, other advanced vascular disease or uncontrolled hypertension because it is sympathomimetic. However, it is often useful as part of a balanced sedative cocktail in such patients.

Ketamine given either intravenously or intramuscularly is popular for ED paediatric procedural sedation. At standard doses, its use is safe, with preservation of oropharyngeal reflexes, and little respiratory depression.^{6,8,22,82–85} At higher doses (exceeding 1.5 mg/kg), sub-clinical respiratory depression can be noted at rates similar to propofol,⁷⁰ but ketamine is associated with lower rates of actual airway intervention across the sedation dosage spectrum.¹⁵

In some EDs, practitioners are hesitant to use ketamine for fear of 'emergence delirium/phenomena'.^{4,83–88} Emergence delirium has been described as either 'patients are agitated,

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restless, and combative, and do not seem cognizant of their surroundings. Patients refuse to be comforted, even by their parents',⁸⁹ and 'combative, excited, and disoriented behaviour that requires transient physical restraint'.⁹⁰ However, emergence phenomena may be something as mild as a non-distressing visual hallucination (e.g. as being on a roller coaster) or as transient diplopia. Given the differing definitions, the rate of adult emergence delirium/phenomena occurring during the recovery phase after sedation varies from less than 1% to greater than 36%.^{70,91–93}

Atropine can reduce hypersalivation⁹⁴ and postprocedure vomiting, but its use is optional because it rarely affects the conduct of the procedure.

Intramuscular ketamine can facilitate a 'no cannula' sedation technique in ED, making it particularly useful for sedation involving anxious and uncooperative pre-school-aged children. Further research into safe and reliable intranasal dosing schedules is underway.

Combinations utilizing ketamine

Midazolam and ketamine

Midazolam (or another benzodiazepine) has been used in combination with ketamine, in an effort to decrease the incidence of 'emergence delirium'; however, recent randomized trials in children show no effect on emergence agitation when midazolam is added to ketamine.^{95–97} Midazolam use has also been associated with higher rates of airway and respiratory compromise during procedural sedation in children,¹⁷ and thus use of adjunctive benzodiazepines with ketamine is not recommended. The only prospective randomized controlled trial (RCT) in adults addressing this issue showed that the prophylactic use of midazolam reduced recovery agitation by 10%.⁹⁸ Midazolam as an adjunctive medication when performing EDPS using ketamine has repeatedly been associated with lower rates of postprocedural emesis^{95,96} but with higher rates of airway/respiratory complications.¹⁷ Midazolam as a sole sedative agent has itself been reported to have a rate of emergence agitation of up to 42%.^{99–101}

Ketamine and propofol ('Ketafol')

Local and international RCT studies have compared 'ketafol' with propofol,^{102,103} midazolam/fentanyl¹⁰⁴ and ketamine alone.¹⁰⁵ Most studies were small and focused on minor outcome differences. Ketamine and propofol is a stable solution and can safely be administered from the same syringe.¹⁰⁶

Although 'ketafol' usually implies a single syringe technique of premixed ketamine and propofol, experienced ED sedationists also utilize ketamine and propofol in separate syringes, with comparable or superior results.¹⁰⁷

The rationale for the addition of ketamine to propofol is to provide intraprocedural analgesia and sedation.¹⁰⁸ The combination aims to optimize sedation safety and efficacy and pain relief, balancing the opposing haemodynamic and respiratory profile of each individual drug. In addition, the antiemetic effect of propofol may counteract the vomiting seen with ketamine use and may minimize the rate of emergence experiences.^{105,109–112}

The authors favour sedation utilizing two separate syringes, ketamine at low dose providing analgesia but not dissociation and targeting depth and duration of sedation using propofol, with optimal doses being in the vicinity of ketamine 0.2 to 0.4 mg/kg and propofol 1.2 to 2.0 mg/kg, both given by titration. Recent studies have identified that higher doses of ketamine intra-procedurally result in greater rate of unpleasant emergence reactions in the postsedation period¹¹³ and higher rate of unpleasant recall of pain or discomfort during the procedure.¹⁰⁷

Other drugs

Dexmetetomidine

Dexmetetomidine is a selective alpha-2 adrenergic agonist with sedative, anxiolytic, and very mild analgesic properties. Chemically, it is related to clonidine but has greater affinity for alpha-2 adrenergic receptors than alpha-1 receptors.¹¹⁴ Dexmetetomidine acts in the CNS on vasomotor centres in the medulla, where it causes decreased sympathetic tone, which results in increased inhibitory GABA activity, leading to sedation and (limited) analgesia.¹¹⁵ It has been used for sedation of adults in the ICU and for paediatric sedation for (nonpainful) radiological investigations, such as computed tomography (CT) and magnetic resonance imaging (MRI), with some success. However, its utility is limited by hypotension and bradycardia mediated by its sympatholytic activity. There is minimal, if any, respiratory depression.

Current ED uses could be for decreasing agitation and motion in a child undergoing CT or MRI scan or as a sedative agent for intubated patients in the ED. Some report that its utility as a paediatric sedation agent is restricted to sedation for CT, MRI, or electroencephalography (EEG) and note that its use demands a longer induction and results in a longer recovery time than propofol when used for similar procedures.

Local anaesthesia

Local anaesthesia can be a very useful adjunct during EDPS, especially in cases of wound repair, cutaneous foreign body removal, and abscess incision and drainage. Infiltration of local anaesthesia in a field block allows for control of pain during the procedure, allowing for painless

completion of the procedure with a lower dose of sedation medication, as well as providing some appropriate postprocedural analgesia. This is particularly important for children. Consideration should be given to the use of appropriate-dose local anaesthesia as local infiltration or field block, where indicated.

Preparation and monitoring

Resuscitation area

EDPS should ideally occur in a resuscitation-capable area of the ED, with two trained physician staff: one to perform the procedure and one to be responsible for the drugs and airway, with the assistance of an ED nurse.⁸ Supplemental oxygen should be given for most cases of EDPS, particularly when using propofol. A Hudson mask or similar is usually preferable to nasal cannula as an oxygen-delivery system. Occasionally, when using ketamine for paediatric EDPS, the use of supplemental oxygen by mask may be excessively upsetting for the child prior to commencement of sedation, and it is perfectly acceptable to sedate the child, then apply oxygen. For removal of nasal foreign bodies or facial laceration repair under ketamine sedation, mask or nasal cannula O₂ may be omitted to facilitate access to the nares and midface.

For propofol sedation, a suitably trained and credentialed medical practitioner must be exclusively available to administer sedation to the patient, and the exclusive availability of an assistant (nurse, trainee or junior doctor) to this practitioner is recommended.¹¹⁶

Monitoring

Suction, oxygen, airway adjuncts and equipment should be prepared and physiological monitoring applied. Monitoring setup includes pulse oximetry, noninvasive blood pressure, heart rate, electrocardiography ECG rhythm and respiratory rate. End-tidal carbon dioxide monitoring is recommended, if available, and highly desirable in cases of propofol sedation. However, it is not considered mandatory for paediatric ketamine sedation, although if available and suitable for the patient and procedure performed, it should be used.^{2,12} IV access is mandatory for all cases, with the exception of sedation using intramuscular or intranasal ketamine, or nitrous oxide sedation. See Table 22.3.2 for essential equipment requirements.

Sedation scoring

Interactive monitoring as verbal and tactile stimulation is used to constantly reassess the depth of sedation. Careful dose titration and subjective evaluation of patient responsiveness throughout the procedure is paramount.^{41,49} Ramsay Sedation Score¹¹⁷ or Wisconsin Sedation Scale¹¹⁸ may

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Table 22.3.2 Essential equipment requirements

S	Suction equipment (connected and checked) <ul style="list-style-type: none"> • Wall suction • Yankauer suckers and tubing • Paediatric suction catheters
O	Oxygen (connected and checked) <ul style="list-style-type: none"> • Supply • Age-appropriate masks including nebulizer attachment • Primed bag valve mask
A	Airway <ul style="list-style-type: none"> • Oro and nasopharyngeal airways • Appropriate selection endotracheal tubes • Stylettes and bougies • Laryngoscope (and video laryngoscope) and selection of blades (tested) • Difficult airway kit including laryngeal mask airway (LMA)
P	Pharmacological agents (should be accessible but need not be drawn up) <ul style="list-style-type: none"> • Adrenaline and atropine • Naloxone and flumazenil • Bronchodilators • Medications for rescue rapid sequence induction (RSI)
M	Monitoring equipment <ul style="list-style-type: none"> • Full noninvasive physiological monitoring in situ • End-tidal CO₂ tubing and transducers (if available)
I	Intravenous access trolley <ul style="list-style-type: none"> • Crystalloids

Table 22.3.3 Ramsey sedation scale

If Awake

Ramsey 1	Anxious, agitated, restless
Ramsey 2	Cooperative, oriented, tranquil
Ramsey 3	Responsive to commands only

If Asleep

Ramsey 4	Brisk response to light glabellar tap or loud auditory stimulus
Ramsey 5	Sluggish response to light glabellar tap or loud auditory stimulus
Ramsey 6	No response to light glabellar tap or loud auditory stimulus

be used. All scales are subject to interobserver variability, are relatively imprecise and are not true objective measures of sedation. However, they require little formal training and are easily used (Tables 22.3.3 and 22.3.4).

Bispectral EEG analysis

Bispectral (BIS) EEG analysis has been studied but is not reliably predictive of conscious state in individual patients.^{74,119,120} Enthusiasm for BIS in EDPS has waned because it has not proven its value over clinical sedation scoring alone.

Table 22.3.4 Wisconsin sedation scale

Level of Consciousness	Stimulus	Score
Agitated, anxious, in pain	Spontaneous without stimulus	6
Awake and calm	Spontaneous without stimulus	5
Drowsy with eyes open or closed, easily aroused	With mild to moderate verbal stimulus	4
Drowsy, arousable	Moderate tactile or loud verbal	3
Can be aroused to consciousness but slow	Requires sustained painful stimulus	2
Can be aroused but not to consciousness	Requires sustained painful stimulus	1
Unresponsive	No response to painful stimuli	0
Score		Interpretation of Wisconsin sedation scale
6	Inadequate sedation	
5	Minimal conscious sedation	
4	Conscious sedation, moderate	
3	Conscious sedation, moderate to deep	
2	Conscious sedation, deep	
1	Deep sedation	
0	Anaesthesia	

Box 22.3.3 Discharge instructions

Recommended adult discharge criteria

- 1 Patient is alert and oriented or has returned to preprocedure state.
- 2 Patient ambulates safely.
- 3 Patient is comfortable and has discharge analgesia arranged.
- 4 Patient is discharged into care of a responsible adult.
- 5 Avoidance of driving or the like for a minimum of 12 h.
- 6 Avoid alcohol or other CNS depressants for 12–24 h.
- 7 Warn patients about potential for pain, unsteadiness or dizziness.

Capnography

Capnography can detect respiratory depression before clinical examination or oximetry.^{121–123} Change in trace character or transient hypercapnoea^{54,55,124} are the early warning signs of hypoventilation or impending upper airway obstruction, especially important in children or those with reduced functional reserve.⁶¹ Such early detection can avoid further sedation being given and result in stimulating the patient or repositioning the airway. Only occasionally is airway adjuncts or bag valve mask ventilation required.^{12,62,66}

Apnoea due to inadvertent deep sedation and detected by capnography is often managed by recommending the procedure, which usually results in enough arousal to stimulate the patient's own respiratory effort. Positive pressure ventilation is provided if apnoea persists.

Postprocedure considerations

Patients should be observed until they have returned to their baseline level of functioning.^{2,13,17} The exact time will depend on the patient and the drugs administered.¹²⁵ No special efforts need be made to darken the room or shield a child from background routine visual and auditory stimuli of the ED after ketamine sedation. Patients receiving propofol do not need prolonged postprocedure monitoring, because resedation following propofol use is rare.⁶⁵ Once the patient has awoken from the sedative episode and can talk, nursing staff have an 'end point' for the cessation of physiological monitoring, confident that patients are unlikely to develop any adverse events at this time.¹²⁶ While it is a humane gesture to provide a cup of tea to an elderly patient or a drink of juice to a small child, it should not be mandatory that the patient ingest this prior to discharge from ED.¹³ Discharge instructions should be provided (Box 22.3.3).

CONTROVERSIES

- Inadequate analgesia provision (oligoanalgesia) still exists in emergency departments (EDs).^{127,128}
- Intraprocedural narcotic use is associated with greater pain recall in ED propofol procedural sedation.
- Ultrashort-acting narcotics do not appear to provide adequate postprocedural analgesia for most conditions requiring ED procedural sedation.

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- The relationship between practitioner skill set and complications has been described, and credentialing programmes have resulted in reductions in complications and greater procedural success being achieved.^{129,130}
- The role of alternative delivery modalities (e.g. patient-controlled sedation or target-controlled infusions) using ketamine or propofol has yet to be elucidated in EDs.
- Randomized controlled trials of novel agents or combinations may present evidence of safer alternatives for certain procedures.

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Full references are available at <http://expertconsult.inkling.com>

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SECTION
23

EMERGENCY IMAGING

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23.1 Emergency department ultrasound

James Rippey • Adrian Goudie

ESSENTIALS

- 1** Ultrasound examination, interpretation and clinical correlation should be available in a timely manner 24 hours a day for emergency department patients.
- 2** Emergency physicians providing emergency ultrasound services should possess appropriate training and hands-on experience to perform and interpret limited bedside ultrasound imaging.
- 3** Ultrasound imaging by emergency physicians is useful for at least the following indications: major trauma, undifferentiated shock, respiratory distress, pain or bleeding in early pregnancy, leg swelling, right upper quadrant pain. Conditions it assesses for include traumatic haemoperitoneum, pneumothorax, pleural fluid, pericardial fluid, abdominal aortic aneurysm, right heart strain, left ventricular systolic dysfunction, hypovolaemia, intrauterine pregnancy, ectopic pregnancy, hydronephrosis, deep vein thrombosis and biliary tract disease. It is also useful to guide difficult vascular access and other invasive procedures.
- 4** Continued research is required in the area of ultrasound imaging and any other known or evolving bedside imaging techniques and modalities.
- 5** Emergency medicine training programmes should provide instruction and experience in bedside ultrasound imaging for their trainees.
- 6** The Australasian College for Emergency Medicine supports the use of bedside ultrasound by emergency physicians, as does the American College of Emergency Physicians, the College of Emergency Medicine in the UK and the International Federation for Emergency Medicine.

Background

Clinical ultrasound followed developments from the use of sonar, where the principle that sound waves could be used to locate objects was developed. Initially, ultrasound machines were large and cumbersome, but advances in technology have improved image quality while reducing machine size, so that today, small machines are able to produce high quality images. As a result

of this improved technology, ultrasound is now available to clinicians in prehospital and diverse hospital environments. There was early adoption of the technique by obstetricians and gynaecologists worldwide and later by other specialties in Europe and Japan. Ultrasound is now used by many different specialties in most countries.

Clinician performed ultrasound, now commonly referred to as point-of-care ultrasound (POCUS), has a different approach to comprehensive

diagnostic ultrasound, which is performed in radiology departments by specialist sonographers. POCUS is generally limited in scope and is targeted to answering a specific question (such as 'Is there an abdominal aortic aneurysm?'), rather than providing a full assessment of an anatomical area (Box 23.1.1). In this regard, it is often viewed more as an extension of the clinical examination, than a technique that competes with other imaging techniques (including comprehensive ultrasound).

The Australasian College for Emergency Medicine supports the use of bedside ultrasound by emergency physicians,¹ as does the American College of Emergency Physicians, the College of Emergency Medicine in the UK and the International Federation for Emergency Medicine, where it is seen as a core skill required of all trainees. It is expected that with increasing experience, the range of conditions for which ultrasound is used in emergency departments (EDs) will increase.

Basic physics of ultrasound²

Sound waves are mechanical waves that transmit energy through the vibration of particles.

Box 23.1.1 Current indications for emergency ultrasound

- Trauma (haemoperitoneum, haemopericardium, pneumothorax)
- Abdominal aortic aneurysm
- Early pregnancy complications
- Biliary disease
- Renal stones and hydronephrosis
- Echocardiography in trauma and shock
- Lung ultrasound in acute dyspnoea
- Proximal DVT exclusion
- Procedural
- Musculoskeletal

DVT, Deep vein thrombosis.

23.1 EMERGENCY DEPARTMENT ULTRASOUND

Ultrasound waves are defined as those that are above the usual range of human hearing (20 to 20,000 Hz). Current diagnostic ultrasound machines are based upon the pulse–echo principle, using pulses of sound waves at frequencies of 2 to 15 MHz, which are reflected back. Processing of these reflected echoes creates the ultrasound data and image.

The ultrasound transducer converts electrical impulses into pulses of sound (via the piezoelectric effect), which are then directed into the body. As the sound wave travels through tissue, it gradually loses energy, which is termed ‘attenuation’. The degree of attenuation differs for different tissues and is also dependent on the frequency of the pulse wave. Upon reaching a tissue interface, some of the energy is reflected back as an echo, due to the differences in acoustic impedance (gel or other coupling material is used to minimize reflection at the probe/skin surface). This reflected echo then travels back through tissue, undergoing further attenuation, until it reaches the transducer, which converts the energy back to an electrical impulse. This returning impulse is then amplified and processed. The time taken for the pulse wave to travel to the tissue interface and back is converted into distance by using the average speed for sound in tissue. The intensity of the returning wave determines the brightness of the displayed pixel. The returning pulses from the different reflecting surfaces along the path of the ultrasound beam generate a single line of the ultrasound image. The ultrasound beam is steered across the field to generate the multiple lines of information that then form the 2D image (termed B-mode, for brightness modulation). Alternatively, if the direction of the beam is kept constant and the changing surfaces are mapped over time then an M-mode image is generated (M stands for motion).

The degree of attenuation is dependent on the frequency of the sound wave, so higher frequency pulses undergo greater attenuation. They also have shorter wavelengths, which improve the resolution of the ultrasound beam (the ability to distinguish two separate objects close together). This leads to one of the most important trade-offs in ultrasound, between resolution and penetration. To obtain high resolution, a high-frequency probe can be chosen, but these will be unable to image deep structures.

To form the image, the ultrasound machine makes certain assumptions about the ultrasound beam and sound impulse. Deviations from these behaviours will result in image artefacts, that is, when the image does not represent the tissue accurately. There are many artefacts, most of which reduce the information available from the image. However, the most clinically important artefacts also can be used diagnostically:

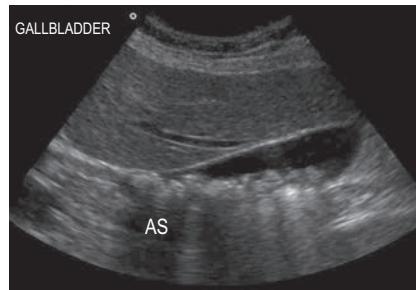


FIG. 23.1.1 Acoustic Shadowing from Gallstones.
AS, Acoustic shadow.

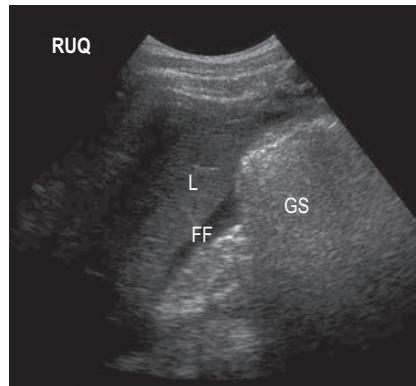


FIG. 23.1.2 Acoustic shadowing from bowel gas in a patient with free fluid. FF, Free fluid; GS, gas shadow; L, liver.

Shadowing: when all of the energy of the ultrasound pulse is reflected or absorbed at a surface (such as air or bone). In this situation, there will be no returning pulses from the tissue distal to the object. This creates a black area on the screen, known as an acoustic shadow. The presence of a shadow behind a brightly reflective surface can thus be used to diagnose a region of calcification, such as a calculus (Fig. 23.1.1). Stones and bones generally give ‘clean’ or black shadows, while gas gives ‘dirty’ or grey shadows due to the superposition of both shadow and reverberation artefact (Fig. 23.1.2).

Enhancement: when an area of interest (such as fluid in a cyst) absorbs less energy than the surrounding tissue, the pulses that have travelled through that area will have more energy than equidistant pulses that did not, resulting in a bright region deep to the area of interest on the image (Fig. 23.1.3). Enhancement is used to confirm the fluid-filled nature of lesions.

Transducer

Different ultrasound transducers are available varying in shape, frequency and the size of the contact area (termed footprint). Transducers may have a small footprint to fit into small areas, such as between ribs, from which the beam spreads in

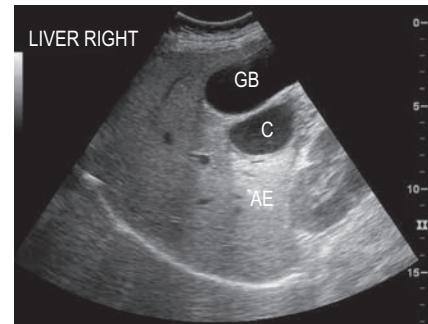


FIG. 23.1.3 Acoustic Enhancement from Fluid-filled Structures. Acoustic enhancement is seen where the ultrasound beam passes through the gallbladder and more prominently where it passes through the gallbladder and pancreatic pseudocyst. AE, Acoustic enhancement; C, pancreatic pseudocyst; GB, gallbladder.

a large arc (e.g. a sector transducer). Alternatively, they may be larger with a flat or slightly curved surface where contact can be maintained, such as a linear probe. Special transducers have been designed for use within body cavities, such as transoesophageal, endovaginal and endo-anal probes. These transducers offer the advantage of reduced distance between the transducer and area of interest, which allows higher frequencies to be used resulting in improved resolution. Very high frequency transducers have been used for intravascular and superficial ocular scanning. Appropriate choice of transducer is important in ensuring the optimal image is obtained.

The scope of emergency department ultrasound

Extended focused assessment with sonography for trauma^{3–6}

Descriptions of the use of ultrasound by clinicians to evaluate trauma patients appeared in the European literature in the 1970s. Reports have subsequently appeared from countries around the world and the technique is now well established. Initially limited to the abdomen and pericardium (focused assessment with sonography for trauma [FAST]), the examination is now routinely extended to include the chest (extended focused assessment with sonography for trauma [EFAST]). With relatively brief training and experience, non-radiologists are able to diagnose haemoperitoneum, pericardial effusions, pleural effusions and pneumothorax with a high degree of sensitivity and specificity, although accuracy does improve with experience.

Clinical examination in abdominal trauma can be difficult and unreliable. Diagnostic peritoneal lavage (DPL), ultrasound (FAST) and computed tomography (CT) have been used to further evaluate this group of patients. In most cases, FAST has replaced diagnostic peritoneal lavage

23.1 EMERGENCY DEPARTMENT ULTRASOUND

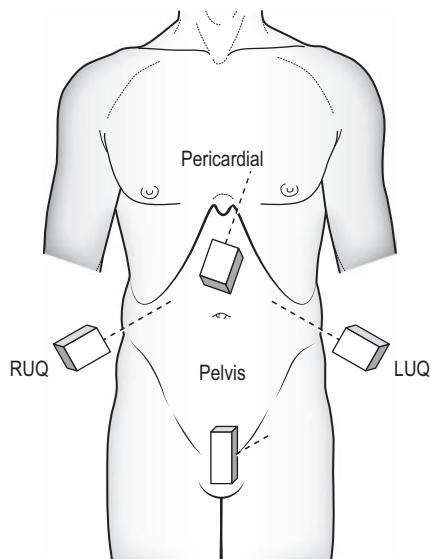


FIG. 23.1.4 Transducer placement for the four views for FAST scanning. *LUQ*, Left upper quadrant; *RUQ*, right upper quadrant.

as it is non-invasive and does not interfere with subsequent interpretation of CT images. CT scanning is highly accurate for diagnosing free fluid, solid organ injury and bony injury, and is slightly less accurate for hollow viscus and diaphragmatic injury.

Studies of ultrasound scanning in trauma have reported varying sensitivity. Much of this variation is due to differences in the gold standard used for the comparison and definition of 'true positive'. Haemoperitoneum (on further imaging, surgical or post-mortem examination), organ injury and clinical stability have all been used in different studies. It must be remembered that the primary role of a FAST scan is to detect free fluid in the peritoneal or pericardial spaces, for which it has high sensitivity and specificity. Solid organ or retroperitoneal haemorrhage may be detected but, even in expert hands, the accuracy is much lower (with as many as two-thirds of injuries being missed). FAST has been shown to be reliable and useful in both pregnant and paediatric patients.

Technique

FAST scanning evaluates four regions for the presence of free fluid: (1) pericardial, (2) perihepatic, (3) perisplenic and (4) pelvic (Fig. 23.1.4). The scan is then extended to the chest (EFAST) where the pleural spaces are examined posterolaterally for fluid, and anteriorly to exclude pneumothorax. The technique is rapid, generally being completed in under 5 minutes.

Free fluid appears as an echolucent area (i.e. black), which is generally linear or triangular in shape in the most dependent area of the peritoneal or pericardial space, although blood clots

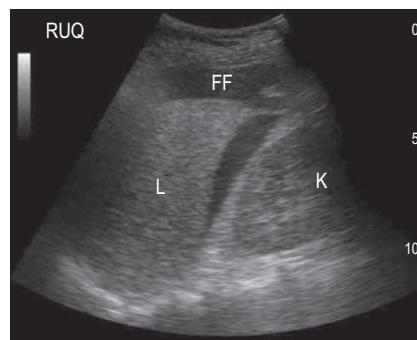


FIG. 23.1.5 Free fluid in the perihepatic view; fluid lies in the Morrison pouch between liver and right kidney. *FF*, Free fluid; *K*, kidney; *L*, liver.

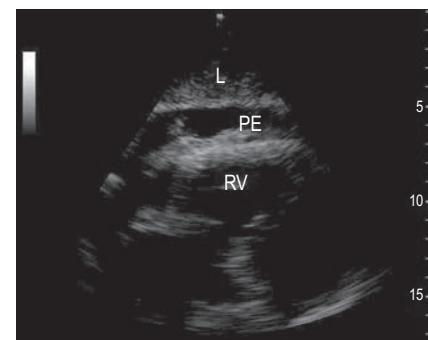


FIG. 23.1.7 Pericardial Effusion With Clot. *L*, Liver; *PE*, pericardial effusion with grey blood clots and black (echo free) blood; *RV*, right ventricle.

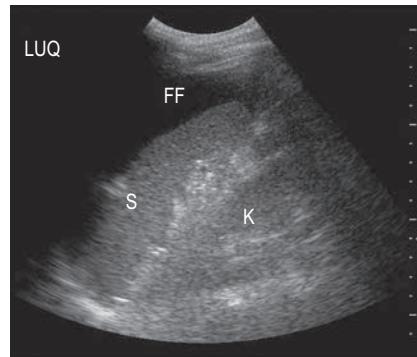


FIG. 23.1.6 Free fluid in the perisplenic view; fluid may lie anywhere around the spleen; in this case, it lies interposed between spleen and diaphragm. *FF*, Free fluid; *K*, kidney; *S*, spleen.

may be seen as echogenic (grey) collections (Figs. 23.1.5 to 23.1.7). While fluid is most commonly seen in the perihepatic space, all spaces should be examined before the result can be considered negative. Small amounts of fluid (<500 mL) may not be detected.

When scanning the chest, the presence of lung sliding or lung pulse is an indication that the visceral and parietal pleura are in contact, excluding a pneumothorax at that point. The presence of a moving transition point between areas of lung sliding and absent lung sliding (the 'lung point' sign) is diagnostic of pneumothorax.

Limitations and pitfalls

- User dependent with learning curve.
- Inadequate views occur in up to 10%, especially if the bladder is empty or with subcutaneous emphysema.
- Cannot distinguish between blood and other forms of intra-abdominal or pericardial fluid, such as ascites or pericardial effusion.
- Retroperitoneal haemorrhage may be missed.
- Solid organ, hollow viscus or diaphragmatic injuries can occur without free fluid.

- Small amounts of free fluid may not be detected.
- Small amounts of pelvic fluid may be physiological in women.
- Fluid-filled bowel can be misinterpreted as free fluid.
- Pericardial fluid may decompress into the pleural cavity.
- Loss of lung sliding may be due to causes other than pneumothorax.

Clinical implications and utility

The limitations of ultrasound in excluding all intra-abdominal injuries requiring laparotomy and the increasing use of conservative management of some injuries, even in the setting of intra-abdominal free fluid, has resulted in there being no universally accepted clinical algorithm based upon EFAST scan results. However, in this regard, EFAST scanning is no different to any other clinical, laboratory or imaging information of the trauma patient, the results of which are routinely used in combination to determine the management plan. Various algorithms incorporating EFAST scanning have been proposed, which generally incorporate haemodynamic stability and EFAST scan result, such as in Fig. 23.1.8. Some algorithms incorporate a semi-quantitative scoring system to estimate the amount of free fluid, with an increased volume of free fluid associated with a greater need for therapeutic laparotomy. A positive abdominal EFAST scan is highly predictive of significant intra-abdominal injury and, based upon the clinical condition of the patient, generally indicates the need for CT or surgical exploration. A negative EFAST scan, stable haemodynamics and clinical observation have been shown to be highly accurate in excluding significant intra-abdominal injury. Some authors advocate serial EFAST examinations in stable patients, suggesting this can reduce the requirement for CT.

Similarly, for pneumothorax, the integration of EFAST findings with other clinical, laboratory

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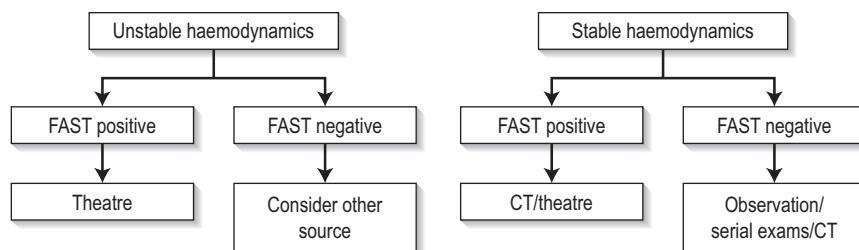


FIG. 23.1.8 Suggested Algorithm Using FAST Results. CT, Computed tomography.

and imaging findings will determine patient management. Conservative management of small pneumothoraces, even in the setting of positive pressure ventilation means that the ultrasound findings must be considered in the setting of the individual patient when management decisions are made.

In the Australasian setting, EFAST is generally accepted as fulfilling a complementary role to CT. Its portability and speed allow it to be used early in the evaluation of trauma patients (e.g. immediately after the primary survey) and this information is then incorporated with other clinical information to risk stratify the trauma patient to help to determine the requirement and timing for either laparotomy, thoracotomy or CT. Repeated examinations, particularly if the patient's condition changes, can be valuable. Providing the limitations of the technique are not ignored, it can rapidly provide vital information to assist with patient management.

Abdominal aortic aneurysm^{7,8}

Abdominal aortic aneurysm (AAA), defined as pathological dilation of the aorta with a diameter >1.5 times the expected anteroposterior diameter of that segment; however, the most commonly adopted threshold is a diameter of 3 cm or more, which occurs in 1% to 9% of the population. Clinical assessment of the abdominal aorta is unreliable and may be especially difficult in the obese or unstable patient with abdominal pain. Clinical presentation of ruptured abdominal aortic aneurysm can be varied, with only 50% of patients demonstrating the classic presentation of hypotension, back pain and pulsatile mass. Other presentations may include abdominal, groin or flank pain, unexplained hypotension, syncope, haematuria or cardiac failure and AAA should be considered in any of these presentations.

Ultrasound is the primary mode of investigation of the abdominal aorta. Ultrasound performed by emergency clinicians has been shown to be rapid, highly sensitive and highly specific (>95%) in assessing aortic diameter. Ultrasound may occasionally detect rupture, but it is not reliable in excluding rupture. In addition to its utility in diagnosing AAA, ED ultrasound is very

beneficial in rapidly excluding AAA in the wide variety of presentations listed above.

The risk of rupture of an AAA increases with the diameter. Although the risk of rupture if the aneurysm diameter is less than 4 cm is <0.5% per year and 1.5% per year for aneurysms 4.0 to 4.9 cm, rupture can still occur. Approximately 10% of ruptured aneurysms measure 5 cm or less.

Technique

The aorta should be identified anterior to the vertebral body and to the left of the inferior vena cava (IVC). It should be followed from the epigastric region to its bifurcation, just above the umbilicus, remembering that, in elderly patients, it may follow an ectatic course rather than following a strictly cranial-caudal course. It must be distinguished from both the superior mesenteric artery (SMA) (which runs anterior to the aorta) and the IVC (ensuring that the venous pulsation of the IVC is not mistaken for the arterial pulse of the aorta). Measurements should be taken both proximally and distally and, if an aneurysm is present, at the widest point. Measurements from both transverse and longitudinal planes should be taken. Measurements are taken from the outer wall to outer wall, including any mural thrombus (Fig. 23.1.9). If the renal arteries or SMA origin are identifiable then the relation to the aneurysm should be noted although, in the ED setting, this may not be possible. Any retroperitoneal haematoma or peritoneal free fluid should be noted.

Limitations and pitfalls

- Pain, obesity or bowel gas may prevent adequate imaging by ultrasound.
- Mistaking the IVC or SMA for the aorta.
- Measuring the lumen without including mural thrombus.
- Attempting to exclude rupture on ultrasound.
- Forgetting that the AAA may be an incidental finding and not the primary cause of the patient's symptoms.

Clinical implications and utility

In the patient with ruptured AAA who is haemodynamically unstable, ED ultrasound allows

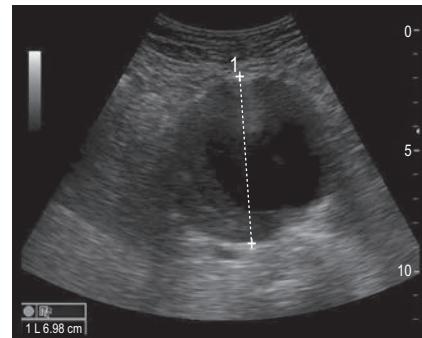


FIG. 23.1.9 Abdominal Aortic Aneurysm.

rapid and accurate diagnosis within the resuscitation area. Rapid diagnosis of these patients is essential to achieve successful treatment. In the stable patient, whose presentation may be atypical, ED ultrasound provides a rapid means of excluding the diagnosis (e.g. in the elderly patient who presents with 'renal colic'). If an AAA is detected in these patients, then further imaging will often be required to determine if the AAA is an incidental finding or the cause of the patient's symptoms. If the AAA is an incidental finding then formal follow-up should be arranged.

Early pregnancy^{9,10}

Ultrasound is the primary imaging modality for early pregnancy and its complications.¹¹ In the ED setting, it is most commonly used for the pregnant patient with pain or bleeding. In addition to transabdominal scanning (TAS), transvaginal scanning (TVS) can be performed with patient consent using a specifically designed probe, which places the transducer close to the pelvic organs and utilizes higher frequencies to produce images of much greater detail than TAS. It does not require a full bladder and should not be a painful procedure. TAS still has an important role, as it allows a broader field of view that allows better assessment of large amounts of free intraperitoneal fluid and may diagnose other causes of pain. Emergency-physician-performed ultrasound for early pregnancy complications has been shown to be safe and to reduce the time patients spend in EDs.

Technique

TAS is performed initially, preferably when the patient has a full bladder, as the pelvic organs will be better visualized. The uterus is identified and examined in both longitudinal and transverse planes (recognizing that the longitudinal axis of the uterus may not necessarily be in a strictly sagittal plane). The endometrial thickness is noted and any fluid collections or gestational sac noted. The adnexa are examined to identify the ovaries and any masses. The pelvis is scanned for

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free fluid. The upper abdomen can be examined to estimate the volume of free fluid if seen. The kidneys also can be examined to identify any alternate diagnoses.

TVS is performed after the procedure is explained and consent is obtained. A chaperone should be present if the sonographer is male. The patient is asked to empty their bladder and the pelvis is elevated slightly off the bed using a foam wedge or similar. The probe is covered with a sterile sheath (e.g. condom) with gel placed inside and outside the sheath. The probe is gently inserted into the vagina and advanced. The uterus and adnexa are then examined in both longitudinal and transverse planes as in TAS. After the scan is complete the probe must be cleaned and disinfected.

Limitations and pitfalls

- Confusing a corpus luteum cyst and ectopic pregnancy.
- Misinterpreting a pseudogestational sac for a gestational sac.
- Not considering heterotopic pregnancy in patients receiving fertility treatment.
- Failure to arrange follow-up if an intrauterine pregnancy is not identified, even if an ectopic pregnancy is not seen.
- Failure to recognize an eccentric or low gestational sac could be an interstitial, cervical or scar ectopic.
- Assuming an empty uterus in a patient with positive β -human chorionic gonadotrophin (β -HCG) is a complete miscarriage.

Clinical implications and utility

The primary aim of ultrasound in evaluating early pregnancy complications in the ED is to locate the gestational sac. Additional information should then be sought for the presence of free fluid, adnexal masses, embryonic size and embryonic cardiac activity (viability). The earliest ultrasound evidence of pregnancy is a small anechoic fluid collection surrounded by an echogenic ring, which can be seen on TVS at approximately 4.5 weeks. However, a pseudogestational sac (due to fluid within the endometrial cavity) can have very similar appearances. Definite signs that the sac is a true gestational sac appear at 5.5 weeks when the yolk sac can be visualized, or later when the embryo can be identified. A heartbeat may be visualized from 6 weeks onward. TAS will show the same features but 1 to 2 weeks later.

Pregnancies that are not identified by ultrasound are termed 'pregnancy of unknown location'. Most will either fail (miscarry or resolve spontaneously) or progress to normal pregnancy. However, 9% to 43% will eventually be identified as ectopic pregnancies (lower rates are seen in centres with more expert scanning ability as they have higher rates of definitively diagnosing

Table 23.1.1 Ultrasound findings of ectopic pregnancy

Ultrasound finding	Accuracy (%)
Absent IUP	5
Any free fluid (no IUP)	50
Mod-large free fluid (no IUP)	60–85
Adnexal mass (no IUP)	95
Adnexal mass + free fluid (no IUP)	97
Ectopic pregnancy seen	100

IUP, Intrauterine pregnancy.

ectopic pregnancy). Quantitative HCG levels have been used to determine when a gestational sac should be identifiable by ultrasound, termed the 'discriminatory zone'. For TVS, this is usually 1500 IU and for TAS 4500 IU (varying between institutions and depending on expertise and equipment). Even though a normal pregnancy may not be expected to be seen in patients with β -HCG levels below these levels, ultrasound should still be performed as it may still show diagnostic findings. In particular, ectopic pregnancies often have lower β -HCG levels than normal pregnancies of corresponding gestation and may be seen, as can the presence or absence of free fluid, which is valuable for risk stratification.

All patients with pregnancy of unknown location require close follow-up with serial β -HCG and repeat ultrasound.

If an intrauterine pregnancy is confirmed, the risk of ectopic pregnancy is very low in spontaneously conceived pregnancies. Heterotopic pregnancy is where both an intrauterine and extrauterine pregnancy coexist and occurs in up to 1:7000 pregnancies in spontaneously conceived pregnancies, but over 1:100 pregnancies in the setting of fertility treatment.

Failure to visualize an intrauterine pregnancy may be due to early dates in a normal pregnancy, failed intrauterine pregnancy (including complete miscarriage) or ectopic pregnancy. Other ultrasound findings in ectopic pregnancy include non-specific findings, such as pelvic blood and adnexal mass (Table 23.1.1).¹² Visualization of a gestational sac (with yolk sac or embryo) outside the uterus is diagnostic, but seen only in 8% to 26% of ectopic pregnancies (Fig. 23.1.10).

Unusual forms of ectopic pregnancy include interstitial, cervical and scar ectopics. In these cases, a gestational sac may be seen, but not within the true uterine cavity. It is recommended that pregnancies that appear low or eccentric should be reviewed by expert sonographers.

Distinguishing between miscarriage and ectopic pregnancy when no adnexal mass has been identified can be difficult on ultrasound.

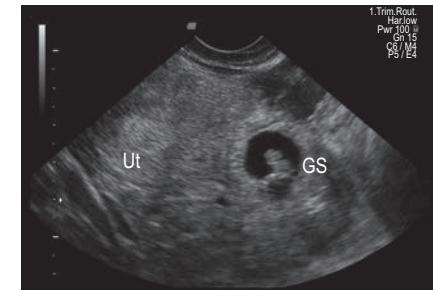


FIG. 23.1.10 Ectopic Pregnancy. A gestational sac (GS) containing an embryonic pole is seen outside the uterus (Ut).

However, if the clinical symptoms have settled, no free fluid is identified on ultrasound and no adnexal masses have been identified, then it is safe to observe or discharge the patient for formal ultrasound review the following day and subsequent follow-up with repeat ultrasound and quantitative β -HCG (see Chapter 19.4).

If an intrauterine pregnancy is confirmed, the gestational age can be estimated by measuring the size of the embryo. Most machines will automatically calculate gestational age based upon this measurement. Cardiac activity can usually be identified by TVS once the embryo is approximately 5 mm (9 mm by TAS). Absent cardiac activity when the embryo is 7 mm or above suggests embryonic demise. Absent yolk sac or embryo on TVS when the gestational sac is 25 mm suggests an empty sac miscarriage (also referred to as a blighted ovum).¹³ Other sonographic signs of poor prognosis for continued pregnancy exist, but they are generally beyond the scope of emergency ultrasound.

Right upper quadrant/gallbladder¹⁴

Upper abdominal pain due to biliary disease is a common presenting complaint to EDs and includes biliary colic, choledocholithiasis, cholecystitis and ascending cholangitis. Many of the patients suspected of having acute cholecystitis will have alternate diseases, and clinical examination is neither sufficiently sensitive nor specific for these patients. Ultrasound is the primary imaging modality for these patients, where it is used to detect the presence of gallstones (see Fig. 23.1.1), other sonographic signs of cholecystitis and bile duct obstruction. It is superior to both scintigraphy and CT for these patients.

Ultrasound has a high sensitivity and specificity for the identification of stones when performed by either radiology or ED staff. However, some stones may be missed and false-positive results also occur. The diagnosis of cholecystitis relies upon associated findings including sonographic Murphy sign, gallbladder (GB) wall thickening, GB distension and pericholecystic

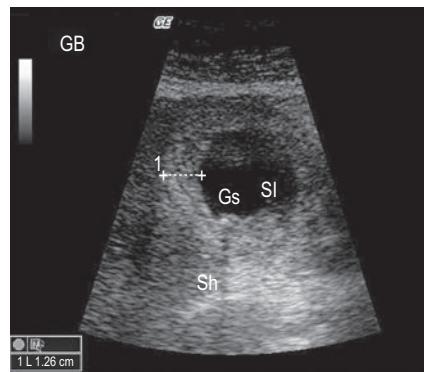


FIG. 23.1.11 Acute Cholecystitis. Transverse image of a gallbladder with thickened wall and pericholecystic fluid. Within the lumen are sludge (SI) and multiple gallstones (Gs) which cast shadows (Sh). Gb, Gallbladder.

fluid (Fig. 23.1.11). GB wall thickening and pericholecystic fluid are both non-specific findings and may be seen in other hepatic or generalized diseases as well as in acalculous cholecystitis. Fasting can cause GB distension. The common bile duct, if visualized, should be measured and examined for stones, although this is technically more difficult and may be beyond the scope of a focused GB examination.

Technique

The GB is usually identified by scanning under the costal margin in a longitudinal plane. Positioning the patient in the left lateral decubitus position and/or deep inspiration may assist. The GB should be scanned throughout its length in both longitudinal and transverse planes. The sonographic Murphy sign is assessed by pressing with the ultrasound probe over the GB. Wall thickness should be measured and is normally less than 3 mm. Gallstones will appear as bright, echogenic masses with posterior acoustic shadowing. Stones tend to be mobile unless impacted in the GB neck or cystic duct. Stones impacted in these positions are technically more difficult to detect and may be missed if not painstakingly searched for. Sludge and polyps also appear echogenic but will not shadow. Whenever possible, the common bile duct (CBD) should be visualized, measured and followed; when dilated, distal CBD obstruction should be considered.

Limitations and pitfalls

- Incorrectly assuming the presence of gallstones explains the patient's symptoms, when they may be an incidental finding.
- Mistaking gas in the duodenum for gallstones in the GB.
- Mistaking a GB that is contracted and/or full of stones for a gas- and food-filled duodenum.

- Symptomatic stones impacted in the GB neck or cystic duct are easily missed.
- Small stones (<3 mm) may not cast shadows.
- Misinterpreting sludge or polyps as stones.
- Misinterpreting other causes of GB wall thickening as cholecystitis.

Clinical implications and utility

In a patient with abdominal pain, the finding of gallstones with a positive sonographic Murphy sign is strongly predictive of cholecystitis. The more sonographic signs of cholecystitis that are seen, the more likely the diagnosis. However, asymptomatic gallstones are common and may therefore represent an incidental finding, especially if the sonographic Murphy sign is absent. In elderly, diabetic or critically ill patients, 5% to 10% of cholecystitis can be acalculous. In those patients thought to have biliary colic or cholecystitis, a negative ultrasound should prompt a search for alternative diagnoses or consideration of further imaging, either formal ultrasound or, if an alternate diagnosis is believed likely, CT.

Renal ultrasound

The primary focus of renal ultrasound in the emergency setting is the detection of hydronephrosis in the presence of acute renal failure or renal colic.¹⁵ As experience increases, users can often detect renal calculi, particularly when located at the vesicoureteric junction. The presence of a ureteric jet excludes complete ureteric obstruction on that side.

Technique

The kidneys are paired retroperitoneal organs lying on either side of the spine between T12 and L4. They have a convex lateral border and a concave medial border and hilum. The normal adult kidney is 9 to 12 cm in length, 2.5 to 4 cm thick and 4 to 6 cm wide. The kidney itself is composed of two distinct areas, the renal parenchyma and the renal sinus.

The adult kidney is scanned using a curvilinear 3.5 to 5 MHz transducer and a renal preset that provides the best contrast resolution and grey map for imaging the kidneys. The patient may be supine, although the kidneys are usually best seen with the patient in a lateral decubitus position. A combination of subcostal and intercostal approaches is often necessary. The kidneys should be imaged in at least two planes, including the sagittal or coronal plane and the transverse plane (Figs 23.1.12 and 23.1.13). On ultrasound, the kidney can be identified by its elliptical shape with a thin echogenic capsule. Normal renal parenchyma has slightly decreased or equal echogenicity relative to the hepatic or

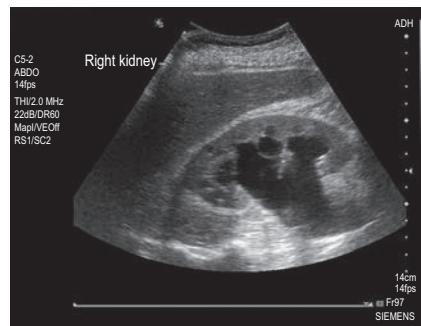


FIG. 23.1.12 Sagittal image of right kidney demonstrating moderate hydronephrosis.



FIG. 23.1.13 Coronal image of left kidney demonstrating a calculus in the renal pelvis with acoustic shadowing.

splenic parenchyma, although this is age dependent with it being comparatively hyperechoic in the elderly. The central renal sinus is particularly echobright due to the fat and fibrous tissue content. The renal pelvis and infundibulum are usually collapsed and not seen except in the setting of hydronephrosis when they become filled with urine, appearing anechoic. The bladder should be full and examined in both the sagittal and transverse planes to complete the study. It should be noted that an excessively full bladder may cause mild dilatation of the pelvicalyceal system; however, this will return to normal following micturition.

Ureteric jets occur when either ureter contracts propelling urine into the bladder. This occurs every 10 to 20 seconds in the euvoilaemic patient with normal renal function and excludes complete obstruction on that side. However, the presence of a jet does not exclude the possibility of a non-obstructive renal or ureteric calculus.

Hydronephrosis is the dilatation of the renal pelvis and calyces and may be secondary to an anatomical obstruction or may be functional in nature (such as with ureteric reflux). Obstructive hydronephrosis may be intrinsic or extrinsic. Depending on the level of obstruction, it may be unilateral or bilateral with or without associated hydroureter. When hydronephrosis is identified, the cause for the obstruction should be sought.

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Common intrinsic obstructive causes seen in the ED include obstructive or partially obstructive renal or ureteric calculi. Bladder outlet obstruction due to prostatic hypertrophy is another common cause of hydronephrosis. Extrinsic or invasive masses in the pelvis obstructing either the ureters or bladder outflow also should be considered.

Hydronephrosis may be described as mild, moderate or severe depending on the extent of dilatation of the renal collecting system:

- *mild*: dilatation of renal pelvis; may have some calyceal filling; however, the calyces remain cupped
- *moderate*: increasing dilatation extending into the pelvicalyceal system with distension and blunting of the calyces, but with preservation of cortical thickness
- *severe*: marked pelvicalyceal dilation with clubbed calyces and associated parenchymal cortical thinning.

Limitations and pitfalls

- Assuming hydronephrosis and obstruction are synonymous.
- Hydronephrosis takes time to develop and more so in the dehydrated patient.
- Hydronephrosis can persist transiently after obstruction is relieved.
- Mistaking an extrarenal pelvis for hydronephrosis.
- Mistaking parapelvic renal cysts for hydronephrosis.

Clinical implications and utility

Ultrasound is less sensitive than plain films or CT in detecting renal calculi. Small stones may often be obscured by the echogenic renal sinus and be hard to detect if they have a weak posterior acoustic shadow. Having said this, stones in the kidney that are greater than 5 mm in size have been shown to be detected in experienced hands with 100% sensitivity sonographically.¹⁶ Renal stones appear as bright, echogenic foci with distal acoustic shadowing and sometimes twinkle artefact when interrogated with colour Doppler. Ureteric calculi are difficult to visualize as they are often obscured by bowel gas in their retroperitoneal position. Therefore a normal appearing kidney and the failure to visualize a calculus does not exclude a ureteric calculus that is non-obstructing or where hydronephrosis has not yet developed.

Deep vein thrombosis

The primary focus of ED ultrasound in the assessment of deep vein thrombosis (DVT) is in the diagnosis or exclusion of a proximal lower limb DVT.

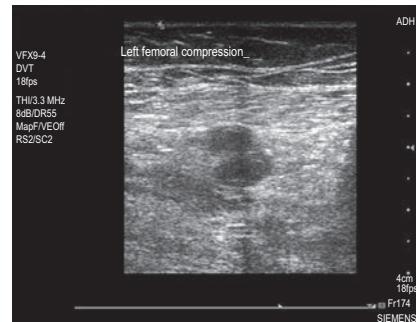


FIG. 23.1.14 Transverse image of the left femoral vein and artery with incomplete collapse of the femoral vein with compression, indicating intraluminal thrombus.

The clinical assessment of DVT is unreliable and inaccurate.^{17,18} Positive findings on sonographic examination of only 11% have been reported for patients referred for suspected acute DVT on the basis of clinical features.¹⁹

Technique

Ultrasound is the imaging modality of choice for assessing for DVT. The technique relies primarily on B-mode imaging with intermittent venous compression, with the main diagnostic criteria used to exclude a DVT being complete collapse of the vein with apposition of the anterior and posterior walls of the vessel.

A broadband linear array transducer with a centre frequency of about 5 MHz is used to examine the femoral, popliteal and sometimes the calf veins. In larger patients, the curved linear array transducer with a centre frequency of 3.5 MHz (as used for abdominal studies) may be substituted. The curved linear array transducer is also used to examine the iliac veins. The machine should be configured to use the lower limb venous preset and the use of harmonic imaging may improve the contrast resolution between the vessel and the surrounding tissue. Transducer compression of the interrogated vessel should be in the transverse imaging plane. Starting at the level of the groin, with the patient in a supine position, the common femoral vein is identified lying medial to the common femoral artery and the vein is compressed to demonstrate collapsibility extending distally in a stepwise fashion with the vein compressed every 2 to 3 cm (Fig. 23.1.14). Where thrombus is present in the vein, pressure with the transducer will not result in its collapse. The popliteal vein may be best examined with the patient in a lateral or prone position with the knee slightly flexed. Colour and spectral Doppler may be used to supplement the findings of intermittent compression. Emergency physicians who had undergone standardized training to

identify clot in the femoral or popliteal veins have shown an accuracy comparable to formal vascular studies.²⁰

Limitations and pitfalls

- Mistaking the saphenous vein for the femoral vein.
- Not recognizing that the incorrectly termed 'superficial' femoral vein is a deep vein (it is correctly referred to as the 'femoral vein').
- Sensitivity of ultrasound for calf DVT detection is much lower than proximal DVT.
- Not recognizing a duplicated femoral or popliteal vein, with one patent and one thrombosed.
- Misdiagnosing chronic clot for fresh clot.
- Not ensuring that initial ED exclusion of proximal DVT is followed up by a formal repeat scan in 7 days if high clinical suspicion or positive d-dimer.

Clinical implications and utility

The accuracy of compression ultrasonography is highest in symptomatic patients, with studies comparing venography with compression ultrasound demonstrating an average sensitivity of 95% and specificity of 98%.²¹ For proximal lower limb DVT, this technique has demonstrated sensitivity of up to 100%.²² The use of colour and spectral Doppler to assess for vessel filling defects and flow patterns has not been shown to increase significantly the sensitivity for proximal DVT detection in the lower limb.^{22–25} It has also been suggested that an abbreviated technique, using only two compression points (the saphenofemoral junction and the lower popliteal vein) has adequate sensitivity, provided repeat examination is performed in 5 to 7 days.^{24,26,27} The accuracy of ultrasound in detecting isolated calf DVT, especially when applied to emergency POCUS ultrasound, is low with success rates as low as 40% reported.²⁸

Thus the aim of focused ED ultrasound in the assessment of DVT is generally to confirm or exclude the presence of clot in the proximal deep veins of the lower limb. A negative compression ultrasound study of the proximal lower limb significantly reduces the likelihood of DVT and discharge from the ED without anticoagulation, with outpatient follow-up for a definitive study can be considered.^{21,29–31}

Emergency echocardiography

Focused use of echocardiography in the ED represents one of the most valuable uses of ultrasound in emergency medicine. Applications include its use in cardiac arrest, undifferentiated hypotension, suspected pericardial effusion and tamponade, chest pain, pulmonary embolus

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and ultrasound guided procedures. The use of cardiac ultrasound in emergency medicine is likely to increase significantly as more emergency physicians learn the technique and look to apply it increasingly in the clinical environment.

Echocardiography provides direct structural and functional information on cardiac structures only inferred by clinical examination, which has been shown to have limited accuracy, and with greater sensitivity and specificity than indirect tests, such as electrocardiography and chest radiography.^{32–34}

Technique

Modern general ultrasound machines can provide good quality transthoracic echocardiography capability. A broadband phased array transducer with a centre frequency of 2 MHz and a small footprint to improve access between the ribs should be used. Ideally, the patient should be positioned on their left side.

The full, standard echocardiographic examination includes parasternal long and short axis views obtained at the left sternal edge in the 2nd to 4th rib spaces, the apical 4-, 5-, 3- and 2-chamber views that are obtained at the cardiac apex and the subcostal views obtained from a subxiphoid position. The standard examination would involve 2-D assessment of cardiac structure and function using B-mode, supplemented by the use of colour and spectral Doppler to assess valvular function and measure chamber pressures using the windows described above.

Where an abbreviated, emergency bedside echocardiographic examination is being used to screen for the presence of tamponade, right ventricular (RV) dysfunction, left ventricular (LV) dysfunction (including absence of contraction) and hypovolaemia alone, simply using B-mode and attaining the parasternal short and long axis views, the apical 4-chamber view and the subcostal view is generally enough.

In cardiac arrest, the subcostal view is used with the patient in the supine position. All preparations are made including charging the defibrillator while cardiopulmonary resuscitation (CPR) continues. During the rhythm check, a loop is recorded and reviewed once CPR recommences. It is imperative that the time without CPR is minimized and echocardiography should not interfere with this.

Emergency physicians have been shown to assess accurately LV function in the hypotensive patient.³⁵

Limitations and pitfalls

- Good views may not be obtainable in a supine patient, especially if ventilated.
- Not appreciating the limitations of focused and abbreviated emergency echocardiography.

graphic studies when compared to formal detailed echocardiographic studies.

- Focused echocardiographic examination aims to detect for tamponade, RV dysfunction, LV dysfunction and hypovolaemia. It does not assess for diastolic dysfunction, regional wall motion abnormality, valvular dysfunction or aortic dissection, the detection of which generally take significantly more experience.
- Confusing pleural and pericardial effusions.
- Confusing pericardial fat pad and pericardial effusion.
- Not appreciating the fluid causing tamponade is not always anechoic, particularly when exudative, purulent or haemorrhagic.
- Not appreciating that a loculated clot or effusion may cause tamponade but not be seen, particularly in the postoperative patient.
- Not appreciating a normal echo does not exclude pulmonary embolism (PE).
- Not understanding that there is difficulty distinguishing between acute pulmonary hypertension from PE and chronic pulmonary hypertension.
- Not appreciating that while a large, round IVC with no respiratory variation infers elevated right-sided pressures, it does not mean administration of intravenous fluid will be futile. In tamponade and RV infarction, for example, additional preload despite a 'full' IVC is often useful.

Clinical indications and utility

In cardiac arrest, the aim of echocardiography is to assess LV activity as well as to exclude the presence of potentially reversible causes, particularly tamponade. In the setting of cardiac arrest, cardiac standstill on initial presenting echocardiographic assessment has important prognostic implications, irrespective of presenting electrical rhythm. Gaspari et al., in a multicentre observational study, demonstrated that the absence of cardiac activity is a very poor, but not absolute, prognostic sign, with only 0.6% of these patients surviving to discharge.³⁶ As is always the case, the user must integrate ultrasound findings into the clinical picture to make a final clinical decision. Cardiac standstill in the newly collapsed patient, the hypothermic patient, the young patient or the toxicological overdose should not be used as the sole criterion to cease resuscitative efforts.

Echocardiography is very useful in determining the cause of undifferentiated hypotension and shock. The primary aim of focused emergency echocardiography in this setting is to assess for tamponade, for RV dysfunction (that in the correct clinical setting would infer massive PE), for LV systolic dysfunction and for hypovolaemia. With increased echocardiographic expertise severe valvular dysfunction also can be rapidly detected.

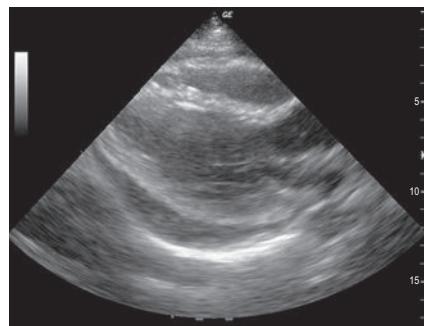


FIG. 23.1.15 Parasternal long-axis view of the heart demonstrating a moderately-sized pericardial effusion.

A pericardial effusion is seen as an anechoic collection of fluid between the visceral and parietal pericardium (Fig. 23.1.15), although an inflammatory pericardial effusion or haemopericardium may exhibit internal echoes. In differentiating between a pericardial effusion and a pleural effusion, a pericardial effusion tapers towards and anterior to the descending aorta and may extend a short distance between the aorta and left atrium; conversely, a pleural effusion will accumulate and extend behind the descending aorta, which is best seen in the parasternal long axis view. When a pericardial effusion is identified, its location and size should be documented and any evidence of tamponade looked for. The size of an effusion can be described as small, moderate or large. A small effusion is ≤ 1 cm in thickness and may be localized. A moderately sized effusion is between 1 and 2 cm and is generally circumferential unless loculated. A large effusion is described as being >2 cm. In a group of 515 patients at high risk for pericardial effusions (103 of whom had pericardial effusions), emergency physicians were able to detect an effusion with an overall sensitivity of 96%, specificity of 98% and accuracy of 97%.³⁷

The risk of tamponade is more a function of the rate of accumulation than total volume of pericardial effusion. There are a number of different echocardiographic features used to define tamponade; however, its precise echocardiographic diagnosis remains complex and controversial. The most frequently used echocardiographic finding to support a diagnosis of tamponade is collapse of the right heart chambers during mid-to-late diastole and, specifically, RV diastolic collapse. In the ED setting, pericardial tamponade should remain a clinical diagnosis. In a patient with signs and symptoms consistent with tamponade, the focus of emergency echocardiography is the identification of pericardial effusion. Its presence is then interpreted and acted upon in the clinical context.

Transthoracic echocardiography lacks sensitivity for diagnosing PE. Echocardiography missed

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16 of 39 patients presenting to an ED with PE, diagnosed by other modalities in a prospective observational study.³⁸ However, there are echocardiographic features associated with PE that, when identified and put into clinical context, can be highly suggestive or diagnostic. These include RV dysfunction or dilatation, McConnell sign (mid and basal RV akinesia with preservation of RV apical function), paradoxical septal motion, acute tricuspid regurgitation and the presence of clot in the right heart. While echocardiography may be a poor tool for diagnosing PE, it may be useful in assessing RV dysfunction caused by PE and may have a role in risk stratifying patients and influencing the decision to use thrombolytic therapy. RV dysfunction is associated with a significantly higher mortality.³⁹ Massive PE with associated hypotension, or when clot is seen in transit through the right heart, is generally managed with thrombolysis or less commonly embolectomy or various interventional radiological therapies. Specific criteria for the use of these aggressive strategies to treat submassive PE remains controversial, but current recommendations are for simple heparinisation and close observation, with invasive intervention only if hypotension develops. (see Chapter 5.5)

When the cause of shock is primarily due to pump failure, then echocardiography demonstrates a poorly functioning, often dilated left ventricle (LV) and/or atrium. Differentiating severe global LV dysfunction (as occurs in cardiogenic shock) from normal LV function or the hyperdynamic LV of hypovolaemia is readily done. More precise calculations of ejection fraction and cardiac output or regional wall motion abnormality are generally beyond the scope of the focussed echo exam.

In shock due to hypovolaemia, echocardiography demonstrates a small LV end-systolic volume with hyperdynamic LV motion. The IVC also tends to be small or collapsed and demonstrates increased respiratory variation. In the spontaneously ventilating patient, inspiratory collapse of over 50%, particularly when the IVC is small, infers a high likelihood of fluid responsiveness.

The use of echocardiography for the acute assessment of chest pain is extremely useful but requires significant expertise and is generally beyond the scope of the ED user. Transthoracic echo can detect the regional wall motion abnormalities associated with cardiac ischaemia and, in expert hands, the sensitivity and specificity are relatively high. Echo too may detect the RV dilatation and dysfunction associated with PE, the pericardial effusion that may be associated with pericarditis, proximal aortic dilatation and even an intimal flap or aortic regurgitation from dissection, but, for these conditions, has much lower sensitivity. Ultrasound can also detect numerous chest wall and pulmonary pathologies

presenting with chest pain that may mimic cardiac pain and thoracic ultrasound is described in the next section.

Lung ultrasound

Lung ultrasound is being increasingly used by critical care clinicians and respiratory physicians to assess the patient with undifferentiated shortness of breath. It is also used to answer a diverse range of specific clinical questions, such as is there a pleural effusion, is there a pneumothorax or is there pulmonary oedema? Finally, it is used to guide pleural procedures, such as effusion drainage or biopsy.

Suggested algorithmic approaches, such as Lichtenstein's 'BLUE protocol' for the patient with acute respiratory failure, claim a diagnostic accuracy of 90.5%.⁴⁰ This protocol assesses for cardiogenic pulmonary oedema, pneumonia, decompensated chronic obstructive pulmonary disease (COPD), asthma, PE and pneumothorax.

It should be recalled that neither bone nor air allows the passage of ultrasound. Because of this, one cannot assess directly behind a rib where an acoustic shadow occurs, nor deep to an air interface, such as the normal pleural surface. This means that thoracic ultrasound can focus on the bony thoracic cage where fractures of ribs and the sternum can be readily detected or on the pleural space where effusions, pleural masses or free air (as in pneumothorax) can be detected and, finally on the lung itself. In aerated lung, assessment can be made only of the visceral pleural surface (and a tiny rim of lung tissue directly adjacent to this). If the lung is not aerated, as occurs with solid tumours, consolidation, collapse or infarction, the solid area of lung deeper to the surface can be explored with ultrasound.

Sonographic assessment of aerated lung relies on two things. First, movement of the lung, with the two pleural surfaces sliding against one another during ventilation and, second, on artefact created by reverberation of ultrasound. This reverberation occurs at the pleural surface and within minute collections of interstitial fluid or fibrosis. Normal ventilating lung is therefore characterized by 'lung sliding' where the very slightly irregular visceral pleural surface can be seen moving to-and-fro past the parietal pleura with inspiration and expiration. Even in normal lung, tiny foci of interstitial or alveolar fluid or fibrosis create short path reverberation artefacts, which appear as bright vertical lines deep to the pleural surface. When these are short they are called comet tails and when they are long they have been termed 'B-lines'. When there is an increasing amount of interstitial or alveolar fluid (or fibrosis) as seen in pulmonary oedema, pneumonitis, acute respiratory distress syndrome, lymphangitis carcinomatosis and

pulmonary fibrosis the number and prominence of these vertical 'B-lines' increases dramatically. More subtle sonographic changes in the pleural surface may allow differentiation between these subgroups; however, often it is clinical correlation that makes the picture clearer.

With pneumothorax lung sliding is lost, as are the vertical comet tail and B-line artefacts. The lung point can sometimes be found where the two pleural surfaces meet and allow some degree of assessment of pneumothorax size. In addition, with pneumothorax, the free air beneath the parietal pleural surface creates a smooth mirror-like effect. Long path reverberation artefacts, known as 'A-lines', occur where horizontal repetitions or reflections of the pleural surface are seen below the actual pleural surface. Lung sliding can also be absent in COPD, bullae or conditions where the lung surface is 'sticky' from inflammation of any cause.

In addition to the diagnostic utility of thoracic and lung ultrasound, having access to ultrasound for procedural guidance is extremely useful. Ultrasound can be used to assess an area of opacity seen on chest x-ray, to determine whether it is solid or liquid and the relation to the diaphragm and heart. If a pleural effusion is confirmed, it can be further characterized as being simple or loculated and as to whether there is debris floating within it. Aspiration or tube placement can then be done after calculating the thickness of the chest wall, the depth of the effusion and the best direction from which to approach. The procedure can be done in real-time or after the patient is positioned, the skin is marked and trajectory planned.

Technique

The pleural surface is interrogated using either the curvilinear abdominal or the high frequency linear transducer. Several different methods for assessment have been described and depend on clinical suspicion, which must be used to guide and then interpret the scan. Integration of lung ultrasound and emergency echocardiography is the best approach to assessing the patient with undifferentiated acute dyspnoea.

In the absence of pleural adhesions or loculations, pneumothorax collects in the most apical portion of the thoracic cage and should be examined for there. If the patient is a supine trauma patient, assessment anteriorly along the mid-clavicular line from clavicle to diaphragm, with the probe in longitudinal orientation is effective.

If considering pleural effusion or haemothorax, examining the bases and costophrenic angles from the front, side and back, usually with the patient sitting up, is best. To assess the lung parenchyma, maximizing the view of the pleura, lining the probe up in the line of the intercostal spaces and so avoiding ribs, is ideal.

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For a non-trauma patient who presents in acute respiratory distress, sitting up, the author tends to examine the chest methodically:

- Anteriorly in the midclavicular line:
- with the probe longitudinally to maximize lung sliding, explore from clavicle to dia-phragm.
- Laterally in the midaxillary line:
- initially with the probe in longitudinal position at the lung base to assess the costo-phrenic angle for fluid, collapse or consolidation,
- then higher with the probe aligned with the intercostal spaces to interrogate the pleural surfaces and lung higher up.
- Posteriorly just medial to the scapulae, which are rotated out the way by flexing the shoulders forward:
- initially with the probe longitudinal at the lung base to assess the costophrenic angle for pathology,
- then higher up the chest with the probe orientated along the line of the intercostal spaces (almost transverse).

Limitations and pitfalls

- Surgical emphysema, obesity or patient position may prevent adequate imaging by ultrasound.
- Assuming lack of lung sliding is diagnostic of pneumothorax – without considering other causes such as COPD, bullae, severe asthma, pleural adhesions, etc., and failing to search for the lung point to confirm the diagnosis.
- Many pathologies can cause an increase in the number of B-lines, not just pulmonary oedema; remember to correlate clinically.
- Pericardial fat pads can be confused with consolidation.

Clinical implications and utility

ED ultrasound allows the rapid assessment of patients in acute respiratory distress at the bedside. Whilst the major sonographic patterns described above are easy to differentiate, relatively diverse pathologies may have similar sonographic patterns. As with all of POCUS integration of the ultrasound findings with careful clinical assessment and appropriate clinical judgement is essential in ensuring the correct diagnosis is made.

Ultrasound-guided vascular access

Vascular access, both venous and arterial, and central and peripheral, is commonly performed in the ED. Widespread availability of machines and increasing familiarity and expertise among the emergency medicine community in using ultrasound to guide all forms of vascular access

has had major positive implications to patients in recent years.

Traditionally, central venous access has been secured using the 'landmark technique', where surface anatomical features are used to predict the location of the internal jugular, subclavian and femoral veins. However, access using this technique has been associated with a 20% failure rate and a 10% complication rate, including inadvertent arterial puncture, excessive bleeding, vessel laceration, pneumothorax and haemothorax.^{41,42} Improved success rates and decreased complication rates have been described using ultrasound-guided central venous access, including reduction in needle puncture time, increased overall success, reduction in carotid puncture, reduction in pneumothorax and a reduction in catheter-related infection.^{43,44} National guidelines from the UK⁴⁵ and the USA⁴⁶ support the use of ultrasound guidance for central venous catheter (CVC) placement. Inadvertent arterial CVC placement can still occur when using ultrasound guidance with the catheter traversing the internal jugular vein before entering the underlying carotid or subclavian artery. Using ultrasound to confirm wire placement prior to dilation, and transducing pressures prior to CVC use are recommended to ensure early recognition and mitigation of this potentially major complication.

Ultrasound guidance is also useful in aiding peripheral vascular access. The basilic, brachial and cephalic veins are frequently not visible clinically, but are readily cannulated using ultrasound guidance. Basilic vein cannulation has been shown to be very successful in the ED setting in patients in whom other peripheral access was difficult.⁴⁷

Technique

A medium to high frequency broad bandwidth linear array transducer is used with a centre frequency of 7.5 to 10 MHz. Specific presets to optimize the needle's visibility have been developed, but a musculoskeletal preset is usually adequate. The procedure is most easily performed with the ultrasound screen, the patient and operator all in line, with orientation checked and optimized. A sterile transducer cover and ultrasound gel are essential. A longer cannula is also particularly useful as the vessels being targeted are generally deep and increased length is required to reach them and ensure adequate vessel purchase.

Two techniques have been described, the static and dynamic techniques. The static technique may be used for very superficial or very large vessels, but is generally considered inferior to the dynamic technique. The static technique is used to locate the vessel, measure its dimensions, confirm relationships of surrounding structures and determine depth below the skin. The vessel is then centred on the screen and the skin marked at the centre of the transducer, corresponding to the vessel's

subcutaneous position. This mark is then used for the puncture site without ultrasound visualization of the needle as it enters the vessel.

The dynamic technique uses real-time ultrasound guidance visualizing the needle tip as it enters the vessel. Higher success rates have been demonstrated with the dynamic technique than with the static technique.⁴⁸

Real-time ultrasound-guided cannulation using both in plane and out of plane transducer orientation relative to the needle have been described. The out of plane orientation is easier to obtain and provides information related to adjacent structures; however, the needle tip is less clearly seen. The in-plane orientation is more difficult to achieve but provides information related to vessel orientation and slope, and provides visualization of the needle in its entirety as it passes through the tissues and enters the vessel.

Clinical implications and utility

In many centres, emergency staff (both medical and nursing) are gaining familiarity and expertise with ultrasound-guided vascular access of all sorts. The increased use of ultrasound to place peripheral cannulae and peripherally inserted central catheter (PICC) lines has meant less trauma for our patients and, in many cases, less need for central line placement.

Miscellaneous applications

Scrotal ultrasound

Patients may present to the ED with scrotal or testicular pain, a scrotal mass or following scrotal trauma. Acute scrotal pain in the absence of trauma may be due to testicular torsion or epididymo-orchitis. Scrotal swelling may be due to hydrocoele, hernia or testicular mass. Scrotal trauma may be associated with testicular rupture, haematoma and testicular ischaemia. Ultrasound is the imaging modality of choice for assessing for testicular pathology and injury.

The scrotum is examined using a high-resolution linear array transducer with the patient in a supine position with the scrotum supported by a towel between the patient's legs.

In testicular torsion, the testis rotates on its axis leading to twisting of the spermatic cord with compromise of both venous drainage and arterial supply. To diagnose torsion, it is important to demonstrate normal flow within the normal testis and absent flow in the affected side.⁴⁹ However, blood flow may be very difficult to identify in normal paediatric testes. In addition with intermittent torsion–detorsion flow may appear normal or even increased in the affected testis. Partial torsion can occur with normal colour Doppler flow detected. Therefore ultrasound cannot exclude testicular torsion, which remains a clinical diagnosis.

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Epididymo-orchitis is the most common cause of scrotal pain in postpubertal men. Sonographically, the epididymis is characteristically thickened. Increased blood flow is demonstrated with colour Doppler in the epididymis or testis, or both. A reactive hydrocoele is common.

Ocular ultrasound

Ocular ultrasound has been used by ophthalmologists as an adjunct to examination for over 40 years. In the emergency setting, it is most useful to examine the eye in those patients where swelling prevents direct visualization of the eye and for disorders for which direct ophthalmoscopy has poor accuracy. After applying gel to the high-frequency linear probe it is gently applied to the closed eyelid and the globe examined in two planes from side to side. The posterior chamber should appear round and echo free. The optic nerve can be identified posteriorly. A retinal detachment appears as a relatively thick and echogenic membrane that may show colour flow on Doppler. In rhegmatogenous retinal detachments, the membrane undulates with eye movement (older detachments tend to move less with increasing fibrosis). Retinal detachments do not cross the optic nerve. Smaller areas of a thick elevated membrane that do not undulate may be seen with other types of detachments or other pathologies, but all of these will generally be beyond the scope of the emergency physician and require an ophthalmologist to distinguish. A vitreous detachment appears as a much thinner, avascular membrane that may only be seen when perpendicular to the beam, which also moves with globe movement. Vitreous haemorrhages appear as either dots or larger echogenic regions which move more quickly than retinal detachments. Studies have shown good accuracy when employed by emergency physicians to diagnose retinal detachment.⁵⁰

Ultrasound has also been used to diagnose globe rupture, foreign bodies and lens dislocation. Some groups have described its use in the diagnosis of intracranial hypertension, by looking at the optic nerve sheath diameter. However, while individual groups have found good accuracy, differences in technique and wide variation in the quoted normal ranges have limited the general applicability of this technique.

Appendicitis

Misdiagnosis of appendicitis on clinical assessment is associated with a negative appendectomy rate of 15%, with rates as high as 40% to 50% reported in some series.⁵¹ Delays in intervention can result in appendiceal perforation with associated increased morbidity and mortality.⁵² The aim in assessing a patient with clinically suspected appendicitis is to adequately identify the appendix to confirm or refute

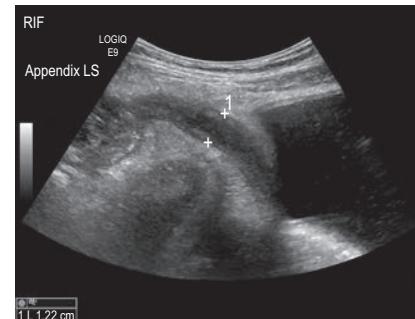


FIG. 23.1.16 Acute Appendicitis. Longitudinal view of the appendix, seen originating from the caecum and draping over the iliac vessels into the pelvis where its tip lies adjacent to the bladder.

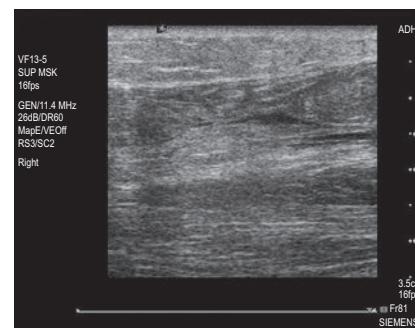


FIG. 23.1.17 Longitudinal view of the tendo Achilles showing a full thickness tear at the level of the musculotendinous junction.

the diagnosis, identify complications, such as perforation, or to identify other causes of the patient's presentation. The appendix is identified as a blind-ending, tubular, aperistaltic structure arising from the posteromedial caecum 1 to 2 cm distal to the ileocaecal junction. The patient should be examined in a supine position using a high-frequency linear array transducer to optimize image resolution. The normal appendix is compressible with a wall thickness equal to or less than 3 mm.⁵³ Increased wall thickness (outerwall to outerwall) of greater than 6 mm with loss of compressibility (Fig. 23.1.16), loss of definition of the mucosa, submucosa and muscularis propria and the visualization of an appendicolith support a diagnosis of appendicitis. Additionally, the detection of peri-appendiceal inflammatory changes in the presence of an abnormal appendix increases the likelihood of appendicitis.⁵⁴ Failure to identify the appendix is common and does not exclude appendicitis.

Musculoskeletal and soft tissue applications

There are numerous musculoskeletal and soft tissue applications for diagnostic ultrasound in emergency medicine. These include foreign body identification, evaluation of suspected tendon tears (Fig. 23.1.17), muscle tears and

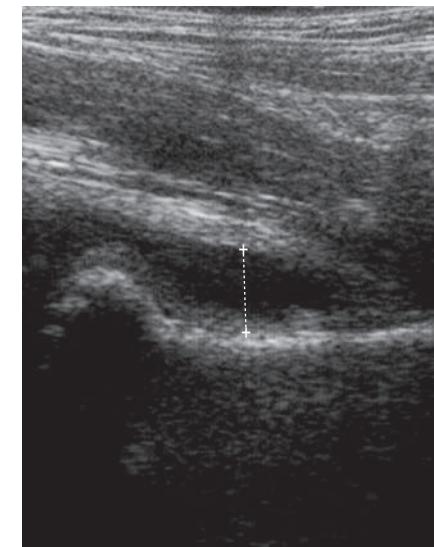


FIG. 23.1.18 Longitudinal view of the right hip demonstrating joint effusion.

haematomas, abscess confirmation and localization, joint effusions (Fig. 23.1.18) and fractures. Most musculoskeletal imaging is done using a broadband, high-resolution, linear array transducer with centre frequency of about 10 MHz.

Ultrasound-guided procedures

Ultrasound is a useful modality for identifying fluid collections and guiding diagnostic or therapeutic aspiration, including thoracocentesis, paracentesis and arthrocentesis. It is also increasingly used by both anaesthetists and emergency physicians to guide nerve blocks.

Training and credentialling¹

In Australasia, both the Australasian College for Emergency Medicine (ACEM) and the Australasian Society for Ultrasound in Medicine (ASUM) make recommendations and provide credentialling pathways in emergency ultrasound. ASUM provides the nationally recognized qualifications the Diploma in Diagnostic Ultrasound (DDU) and the Certificate in Clinician Performed Ultrasound (CCPU).

In 1999, ACEM proposed a policy supporting the use of ultrasound by emergency physicians for at least the detection of traumatic haemoperitoneum, abdominal aortic aneurysm, pericardial fluid, ectopic pregnancy, renal and biliary disease. The subsequently published policy document supported a credentialling process for training in FAST and AAA studies and included recommendations on training requirements. These requirements mandated a minimum of 25 FAST exams with at least 5 positive scans for intraperitoneal, pleural or pericardial fluid and 15 AAA exams of which 3 should demonstrate an

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aneurysm for credentialling purposes. All of these training exams should be confirmed by a gold standard (other study, surgical findings, clinical course, etc.) and be reviewed by a suitably qualified reviewer. The requirements also included attendance at an ultrasound workshop that would cover the basic information for an emergency physician to perform and interpret EFAST and AAA studies. Guidelines for the Minimum Criteria for Ultrasound Workshop were published by ACEM in 2000. These policies were reviewed in 2011, and requirements for credentialling in Basic Echo in Life Support were added.

ASUM is the recognized national training, qualifying and credentialling body in medical ultrasound. ASUM offers two qualifications to medical practitioners performing ultrasound: the CCPU and the DDU. Both of these qualifications are endorsed by ACEM for the purposes of training and credentialling in emergency ultrasound and describe a scope of practice that extends beyond those described by the College. Further details can be obtained from the ASUM website.

In 2005, the Royal College of Radiologists in the UK, in consultation with the clinical colleges, published a document entitled 'Ultrasound Training Recommendations for Medical & Surgical Specialties'. This document defines three levels of competency with suggested training and practice requirements for each level and has been endorsed by the College of Emergency Medicine (UK).

The 2001 American College of Emergency Physicians (ACEP) Policy Statement, Emergency Ultrasound Guidelines, reviewed the previous criteria for achievement of competency to perform focused clinical ultrasound. These recommendations included a 16-hour introductory course and a minimum of 25 ultrasound examinations for each defined primary modality.

Although the minimum training requirements for emergency physicians to become proficient in focused emergency ultrasound remains unclear, the recommendations from ACEP, ACEM, ASUM (for the CCPU) and the training recommendations of the Royal College of Radiologists (UK) for clinical ultrasound are similar and have been promulgated in a consensus document by the International Federation for Emergency Medicine.

The increasing technological sophistication, portability and affordability of ultrasound machines has led to an increasing demand for ultrasound as a diagnostic tool to be devolved to the clinician managing the patient. This is no more so than in emergency medicine where ultrasound has the potential of establishing a broad range of applications and indications that extend beyond EFAST and AAA detection as is described by the training curricula and guidelines above. The challenge now lies in developing adequate training and supervision networks to allow these skills to be learnt and maintained.

CONTROVERSIES AND FUTURE DIRECTIONS

- The scope of practice of emergency ultrasound is likely to continue to expand within EDs. Although the core uses for emergency physicians will continue to focus on unstable patients, the broad utility of ultrasound and its ability to add information to clinically challenging situations is likely to result in its application to a broader patient group.
- The major rate-limiting step remains initial access and supervision of training.
- Paradoxically, skill maintenance in these so-called 'more advanced' applications of emergency ultrasound may be easier to achieve given that the majority of emergency physicians have far greater exposure to these patient groups than those with suspected haemoperitoneum in the setting of trauma or ruptured AAA.
- The amount of training required by clinicians to achieve competency and to maintain the sensitivity and specificity of an ultrasound study remains to be determined.

Full references are available at <http://expertconsult.inkling.com>

23.2 Computed tomography scanning in emergency medicine

Stephen J. Dunjee • Swithin Song

ESSENTIALS

- 1 Computed tomography (CT) scans are a major diagnostic modality in emergency medicine.
- 2 Emergency physicians are ordering CTs more frequently than previously for a variety of reasons.
- 3 Artefacts are occasionally encountered in CT scans, and clinicians should be familiar with these artefacts.
- 4 Contrast media reactions and carcinogenic effects of radiation are recognized potential adverse effects of CT scanning.

Introduction

Computed tomography (CT) was developed in 1971 by Godfrey Hounsfield and Allan Cormack and adopted into medical practice. By the early

1980s, CT scanning was in general clinical use in the United States, and within a generation, most large emergency departments acquired their own dedicated scanners. Emergency medicine has embraced the utilization of CT

scans, as it significantly aids in clinical diagnosis. It has revolutionized the approach to patients with traumatic injury, neurological emergencies, abdominal pain and chest pain. It is cost-effective and fast. It is, however, a modality that presents some risks to patients, and clinicians need to be prudent in their use. It is also an area of considerable development, with CT scanners becoming faster and more precise, and therefore increasing utility.

Development science

CT scan machines consist of a gantry around a patient, with an x-ray source on one side of the gantry and detectors on the opposite side, moving in synchrony. Early scanners imaged one slice at a time ('step and shoot'), with the table stationary while a static image was acquired. This produced a series of parallel slice

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images (tomographic images) of a region of the body. The beam produced by the source can be adjusted, producing widths from 1 to 20 mm. Traditionally, images were produced which displayed the volume of data as axial slices (perpendicular to the long axis of the body), but current



FIG. 23.2.1 Axial CT of head.



FIG. 23.2.2 Coronal CT of head.

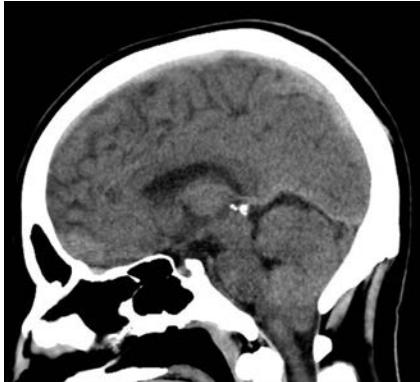


FIG. 23.2.3 Sagittal CT head.

scanners are able to display the collected data as multiplanar slices which improves diagnostic yield ([Figs 23.2.1 to 23.2.3](#)).

Helical (spiral) CT scanners move the patient rapidly and continuously through a circular gantry opening that is equipped with a source and multiple detectors, which are continuously rotating and provide volumetric acquisition. The source describes a helical trajectory relative to the patient.

Windows

The objects displayed in a scan can be differentiated from adjacent organs by their differential attenuation of the x-ray beam based on their individual density. The density of the tissues is measured in Hounsfield units (HU). Water has a density of 0, and tissues denser than water have values greater than 0, while less-dense tissues have negative values. The accepted convention is for high-density structures to be displayed in lighter shades and low-density structures to be displayed in darker shades. The denser a structure, the lighter the shade displayed. The scale extends up to about +4000 for very dense metals, with cancellous bone about +700 and dense bone about +3000. Blood is in

the range of +35 to +45 and muscle about +40. At the other end of the scale, air is -1000, lung -700 and fat -84 ([Figs 23.2.4 and 23.2.5](#)).

Humans can only perceive a limited number of grey shades, and so to highlight the tissues of interest, the full range of density values is not displayed. Instead, the display shows a narrow portion of the full range to allow clear differentiation of one tissue from another and pathological tissue from normal tissue.

For example, bone windows are a preset that will shift the grey scale displayed to centre on the range of densities which are typical of bone and allow detection of subtle abnormalities, such as fractures. As a consequence of focusing the display on such high-density structures, there is a marked decline in the ability to assess soft tissues on bone windows.

Display convention

The accepted convention for displaying images is for the right side of the patient to be on the left side of the image.

Artifacts

There are some imaging artefacts that affect the quality of the images generated and hence the diagnostic quality of the scan. These artefacts are classified as physics-based artefacts, patient based, scanner based and multi-section based. Most emergency physicians (EPs) are familiar with patient movement ([Fig. 23.2.6](#)) and metallic artefacts ([Figs 23.2.7 and 23.2.8](#)).

Physics-based problems include beam hardening (resulting from the absorption of low-energy photons after passage through an object, leaving only high-energy photons and a higher energy beam), which can produce the streaks and dark bands. Undersampling is another physics-based problem, in which the distance between CT samples is large enough to create mis-registration of information about small objects or sharp edges. Partial volume averaging is when the densities in a single CT is averaged rather than displaying separate



FIG. 23.2.4 Axial CT of lung using lung windows preset.



FIG. 23.2.5 Axial CT chest using preset for CT angiogram.

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individual densities. This occurs because every CT slice displayed is a 2D representation of a finite 3D thickness of tissue.¹ Ring artefacts, a scanner-based problem, occur due to mis-calibration or failure of one or more detector elements (Fig. 23.2.9).

Current uses and indications

While the overall usage of CT scanning is dramatically increasing, evidence suggests a higher rate of increase in emergency medicine. A 2011 study showed that in the United States between 1995 and 2007, the number of CT studies performed increased from 2.7 million to 16.2 million—nearly a sixfold increase.²

By the end of the study period, the presenting complaints topping the list of those undergoing



FIG. 23.2.6 Pseudofracture of C6 from patient movement.

CT were abdominal pain, headache and chest pain. The percentage of patient visits associated with CT for all complaints increased most substantially among those who underwent CT for flank, abdominal or chest pain. Other high-use areas include shortness of breath, trauma and headache, being more marked in the elderly.

Indications for emergency department CT scans have increased, as CT is diagnostically more sensitive than plain x-rays, supplanting plain films in assessing skull fractures, cervical spine injury and renal colic.

The long-held belief of the accuracy of clinical examination is being challenged in this era of good diagnostic tests. In the last decade, there has been a dramatic increase in the number of CT scanners, with moderate-sized country hospitals and most large urban emergency departments having their own dedicated scanners. During the



FIG. 23.2.8 Coronal CT abdomen with metallic artefact obscuring bladder.

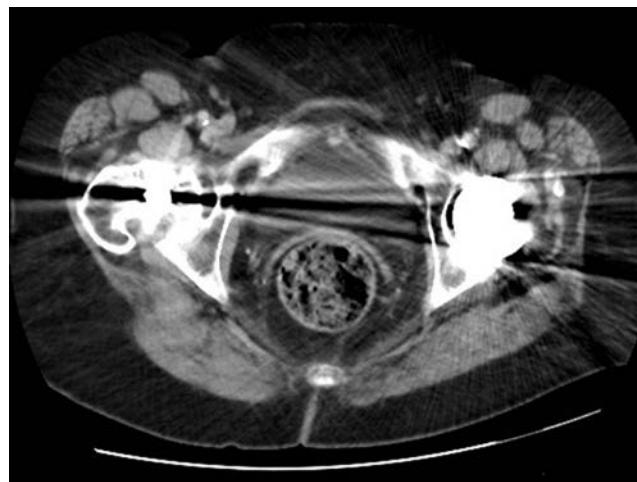


FIG. 23.2.7 Metallic artefacts from hip prostheses.

same period, scanners have become faster with improved diagnostic accuracy. All of these factors drive the increase in scans performed. CT scans are now used for chest pain (for suspected acute coronary syndrome, coronary artery disease and aortic dissection), not just for suspected pulmonary embolism. Surgeons now aim to avoid unnecessary surgery and are increasingly unwilling to take patients for exploratory laparotomies without a prior CT scan to provide a definitive or tentative diagnosis.

Problems

There are some significant problems that continue to present challenges for physicians requesting CT studies.

Weight constraints

Most scanners have a patient weight limit, with the maximum of about 250 kg depending on the unit used, or a patient circumference limit. Some manufacturers are developing bariatric scanners.

Unstable patients

A CT suite is usually limited in its provision of resuscitative care. Even with oxygen and suction outlets and full monitoring, these spaces are primarily designed for imaging, not resuscitation. Although current CT scanners can perform in a short time interval, the process of manoeuvring patients into the room, off the trolley and changing over tubing and monitoring has changed little over the years. Consequently, scanners that can perform a whole-body scan in a few minutes have made surprisingly little difference to the time in the CT scan suite. Patients still die in the relative isolation of these suites, and it is still important for physicians to ensure that their patients are as stable as possible prior to leaving the resuscitation area. Patients who cannot be stabilized because of the severity of their injuries should go straight to the operating theatre rather than be imaged.



FIG. 23.2.9 Ring artefacts in a very bariatric patient.

Allergy to computed tomography contrast media

There is significant lack of understanding in the medical community regarding reactions to contrast media. Contrast molecules are so small that they are not capable of acting as antigens, and although they can create an allergic type reaction, it is probably not IgE mediated. Reactions range from minor skin reactions up to more severe anaphylactoid reactions (bronchospasm, angio-oedema, hypotension). IV contrast reactions are more common in atopic individuals and those with previous allergic reactions, but the most important risk factor is a previous contrast reaction. Determining the incidence of such reactions is difficult because of underreporting and because concomitant illness can produce similar symptoms in some patients. The American College of Radiologists manual on contrast media suggests rates of 0.2% to 0.7% overall, with the rate of serious reactions of about 1 or 2 per 10,000.³

Iodine is an essential element, and it is not possible to be allergic to it. Although shellfish are a rich source of iodine, allergy to shellfish is due to the proteins found in the muscle of the shellfish, and so the widely held belief that shellfish allergy precludes the use of contrast agents is not based on fact.

For patients who are at risk of a reaction, it is wise to have medication on hand to manage a severe response easily. The usefulness of prophylactic steroids for emergency patients is dubious. One recommendation suggests:

Do not delay emergent studies for steroid premedication. Only lengthy 12-hour premedication protocols have shown any effect on reaction rates and this small benefit was manifested primarily by decreasing minor reactions. No steroid protocol has shown a significant benefit in decreasing severe or fatal reactions.⁴

Contrast-induced nephropathy

Contrast-induced nephropathy is a concerning complication for those receiving IV contrast media. It has been estimated to have a mortality rate of up to 36% in hospital and a 19% 2-year survival, as well as prolonged hospitalization. Contrast media have also been estimated to be used in approximately 50% of scans currently performed, and CT scan usage is increasing at an exponential rate.

Under normal physiological conditions, nearly all of the contrast medium is eliminated through the kidneys. The resulting concentration in the renal tubular system is up to 100 times the concentration in plasma and approaches $\leq 30\%$ of the concentration of the injected solution. With

contrast concentrations of this magnitude, it is not surprising that this could be a cause of acute kidney injury.

Recent evidence challenges long-held beliefs about contrast-induced nephropathy (CIN). A turning point has been the adoption of a more uniform way of diagnosing and describing the illness (change in the baseline creatinine of $\geq 25\%$ and/or an absolute elevation of creatinine from baseline values of 0.5 mg/dL).

Studies focusing on contrast-enhanced CT show an overall incidence of CIN, with the current generation of non-ionic contrast media, to be in the range of about 5%. Very recent work examining contrast media away from cardiac catheterization has questioned whether the media induce CIN at all, and suggests that there is no difference in rates of acute kidney injury in unwell patients receiving contrast versus those who are scanned without contrast.⁵ Traditionally, risks for developing CIN include renal insufficiency, age (older than 55), hypovolaemia, longstanding diabetes and patients taking metformin. It appears that baseline renal insufficiency is the only well-supported independent risk factor.

There have been many agents used as attempted prophylaxis against development of CIN, including *N*-acetylcysteine (NAC), vasodilators, such as fenoldopam, calcium channel blockers, theophylline, but the only well-accepted measure for at-risk patients is adequate hydration. This position is supported by the American College of Radiology, but the ideal volume and rate of administration is not known. Isotonic fluids, such as normal saline, are preferred. Most guidelines suggest 6 to 12 hours of infusion prior to the procedure and for up to 4 hours afterward.⁶ Clearly these recommendations are impossible to implement for emergent patients.

Radiation

CT scanning is a source of ionizing radiation, which is capable of overcoming the binding energy of electrons and is able to knock them out of orbit, creating ions. Although x-rays can ionize DNA directly, it is the production of hydroxyl radicals from ionization of water molecules that produces strand breaks and base damage. Although there is some capacity to repair damaged DNA, unresolved damaged DNA can induce cancer. At the doses delivered in normal scanning, there is a small risk of radiation-induced carcinogenesis. This is supported by the historical evidence supplied by Japanese survivors of the atomic bombs dropped in 1945. The group who received low doses of radiation in the range 5 to 150 mSv (mean 40 mSv, which approximates the organ dose from a typical CT involving two to three scans in an adult) showed a significant increase in the risk of cancer.

Spiral (or helical) CT is rapidly becoming the dominant type of scanner used and, under typical use (with a pitch of 1 or greater), the radiation dose is comparable to conventional CT. Slice thickness, the number of slices obtained and the pitch affect radiation exposure. Pitch is a ratio defined as the distance the table travels during one rotation of the radiation source divided by the section thickness

In pregnancy

Radiation damages DNA, and a foetus with rapidly dividing and differentiating cells is more susceptible to these effects than adults. Large doses of radiation can lead to growth retardation, birth defects, cancers, mental retardation and even fetal death, but modern diagnostic studies are well below the threshold that would cause such catastrophic effects.⁷ Exposure to less than 5 rads has not been associated with deleterious effects on a foetus.

In context, an abdominal x-ray exposes a foetus to about 100 mrad, a lumbar spine x-ray to 50 to 150 mrad, a CT of pelvis to 250 mrad and a CT of abdomen or lumbar spine to 3.5 rad.

Apart from the risks of radiation, there are often questions about the safety of contrast media. It is generally considered safe to give contrast media in all trimesters of pregnancy, although there are theoretical risks of thyroid depression in the foetus/neonate because contrast media molecules are small enough to cross the placental barrier and to be excreted in breast milk. Some centres direct pregnant or lactating women to discard breast milk for up to 24 hours after contrast administration, although this is likely unnecessary.

In childhood

There has been a marked increase in the use of diagnostic CT scanning in the paediatric population, driven in part by the decrease in time to perform a scan, which eliminates the need for anaesthesia.

The largest growth has been in the diagnosis of acute appendicitis, in which CT is cost effective and accurate, although ultrasound represents a safer option.

The increased risk of carcinogenesis is even more marked in the paediatric population for two reasons: they are more radiosensitive, and they also have more years of life in which to develop a radiation-induced cancer.

Overuse

Widespread acceptance of the use of CT scanning, the development of new indications, its speed and accuracy in diagnosis, liability

23.2 COMPUTED TOMOGRAPHY SCANNING IN EMERGENCY MEDICINE

issues and the improved access to scanning are among a long list of reasons why the number of scans generated by emergency departments is increasing.⁸

While this change is mirrored throughout medical practice, the potential for inappropriate overuse of CT in emergency medicine is an area of concern. Unnecessary scans expose patients to radiation (particularly if there are consecutive or multiple scans done in a short period) and are expensive (particularly if compared with modalities like plain x-ray or ultrasound).

Some estimates have suggested a sevenfold increase in total medical radiation exposure from the 1980s to 2006 for the population of the United States. While CT scanning in that period only accounted for 17% of x-ray imaging, it was responsible for 49% of the total estimated dose.

In the same population, emergency medicine generates about one-third of the CT scans performed. The benefits for patients in EDs are not disputed.

Some studies suggest that there are significant numbers of inappropriate tests ordered from emergency departments, in part driven by a fear of medical liability.

EPs respond by pointing out that although the CT radiation dose is significant (10 to 20 mSv, which is associated with a lifetime risk of fatal cancer in about 1 per 2000 scans), more than 1 in 2000 patients will have potentially life-saving information provided by a CT. To many frontline doctors, the long-term risks are theoretical and poorly quantified compared with the risk of missing significant pathology in the here-and-now.

One area of medicine in which CT scanning has revolutionized care is trauma management. Rapid, high-quality scanning has unequivocally led to better outcomes in many patients but, even here, questions are being asked. The pan-scan has been enthusiastically embraced and quickly become a standard of care before any rigorous scientific evaluation.

An Australian study compared radiation exposure with trauma patients before and after the introduction of a diagnostic algorithm employing a 64-slice scanner.⁹ Their findings were challenging, suggesting that patients were 1.7 times more likely to receive a radiation dose exceeding 20 mSv compared with a conventional CT work-up, but did not significantly benefit from the procedure in terms of the incidence of missed injuries (0.6% vs. 0.9%).

Only one-fifth of the patients in the study fulfilled the criteria for major trauma. The authors went on to suggest that the pan-scan may be 26 times more likely to harm the patient in the long term than assist them in the acute setting.

CT scanning should not be requested in a frivolous fashion, without regard for potential long-term health risks. The speed of the investigation

and the quality of the diagnostic information should always be balanced against the knowledge that the scan may harm the patient.

Clinical decision rules

EPs are responsible for ensuring that they make sensible and appropriate decisions for their patients and that their choice of CT as a modality takes account of the risks to the patient. It is unfortunately true that there has been such a proliferation of guidelines that sometimes clinicians are hard pressed to know which one to follow. There are, for example, no less than three widely accepted and well-validated decision rules for determining the need for CT in head injury (Canadian Head CT rule, New Orleans Criteria, NEXUS II). The American College of Radiologists has developed a comprehensive list of appropriateness criteria that relate possible investigations to the presenting complaint, covering the full gamut of clinical presentations and made in conjunction with appropriate input from clinicians.

Diagnostic accuracy of emergency physicians

EPs are often required to interpret a CT scan. Early studies did not suggest this was done well. Many studies have examined the ability of EPs and registrars (Emergency Medicine residents in North America) to interpret head CT scans. In the specific clinical setting of stroke, compared with the gold standard of interpretation by neuroradiologists, EPs performed relatively poorly in recognition of both haemorrhage and early ischaemic changes (accuracy 60%), but neurologists and general radiologists only achieved a result of 80%.

A study examining EPs' abilities to assess head CT for trauma concluded that, without extra training, EPs should not be interpreting such scans. While there is debate about whether the non-concordance between EPs and radiologists leads to poor clinical outcomes, there are numbers of studies that demonstrate the improvement that is possible with focused teaching.

There is no doubt that improvement in training must occur because, despite the advent of teleradiology, there will still be occasions when the situation dictates that an EP perform the initial interpretation of a CT scan.

Advances in CT scanning

There have been a number of technological innovations in the last decade that have improved imaging diagnostic quality, reduced radiation dose, and expanded the diagnostic capabilities of CT scanners.¹⁰ These innovations include **higher slice systems, iterative reconstruction, new detector technology, spectral CT imaging and advances in cardiac imaging.**

New standards of care were introduced when 64 slice scanners became available and were widely deployed across all health care systems. Since that time, **higher slice systems were introduced** (80, 128, 256, 320 and 640 slice) and soon superseded the older systems. Proponents for the new systems point out that the increased price tag is justified by the increased image area coverage, reduced radiation and reduction in the need for repeat scans. They improve image quality, reduce stitching artefacts and benefit cardiac scans by completing scans in milliseconds and hence avoiding movement artefacts.

Iterative reconstruction is an innovation that reduces radiation dose and improves image quality. This is achieved with software that revises the image repeatedly with multiple iterations to clarify the image, pixel by pixel, and clean up artefacts. This promotes diagnostic image quality with low-dose scanning.

New detector technology utilizing micro-electronic circuits reduces electronic noise and produces sharper images.

Spectral CT imaging is based on viewing the same anatomy at two different kV energies, which breaks down x-ray photons by chemical elements, similar to the way a prism breaks down light. This is done either with a dual source scanner, or by using fast kV switching between different energies during the scan (or using detector elements that record different kV levels during a scan). The result is that different anatomical features are enhanced at different energy levels, and it may avoid the need to scan a patient multiple times. The software can highlight or eliminate chemical compounds based on anatomic number. This means that one can create contrast and non-contrast images from one scan (since iodine contrast can be removed by spectral filters to create a virtual non-contrast scan), and can also differentiate between contrast and a calcified plaque in a blood vessel. One can also differentiate between different types of kidney stone, reduce metal artefact and more clearly identify pulmonary emboli.

Cardiac imaging advances mean that cardiac CT scanning, which was an anatomical imaging modality (without functional quantification of blood flow/perfusion) is now being offered with CT perfusion assessment software that tracks the iodine contrast concentration in the myocardium throughout the cardiac cycle. Areas of low contrast correspond with areas of perfusion defects. Cardiac CT scan, it is argued, will allow for more timely discharge of patients without coronary causes and reduce the need for unnecessary nuclear medicine cardiac scans or cardiac coronary artery catheterizations.

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23.3 Magnetic resonance imaging in emergency medicine

James Rippey

ESSENTIALS

- 1** Magnetic resonance imaging (MRI) is becoming more readily available in Australian hospitals and is becoming part of many imaging diagnostic algorithms.
- 2** The most common indication for MRI in the emergency department (ED) is suspected acute spinal cord pathology.
- 3** MRI is well suited to imaging soft tissues, particularly the central nervous system, musculoskeletal tissues and abdominal organs.
- 4** Lack of ionizing radiation makes MRI a good choice for younger patients and pregnant women, although it is generally avoided in the first trimester.
- 5** Disadvantages for EDs include the time taken for a scan and difficulties with monitoring and resuscitation in the scanner, making MRI unsuitable for most unstable patients.

Introduction

Magnetic resonance imaging (MRI), like each of the other imaging modalities, has its unique strengths and weaknesses. Emergency diagnostic imaging algorithms are complex and vary according to the clinical condition, the question being asked, patient factors, local availability and expertise. In Australasia, there are rapidly increasing numbers of MRI machines, together with appropriately trained staff. Many diagnostic algorithms are being revised to include MRI as a realistic imaging alternative. While the indications for urgent MRI are increasing, the major indication for emergency MRI remains suspected acute spinal cord pathology.

The main strength of MRI lies in its ability to image soft tissues at extremely high resolution, both spatially and with unparalleled levels of soft tissue contrast. It also has the ability to create two-dimensional slices in any plane; these multiplanar capabilities allow comparison of adjacent tissues from any angle.

Different MRI techniques allow different anatomical and pathological features to be demonstrated. MRI is particularly good at imaging the structure and pathology of brain, spinal cord and nerves, muscle, tendons and ligaments, cartilage, bone marrow and solid abdominal organs. The advent of magnetic resonance angiography (MRA) makes it an alternative to computed tomography angiography (CTA), particularly in those with contraindications to CT contrast media or those more vulnerable to ionizing radiation. Finally, the ability to perform electrocardiogram (ECG)-gated imaging has enabled unsurpassed dynamic noninvasive cardiac imaging.

MRI has imaging limitations in cortical bone and air-filled spaces (particularly lung) and thus tends not to be the imaging choice for assessing these tissues.

The lack of ionizing radiation makes MRI an attractive alternative to CT, particularly in younger patients, especially children and women of child-bearing age. MRI's apparent safety in pregnancy is another advantage.

Currently, the main limitations of MRI lie in its lack of availability, expertise and associated high costs. From the perspective of emergency medicine, even when availability is not an issue, a major disadvantage is the time it takes to complete a scan. The patient is in an inaccessible, confined space, usually with limited monitoring for the duration of the 30- to 60-minute scan. MRI is therefore unsuitable for the unstable patient. If a patient is stable and intubated, specialized anaesthetic and monitoring equipment and expertise in using it is required to ensure patient safety.

Patients with metallic foreign bodies or electronic implants are often unable to have MRI, which can also limit its use.

Technical issues

Put very simply, the steps of an MRI involve putting the patient into a powerful magnet, sending in a radio wave and turning the radio wave off; the patient then emits a signal which is received and used for reconstruction of the image.

Components

The traditional MRI suite is centred around the MRI scanner, with its mobile patient table that moves the patient in and out of the MRI tunnel (Fig. 23.3.1). Current machines have a bore (internal diameter of the tunnel) of up to 70 cm and utilize short bore architecture that allows the tunnel to be approximately half the length of that required in the previous generation of MRI scanners. The machine houses a superconductor magnet, the strength of which is measured in Tesla. Most current machines operate at 1.5 or 3 Tesla. A 3-Tesla magnet creates a magnetic field around the patient 60,000 times the strength of the earth's magnetic field. In addition to the magnet, there are radiofrequency transmitter

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FIG. 23.3.1 Typical 3-Tesla short bore, 70-cm opening diameter magnetic resonance imaging machine.

and receiver coils that send and receive radio-frequency pulses. These briefly disturb the magnetic field and ultimately create the MRI image. Another three sets of gradient coils provide additional linear electromagnetic fields important for spatial information—determining the origin of the signal in the three-dimensional space. It is these coils banging against their anchoring devices that cause the loud noises associated with MRI.

The high magnetic field generated by MRI means metallic objects within range can become projectile missiles, and great care has to be taken to ensure metal objects are well secured or do not enter the room. The magnet can also interfere with electronic equipment, such as computers, monitors and medical equipment such as pacemakers, and these must be kept away. Finally, the receiver coils are highly sensitive and are designed to detect very minor fluctuations in returning radio waves (which are a form of electromagnetic radiation). External radio waves can interfere with the waves received by the coils, and this noise will create artefacts interfering with image production. To minimize this, the entire MRI room is secured inside a Faraday cage, whose external conducting surface blocks or markedly attenuates any outside potentially interfering radio waves. The MRI control room and computer terminals with operating console are located immediately adjacent to, but outside the MRI room, in a similar fashion to the CT control room.

Creating an image

MRI depends on the alignment of hydrogen nuclei or positively charged protons within organic compounds in the body. Hydrogen nuclei act like tiny bar magnets. Under the influence of the external MRI magnet, mobile hydrogen ions align and spin in the orientation of the MRI magnet's field, creating a magnet of the patient's body. In addition to aligning and spinning on their own axis, protons also rotate or 'precess', as would a spinning top with a slight wobble, around a central axis.

Pulses of electromagnetic energy, called radiofrequency or RF pulses, are then sent into the area being imaged. This briefly disturbs the orientation and precession of the aligned protons. A transient reduction in the longitudinal magnetic field results, and a new magnetic vector in the transverse direction, called transversal magnetization, is created. Once the RF pulse is stopped, the protons relax back to their initial aligned state and the longitudinal and transverse magnetic vectors return to their original state. The realignment rate depends on tissue characteristics and water content. As the magnetic vectors realign, electric currents are induced and the MRI signal and signal intensity created. The receiver coils receive these minute pulses of newly created electromagnetic radiation, and these are interpreted to create the ultimate image.

Different magnetic resonance imaging techniques

Numerous different MRI imaging sequences and techniques have been developed to create the optimal images for varying body tissues and pathology. The following is not an exhaustive list.

T₁ and T₂ imaging

These are the most common MRI images with which we are familiar.

T₁-weighted images (anatomical) create high-definition anatomical images with optimal tissue contrast resolution. In these images, fat is white and water is black. The resultant image gives detailed representation of the internal structure of soft tissue organs. T₁ is a time constant that refers to the time it takes for the changes in longitudinal magnetization induced by the RF pulse, to return toward the original state. Measuring this tends to define structural tissue proteins and fats optimally.

T₂-weighted images (pathological) highlight pathological processes where there is increased water content within tissues (Fig. 23.3.2). Most pathological processes involve an element of tissue oedema, and, whether it be trauma, infection, infarction or neoplasia, these images highlight water. Water is seen as white in these images. T₂ is a time constant that refers to the time it takes for the changes in transversal magnetization induced by the RF pulse, to return toward their initial state. Measuring this tends to highlight water optimally.

Other MRI techniques each aimed at highlighting other anatomical or pathological features are shown in Fig. 23.3.3. The *left* image (A) is a FLAIR (fluid-attenuated inversion recovery) sequence that nulls fluid and can highlight periventricular demyelination; the *central* image (B) is a T₂ gradient image which detects haemoglobin and its breakdown products; the *right-hand* image (C) is a diffusion apparent diffusion coefficient (ADC) image detecting cell injury in early stroke.

Angiography and gadolinium

MRA can be done with or without contrast media (Fig. 23.3.4 shows non-contrast MRI). Flow itself alters the MR signal simply by moving the protons that have been exposed to the RF pulse. This can leave what is called a flow void phenomenon, and, using this, the machine can create an angiographic image.

Where a contrast agent is used, the paramagnetic rare earth gadolinium (Gd) is the agent of choice. Its use creates excellent angiographic images. In addition, Gd does not cross the normal blood–brain barrier. However, if this is disrupted, as can occur in many pathological processes, Gd improves lesion detection and

diagnostic accuracy. Gd is not an iodinated contrast medium and is generally very well tolerated.

The sagittal images of the lumbar spine shown in Fig. 23.3.5 demonstrate a tumour involving the L1, causing some cord compression. The *left* image is T1, the *centre* T2 and the *right* a T1 fat-saturated post-Gd image where the tumour with its abnormal vasculature is most obvious.

Diffusion- and perfusion-weighted imaging

MRI imaging changes occur early after stroke and can be detected prior to any visible change on CT. Diffusion-weighted imaging assesses water

diffusion across cell membranes. There is no water movement across cell membranes when cells are damaged. Diffusion imaging is used to define areas of newly infarcted cerebral tissue. These changes can occur as early as 10 minutes after infarction. Perfusion imaging aims to detect the potentially salvageable cerebrovascular accident 'penumbra' surrounding the non-viable ischaemic core, with a view to decision-making regarding thrombolysis and revascularization.

Cardiac imaging

Cardiac imaging is done by using ECG gating and imaging the heart over several cardiac cycles.

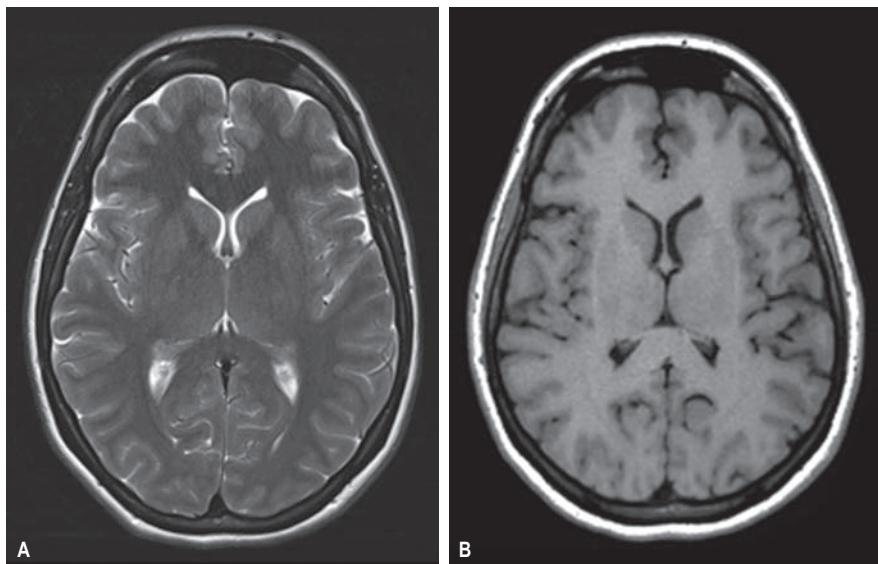


FIG. 23.3.2 (A) T2-weighted magnetic resonance image of the brain where water is bright and pathology involving oedema is best demonstrated. (B) T1-weighted magnetic resonance imaging where water is black and anatomic features are well demonstrated, maximizing soft tissue contrast.

Sequentially timed images taken from separate cardiac cycles are stitched together to create an animation representative of a single cardiac cycle. The result is a very high resolution, dynamic study of heart function and blood flow within the heart (Fig. 23.3.6).

Monitoring patients in the magnetic resonance imaging

The patient in the MRI suite is particularly vulnerable. His or her physical movement is restricted while in the MRI tunnel, he or she is inaccessible to immediate assistance and there are particular challenges with traditional patient monitoring in the MRI environment. This makes MRI unsuitable for the unstable patient and makes those requiring sedation or general anaesthesia a far greater challenge.

As a minimum requirement, visual camera and verbal monitoring are mandated for all MRI machines, ensuring some degree of immediate communication between radiographer and patient.

If any sedation is required, it is essential the patient have oxygen saturation monitoring. There are MRI-compatible units, with no ferromagnetic components, often fiberoptic, suited to this purpose and available in most units.

Patients who are under general anaesthetic require highly specialized anaesthetic staff and equipment. This form of remote anaesthesia requires unique training and practice. MRI-compatible and prepared equipment is required. This includes specially prepared ventilators and monitors. Attention to detail is required regarding all the equipment involved. Even inappropriate ECG dots and leads can heat and cause injury.

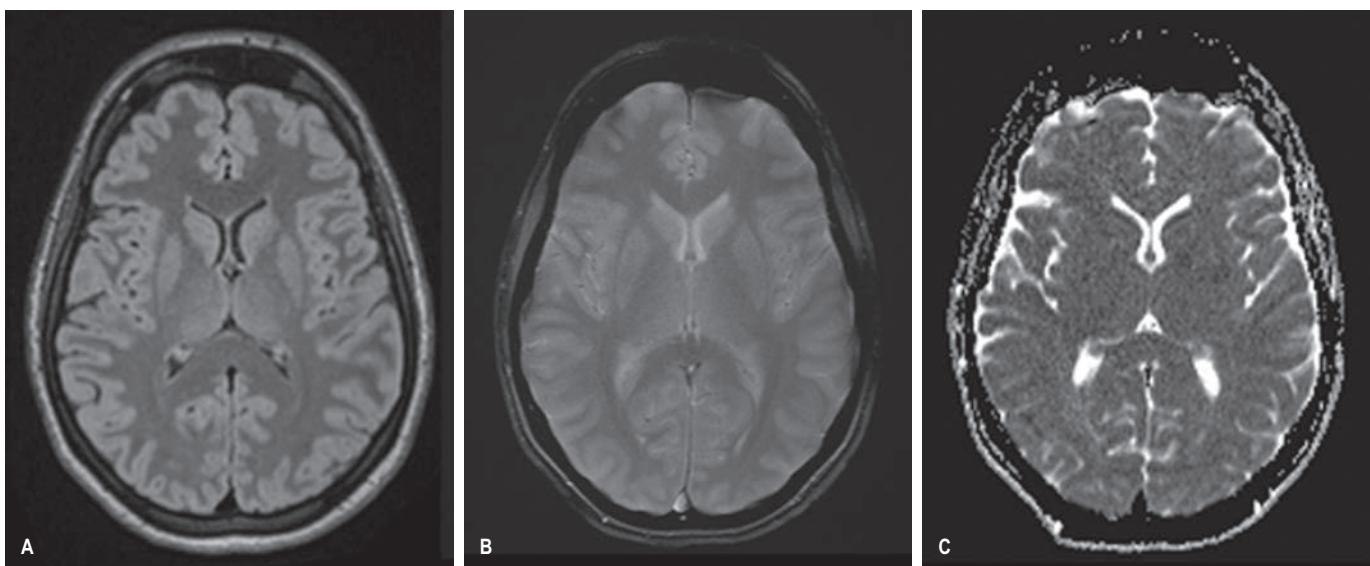


FIG. 23.3.3 Other Magnetic Resonance Imaging Techniques. *Left:* (A) FLAIR (fluid-attenuated inversion recovery) sequence; *centre:* (B) T2 gradient image; *right:* (C) diffusion ADC image.

23.3 MAGNETIC RESONANCE IMAGING IN EMERGENCY MEDICINE

Indications for magnetic resonance imaging

In most parts of the world, access to MRI, with its great cost and requirement for highly specialized radiography and radiology staff, is extremely limited. Australasia falls into the category where truly emergent MRI requests can usually be met by most tertiary hospitals. Arranging the scan in a public hospital generally requires consultant-to-consultant discussion and involvement of the inpatient specialty team.

Where there are reasonable imaging alternatives to MRI, diagnostic imaging guidelines have been designed to create effective alternative pathways.

Suspected acute spinal cord and cauda equina pathology

MRI is the investigation of choice when it comes to imaging the spinal cord, spinal nerves,

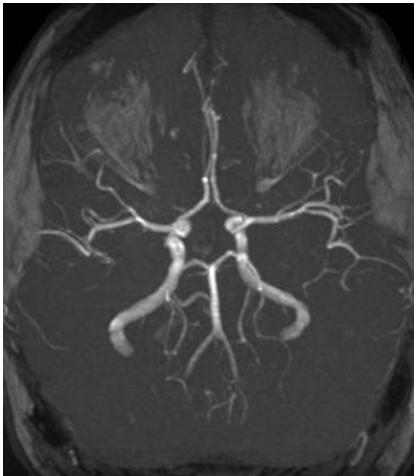


FIG. 23.3.4 Noncontrast magnetic resonance imaging demonstrating the circle of Willis.

intervertebral discs and ligaments of the spine. Where there are long tract signs and suspicion of an acute spinal cord-threatening lesion, most would proceed directly to MRI. In the setting of trauma, a CT to define bony injury is usually performed prior to MRI.

MRI clearly defines any pathological process affecting the cord, cerebrospinal fluid (CSF) space and surrounding soft tissues. In the emergency setting, trauma with cord injury (Fig. 23.3.7) or contusion may occur, and MRI gives additional information regarding spinal ligamentous injury. Other common cord-threatening pathology includes malignancy, which may originate in the vertebrae, most commonly the bodies, and extend into the spinal canal or may invade the canal through the spinal foramina. Malignant deposits, particularly metastases, may also originate within the spinal canal, involving the cord or dura. Infective processes, such as discitis and epidural abscess, are not infrequent causes of acute cord compression and are more common in IV drug users, the immunosuppressed and those who have had spinal procedures. Vascular phenomena, such as epidural haematoma, arteriovenous (AV) malformation with bleed, aneurysms and spinal cord infarction can all be defined by MRI. Degenerative conditions, such as disc prolapse (Fig. 23.3.8) and spinal canal stenosis from any cause, may also threaten the cord.

Rapidly defining the cause of the spinal cord lesion enables surgical planning or, if a malignant process, consideration and planning for radiotherapy.

Stroke

MRI is an excellent modality for defining any brain pathology, and stroke is no exception. In addition to confirming the presence of stroke and excluding the presence of haemorrhage, MRI can detail

the extent of brain injury, the vascular supply and any ischaemic penumbra and can assess for dissection or other predisposing vascular causes.

Unfortunately, even if immediately available, performing an MRI and then preparing and reporting the images often puts the patient outside the window of benefit for thrombolysis. CT is far more accessible and provides adequate information for the majority of cases, and this is currently the accepted 'gold standard'.

The exception is the posterior circulation and suspected brainstem infarction where MRI is superior to CT and generally required before interventional attempts at revascularization.

Headache

CT scan is usually the first choice for investigation of headache, but MRI may be considered among patients at high risk of the effects of ionizing radiation. MRI is performed where consideration for intervention for brain tumours, acoustic neuroomas and pituitary tumours is being made. Where patients are young or cannot have iodinated contrast and sinus venous thrombosis is being considered, MR venography would be performed over CT venography; however, in most people, CT is adequate to define sinus venous thrombosis and other sinister causes of headache.

Angiography

MRA and CTA are considered similar in their utility for imaging blood vessels. Dissection is well imaged with either modality, and factors that would swing one in favour of MRI include a young patient age (MRI avoids radiation) and allergy to CT contrast.

Occult fracture detection

In the Australasian setting, it is unusual to attain an MRI to assess for occult fracture. Hip and scaphoid fractures are the classic examples where early detection and intervention can benefit the patient. CT scan has lower sensitivity than MRI for detecting occult hip fractures, but it remains reasonable. Where concern remains, a bone scan will give the answer. Similarly, for scaphoid fractures, CT or bone scan or immobilization and delayed repeat plain films at 10 days are reasonable alternatives.

Soft tissue musculoskeletal injury

MRI is increasingly being used to assess for soft tissue injury when complex injuries are suspected. Requests generally come from the orthopaedic team involved in the patient's care. MRI can image injuries to muscles, tendons, ligaments, joint capsule and cartilaginous surfaces extremely well (Fig. 23.3.9). Acute shoulder and knee injuries are most commonly assessed with MRI, but complex elbow, wrist, foot and ankle injuries can also be assessed by MRI.

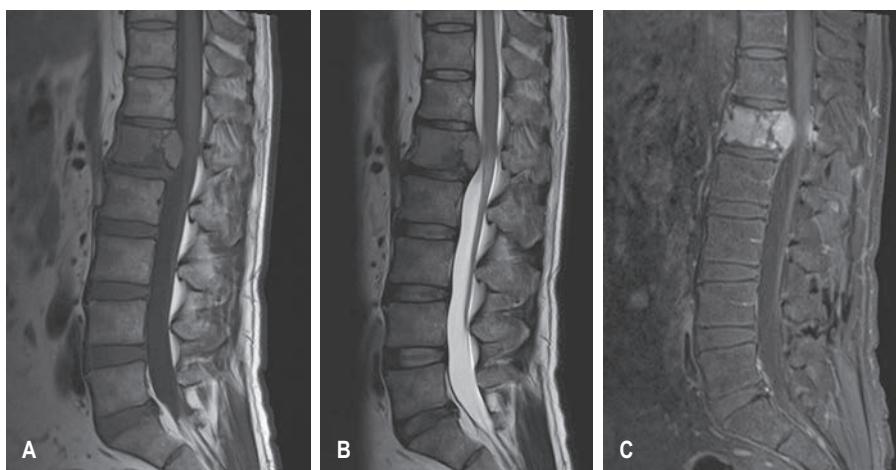


FIG. 23.3.5 Sagittal images of the lumbar spine showing tumour involving the L1, causing some cord compression. The left image (A) is T1, the centre (B) is T2 and the right (C) is a T1 fat-saturated post-gadolinium image where the tumour with its abnormal vasculature is most obvious.



FIG. 23.3.6 Magnetic resonance imaging four-chamber cardiac view.



FIG. 23.3.9 Coronal knee magnetic resonance imaging showing ACL and MCL ligamentous disruption.

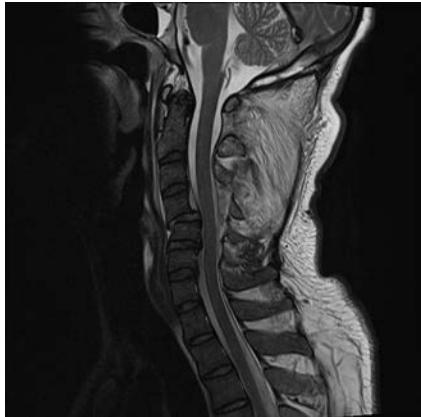


FIG 23.3.7 T2 sagittal image of an acute cervical spine injury with bifacet dislocation and marked anterior displacement of the body of C4 on C5, with some cord oedema. The anterior and posterior longitudinal ligaments are well demonstrated.



FIG. 23.3.8 T2 image shows L4/5 disc prolapse with marked narrowing of the spinal canal and cauda equina compression.

Where there is complex fracture/dislocation and the relationship of adjacent bones and bone fragments need defining, CT is more appropriate.

Magnetic resonance cholangiopancreatogram (MRCP)

MRCP can image the liver and biliary tree well. Ultrasound is generally the first imaging modality used to investigate for biliary pathology. Where concern remains and ultrasound imaging has not been definitive, MRCP can help. This is most common with distal biliary obstruction where ultrasound has not been able to image the extreme distal common bile duct. An effective alternative is endoscopic retrograde cholangiopancreatogram (ERCP) and endoscopic ultrasound. The

advantage of ERCP is that therapeutic interventions, such as stone retrieval or stenting, can be carried out at the same time.

Appendicitis in pregnancy

Ultrasound is the first indicated investigation. MRI may sometimes be used where there is diagnostic uncertainty.

Contraindications, precautions and limitations

There are numerous contraindications to MRI, and pre-MRI safety checklists can be found at

www.mrisafety.com. MRI technicians should be made aware of any implanted metallic, prosthetic, electronic or drug delivery device. The pre-MRI questionnaire also covers past medical history, particularly renal dysfunction and allergies.

Ferrous and metallic materials

The high magnetic field generated by MRI can move and heat metallic materials. While most joint and heart valve prostheses are now MRI compatible, older prostheses, implanted metallic medical devices, aneurysm clips and metallic shrapnel, especially intraocular metallic foreign bodies, are contraindications to MRI.

Metallic drug transdermal drug infusion patches often contain metal and can heat.

Some tattoos and permanent makeup contain iron oxide and can heat in the MRI environment, although this is rare.

Electronic implants

The intense magnetic field can affect electronic and magnetic equipment. Cardiac pacemakers, implantable cardioverter defibrillators, implanted nerve stimulators, cochlear implants and other electronic implants can be affected. Some are now MRI compatible; however, most are a contraindication to MRI. The website www.mrisafety.com has lists of thousands of implants and devices that have been tested in MRI machines and is recommended by RANZCR as a resource for obtaining information on patient's implanted devices.

Noise

The MRI is very loud, with constant banging heard. Ear protection is recommended.

23.3 MAGNETIC RESONANCE IMAGING IN EMERGENCY MEDICINE

Pregnancy

There has been no demonstrated adverse effect from MRI or Gd-based contrast media to the mother or embryo/foetus. However, the evidence in this setting is limited and, with regard to MRI exposure, the ALARA (as low as reasonably acceptable) principle is followed. MRI should be pursued only where potential benefits outweigh the risks. In general, it is considered prudent to avoid MRI in the first trimester.

Gadolinium

Gd can rarely cause nephrogenic systemic fibrosis (NSF). This disabling disease is more likely in patients with underlying renal disease. It is recommended that patients older than 60, those with hypertension or diabetes or a history of renal disease (including transplant or a single kidney), those within a month of a liver transplant or those with an acute deterioration in renal function have renal function tested prior to MRI. If their renal function is not normal, further discussion and consideration of the risk benefit ratio of Gd should be made in conjunction with the MRI radiologists.

Weight and size limits

Different MRI machines can tolerate different patient weight and size limits. Some tolerate patients up to 250 kg. Occasionally, it is the patient diameter or shape rather than absolute weight that limits entry to the MRI tunnel.

Claustrophobia

The MRI tunnel frequently causes claustrophobia. Non-pharmaceutical management may include patient education, allowing a patient companion to accompany the patient, continuous verbal contact, headphones with audio, use of prone and/or feet first positioning, use of a blindfold, fan, bright

lights, aromas or other relaxation techniques or watching videos or movies via mirrors.

Despite these measures, sedation is sometimes required and should be done only with oxygen and saturation monitoring and a single dedicated and trained person responsible to supervise and monitor the sedation.

Conclusion

The increasing availability of MRI within Australasia, together with improving imaging times and a diverse range of MRI techniques, mean MRI is becoming the imaging modality of choice for an increasing number of indications.

Currently, it is generally used in conjunction with other imaging modalities, particularly if they have been unsuccessful, in imaging soft tissue structures and pathology.

The required isolation of the patient for the duration of the scan and difficulty in monitoring and managing anaesthetized patients in the MRI mean it is not the place for unstable critically unwell patients.

CONTROVERSIES AND FUTURE DIRECTIONS

- Although currently most commonly limited to tertiary centres, as with other expensive technologies, magnetic resonance imaging (MRI) is likely to diffuse more widely through the hospital system.
- The indications for MRI from emergency departments are likely to expand as scanners become more widely available.
- Scanners which can accommodate the sitting patient are being developed, and these may enable wider access to MRI.

Acknowledgements

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SECTION 24

ENVIRONMENTAL EMERGENCIES

Edited by *Mark Little*

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24.1 Heat-related illness

Ian Rogers

ESSENTIALS

- 1** Exercise-associated collapse is the most common heat- and exercise-related illness. It is due to an impaired compensation for the drop in blood pressure that occurs when muscle pumping ceases and venous return drops at the cessation of exercise. It responds rapidly to supine posture followed by rest and oral fluids. No other medical interventions are usually required.
- 2** Heatstroke is a true medical emergency, where rapid cooling using tepid spraying, fanning and ice packs is essential to minimize morbidity and mortality.
- 3** Water immersion may cool patients more rapidly but is not always practical in the emergency department. Its major role may be in the pre-hospital setting where early intervention may be life-saving.
- 4** Patients with drug-related hyperthermia may die from the complications of the high temperature, not from direct drug toxicity. Early and aggressive treatment of hyperthermia using similar methods to that for heat stroke and before complications occur is vital.

with a brief loss of consciousness. The primary mechanism is a failure of prompt baroreceptor responses and not haemodynamically significant dehydration. Severe heat-related dehydration is rare.

The other, more serious, heat-related disorders are all associated with, or have the potential for, significant hyperthermia which if not treated promptly results in similar pathophysiology at a cellular and organ system level. A core body temperature around or greater than 41.5°C results in progressive denaturing of a number of vital cellular proteins, failure of vital energy-producing processes and loss of cell membrane function. At an organ system level these changes may manifest as rhabdomyolysis, acute pulmonary oedema, disseminated intravascular coagulation, cardiovascular dysfunction, electrolyte disturbance, renal failure, liver failure and permanent neurological damage.^{2,3} Any or all of these complications must be expected in severe heat illness.

The hallmark of heatstroke is failure of the hypothalamic thermostat, leading to hyperthermia and the associated additional pathophysiological features described above. Clinically, heatstroke can be divided into 'exertional heatstroke' due to exercise in a thermally stressful environment, and 'classic heatstroke', which occurs in patients with impaired thermostatic mechanisms. Common risk factors for heatstroke are listed in **Box 24.1.1**.

Certain drugs produce hyperthermia by mechanisms in addition to interference with thermostatic function. These mechanisms and the appropriate treatment are described in detail elsewhere.

Introduction

Heat-related disorders have a broad range of potential aetiologies and manifestations. In some the primary disorder is a failure of thermal homoeostasis, whereas in others the hyperthermia is secondary to other processes. The major heat-related illnesses to consider are exercise-associated collapse (EAC), heatstroke, and the drug-related heat illnesses neuroleptic malignant syndrome, serotonin toxicity and malignant hyperthermia. Whilst still in common use¹ the term 'heat exhaustion' should be discouraged

as it has no defining pathophysiology or clinical syndrome, and has become a catch-all term for any illness in the context of a thermally stressful environment.

Epidemiology and pathophysiology

EAC is the most common heat-related illnesses presenting either to medical tents at sporting events or to emergency departments (EDs). EAC manifests at the end of a race when muscle pump enhanced venous return ceases and cardiac output drops. This leads to collapse, often

24.1 HEAT-RELATED ILLNESS

Box 24.1.1 Heatstroke risk factors

Behavioural

Army recruits
Athletes
Exertion
Inappropriate clothing
Elderly
Inappropriate exposure to high heat/humidity
Babies left in cars
Manual workers
Pilgrims

Drugs

Anticholinergics
Diuretics
Phenothiazines
Salicylates
Stimulants/hallucinogens

Illness

Delirium tremens
Dystonias
Infections
Seizures

Prevention

Prevention of exertional heatstroke should focus on the education of at-risk groups. Dehydration is not as important aetiologically in heatstroke as once thought. Exertional heatstroke is most often reported in shorter, high intensity exercise where marked dehydration is unlikely. So although adequate fluid intake is needed for prolonged exercise it is not a key factor in heatstroke prevention. As high ambient temperatures and high humidity predispose to exertional heatstroke, exertion in these environments should be limited. Sporting organizations and workplaces are encouraged to minimize risk by using tools that take such factors into account. These tools include the wet bulb globe temperature measurement and formal heat stress scoring systems.

Clinical features

Exercise-associated collapse

The clinical presentation of EAC will be familiar to all emergency practitioners as it mirrors that of poor cerebral perfusion from any other cause. Patients complain of nausea, vomiting, malaise and dizziness. There may be a history of collapse, and there is likely to be a tachycardia and (orthostatic) hypotension. The orthostatic hypotension typically manifests at the end of physical exertion by collapse, often with brief loss of consciousness. In this syndrome, and in distinction to heatstroke, the core temperature will be less than 40°C and neurological function will rapidly return to normal once the patient is supine.

Heatstroke

The classic clinical features of heatstroke are neurological dysfunction, core temperature above 41.5°C and hot, dry skin. However, relying on this classic triad to make the diagnosis will result in a number of cases being missed. Loss of consciousness is a constant feature of heatstroke³ but by the time of ED presentation conscious state may be improving, although some neurological abnormality will persist. Temperature readings may be misleadingly low, due either to effective prehospital care or to measurements at inappropriate sites, such as the oral cavity or axilla. Profuse sweating is a much more common feature than previously thought.³ Other clinical features may include tachycardia, hyperventilation, seizures, vomiting and hypotension.

Clinical investigation

Diagnosis of the hyperthermic disorders is based on the history, clinical picture and exclusion of alternative diagnoses. Investigations are thus directed towards excluding other possible causes of temperature elevation (e.g. infection, metabolic disorders) and evaluation of the specific complications of hyperthermia.

Patients with a presumed clinical diagnosis of EAC should still have serum electrolytes and creatine kinase measured to exclude exercise associated hyponatraemia and rhabdomyolysis respectively. Should mental state not rapidly normalize with supine posture then an urgent finger prick or serum glucose estimation is needed. Collapsed athletes should also have an ECG to identify unrecognized cardiac abnormalities.

All other heat disorders warrant a far more extensive laboratory and radiological work-up, as multiorgan system dysfunction is the rule.^{2,4} Tests must include an ECG, serum electrolytes, disseminated intravascular coagulation (DIC) screen, liver function tests, muscle enzyme assays, renal function and urinalysis, serum glucose and a chest x-ray.

Treatment

Exercise-associated collapse

EAC responds rapidly to supine posture (ideally with the legs elevated), rest and oral fluids. Intravenous normal saline is rarely required as few athletes will be profoundly dehydrated. The use of 'routine' intravenous (IV) normal saline in collapsed athletes should be actively discouraged as it will worsen exercise associated hyponatraemia where there is usually already fluid overload with persistent and inappropriate antidiuretic hormone levels.

Heatstroke

This is a true medical emergency. Early recognition and aggressive therapy in the field and in hospital can prevent substantial morbidity and mortality. The key management is aggressive cooling. Cooling rates of at least 0.1°C/min should be achievable. Several cooling methods have been proposed, including evaporative cooling, iced water immersion, ice slush, cool water immersion, iced peritoneal lavage and pharmacological methods.^{1,5} A combination of methods is most widely used in EDs. All of the patient's clothing should be removed and the patient sprayed with a fine mist of tepid water while gentle fanning is commenced (a ceiling fan is ideal). At the same time, areas with vascular beds close to the surface (neck, axillae and groins) should be packed with ice bags. This technique facilitates patient access and monitoring when compared to methods such as ice-bath immersion even though an iced bath may offer more rapid cooling. In the field ice-bath immersion may be preferred, but in the ED covering the patient with regularly replaced towels that have been soaked in iced water may offer a compromise between the efficacy of immersion cooling and the need for monitoring and accessibility. Intravascular cooling devices, while able to rapidly cool, are cumbersome to set up and not widely available. As such in heat stroke, where time is of the essence, their use is not encouraged. Although ice cold IV fluids can also aid in rapid cooling, fluid requirements in heatstroke can be difficult to estimate and balance.

In hospital, shivering, seizures and muscle activity may need to be controlled with pharmacological agents such as chlorpromazine, benzodiazepines and paralyzing agents. Aspirin and paracetamol are ineffective and should be avoided. Intravenous fluids need to be used cautiously and may need titrating to central venous pressures. Maintain adequate oxygenation but avoid hyperoxia. Ventilatory support may be required. Urine flow needs to be maintained with initial volume loading, and later with mannitol or furosemide, to prevent secondary renal injury, especially from rhabdomyolysis. Electrolyte, acid–base and clotting disturbances should be closely monitored and treated by standard measures. Heat stroke due to drug-related causes is treated using the same cooling methods as described above; however specific drug therapies may be indicated and are described elsewhere.

Prognosis and disposition

In heatstroke both the maximum core temperature and the duration of temperature elevation are predictors of outcome. Prolonged coma and oliguric renal failure are poor prognostic signs.²

Mortality is still of the order of 10%, but most survivors will not suffer long-term sequelae.^{2,3} Any patient with suspected heatstroke should routinely be referred to the intensive care unit for ongoing care. Most cases of EAC will be suitable for short-stay ED treatment or indeed simply for treatment on-site in an event medical tent.

CONTROVERSIES

- 1** Although debate is likely to continue about the most effective cooling therapy in heatstroke, this is largely of academic interest as all methods seem to achieve the desired outcome of rapid temperature drop. Of more interest will be research that focuses on the cellular mechanisms of the damage seen with hyperthermia. Such research may lead to the development of pharmacological agents that can prevent or treat heatstroke.
- 2** Whilst the term 'heat exhaustion' is still frequently used, its use should be actively discouraged as it has no defining pathophysiology or distinct clinical syndrome.
- 3** The long-standing dogma that vigorous hydration prevents heat illness is now challenged. A greater concern now is to highlight the risks of promotion of aggressive hydration strategies in sport.

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24.2 Hypothermia

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ESSENTIALS

- 1** Hypothermia is categorized into mild (32°C to 35°C), moderate (29°C to 32°C) and severe ($<29^{\circ}\text{C}$) on the basis of a rectal or other core temperature reading.
- 2** Moderate-to-severe hypothermia produces progressive delirium and coma, hypotension, bradycardia and failure of thermogenesis.
- 3** The electrocardiograph will often show slow atrial fibrillation and an extra positive deflection in the QRS (the J or Osborn wave) in leads II and V_3 to V_6 with worsening hypothermia.
- 4** Endotracheal intubation is safe in hypothermia. Ventilation and acid–base status should be manipulated to maintain uncorrected blood gases within the normal range.
- 5** Endogenous rewarming, consisting of drying the patients and placing them in a warm, dry and wind-free environment, should form part of all rewarming protocols.
- 6** In most cases of moderate-to-severe hypothermia rewarming can be achieved with endogenous rewarming plus forced-air rewarming blankets without the need to resort to more aggressive techniques.
- 7** In the arrested hypothermic patient rewarming should be with cardiopulmonary bypass or warm left pleural lavage.

moderate and severe are often grouped together as they typically share the clinical features of absence of shivering and altered mental state. These categorization systems can be used both out of and in hospital as a guide to selecting rewarming therapies and prognosis. Mild hypothermia is considered the stage where thermogenesis is still possible; moderate is characterized by a progressive failure of thermogenesis; and severe by adoption of the temperature of the surrounding environment (poikilothermia) and an increasing risk of malignant cardiac arrhythmia. Nevertheless, there are substantial differences between individuals in their response to hypothermia.

Epidemiology and pathophysiology

Hypothermia may occur in any setting or season.¹ True environmental hypothermia occurring in a healthy patient in an adverse physical environment is less common in clinical practice than that secondary to an underlying disorder. Common precipitants include injury, infection, systemic illness, drug overdose and immersion, and are outlined in more detail in Table 24.2.1. The elderly are at greater risk of hypothermia because of reduced metabolic heat production and impaired responses to a cold environment. Alcohol is a common aetiological factor and probably acts by a number of mechanisms, including cutaneous vasodilatation, altered behavioural responses, impaired shivering and hypothalamic dysfunction.

Introduction

Hypothermia is defined as a core temperature of less than 35°C . This can be measured at a number of sites (including oesophageal, right heart, tympanic and bladder). Rectal remains the routine in most emergency departments (EDs),

despite concerns at how rapidly it equilibrates to and reflects true core temperature. Conventionally, hypothermia is divided into three groups: mild (32°C to 35°C), moderate (29°C to 32°C) and severe ($<29^{\circ}\text{C}$) on the basis of measured core temperature. In a field setting, where core temperature measurements may not be possible,

24.2 HYPOTHERMIA

Table 24.2.1 Hypothermia aetiologies

Environmental	Cold, wet, windy ambient conditions Cold water immersion Exhaustion
Trauma	Multitrauma (entrapment, resuscitation, head injury) Minor trauma and immobility (e.g. # fractured neck of femur (NOF), # fractured neck of humerus (NOH)) Major burns
Drugs	Ethanol Sedatives (e.g. benzodiazepines) in overdose Phenothiazines (impaired shivering)
Neurological	Cerebrovascular accident (CVA) Paraplegia Parkinson's disease
Endocrine	Hypoglycaemia Hypothyroidism Hypoadrenalinism
Systemic illness	Sepsis Malnutrition

Clinical features

The clinical manifestations of hypothermia depend on both the degree of core temperature drop as well as the features of the underlying aetiology. Individual variation in presentation is common.

Mild hypothermia manifests clinically as shivering, apathy, ataxia, dysarthria and tachycardia. Moderate hypothermia is typically marked by a loss of shivering, altered mental state, muscular rigidity, bradycardia and hypotension. In severe hypothermia signs of life may become almost undetectable, with coma, fixed and dilated pupils, areflexia and profound bradycardia and hypotension. The typical cardiac rhythm of severe hypothermia is slow atrial fibrillation. This may degenerate spontaneously, or with rough handling, into ventricular fibrillation or asystole. In the field, moderate and severe hypothermia are often grouped together, with the key clinical feature of absent shivering suggesting the loss of the ability to rewarm without medical intervention.

Many complications may also manifest as part of a hypothermia presentation, although at times it may be difficult to separate cause from effect. These include cardiac arrhythmias, thromboembolism, rhabdomyolysis, renal failure, disseminated intravascular coagulation and pancreatitis.

Clinical investigation

Mild hypothermia with shivering and without apparent underlying illness needs no investigation in the ED.

Moderate or severe hypothermia mandates a comprehensive workup to seek common precipitants and complications that may not be clinically apparent.

Biochemical and haematological abnormalities are frequently associated with hypothermia,¹ although there is no consistent pattern. Blood tests indicated include sodium, potassium, glucose, renal function, calcium, phosphate, magnesium, lipase, creatine kinase, ethanol, full blood count and clotting profile. Blood gases if taken should be accepted at face value, rather than adjusting for the patient's temperature.

Impaired ciliary function, stasis of respiratory secretions or aspiration may be expected in moderate-to-severe hypothermia, so chest radiography should be routine. Other radiology may be indicated if a trauma-related aetiology is suspected.

A 12-lead electrocardiograph (ECG) and continuous ECG monitoring should be routine in moderate-to-severe hypothermia. The typical appearance is slow atrial fibrillation, with J or Osborn waves most prominent in leads II and V₃ to V₆ (Fig. 24.2.1). The J wave is the extra positive deflection after the normal S wave. These changes become more common and prominent with increasing severity of hypothermia, typically occurring below 32°C.²

Treatment

General

The general and supportive management of hypothermia victims largely follows that of other critically ill patients. However, some syndrome-specific issues demand careful attention.

Muscle glycogen is the substrate preferentially used by the body to generate heat by shivering. All hypothermics, therefore, need glucose. In mild cases this can be given orally as sweetened drinks or easily palatable food. With more severe

hypothermia gastric stasis and ileus are common, and glucose should be given intravenously: 5% dextrose can be infused at 200 mL/h. Additional volume resuscitation should be gentle, bearing in mind the contracted intravascular space in severe hypothermia, and that hypotension that would be classified as severe at a core temperature of 37°C is a normal physiological state at 27°C. All intravenous fluids should be warmed to minimize ongoing cooling. Endotracheal intubation by a skilled operator is safe in severe hypothermia. Intubation is indicated as in any other clinical condition to provide airway protection or to assist in ventilation.

Ventilatory support and, where necessary, manipulation of acid–base status, should be titrated to maintain uncorrected blood gas pH and partial pressure of CO₂ (PCO₂) within the normal range.

The slow atrial fibrillation so common in more severe hypothermia is a benign rhythm and requires no chemical or electrical correction. It will revert spontaneously with rewarming. Pulseless ventricular tachycardia and ventricular fibrillation should largely be managed along conventional lines. However, if initial direct current (DC) shocks are unsuccessful, then others are unlikely to be so until the patient is warmer. Repeat countershocks are generally reapplied with every 1°C increase in core temperature. Magnesium may be the antiarrhythmic drug of choice in hypothermia.

The pharmacokinetics and dynamics of most drugs are substantially altered at low body core temperatures. Indeed, for many of the common drugs used in an ED they are unknown. Insulin is known to be inactive at <30°C. Hyperglycaemia, due in part to loss of insulin activity, is common in hypothermia, but should probably be managed expectantly until sufficient rewarming has occurred to ensure full endogenous insulin activity.

Rewarming therapies

Strategies for rewarming in hypothermia have only a limited evidence base on which to base recommendations and little has changed in recent decades, despite some enthusiasm for more complex devices such as endovascular temperature control catheters.³ Although more invasive and rapid techniques are advocated for more severe hypothermia, there is little evidence to support this advice. The traditional concern of afterdrop (a paradoxical initial drop in core temperature with rewarming) is probably of little or no relevance in a clinical setting.⁴

Rewarming therapies are broadly divided into three groups: endogenous rewarming, which is allowing the body to rewarm by its own endogenous heat production; external

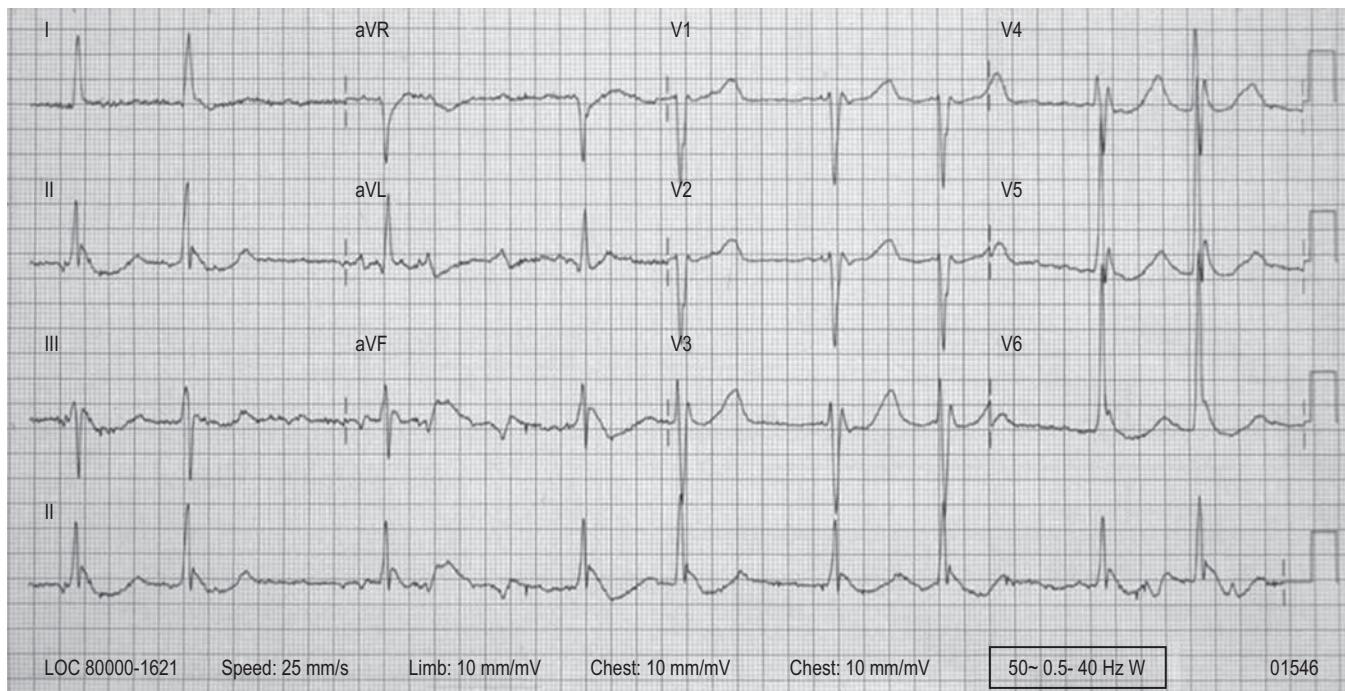


FIG. 24.2.1 ECG in hypothermia: slow atrial fibrillation, shivering artefact and J waves in leads II, V₃ to V₆ in a patient with a core temperature of 29.1°C.

Table 24.2.2 Rewarming therapy classification

Endogenous rewarming	Warm, dry, wind-free environment Warmed intravenous fluids (to prevent cooling)
External exogenous rewarming	Hot bath immersion Forced-air blankets Heat packs Body-to-body contact
Core exogenous rewarming	Warmed, humidified inhalation Left pleural cavity lavage Extracorporeal circulation

exogenous rewarming, which is supplying heat to the outside of the body; and core exogenous rewarming, which is applying the heat centrally. The classification of the commonly utilized rewarming therapies is outlined in *Table 24.2.2*.

Endogenous rewarming is a mandatory component of any emergency rewarming protocol. It consists of drying the patient, covering them with blankets, placing them in a warm and wind-free environment, and warming any intravenous or oral fluids that are administered. Endogenous rewarming alone can be expected to reheat at a rate of about 0.75°C/h. For most patients above 32°C (the level at which shivering thermogenesis is typically preserved), endogenous rewarming is the only therapy required. The exception is the exhausted patient in whom shivering has ceased at a core temperature higher than expected. Although more sophisticated techniques, such

as bath immersion, will more rapidly reheat a mildly hypothermic patient, there is no evidence that an increased rewarming rate improves prognosis in this group.

In moderate hypothermia, endogenous heat production is likely to progressively fail and more aggressive exogenous rewarming therapies are indicated. Hot-bath immersion has the theoretical disadvantage of causing peripheral vasodilatation, with shunting of cool blood to the core and further cooling. This might be expected to increase core afterdrop and produce circulatory collapse. In fact, rewarming rates of at least 2.5°C/h with minimal afterdrop have been achieved using baths at 43°C.⁴ Nevertheless, substantial practical difficulties are obvious with monitoring a more seriously ill patient immersed in a bath. This method of rewarming can only be recommended for otherwise healthy patients who

are expected to make a rapid recovery from accidental environmental hypothermia (e.g. immersion in very cold water).

The therapy that has been best studied and most widely used in moderate hypothermia is forced-air rewarming.⁵ Forced-air rewarming is achieved by covering the patient with a blanket filled with air at 43°C. These devices direct a continuous current of air over the patient's skin through a series of slits in the patient surface of the blanket. This method produces minimal, if any, afterdrop, is apparently without complication, and should produce rewarming at about 2.0°C/h. Warm humidified inhalation may be added to this, and its value is largely by preventing ongoing respiratory heat loss.⁶ Body-to-body contact and chemical heat packs are often recommended as field treatments for all degrees of hypothermia. In mild hypothermia, whilst they provide comfort it seems that the benefit of any heat they deliver is negated by an inhibition of shivering thermogenesis. In more severe cases, where shivering is absent, it may be that even the small amount of exogenous heat they deliver is beneficial.

In severe hypothermia more aggressive exogenous rewarming therapies may be indicated in order to rapidly achieve core temperature above 30°C, the threshold below which malignant cardiac arrhythmias may occur spontaneously. Bladder, gastric or peritoneal lavage with warm fluids are all relatively ineffective methods of heat transfer,

24.2 HYPOTHERMIA

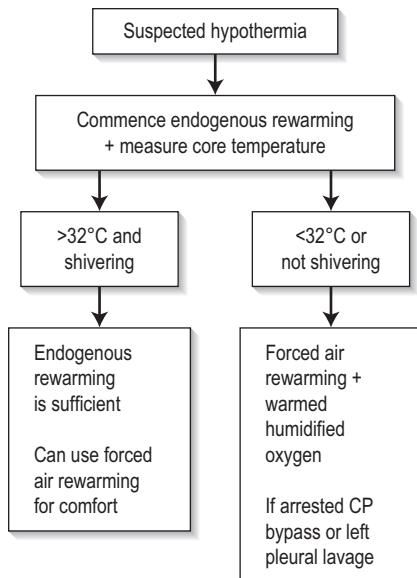


FIG. 24.2.2 A recommended rewarming algorithm in hypothermia. CP, cardiopulmonary.

and as such are not recommended for use in emergency situations. When available, full cardiopulmonary bypass achieves rewarming rates of about $7.5^{\circ}\text{C}/\text{h}$ without core afterdrop. Pleural lavage using large volumes of fluid warmed to 40°C to 45°C through an intercostal catheter may be nearly as effective.⁷ Both techniques have the advantage of delivering heat to the heart which acts as a heat pump to distribute rewarming to key core organs,

but are clearly invasive and carry associated risks. These risks are certainly acceptable in a hypothermic arrest, but in the non-arrested patient a slower rate of rewarming using forced-air and warm humidified inhalation may be more appropriate.

A suggested rewarming algorithm is shown in Fig. 24.2.2.

Prognosis and disposition

Attempts at developing a valid outcome prediction model for hypothermia are likely to be frustrated by its multifactorial aetiology. Recovery with appropriate treatment is likely from accidental environmental hypothermia when there is no associated trauma. To date, the coldest patient to survive accidental hypothermia neurologically intact had an initial measured temperature of 13.7°C .⁸ Although increasing severity of hypothermia does worsen prognosis, the major determinant of outcome is the precipitating illness or injury. Reported mortality rates vary from 0% to 85%.

Mild hypothermics without associated illness or injury can be safely managed at home in the care of a responsible adult. Moderate hypothermia may be treatable in a short-stay observation ward, but often requires a longer inpatient stay to manage underlying illness or injury. Severe hypothermics are at risk of multiorgan system complications and should be considered for admission to an intensive care unit.

CONTROVERSIES

- The question of which rewarming therapy to use will only be answered when the focus moves to randomized clinical trials measuring clinically relevant outcomes, such as morbidity and mortality, rather than surrogate markers such as rewarming rate and core afterdrop.
- The role of more technologically advanced rewarming techniques is not yet clear, and as yet no advantage has been shown over longstanding and low technology approaches.

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24.3 Dysbarism

David R. Smart

ESSENTIALS

- 1** Dysbarism is the term given to medical complications of exposure to gases at higher than normal atmospheric pressure. It includes barotrauma and decompression illness.
- 2** An understanding of the pathophysiology of dysbarism requires an understanding of the gas laws.
- 3** Barotrauma occurs as a consequence of excessive expansion or contraction of gas within enclosed body cavities. It principally affects the middle ear, the sinuses and the lungs. Lung barotrauma may result in gas embolism, pneumomediastinum or pneumothorax. Inner-ear barotrauma is rare but serious and may mimic vestibular decompression illness.
- 4** Decompression illness occurs when gas bubbles develop within the body. This may occur as a complication of pulmonary barotrauma or when a diver whose tissues are supersaturated with nitrogen (or other breathing gas such as helium), ascends too rapidly.
- 5** The clinical manifestations of decompression illness may affect many body systems and are extremely variable in nature and severity. Loss of consciousness or neurological symptoms and signs (including cognitive dysfunction) indicate serious decompression illness.
- 6** If a diver becomes unwell during or after diving, then diving is the likely cause of the illness, until proven otherwise. Early consultation with a diving medicine specialist is mandatory, especially where retrieval to a recompression facility may be necessary.
- 7** The seriously injured diver should be managed lying flat and urgently referred for recompression treatment. The diver should not exceed 300 m altitude during retrieval for recompression treatment.
- 8** Nondiving causes of dysbarism include caisson work, altitude decompression, recreational use of compressed gases (nitrous oxide and helium) causing pulmonary barotrauma and gas embolism and medical adverse events where gas enters the circulation. These cases are likely to benefit from early recompression with hyperbaric oxygen.

Box 24.3.1 Atmospheric pressure at sea level in various units

1 Atmosphere absolute (ATA)
101.3 kPa (SI units)
1.013 Bar
10 m of sea water (MSW)
760 mm of mercury (mm Hg)
14.7 pounds per square inch (PSI)

Table 24.3.1 Depth vs pressure and gas volume (Boyle's law)

Depth (m)	Absolute pressure (ATA)	Gas volume (%)
0	1	100
10	2	50
20	3	33
30	4	25
40	5	20

The proportionate change in volume is greatest near the surface (Table 24.3.1).

Dalton's law states that the total pressure (P_t) exerted by a mixture of gases is equal to the sum of the pressures of the constituent gases (P_x , P_y , P_z):

$$P_t = P_x + P_y + P_z$$

Therefore as divers breathe air at increasing atmospheric pressure, the partial pressures of nitrogen and oxygen increase:

$$\begin{aligned} \text{Surface} &= 1 \text{ ATA} \\ &= 0.8 \text{ ATA N}_2 + 0.2 \text{ ATA O}_2 \\ 10 \text{ m} &= 2 \text{ ATA} \\ &= 1.6 \text{ ATA N}_2 + 0.4 \text{ ATA O}_2 \\ 40 \text{ m} &= 5 \text{ ATA} \\ &= 4.0 \text{ ATA N}_2 + 1.0 \text{ ATA O}_2 \end{aligned}$$

A diver breathing air at 40 m is inhaling a gas with a partial pressure of oxygen equivalent to breathing 100% oxygen at the surface. At partial pressures above 3 ATA, the PN_2 affects coordination and judgement ('nitrogen narcosis'). Oxygen may also become toxic at partial pressures greater than 1 ATA. Recreational scuba diving generally has a limit of 40 m because of these effects.

Introduction

This chapter focuses on medical problems that develop secondary to breathing gases at higher than normal atmospheric pressure (dysbarism). This usually occurs in the context of scuba (self-contained underwater breathing apparatus) diving, a popular recreational activity in Australasia. Diving is generally very safe and serious decompression incidents occur approximately 1:10,000 dives. However, because of a high participation rate, between 200 and 300 cases of decompression illness are treated in Australia each year.¹ It is estimated that 10 times that number of divers experience less serious health problems after diving. Emergency physicians are often the first medical staff to assess the diver after a diving accident and it is essential they understand the risks and potential injuries.

Diving physics and physiology

An understanding of pressure and some gas laws is essential to understand the pathophysiology of diving injuries. The air pressure at sea level is 1 atmosphere absolute (ATA). Multiple units are used to measure pressure (Box 24.3.1). For every 10 m a diver descends in seawater, the pressure increases by 1 ATA. This pressure change impacts on gas spaces within the body according to Boyle's law.

Boyle's law states that, at a constant temperature, the volume of a gas varies inversely to the pressure acting on it:

$$PV = k$$

where P = pressure, V = volume and k = constant.

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Henry's law states that at a constant temperature the amount of a gas that will dissolve in a liquid is proportional to the partial pressure of the gas in contact with the liquid:

$$Q = kP_{\text{gas}}$$

where Q = volume of gas dissolved in a liquid, k = constant and P_{gas} = partial pressure of the gas.

Henry's law is relevant in diving illness because it is the basis of decompression illness (DCI). As the ambient pressure increases, the diver is exposed to increasing partial pressures of nitrogen (or other gas such as helium), which dissolves in bodily fluids. The amount of nitrogen absorbed depends on both the depth (which determines the partial pressure of nitrogen) and the duration of the dive. Tissues also take up nitrogen at different rates depending on their blood supply and permeability. Eventually, the tissues become saturated with nitrogen and no further absorption occurs. As the diver ascends and ambient pressure decreases, the partial pressure of nitrogen in some tissues will exceed ambient pressure, resulting in tissue supersaturation. If the diver ascends slowly enough, nitrogen diffuses out of the tissues and is transported, safely dissolved in the blood, to the lungs for elimination. This is known as 'off-gassing'.

If the diver ascends too rapidly, sufficient nitrogen bubbles will form in their body to cause decompression illness. Oxygen does not cause problems because it is rapidly metabolized by the tissues.

Barotrauma

Barotrauma occurs when changes in ambient pressure lead to expansion or contraction of gas within enclosed body cavities. The change in gas volume distorts or tears adjacent tissue. Injury by this mechanism may occur to the middle ear, inner ear, sinuses, lungs, eyes (via the diver's mask) and rarely, the gut. Different injury patterns occur in breath-hold divers (snorkellers) compared to those breathing compressed air. Both breath-hold and scuba divers may experience injury of the middle and inner ear, sinuses and eyes if they do not equalize pressures in the gas spaces as they descend. Breath-hold divers are unlikely to injure their lungs as their lung volumes reduce as they descend and return to their original volume as they ascend to the surface by the increasing ambient pressure.

Middle-ear barotrauma

Pathophysiology

Middle-ear barotrauma (MEBT), the most common medical disorder of diving, usually occurs during descent. Increased ambient pressure results in a reduction of middle-ear volume. If

equalization of the volume via the eustachian tube is inadequate, a series of pathological changes results. The tympanic membrane (TM) is deformed inwards, causing inflammation and haemorrhage. Middle-ear mucosal oedema is followed by vascular engorgement, effusion, haemorrhage and, rarely, TM rupture.

Clinical features

Symptoms of middle-ear barotraumas include ear pain, tinnitus and conductive hearing loss. Mild vertigo may also be experienced. More severe vertigo and pain occur if water passes through a perforated TM. Severe vertigo and significant sensorineural hearing loss should alert the emergency physician to possible inner-ear barotrauma (IEBT) (see below). MEBT severity is graded by visual inspection of the TM (Table 24.3.2). An audiogram is useful to document any hearing loss.

Treatment

Treatment of MEBT consists of analgesia, decongestants and ear, nose and throat (ENT) referral if there is TM perforation or suspected IEBT. Antibiotics are indicated for TM rupture because of potential contamination with water. The patient should not dive again until symptoms and signs have resolved, any TM perforation has healed, and the eustachian tube is patent.

Inner-ear barotrauma

Pathophysiology

Sudden pressure changes between the middle and inner ears can cause rupture of the round or oval windows or a tear of Reissner's membrane. This usually occurs during rapid descent without equalizing or forceful Valsalva manoeuvres.

Clinical features

Symptoms include sudden onset of tinnitus, vertigo, nausea and vomiting, vestibular symptoms and profound sensorineural hearing loss, which may not be apparent until the diver has left the water.² Onset of symptoms after the dive while

Table 24.3.2 Grading of severity of middle-ear barotrauma

Grade 0	Symptoms without signs
Grade 1	Injection of TM along handle of malleus
Grade 2	Slight haemorrhage within the TM
Grade 3	Gross haemorrhage within the TM
Grade 4	Free blood in middle ear
Grade 5	Perforation of TM

TM, Tympanic membrane.

performing an activity that increases intracranial pressure (e.g. heavy lifting) suggests IEBT. Coexistent middle-ear barotrauma is absent in about one-third of cases.

The main differential diagnosis is DCI involving the inner ear or vestibular apparatus. Frequently it is difficult to distinguish between IEBT and vestibular DCI, although the latter is frequently accompanied by other symptoms or signs of DCI. Because of this overlap in clinical syndromes, early specialist advice should be sought.

Treatment

Treatment of IEBT consists of avoidance of activities that increase intracranial pressure and urgent (same day) ENT referral for more detailed assessment and audiology. Surgical repair may be undertaken when vertiginous symptoms are severe. Vomiting should be treated with antiemetics and the diver kept supine with their head on a pillow. If DCI is excluded, then a 45° semirecumbent position is preferred. If DCI cannot be excluded the diver should have a trial of recompression. In one series, exposure to pressure did not worsen IEBT. The benefit of steroids in IEBT has not been confirmed.²

It was thought that further diving was contraindicated after IEBT, but recent case data suggest that diving might be possible following full recovery of hearing.

External ear barotrauma

Ear-canal barotrauma is very rare and only occurs if there is a complete obstruction of the canal (usually by wax or ear plugs), creating a noncommunicating gas cavity between the obstruction and the TM. Treatment is symptomatic. ENT specialist referral may be necessary if the TM cannot be visualized.

Sinus barotrauma

Pathophysiology

Mucosal swelling and haemorrhage occur if the communication of the sinuses with the nasopharynx is blocked and equalization of sinus pressure is not possible during descent. The frontal sinuses are most commonly involved.

Clinical features

Sinus pain usually develops during descent. Maxillary sinus involvement can refer pain to the upper teeth or cheek. There may be resolution of the pain at depth, due to mucosal oedema and blood filling the volume deficit left by gas compression. Pain and epistaxis may occur as the diver ascends. The pain usually persists after diving. Tenderness will be noted over the affected sinus. In doubtful cases, a sinus computed tomography (CT) scan will assist the diagnosis.

Treatment

Treatment includes analgesia, decongestants and recommendations to avoid diving until asymptomatic. Antibiotics may be required if secondary infection occurs.

Mask squeeze

If divers fail to exhale air into their masks on descent, the reduced volume inside the mask can cause pain, petechiae and conjunctival haemorrhage. In assessing these divers, it is important to confirm that they have normal visual acuity and fundi are normal. The condition is usually self-limiting.

Gastrointestinal barotrauma

Expansion of gas within the gastrointestinal tract on ascent can occasionally cause colicky abdominal pain. Rupture of the stomach is rare but has occurred where panic or equipment failure has led to air swallowing and rapid ascent. The affected diver presents with abdominal pain and distension. Shoulder pain may be due to diaphragmatic irritation or coexisting DCI. Subdiaphragmatic free air may be visible on an erect chest x-ray. The differential diagnosis includes pulmonary barotrauma, because air can enter the peritoneum via the mediastinum and oesophageal or aortic openings in the diaphragm. The diagnosis is confirmed with endoscopy and surgical repair is necessary.

Dental barotrauma

Severe tooth pain may occur with descent or ascent if air is trapped under a decaying tooth or recent filling. Percussion of the involved tooth is painful. Treatment is with analgesia and dental repair.

Pulmonary barotrauma

Pathophysiology

Breathing compressed air at depth, the diver's lungs contain greater amounts and density of gas than on the surface. Divers are trained to breathe continuously during ascent or to exhale continuously if they have lost their air supply. Pulmonary barotrauma results when a diver ascends without exhaling adequately and the expanding gas in the lungs exceeds the lung's elasticity, tearing alveoli. This occurs most commonly when a diver runs out of air, panics and ascends too rapidly. Even a change in pressure over 1 m near the surface is sufficient to cause lung barotrauma. It has been reported in student divers training in swimming pools and in helicopter escape training. It can also occur with a normal ascent if there is a localized area

of lung that does not empty properly, as is possible in divers with asthma, reduced pulmonary compliance or air trapping.

The resultant clinical syndromes depend on the sites at which the air escapes and include arterial gas embolism (AGE), pneumomediastinum and pneumothorax.

Clinical features

Onset of symptoms is usually rapid. If pneumomediastinum or pneumothorax is detected after diving, it is essential to look for features consistent with associated gas embolism. These include impairment or loss of consciousness, cognition impairment including loss of memory, or neurological abnormalities. Sometimes the abnormalities are subtle (or transient) and tests of cognition and memory should be performed in addition to a detailed history and thorough examination.

Treatment

If AGE is suspected, then the affected individual should be kept supine and urgent recompression treatment is required. Management of AGE is discussed under the heading of decompression illness. Lung barotrauma is regarded as the cause of AGE. Subtle signs of extra-alveolar air suggesting pulmonary barotrauma are present in nearly half with more sophisticated imaging, such as CT.

If divers present with a pneumomediastinum or pneumothorax, then they may have up to 50% chance of AGE. The signs of AGE in these circumstances may be subtle with only a brief period of loss of memory or dizziness.

Pneumomediastinum and subcutaneous emphysema in the absence of AGE can usually be managed conservatively. If symptoms are severe, 100% oxygen can accelerate resolution of the trapped gas. If recompression is required for coexistent AGE, then the pneumomediastinum does not require any specific additional management unless a pneumothorax is present.

Isolated pneumothorax resulting from pulmonary barotrauma is very uncommon. Pneumothorax from pulmonary barotrauma should be managed identically to non-diving-related causes and recompression is not necessary. If recompression is required for coexisting AGE, a chest tube with a Heimlich valve should be placed before commencing treatment, because the size of any remaining pneumothorax will increase markedly on depressurization.

Following acute management of pneumomediastinum and pneumothorax, the divers should be referred to a diving medical specialist for long-term follow-up, because the conditions will impact upon their future diving fitness.

Decompression illness

Classification and criteria for diagnosis

Diving accidents involving bubbles were traditionally divided into *decompression sickness* (DCS; due to nitrogen bubbles coming out of tissue) and *arterial gas embolism* (AGE; due to pulmonary barotrauma releasing air into the circulation). DCS was then classified as type I or II. Type I DCS involves the joints or skin only; type II involves all other pain, neurological injury, vestibular and pulmonary symptoms.

In the 1990s, the term DCI was proposed to include both DCS and AGE, for the following reasons:

- It can be difficult to distinguish clinically between cerebral arterial gas embolism (CAGE) and neurological DCS.
- AGE can be caused by arterialization of venous bubbles released from tissues.
- Prehospital and emergency management prior to recompression is identical.
- The division of DCS into type I and type II is inadequate for research purposes and divers classified as type I have been found to have subtle subclinical neurological manifestations.
- Symptomatic classification is adequate to guide management.
- The current classification system describes DCI in terms of four components:
 - onset (acute/chronic)
 - evolution of symptoms (spontaneously resolving/static/progressive/relapsing)
 - body system affected (musculoskeletal/cutaneous/lymphatic/neurological/vestibular/cardiorespiratory)
 - presence/absence of barotrauma.

For example, a diver may be classified as having acute progressive neurological DCI with no evidence of barotrauma. The classification has been generally adopted in Australia and New Zealand, but not in North America. DCI is a satisfactory term from a management perspective but, from a scientific perspective, it does not describe differing aetiologies and pathophysiology.¹

Pathophysiology³

DCI occurs if excessive nitrogen comes out of solution to form bubbles which gain access to the venous and lymphatic systems or if bubbles form within tissues themselves. The formation of bubbles requires tissues to be supersaturated with nitrogen and for ascent to be excessively rapid. As bubbles form in tissues, they distort tissue architecture, which results in impaired function, pain and inflammation and is probably responsible for most musculoskeletal symptoms.

Many bubbles entering the venous system do not cause symptoms. In fact, using ultrasonic detection methods, intravascular

24.3 DYSBARISM

microbubbles are detected after approximately 60% of routine dives. It appears that these bubbles are safely filtered by the lung and diffuse into the alveoli.

Bubbles entering the arterial system are more likely to cause serious problems. This can occur under several circumstances. Large volumes of bubbles may overwhelm the pulmonary filter and arterialize. Bubbles may also bypass the lungs via a right-to-left shunt. Up to one-quarter of the population may have a patent foramen ovale (PFO). Under normal circumstances, the foramen is kept closed by the pressure difference between the left and right atria. However, after diving, the pressure differential may reverse during a Valsalva manoeuvre or with acute increases in right-sided pressures associated with a large pulmonary gas load. A PFO is associated with cerebral, spinal, vestibular and cutaneous decompression illness.^{4,5}

Alternatively, gas can enter the circulation following pulmonary barotrauma. Air entering the pulmonary arterial system is carried to the pulmonary capillaries where it is trapped and reabsorbed by the alveoli. Air entering the pulmonary venous system, however, will pass through the heart and result in AGE.

Gas bubbles entering the circulation (either from tissues or barotrauma) cause both mechanical and biochemical abnormalities. Trapping in the pulmonary circulation may result in elevation of right heart and pulmonary pressures, leading to increased venous pressures, reduced cardiac output and impairment of tissue microcirculation. Arterial bubbles can cause end-organ ischaemia, although most pass through the capillaries and into the venous system. Most of the deleterious effects are a consequence of secondary inflammation of the vascular endothelium.

Bubble–endothelial interaction activates complement, kinin and coagulation systems and precipitates leucocyte adherence. This results in increased vascular permeability, interstitial oedema and microvascular sludging. The end result is ischaemia and haemoconcentration. Increased vascular permeability of the cerebral circulation will produce cerebral oedema. Vasospasm and reduced flow occurs approximately 1 to 2 hours after bubbles have passed through the arterial tree. This explains the commonly observed clinical course of a diver with a cerebral AGE experiencing an initial deterioration (bubble emboli), followed by spontaneous improvement (bubbles pass through the cerebral capillaries) and then a subsequent secondary deterioration. Animal studies have demonstrated that bubbles travel against arterial flow because of their buoyancy and lodge in the highest point of the body (hence the logic of maintaining supine position after decompression accidents).

Prevention

A number of dive tables and computer algorithms have been developed in an attempt to avoid nitrogen supersaturation of tissues and improve diver safety. Limits are placed on depth, time and ascent rates to allow safe decompression after diving. However, as with all mathematical models which attempt to predict biological behaviour, the dive tables are far from perfect. One series has shown that 39% of DCI cases were within the limits of the table they were using and 24% within the limits of the conservative Canadian Defence and Civil Institute of Environmental Medicine (DCIEM) tables. The occurrence of DCI is a probabilistic event where risk increases with increasing depth, time, numbers of dives, numbers of ascents and rates of ascent.

Flying after diving can precipitate DCI. Even if there are no bubbles at the end of the dive, excess nitrogen remains in the tissues and is slowly off-gassed. Further reduction in ambient pressure at altitude can cause bubbles or enlarge pre-existing asymptomatic ones. Current guidelines advise against flying for 12 hours after a single short no-decompression dive and 24 hours following multiple or decompression dives.

Clinical features

Onset of any symptoms during or in the hours after diving should be regarded as DCI until proven otherwise. Failure to recognize and treat milder cases can lead to permanent morbidity because the disease can progress as the bubble load increases with time. Common non-neurological symptoms include profound fatigue, myalgia, periarthritis pain and headache. Shoulders and elbows are the joints most commonly involved. The pain is usually a dull ache, which may initially be intermittent and migrate from joint to joint, but later becomes constant. Movement aggravates the pain, but local pressure with an inflated sphygmomanometer cuff may improve it. Paraesthesia and numbness may accompany the pain suggesting concomitant neurological disease.³

Early onset of symptoms or signs (up to 1 hour), especially those that are neurological in nature, indicates a serious decompression emergency and recompression is a time-critical treatment. Milder syndromes of decompression illness may develop up to 24 hours after a dive or even later if there is a precipitant, such as heavy exercise or ascent to altitude (e.g. flying).

In general, pulmonary barotrauma that results in AGE has a dramatic clinical presentation and the onset of major neurological symptoms and signs occurs within seconds to minutes after the dive. DCI caused by intravascular bubbles from barotrauma can be rapidly fatal and has a mortality of 5% in sport divers who reach a recompression chamber alive. In Australia, it is

the second most common cause of diving-related death after drowning. The brain is the organ most commonly affected, probably because of the vertical positioning of the diver on ascent. Cerebral gas emboli can cause sudden loss of consciousness, convulsions, visual disturbances, deafness, cranial nerve palsies, memory disturbance and asymmetric hemiplegias. Hemiplegia is much less common than asymmetric hemiplegias. Symptoms usually begin within 10 minutes of surfacing. Sudden loss of consciousness on surfacing should be assumed to be due to cerebral gas emboli. Spontaneous improvement may occur with first aid measures, but relapse is common.

Coronary arterial emboli rarely may present as acute myocardial infarction or arrhythmia. Abdominal organs and skin may also be embolised. Elevation of serum creatine kinase (predominantly from skeletal muscle), serum transaminase and lactate dehydrogenase levels in divers with AGE suggests that emboli are distributed more extensively than previously recognized. Peak creatine kinase (CK) may be a marker of the degree and severity of AGE.¹

Onset of DCI due to gas bubbles coming out of solution can be equally as dramatic (especially after rapid ascents from deep dives), but frequently evolves over hours postdive. DCI caused by bubbles released from tissues usually causes symptoms within 1 hour of completing a dive and 90% of cases have symptoms within 6 hours. Neurological symptoms occurring around 30 minutes after a dive suggest an associated PFO.^{4,5} Neurological DCI may present as personality change, headache, memory loss, visual defects, convulsions, confusion and altered level of consciousness. A flat affect may be the only symptom. The vestibular system can also be involved, with dizziness, vertigo, vomiting, nystagmus and ataxia.

Spinal-cord involvement occurs in up to 60% of cases of neurological DCI. The exact cause of spinal DCI is still debated. It may be a result of venous infarction of the cord due to obstruction of the epidural vertebral venous plexus. Other explanations include ischaemia and inflammation from bubble emboli or the formation of local bubbles within the spinal cord (autochthonous bubbles). Symptoms include back pain, paraesthesia and paraparesis, with bowel and bladder involvement. It is potentially disastrous to misdiagnose back pain coming on a few minutes after a dive as musculoskeletal pain and not consider spinal cord DCI.

If the bubble load overwhelms the pulmonary filter, a diver can present with a syndrome known as pulmonary DCI or 'the chokes'. The symptoms of this syndrome include dyspnoea, pleuritic substernal chest pain, cough, pink frothy sputum, cyanosis and haemoptysis. It indicates the diver has sustained a large intravascular gas load, so

a careful inquiry about other symptoms of DCI is mandatory and, if present, recompression is advised. Diving-related pulmonary oedema and saltwater aspiration syndrome are the major differential diagnoses.

A variety of rashes may be caused by cutaneous bubbles; however, these syndromes affect less than 10% of divers. The most common presentations are pruritus with no rash, a scarlatiniform rash with pruritus and *cutis marmorata*. *Cutis marmorata* begins as a spreading erythema but subsequently develops a marbled appearance of pale areas surrounded by cyanotic mottling.

Assessment of the injured diver

The injured diver requires simultaneous assessment and treatment. One hundred percent oxygen treatment should be continued during the assessment. If the history suggests AGE, the patient should be kept in the horizontal position to avoid re-embolization.¹³ If symptoms are progressing rapidly, the examination should be brief but thorough so as to ensure rapid access to recompression. In serious cases, some of the historical information may be obtained once the diver is receiving treatment in the recompression chamber.

The diagnosis of DCI is made on history and examination. A full dive history must be obtained, in addition to the medical history. Important details include the number of dives over recent days, depth, bottom time (the time from beginning descent to beginning direct ascent), performance of any decompression or safety stops, dive complications such as rapid ascents, surface interval between dives and the time interval between completing the dive and onset of symptoms. Previous dive experience, equipment used and gases breathed should also be recorded. A history of using surface supply equipment (the 'Hookah' apparatus) should alert the examining physician to the possibility of carbon monoxide poisoning and carboxyhaemoglobin measurement is required. Cold water, hard exercise during the dive, increasing age, multiple ascents and repetitive dives are predisposing factors in the development of DCI. Any exposure to altitude (>300 m) or heavy exercise postdive should be recorded.

A thorough examination, particularly of the neurological system, to detect subtle abnormalities is required. It is also helpful to perform basic tests of cognitive function, such as the mini-mental state examination. For milder static DCI syndromes with delayed presentation, the sharpened Romberg test provides useful information. It is performed by asking the patient to stand heel-to-toe with open palms on opposite shoulders. The patient is stable. They are then asked to close their eyes and timed until they

lose balance or achieve 60 seconds. A score of less than 60 seconds is suggestive of DCI in an injured diver. This test should not be performed if the history was suggestive of AGE or if there are neurological symptoms or signs.

Clinical investigations

Recompression should only be delayed for investigations if they will directly alter management. A full blood count and electrolytes are useful in that intravascular fluid depletion is common in severe DCI and the degree of haemoconcentration may correlate with eventual neurological outcome. Serum CK and liver function tests (LFTs) may be indicators of gas embolism; however, these do not influence clinical management. The blood glucose level should be checked in divers with impaired consciousness. Divers with neurological presentations should not be moved from the horizontal position until they are recompressed. If CAGE due to pulmonary barotrauma is suspected and CT is available, a supine CT scan of the thorax assists diagnosis of pneumothorax or pneumomediastinum. Emergency bedside ultrasound can be used to confirm/rule out a pneumothorax. Magnetic resonance imaging has no role in the acute investigation of DCI.

Treatment

First aid

Initial resuscitation is along standard basic and advanced life support protocols. One hundred percent oxygen provides the maximum gradient for diffusion of nitrogen (or other inert gas) out of the bubbles. A large consecutive comparative series involving over 2000 divers has demonstrated that first aid oxygen significantly improves outcomes for divers with decompression illness.⁶ Oxygen should be administered in the prehospital setting and continued until and during recompression. Failure to improve on oxygen does not rule out DCI. Conversely, complete improvement on oxygen does not obviate the need for recompression. The diver should be transported supine or in the left lateral position if unable to protect their airway. The diver should be prevented from sitting or standing up, to avoid bubbles redistributing from the left ventricle to the brain. If intubation is required, the endotracheal tube cuff should be filled with saline just prior to recompression to avoid a change in volume and a tube leak as ambient pressure increases.

Intravenous isotonic crystalloids should be commenced and titrated to response. Glucose-containing fluids are to be avoided because they may exacerbate CNS injury. Divers who present after several days with mild symptoms may be adequately managed with oral fluids. A urinary catheter should be inserted for spinal cord DCI with bladder involvement. Hypothermia should be corrected.

Retrieval

Long-distance retrieval can either be by air transport pressurized to 1 ATA or by portable recompression chambers. There is little debate that the longer the delay in recompression of severe DCI, the worse the outcome. However, Australian experience suggests that the number of cases where a portable chamber would have made a difference is so small that their use is unwarranted, largely because of the time required to prepare and transport portable chambers. Commercial aircraft are pressurized to 0.74 ATA (2440 m) and not appropriate to retrieve DCI patients, unless arrangements can be made to fly lower and pressurize to sea level. Road retrieval is not suitable over great distances or where an altitude of 300 m will be exceeded. Consultation with a hyperbaric physician should occur if retrieval is difficult.

Recompression

Recompression in a hyperbaric chamber is indicated even if the diver becomes asymptomatic with first aid, because otherwise many will relapse. The relapse may be more severe than the original presentation, due to the pathophysiological changes already initiated by bubbles in the microvasculature and tissues or redistribution of bubbles. Response to recompression is determined by time to recompression and the initial severity of injury. Recompression should always occur as soon as possible. Treatment commenced later than 4 hours after injury is associated with a poor response. Mild cases often respond despite longer delays to recompression.

Two types of hyperbaric chamber are available to administer recompression treatment:

- *Multiplace* chambers can accommodate more than one person, including a clinician attendant and are compressed on air while the patient breathes 100% oxygen via a head hood, demand regulator or endotracheal tube. Air breaks to lessen the risks of oxygen toxicity are provided by removing the head hood in a multiplace chamber. Full monitoring and mechanical ventilation are possible. All hyperbaric facilities in Australasia use multiplace chambers.
- *Monoplace* chambers accommodate one patient only and are usually compressed with 100% oxygen. These are more frequently used to treat nondiving medical illness; however, in other countries, they may be used for definitive treatment of divers.

Hyperbaric oxygen has the following beneficial effects:

- Reduction in bubble size in accordance with Boyle's law. This relieves the obstruction caused by intravascular bubbles and the tissue distortion of extravascular bubbles.

24.3 DYSBARISM

- Increased the outward diffusion gradient for nitrogen, further reducing bubble size. Reduction of endothelial inflammation caused by the bubbles.
- Relief of tissue ischaemia and hypoxia. There are no published randomized trials comparing recompression protocols and hence no international agreement on how to manage DCI. The general consensus is that initial treatments should begin with a standard 2.8 ATA (18 m) table breathing 100% oxygen. Some studies have suggested a benefit from initially recompressing deeper, however, this procedure is not universally accepted and subject to considerable debate.⁷

The identical Royal Navy 62 (RN62) and US Navy 6 recompression tables have become the standard of care for initial treatment of diving accidents in Australia and New Zealand.¹³ These are 18 m tables, lasting 4.75 to 7.25 hours (Fig. 24.3.1). Recompression is followed by gradual decompression. A response to treatment is usually evident after two oxygen periods at pressure. If there is a partial response then there is the option of extending the table at 2.8 ATA. If there is minimal or no response and there is no doubt about the diagnosis, then it is reasonable to proceed to a deeper table (most units use the Comex 30 table). Because of the risks of oxygen toxicity at greater than 2.8 ATA, a combination of helium and oxygen (heliox) is used. Further daily recompression is carried out until the patient stops improving or becomes asymptomatic and then one additional treatment is performed. Follow-up treatments are usually at 18 m, using either the RN61 table (18 m for 45 minutes, ascent to 9 m over 30 minutes, 9 m for 30 minutes then ascent over 30 min)

or the 18:60:30 table (18 m for 60 minutes then ascent over 30 minutes).

In-water recompression is dangerous and difficult and should only be considered if retrieval is impossible. Hypothermia and oxygen toxicity pose serious risks during in-water treatment and supervision by experienced appropriately trained personnel is essential.

Adverse effects of hyperbaric oxygen

Adverse effects of hyperbaric oxygen are uncommon. Even in nondivers, significant middle-ear barotrauma interrupting treatment occurs in 1/170 treatments. Claustrophobia is even rarer at 1/910 treatments.

The most serious adverse effect is oxygen toxicity and the attendant must continually watch for signs of its development. Toxicity is due to the formation of oxygen free radicals, which overwhelm the body's antioxidants. It can affect the brain and the lung.

Cerebral oxygen toxicity can occur with exposures above 2 ATA oxygen. The most common presentation of cerebral oxygen toxicity is muscle twitching, particularly of the lips and face. The incidence of convulsions in divers treated at 2.8 ATA on the RN62 is 0.29%.⁸ Other possible symptoms include apprehension, vertigo, visual disturbance, nausea, confusion and dizziness. If the oxygen is removed at this stage, progression to generalized convulsions may be avoided. Convulsions can, however, occur without premonitory symptoms. Treatment is as for any generalized convulsion, although removal of the oxygen will almost always stop it. Decompression should not be attempted during the convolution as this may

cause pulmonary barotrauma. Oxygen can be safely reinstated 15 minutes after all symptoms have resolved. Predisposing factors to cerebral oxygen toxicity include fever, steroids, a past history of epilepsy and carbon monoxide poisoning. Incidence is directly proportional to time of exposure and inspired oxygen partial pressure. Pulmonary oxygen toxicity manifests initially as an asymptomatic reduction in vital capacity, followed by cough and retrosternal pain. It may occur with prolonged exposure to partial pressure of inspired oxygen, $P_O_2 > 0.5 \text{ ATA} \geq 0.5 \text{ ATA}$. The symptoms usually abate when treatment is completed. Up to 10% reduction in vital capacity has been measured during extended treatments, which reverses within 24 hours.

Adjvant therapies for DCI

Lignocaine was suggested as potentially being neuroprotective for cerebral arterial gas embolism based on cardiac research. However, despite showing initially promise for patients undergoing open-heart surgery, subsequent larger randomized controlled trials (RCTs) failed to demonstrate benefit. In a double-blind RCT, the nonsteroidal antiinflammatory drug tenoxicam had demonstrated benefit in shortening recovery times following decompression illness. There was a reduction in total recompression requirements.⁹

Prognosis after treatment

Relapses may occur after initial recompression. All neurological cases should be observed in hospital to allow immediate recompression if deterioration occurs.

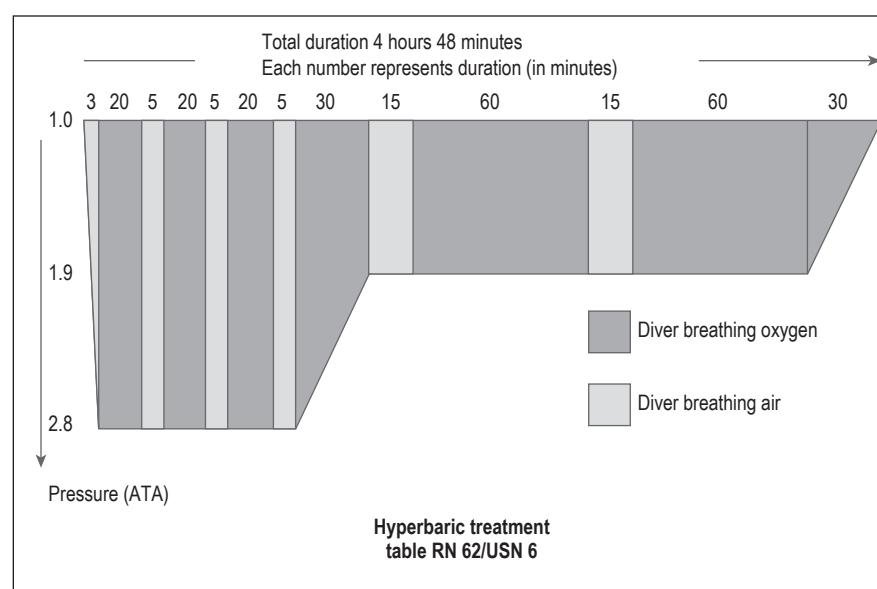


FIG. 24.3.1 Royal Navy Treatment table 62/US Navy treatment table 6.

Residual symptoms occur in up to 30% of cases and are more likely where recompression is delayed. Delays to treatment are not unusual with a mean time to recompression of 68 hours in one series. There is no clear time interval after diving that recompression becomes ineffective. Many divers with DCI still respond to treatment even when delayed for 7 to 10 days and therefore any diver with unexplained symptoms after diving should be referred to a diving medicine specialist.

Flying after treatment and return to diving

Recommendations for flying and diving after treatment for DCI vary greatly and are not evidence based. Flying should be avoided for at least 1 week after treatment to avoid relapse. It is reasonable to permit resumption of diving after 4 weeks if there are no residual symptoms or signs. Because of the risk of recurrence, further diving is contraindicated if the DCI is thought to be due to pulmonary barotrauma, or where there are residual neurological signs or symptoms.

Other issues

Vertigo and headache in divers

These two symptom complexes are challenging to assess and diagnose. There are several possible serious causes of vertigo in divers. Vertigo developing while the diver is underwater is extremely dangerous; it can induce panic and lead to a rapid ascent. It can disorientate the diver and if vomiting occurs, there is risk of airway obstruction. All cases of vertigo in divers (even if resolved) require specialist assessment.

The most common cause, alternobaric vertigo, begins just as divers commence their ascent and is caused by unequal middle ear pressures. It usually lasts only a few minutes. Middle-ear barotrauma can also cause mild vertigo. Other causes include inner-ear DCI, inner-ear barotrauma and TM rupture. Persistent acute vertiginous symptoms may indicate a more serious cause, such as neurological DCI or IEBT.² Headache occurring during or after diving has a number of possible diving-related causes, such as sinus and mask squeeze, carbon dioxide accumulation, carbon monoxide toxicity, decompression illness, patent foramen ovale, ill-fitting wetsuits, temporomandibular dysfunction and marine envenomation. It is recommended that for all divers presenting with vertigo or headache, there is early consultation with a diving medicine specialist.

Oxygen toxicity

Cerebral oxygen toxicity in the diver underwater causes the same problems as in the hyperbaric chamber. Divers are more likely to develop

toxicity underwater than in the chamber because immersion, exercise and carbon-dioxide retention increase the risk. The use of oxygen-enriched gases, such as nitrox, may increase the risk of cerebral oxygen toxicity. Enriched-air divers should ensure they stay at depths that maintain an oxygen partial pressure of less than 1.4 ATA.

Nitrogen narcosis

Nitrogen narcosis is due to the anaesthetic effect of nitrogen dissolved in lipid membranes. Symptoms are similar to those of alcohol intoxication. Some divers experience it at 30 m and almost all by 50 m. Loss of consciousness occurs at 90 m. This condition will not present to the emergency department because it is immediately reversible on ascent. However, it may result in other diving accidents, such as rapid ascent or near drowning. Because of nitrogen narcosis, divers planning to dive deeper than 50 m use alternative breathing gases such as heliox.

Gas contamination

Contaminants may be added during filling or already in the diver's tanks. Common contaminants include carbon dioxide, carbon monoxide and oil. Increasing partial pressures of the contaminants at depth may result in toxicity. Contamination is rare but must always be included as a potential cause when injured divers present, especially with headache, shortness of breath or loss of consciousness at depth.

Diving-related pulmonary oedema

Pulmonary oedema in the diver may be caused by DCI, near drowning or immersion itself. Pre-existing cardiovascular disease, increasing age (>40), female gender, hypertension and beta blockade appear to be risk factors for immersion-induced pulmonary oedema. Symptoms often begin while the diver is still at depth, distinguishing it from DCI. The condition has been reported when immersed but not diving (e.g. swimming). Treatment is supportive and recompression is not required provided DCI can be excluded. However, if detected, the occurrence of pulmonary oedema as a result of diving has long-term ramifications for future diving fitness.

CONTROVERSIES

- What position is best for managing the injured diver?* There are no controlled trials assessing the best position to manage an injured diver. The current recommendation is to maintain a supine position for all suspected or confirmed neurological presentations, based on expert opinion and known pathophysiology.

- Should intravenous or oral fluids be administered?* Based on expert consensus and known pathophysiology, the injured diver is usually dehydrated. Fluid management is regarded as an important adjunct to recompression. In an acute diving accident <12 hours, where consciousness or airway reflexes are impaired or where there is nausea and vomiting, IV salt-based crystalloids should be administered, due to the need for 100% oxygen and the possible risk of oxygen toxicity during the initial treatment phase at 2.8 ATA. In the less acute presentation of static DCI, oral fluids may be acceptable, although there are some risks if an oxygen toxicity seizure occurs during treatment at 2.8 ATA.
- Should we compress divers deeper than 2.8 ATA during treatment?* This is very controversial, with reports of deep tables being used successfully in Hawaii.⁷ To date, there are no completed randomized controlled trials comparing outcomes of different treatment pressures.

Important phone numbers

Listed below are 24-hour services offering advice on management, retrieval and location of the nearest hyperbaric facility:

Australia

Divers Alert Network 1800 088 200
+61 8 8212 9242 (outside Australia)

New Zealand

Diver Emergency Service 0800 4337 111

USA

Divers Alert Network (DAN) (919) 6849111

UK

British Hyperbaric Association National Diving Accident Helpline 07831 151523
Diving Diseases Research Centre, Plymouth
01752 209999

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24.4 Radiation incidents

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ESSENTIALS

- 1** Radiation accidents are rare but require well-planned protocols for successful management. The principal challenge will be managing large numbers of people who have concerns about their exposure to radiation, or contamination with radioactive material as a result of an incident.
- 2** The management of life-threatening illness or injury always takes precedence over the radiation aspects of the patient's condition.
- 3** Removing the patient's clothing and washing exposed skin and hair can reduce the level of external contamination by up to 90%.
- 4** The presence of qualified radiation physicists with appropriate radiation monitoring equipment is invaluable when dealing with (potentially) contaminated patients.
- 5** Effective triage for exposure to radiation is based on early clinical symptoms and lymphocyte counts.
- 6** Following whole-body irradiation, survival is likely only from the haemopoietic and milder gastrointestinal syndromes.
- 7** Blocking and chelating agents can successfully reduce the incorporation of radioactive substances into body tissues if they are given early.
- 8** Early involvement of a haematologist can assist in triaging patients for cytokine modulators to facilitate autologous marrow recovery.
- 9** Haemopoietic stem cell transplantation can increase the survival rates of more severely affected patients but resources around the nation are limited.

Introduction

In August 1945, the first atomic fission bombs were detonated above the Japanese cities of Hiroshima and Nagasaki with devastating effects. Most radiation incidents, however, have been accidental with the most serious occurring in 1986 at Chernobyl in the former Soviet Union when a nuclear reactor unit exploded, dispersing radioactive material over a wide area. One hundred and thirty six people developed the acute radiation syndrome, of which 28 died. The majority of incidents, however, have involved small numbers of people and many have occurred as a result of deliberate bypassing of safety procedures.

There were no deaths from exposure to radiation or cases of radiation sickness following the 2011 Fukushima accident but over 160,000 people had to be evacuated from their homes to ensure this.

In Australia, the Australian Radiation Incidence Registry records all accidents where exposures occur that are not 'within the limits known to be normal for the particular source of radiation and for the particular use being made of it'. Strict licensing and control systems, coupled with improving technology and training, have helped to minimize the number of Australian radiation incidents.

The advent of terrorism has increased the risk of multiple casualty incidents.

Radiation sources and incidents

Worldwide, the most common radiation sources are

- X-ray equipment: used for medical diagnosis and treatment, industrial and commercial inspections, irradiations and research.
- Accelerators: used for medical treatments, industrial irradiation, the production of radioisotopes and research.
- Radioactive materials: used for medical diagnosis and treatment, industrial radiography, quality control and tracing techniques, soil density and moisture tests, and research. Radioactive material may be unsealed or contained within sealed containers.
- Nuclear processing and reactor plants: used for processing uranium and plutonium for fuel purposes and nuclear weapons, power production and research.

With x-ray equipment and accelerators, the victim may be exposed to radiation but this does not make the tissues radioactive. These patients pose no threat to others, including medical attendants.

Unsealed radioactive material has the potential to cause radioactive contamination. This may be external on clothing or skin or internal following inhalation, ingestion or absorption through body orifices, mucous membranes and wounds. Following internal contamination, radioactive material may become incorporated into the patient's tissues.

Other than for accidents involving nuclear processing and reactor plants, or nuclear explosions, incidents usually lead to either exposure or contamination.

There are no nuclear reactors in Australia except for the occasional visiting nuclear powered warship. These vessels are closely monitored while in Australian ports.

Terrorism

The most likely means for terrorist organizations to deploy radiation is a radiation dispersal device (RDD) or 'dirty bomb'. These weapons

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use conventional explosives to spread radioactive substances.

RDDs are sometimes called 'weapons of mass disruption' because of the fear they engender in the population, multiple casualties, contamination of widespread areas and the economic cost.¹ Immediate injuries are generally the result of blast or thermal effects. Few contain sufficient material to cause acute radiation injury. Only those trapped near the site of detonation run this risk. However, radioactive material will be spread over a large area and many people might be exposed to the risks of low-dose radiation. Hospital staff treating the victims of RDD explosions are at negligible risk provided they wear appropriate protective equipment. Unlike surface burst nuclear weapons, RDDs do not cause fallout downwind of the detonation.

Radioactive material without the explosive component may constitute a radiation exposure device (RED) and could potentially be hidden in a crowded space, such as a theatre, where it could cause occult irradiation. Industrial sources are the most prevalent REDs in the civilian sector. An improvised nuclear device (IND), like a small nuclear weapon, produces blast, thermal and radiation energy, exposing people to high-dose external radiation, inhalation of radioactive materials, particulate contamination and ingestion of radioactive materials in the food chain.

Measuring radioactivity

Radioactivity of an isotope is expressed as the average number of atoms that disintegrate per second. The becquerel (Bq) is the International System of Unit (SI unit) for one nuclear disintegration per second. The activity of a given mass of a radioactive substance with a short half-life will decrease with time.

Ionization in air caused by radiation can be measured by portable dosimeters to give an estimate of the levels of radioactivity at the site of an incident. This is used to calculate the exposure level of a patient with acute radiation illness. The units used are Roentgens. Dosimeters are also used in hospitals to measure the level of radiation to which staff members have been exposed or to monitor patients during decontamination.

The absorbed dose of radiation is the amount of ionization energy deposited in matter by ionizing radiation. One gray (Gy) is equivalent to one joule per kilogram. The effect of a given dose of radiation depends on the type of radiation emitted and the tissue type irradiated.

Type of radiation emitted

Different types of ionizing radiation transfer energy to tissue at different rates. The sievert (Sv) is the international unit of effective radiation dose and is obtained by multiplying the absorbed

dose measured in Gy by a quality factor to reflect the different effects of each radiation type and their potential biological damage. For beta and gamma radiation $1 \text{ Sv} = 1 \text{ Gy}$. Alpha and neutron radiation deposit more energy in tissue so the quality factor is higher.

Alpha particles, composed of two protons and two neutrons, do not penetrate the dermis but may cause local damage if ingested, inhaled or absorbed through open wounds. Beta radiation, consisting of electron-like particles, travels about a metre through the air and is stopped by clothing. It often causes radiation injury to exposed skin. Gamma particles have no mass and are similar to x-rays, penetrating the body freely and causing the acute radiation syndrome if the trunk is involved. Neutrons are produced only during nuclear detonations and, while they can technically make an irradiated victim emit radiation, this is not clinically significant.

Grays are the preferred measure for determining acute effects while sieverts are more useful in predicting chronic effects.

The average natural background radiation is 2 mSv per annum in Australia. The Australian National Occupational Health and Safety Commission's standard for a worker is a maximum effective dose of 50 mSv in any year (or 20 mSv/year averaged over 5 years).

Pathophysiology

Radiation damages tissue both directly and indirectly by the production of free radicals from water molecules. Direct damage to cell membranes may cause changes in permeability and the release of lysosomes. Germinal, haemopoietic and gastrointestinal epithelial cells are relatively radiosensitive. The cells of bone, liver, kidney, cartilage, muscle and nerve tissue are relatively radioresistant. The delayed effects of radiation depend on whether the dose is lethal or sublethal to the tissue involved.

Lethal (deterministic) injuries are threshold dependent. Cells are killed when they receive more than a certain radiation dose, which varies with different tissues. Clinical expression occurs when the amount of cell killing cannot be compensated for by proliferation of viable cells. The acute and chronic radiation syndromes are deterministic. The earliest delayed effect of acute radiation injury, cataract formation at about 10 months, is an example of this type of injury.

For sublethal (stochastic) injuries there is no threshold level of radiation and the consequence is based on statistical probability. Sublethal injury to chromosomes is the most important effect of ionizing radiation. Double-strand breaks are not easily repairable, especially if the damage occurs simultaneously to both strands. This results in broken chromosomes with no template

for repair. The exposed ends of chromosome fragments may join up at random, resulting in morphological chromosomal abnormalities. Sublethal damage to chromosomes is implicated in the development of tumours. Although the incidence of malignancy in adults is increased by radiation exposure, the age at which malignancies are clinically expressed does not change. The estimated increase in lifetime risk of fatal cancer is 0.008%/mSv of gamma radiation exposure.² Therefore an individual who is exposed to 100 mSv (twice the acceptable Australian occupational annual exposure) has a 0.8% increase in the lifetime risk of fatal cancer.

Radiation exposure to the gonads may produce temporary or permanent infertility in men depending on the dose. With temporary infertility, there is preservation of the secondary sexual characteristics. In the female, however, all ova are present at birth and larger radiation doses are required to produce sterility. Radiation-induced infertility in females is associated with premature menopause.

Children are more prone to radiation-induced carcinogenesis because they have a higher number of future cell divisions and a longer life span. The fetus is exceptionally susceptible to radiation injury.

Acute radiation exposure

Radiation exposure accidents usually involve penetrating radiation, such as high-energy x-rays or gamma rays. The effects are primarily due to the loss of cells in the body. Acute exposure is more dangerous than chronic, as it does not allow time for cell replacement or tissue recovery. Clinically, radiation exposure may produce a generalized acute radiation syndrome or a localized irradiation injury.

The acute radiation syndrome

The acute radiation syndrome refers to the effects of radiation on one or more body systems. The haemopoietic tissue alone is affected at doses of 1 to 4 Gy and produces pancytopenia with its consequent risks of infection, bleeding and anaemia. Above 6 Gy, gastrointestinal effects are also manifest and the prognosis is poorer. The neurovascular syndrome occurs with doses above 20 Gy and is manifest by leaky capillaries, hypotension and a progressive decline in mental function with eventual death in weeks to months. The symptoms depend on the part of the body irradiated, the dose and the time over which it is delivered.

Clinical features

The course of the illness can be divided into four phases:

- the prodromal phase, which generally lasts up to 48 hours;
- a latent period, lasting hours to weeks;

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- the manifest illness period;
- death or recovery.

The prodromal symptoms are due to the effects of radiation on cell membranes and the release of vasoactive amines. The symptoms are nonspecific, with anorexia, nausea, vomiting, weakness, fever, conjunctivitis, erythema and hyperesthesia. The time to emesis, presence of diarrhoea and duration of symptoms are markers of the severity of the exposure.¹

The phase of manifest illness corresponds to the loss of cells. The haemopoietic syndrome occurs alone with whole-body radiation doses of between 1 and 4 Gy. It is due to loss of stem cells in the bone marrow. At these doses, some stem cells survive and recovery is therefore possible. The latent period lasts from 2 to 20 days and is followed by a rapid fall in the number of white blood cells and platelets. Recovery commences about 30 days after exposure, regardless of the exact dose.

The gastrointestinal syndrome predominates with radiation doses greater than 6 Gy. The prodromal symptoms are more severe. Early bloody diarrhoea suggests death within 2 weeks. The gastrointestinal symptoms recur during the manifest illness phase and can be very severe leading to dehydration and electrolyte imbalance. This syndrome is due to the loss of stem cells in the small intestinal mucosal crypts. It is superimposed upon the haemopoietic syndrome with both occurring after a short latent period of under a week.

The neurovascular syndrome occurs with doses of greater than 20 Gy and is characterized by leakage of fluid into tissues and hypotension. The latent period is just a few days. Leakage into the brain causes neurological symptoms. These effects are superimposed on those due to gastrointestinal and haemopoietic damage. At very high doses, greater than 30 Gy, there is incapacitation usually within the first few minutes and certainly within 40 minutes. The effects are largely due to disruption of cell membranes and electrochemical inactivation of neurons. Death can be anticipated within hours. In a nuclear detonation, however, death from other injuries is more likely in those close enough to receive this level of exposure.

Absorbed dose estimation

Dose reconstruction from a small source is readily calculated by a radiation physicist once the activity of the source, the distance and time a person spent near it are known, but exposure from larger sources requires computer modelling and real-time environmental radiation measurements. Initial assessment must therefore be based on clinical and laboratory information, specifically:

- The presence and timing of emesis and other prodromal symptoms

- Lymphocyte depletion over time and other haematological changes
- Amylase, C-reactive protein (CRP) changes over time

Dicentric analysis is the gold standard but also takes time.

Protracted vomiting within one hour postirradiation is indicative of a dose in the 6 to 8 Gy range. For a time to emesis of approximately 2 hours, the effective dose is likely to be at least 4 Gy. Vomiting at 4 hours is indicative of a dose in the 2 Gy range. If the patient has not vomited within 10 hours the dose is likely to be <1 Gy. However the absence of vomiting does not preclude a significant exposure and hence triage must not be based solely on vomiting alone.³

Whole-body irradiation may produce early erythema but rarely within 24 hours and only after doses greater than 6 Gy.

Clinical investigations

The threshold for admission on initial presentation will depend on the number of casualties but, in general, patients who do not vomit within 6 to 8 hours can be managed as outpatients. A useful triage tool for patients *without* other injuries or chronic illnesses utilizes a combination of the neutrophil/lymphocyte count and the presence of emesis at 4 or more hours postexposure:

$$T = N/L + E, \text{ where } E = 0 \text{ if no emesis and } E = 2 \text{ if emesis.}$$

If T is >3.7 , the patient requires admission for further evaluation as the radiation dose is likely >1 Gy.⁴

Acute radiation exposure is confirmed by laboratory investigation. Lymphocyte counts should be taken every 6 to 12 hours for 48 hours.

A lymphocyte count of $1000/\text{mm}^3$ at 24 hours suggests a dose of at least 2 Gy and the eventual development of the haemopoietic syndrome. A count of $500/\text{mm}^3$ suggests a radiation dose of 6 Gy and the subsequent development of both the gastrointestinal and haemopoietic syndromes. A fall of 50% in the lymphocyte count in the first 24 hours is suggestive of a potentially lethal radiation exposure.

The lymphocyte count at 48 hours is useful for admitted patients to further refine the likely dose and clinical course:

- No symptoms and lymphocytes $>1500/\text{mm}^3$ after 48 hours—unlikely to require clinical support but should be observed periodically.
- Nausea, vomiting, erythema and lymphocytes between 800 and $1500/\text{mm}^3$ at 48 hours—probable serious injury, which will require clinical support.
- Pronounced nausea, vomiting, diarrhoea, erythema and lymphocytes between 100 and $800/\text{mm}^3$ at 48 hours—probable life-threatening injury, which will require maximal clinical support.

- Early vomiting and bloody diarrhoea, erythema and lymphocytes $<100/\text{mm}^3$ at 48 hours—lethal injury.

The US Department of Health and Human Services has an online calculator, which uses lymphocyte depletion kinetics and emesis to estimate the radiation dose.⁵

The lymphocyte count may be less useful if there is significant concomitant trauma or at low levels of exposure. A dose-dependent increase in serum amylase is evident after 24 hours.

Cytogenetic studies using blood collected at 48 hours in a lithium heparin tube examine the number and structure of chromosomes. Radiation dose is reflected in the number of excess acentric and dicentric forms. T lymphocytes are relatively long-lived and reliable dose estimates can be made up to 5 weeks after collection of the sample. Newer methods are quicker and can detect very low doses (0.1 Gy).

Treatment

Supportive treatment includes maintenance of fluid and electrolyte balance, nutritional supplementation, antiemetics such as ondansetron, and antidiarrhoeals. Colony stimulating factors should be commenced as soon as possible if the radiation dose was >2 to 3 Gy and be continued until the lymphocyte count reaches $1000/\text{mm}^3$.^{3,4} Control of infection commences in the prodromal phase, with identification and aggressive treatment of any potential infection, so that the patient is in optimal condition to survive a period of manifest haemopoietic depression. To reduce the infection risk, patients may be kept home during the latent period and admitted to hospital when neutropenia develops. Hospital management involves strict isolation and laminar airflow units. The prophylactic administration of antibacterial, antiviral, antifungal and antihelminthic therapy is reserved for the most severely neutropenic. Nonabsorbable agents are commonly used to sterilize the gastrointestinal tract. Anaerobic agents should be included if there is gut injury.

Management of neutropenia follows the principles established in the management of bone marrow suppression secondary to chemotherapeutic agents. Fever is investigated and managed with empirical therapy in the first instance. If as many as 10% of the stem cells remain intact, the blood cells will repopulate. Platelet transfusion must be commenced early, especially if surgical procedures are required. The role of stem cell transplantation is evolving. Early reintroduction of enteral nutrition is important to maintain gastric acidity and prevent infectious organisms spreading from the gut to the respiratory system. Povidone-iodine or chlorhexidine is used for skin disinfection and shampoo. Meticulous oral hygiene must be maintained.

Prognosis

The LD_{50/60} is the dose at which half the victims succumb within 60 days. Without treatment, the LD_{50/60} is 3.5 to 4 Gy. With supportive care, antibiotics and transfusions, the LD_{50/60} is almost doubled to around 5 to 6 Gy. Early colony stimulating factors and intensive care increase the LD_{50/60} to 6 to 8 Gy. Bone marrow transplantation may be used in patients exposed to 8 to 10 Gy and occasionally patients have survived.

Survival from the cardiovascular and neurovascular syndromes does not occur.

Combined injuries

Combined injury occurs when there is additional trauma, either physical or thermal, in addition to the radiation injury. The effects of the radiation exposure may become apparent earlier and may be more severe when other injuries are present. Healing of tissues, including callus formation at fracture sites, will be delayed even with subclinical radiation doses. Radiation exposure increases the mortality when combined with other injuries or pre-existing conditions that result in immunosuppression, blood loss and danger of infectious complications. All administered blood products should be irradiated to remove the T-cell population and minimize graft-versus-host reactions. Platelets should be transfused if the platelet count falls below $20 \times 10^9/L$ and, if surgery is anticipated, it should be maintained higher than $75 \times 10^9/L$. Emergency surgery, including the excision of dead tissue and the closure of wounds, should be completed within 48 hours while some white blood cells remain. For thermal burns, early excision of potentially septic tissue and skin grafting are indicated. Wound closure is an important means of reducing vulnerability to infection. Nonurgent surgery should wait until any bone marrow suppression resolves.

Radiation pneumonitis may develop some time following the exposure and be confused with acute respiratory distress syndrome (ARDS).

Local irradiation injuries

The majority of local irradiation injuries occur when operators of x-ray diffraction units inadvertently place their fingers or hands in the direct x-ray beam. Other accidents have occurred when radioactive sources, often from industrial radiography equipment, are detached and then picked up and placed in the pockets of workers. There have been misadministrations of radiation to patients undergoing radiotherapy. The higher the dose the greater the severity and the earlier the onset of the local injury. The smaller the area irradiated, the higher the dose required to produce a particular change.

Clinical features

Early symptoms may include erythema, tenderness, itching, tingling and a changed sensitivity to heat and cold. At 14 to 28 days hair epilation occurs at 3 Gy, erythema recurs at 6 Gy, dry desquamation at 10 to 15 Gy, wet desquamation at 15 to 25 Gy and deep ulceration/necrosis at >25 Gy.³ If the area irradiated includes the epigastrium, nausea and vomiting may also occur. The degree of radiosensitivity of the skin depends on the thickness of the epidermis. The most sensitive areas are those that are also moist and subject to friction, such as the axillae, groins and skin folds. The least sensitive areas are the nape of the neck, scalp, palms and soles.

If irradiated skin appears normal at 72 hours, any subsequent changes are likely to be less severe. Erythema may be delayed for up to 30 days but is then unlikely to progress to ulceration. Pain is minimal unless ulceration occurs or the dose is extreme. Magnetic resonance imaging (MRI) and Doppler studies may help define the extent of the damage. Late effects include progressive tissue atrophy, fibrosis and chronic radiodermatitis with tissue breakdown. There may be stiffness and tenderness and decreased sensitivity to temperature change.

Treatment

Mild injuries may be simply observed. An effort should be made to protect the area from additional trauma. Progress may be monitored with serial photographs. Topical corticosteroids may help. For more severe injuries, particularly with pain, local debridement and skin grafting may be necessary but should be delayed until the full extent of the lesion is known. Ideally, surgeons experienced in managing chronic vascular disease should be consulted. Amputation is reserved for gangrene. Skin grafts are indicated for areas of exposed cartilage or bone or for severe scarring. Topical antibiotics are often prescribed in an attempt to reduce infection. Vascular therapy with hyperbaric oxygen and pentoxifylline may be useful. In the long term, the irradiated area must be watched for the possible development of neoplastic change.

Contamination with radioactive material

The care of individuals who are contaminated with radioactive material requires similar preparation and precautions as for those contaminated with hazardous chemicals. Radioactive contamination has the advantage that it can be readily detected by instruments when on the skin. With the exception of Chernobyl, survivors of radiation accidents have not been sufficiently contaminated so as to pose a threat to emergency or

hospital personnel using appropriate precautions and procedures.

Prevention at a site using radioactive materials

All staff using shielded or unshielded radiation sources in their daily work must be thoroughly trained in their safe use. Facilities using unshielded radioactive material must have procedures in place to deal with spillage and other accidents and all workers must be adequately trained in emergency procedures.

Preparedness at site

Emergency equipment must include appropriate monitors for detecting ionizing radiation or contamination, facilities for decontaminating victims and plastic bags for biological and other samples. Appropriate blocking or chelating agents should be stocked at the facility. Emergency planning must include early warning of the receiving hospital so that adequate preparations can be made prior to the arrival of patients.

Scene management

For incidents involving small numbers of patients, members of the rescue team should put on the protective clothing normally used by personnel working with radioactive material at that site. This includes gloves, facemask and cap. Gowns may be covered with large plastic aprons to make them waterproof. Additional measures, such as taping plastic bags over shoes, may be used if the normal protective clothing is judged inadequate. The implementation of life-saving procedures may make it necessary to forgo some of this protection. Contamination of the rescuer will be low and decontamination can be carried out later.

Serious illness or injury is not due to radiation *per se* and should be treated on its own merits. Unless the patient's condition is serious, external decontamination begins at the scene so as to minimize internal contamination and incorporation of the radionuclide into the body tissues and to reduce the risk of contaminating other persons and the hospital environment. As much as 80% of contaminating material may be on the clothing.⁶ Accordingly, the victim's outer clothing should be removed at the earliest practicable stage. If monitoring is not available, it should be assumed that all outer clothing is contaminated. The person removing the contaminated clothing must wear protective clothing and limit contact with the outside of the victim's clothing. The victim is then wrapped in plain sheets and transferred to hospital. If small contamination spots on the skin cannot be easily removed at the scene, they should be dressed and the victim transported to hospital.

At larger incidents, it may also be necessary to establish a controlled area, the periphery of

24.4 RADIATION INCIDENTS

which is located just beyond the region where contamination is detected above background levels. Rescue team members should wear the maximum level of personal protective equipment available. This should be removed at the perimeter of this area prior to both patient and rescuers leaving. Monitoring of all personnel leaving the area should be undertaken if facilities are available.

Portable vacuum units with high efficiency particulate air filters have reportedly been used to facilitate rapid decontamination outdoors.

Emergency department

The elements of planning for the management of radiation accident patients are similar to those for other types of emergencies, namely prevention, preparedness, response and recovery.

Facilities using unsealed radioactive sources should be identified in advance. These include nuclear medicine departments, scientific laboratories and nuclear facilities. An emergency department (ED) response plan should be developed and emergency response team membership designated. Equipment for monitoring, decontamination and contamination control should be in place. Regular practice is essential.

A decontamination area must be designated and be itself capable of adequate decontamination. Ambulant patients and lower acuity stretcher-bound patients should be decontaminated outside the ED. Waste water may be legally discharged into normal draining systems if it does not exceed specified limits. In the clinical setting of a few patients, this is unlikely. Incidents involving contaminated or possibly contaminated patients rapidly deplete a receiving hospital's emergency response. If multiple patients with possible contamination are being managed, the hospital may need to defer where possible the arrival of other patients.

Hospital protocols should include plans for dealing with relatives, the press and the public. The timely release of appropriate information is important. Persons issuing this information should be well versed in radiation medicine, as the avoidance of questions and confusion in answers may generate public uncertainty and panic. Security personnel will be required to restrict the entry of unauthorized persons to the treatment area.

Decontamination process

Life-saving procedures resulting from trauma or burns should take priority over consideration of the radiation aspects of the patient's condition, even if preparations to minimize the spread of contamination have not been completed. A radiation physicist with appropriate monitoring equipment should be present in the ED. However, if patients arrive before monitoring

is available, treatment of severe injury should proceed immediately and subsequent decisions regarding decontamination should be based on the patient's likely exposure.

In the ideal situation, all patients should be monitored at triage and, if found to be contaminated, those without severe injury should be showered and remonitored prior to admission to the ED. This is especially so if whole-body contamination has occurred, for example from a gaseous plume from a reactor accident. Washing starts with the hair and works downwards. Patients should bend forward while washing their hair so that any contamination is not washed into their eyes, nose or mouth. Wounds should be covered with a waterproof dressing before showering to avoid washing contaminated water into them.

Because some patients with severe injury will require immediate admission to the ED, adequate preparations are necessary. The floor of the entry and some treatment cubicles should be covered with plastic and any nonessential items removed. Access to this controlled area must be strictly supervised and there should preferably be a buffer zone. Disposable fluid-repellent gowns are ideal but surgical gowns covered by plastic aprons are satisfactory. Lead aprons as used in x-ray departments are not satisfactory; these prevent exposure but not contamination and are heavy and hot to wear. Plastic bags are taped over the shoes and the cuffs of overalls should be taped and secured to the outsides of overshoes. Facemasks are required to protect against airborne contamination but they do not protect the face from being touched by contaminated hands. Trauma masks with clear plastic visors are the best option. Two pairs of gloves should be worn. The inner ones should be surgical gloves taped to the sleeves. The outer gloves are not taped down and should be changed frequently. Hair cover is desirable. Personal radiation dosimeters should be worn outside clothing by key treating personnel in closest proximity to casualties.⁷ Rubbish bins lined with garbage bags serve as waste receptacles and should be emptied promptly to minimize the amount of radiation in the department.

Once the patient is in the controlled area, all clothing should be removed and other medical conditions assessed and treated. Blocking agents can be administered if they have not already been given. All mucosal surfaces should be swabbed to aid in the assessment of likely internal contamination. These include nostrils and ears, the mouth and rectum. The swabs should be placed in sealed labelled plastic bags and sent for radiation assessment and identification of the chemicals involved. Blood samples should be drawn for a baseline complete blood count, differential and absolute lymphocyte counts and later cytogenetic analysis. A serum amylase

is also important, as the parotid is very sensitive to radiation.

External decontamination utilizes the principles of barrier nursing and contamination control. Staff should stand back from the patient except when actually examining them or performing procedures. Radiation exposure is inversely proportional to the distance from the source squared. Hospital personnel should be rotated during the decontamination procedure to minimize the perceived risk to any one individual. Pregnant staff should not be involved. Staff members should shower following completion of their turn in decontamination.

The priority areas for external decontamination are wounds and orifices, as it is through these that the risk of subsequent internal contamination is greatest. Other priority areas include the hands, face and head, as early contamination removal reduces spread. Decontamination of intact skin is the last priority.

Wounds are decontaminated in the same manner as when removing dirt or bacteria. Deeper wounds should be opened up and thoroughly irrigated. Burnt areas also should be carefully irrigated. Metal fragments should be removed with forceps. Deep debridement and excision of a wound is rarely necessary in extreme cases where highly toxic material is embedded in the tissues. Decontamination efforts should continue until the radiation level is at background levels or there is minimal reduction with further washing.

The mouth is decontaminated by gentle irrigation and frequent rinsing with 30% hydrogen peroxide solution. Brushing of the teeth with toothpaste is helpful, as toothpaste contains chelating agents. External ear canals should be irrigated and nasal douches can be effective. The eyes are rinsed by directing a stream of water or saline from the inner canthus to the outer canthus, so that material is not forced into the lacrimal duct. Hair should be shampooed several times with the head deflected backwards over a basin to keep water from the eyes and ears. A hair dryer is used to dry the hair. Clipping of hair may occasionally be necessary.

The skin is washed initially with warm water and mild soap. If this is ineffective, 0.5% hypochlorite or stronger detergents can be used. If the skin becomes damaged or red and sore, cleansing should be discontinued. If contamination is only discovered after patients are admitted to an ED, the entire area through which they have passed should be taped off, surveyed with the help of a radiation physicist and, if necessary, decontaminated. Staff should put on protective clothing and remove nearby patients so as to create a spacious treatment area. Following a radiation incident, all equipment, instruments and work areas used in treating contaminated patients must be thoroughly cleaned.

Monitoring decontamination

Radiation physicists should check the background level of radiation in the ED from time to time so that they have a baseline from which to assess each patient's exposure. Scanning should occur slowly to avoid missing radiation. Headphones should be used or the sound turned off to avoid alarming patients.

Internal contamination

Internal contamination causes no acute clinical effects and it is usually not feasible to confirm its presence before commencing treatment directed at the reduction of absorption, prevention of incorporation into tissues and promotion of elimination. Significant internal contamination has traditionally occurred through wounds or body orifices in small-scale accidents. It could readily occur on a wider scale following the explosion of an RDD, a reactor accident or a nuclear detonation. Absorption would be by inhalation of contaminated air and/or ingestion of foodstuffs contaminated by fallout. Radionuclides that have short effective half-lives, such as technetium used in nuclear medicine ($t_{1/2} = 5$ hours), pose no danger. For isotopes with effective half-lives measured in days, the decision to treat will depend on the likely intake especially via the lungs, whether the drug is concentrated in tissue, such as iodine in the thyroid or uranium or americium in bone, whether the emission is high energy as with cobalt and whether the chemical itself is toxic. The effective half-life combines radioactive and chemical properties and describes the rate of elimination without decontamination.

To assist in the determination of the extent of internal contamination, a 24-hour urine sample should be collected. If gastrointestinal contamination is suspected, a 24-hour stool sample should also be collected.

The commonest isotopes found in Australia are iodine¹³¹, cobalt⁶⁰, caesium¹³⁷, tritium³, americium²⁴¹ and uranium^{235/238}.

Selection of the appropriate technique or drug depends on knowledge of the radionuclide

involved and its physical form.^{4,8} For example, natural uranium is not a significant radiation hazard but enriched uranium found in fuel rods or weapons emits significant levels of gamma radiation if sufficient quantity is present.

Administration of stable iodine in the form of potassium iodate or potassium iodide tablets will reduce uptake by the thyroid gland by up to 90% if given less than 2 hours after intake and by about 50% if in less than 3 hours. Penicillamine will chelate cobalt and Prussian blue will chelate caesium. Sodium bicarbonate and tubular diuretics will increase the excretion of uranium. These agents may be useful for up to 2 weeks. Mobilizing agents, such as antithyroid drugs, increase the natural rate of turnover of a biological molecule and thereby increase excretion. Gastrointestinal decontamination is unusual but an enema might be used to empty the bowel.

Likely developments over the next 10 years

- The cumulative effects on patients of low-dose radiation from repeated diagnostic examinations are by far the largest source of radiation exposure from human activity. Critically appraising the need for complex and repeated examinations and utilizing imaging algorithms to select the most appropriate modality is increasingly important.
- The specialists most used to managing inpatients with acute radiation illness are haematologists and oncologists. Advances in care in these specialties are likely to improve the treatment available.
- There is more of a focus on planning for possible multicasualty incidents now with considerable research into countermeasures that might reduce the effects of radiation and quicker means of dicentric analysis. Thiol compounds with radical scavenging properties, or derivatives thereof, may prove useful.⁹
- The most effective life-saving opportunity in the first 60 minutes following a nuclear explosion will be to shelter people safely

in possible fallout areas in the nearest basement or in the middle of buildings, but not in cars. This is called sheltering in place. In most cases, effective self-decontamination can be performed if straightforward instructions are provided. The appropriate time to evacuate the fallout area should be determined by authorities on the basis of environmental monitoring and communicated to the population in a timely fashion.¹⁰

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24.5 Drowning

David Mountain

ESSENTIALS

- 1** The incidence of non-fatal drownings requiring medical assessment to fatal drownings is around 2 to 20 times greater than fatal drowning.
- 2** The highest rates of drowning occur in children from 1 to 4 years of age and young adult males. In adults that die, many are intoxicated.
- 3** A total of 10% to 20% of fatal drownings have minimal aspiration with asphyxia probably due to laryngospasm, shunting and mucus plug formation. Differences between fresh- and salt-water drowning are unimportant for management.
- 4** Hypothermia following warm-water ($>10^{\circ}\text{C}$) drowning carries a very poor prognosis. Hypothermia following cold-water ($<10^{\circ}\text{C}$) drowning occasionally sees intact neurological outcome after prolonged (>30 minute) resuscitations.
- 5** Better outcomes are associated with initiation of good-quality CPR, with assisted ventilation being the essential component (i.e. aBc), within 10 minutes of witnessed drowning.
- 6** Spontaneously breathing patients should be managed on their side. Active lung drainage procedures and the Heimlich manoeuvre are contraindicated.
- 7** Positive end-expiratory pressure/continuous positive airway pressure are useful therapies in the hospital. Artificial surfactant and inhaled nitric oxide have equivocal results. Extracorporeal membrane oxygenation is being used more frequently for severe lung injury but without good outcome data in drowning.

Introduction

Australia, the driest inhabited continent, has one of the highest reported incidences of drowning in the developed world. It is a major cause of death and disability in youths with peaks in young children and young adult males. Nomenclature and definitions are now generally agreed with all respiratory distress (of any level, e.g. cough, wheeze, rales) from immersion or submersion defined as drowning (fatal or non-fatal).

Good outcomes are mainly determined by pre-hospital factors, particularly witnessed drowning, short immersion times, early cardiopulmonary resuscitation (CPR), prehospital signs of life, and early access to emergency medical services (EMS). An accurate history, well-run resuscitation and informed judgement on prognosis will optimize outcomes, resource use and aid patient management and family interactions. Patients with spontaneous respiration and/or neurological responsiveness on arrival in the emergency department (ED) are expected to recover unless acute respiratory distress syndrome (ARDS) supervenes. Treatment after a non-fatal drowning is mainly supportive,

although extracorporeal membrane oxygenation (ECMO) and direct lung therapy may improve future outcomes.

In many areas, preventative and educative measures (e.g. pool fencing, life vests, life guards, boat licensing) have reduced fatality rates dramatically. Emergency physicians should be strong advocates for these initiatives.

Epidemiology

Rates of drowning have significantly declined worldwide over the last 2 to 3 decades but it is still a major cause of death and disability in young populations. Overall, males drown more frequently, in most age groups with ratios up to 9:1. This seems to have declined recently with ratios around 2 to 4:1. Groups with highest rates of drowning include infants 0 to 4, (up to 10x higher than 5 to 15, particularly males), young adult males (15 to 30 years), epileptics (up to 20x higher), overseas visitors, the mentally disabled and those from deprived/under-resourced communities with poor public health initiatives. More recently, richer populations are over-represented in countries with high rates of home pools.

In young adult males, bravado, inexperience and alcohol lead to many deaths. Alcohol is found in 14% to 60% of adult drownings. The majority of male adult drownings are related to recreational activities. In the elderly, underlying medical illnesses and suicide attempts are more frequently seen. Most of these factors (except age) are associated with worse outcomes. Cold water has been associated with worse outcomes overall (shorter time to submersion in icy waters), although very occasionally younger patients may survive prolonged immersions potentially by rapid brain cooling.

The ratio of those who initially survive (but require medical attention) to fatal drownings is not accurately known because of differences in nomenclature, definitions and the inability to collect all attendances related to drowning, but is estimated at between 2 and 20:1. In a well-conducted observational study from the Netherlands, the ratio of patients admitted to the intensive care unit (ICU) following drowning compared with those who died before admission was 2:1.

Prevention

Prevention of drowning is a major area for ongoing research and an area emergency physicians should strongly advocate for preventative strategies of proven benefit. Marked reductions in drowning rates in developed countries are suggestive prevention works.

Patrolled beaches with shorter submersion times, early, good quality CPR with assisted breathing and early EMS activation are associated with better outcomes. Important educational initiatives include early swimming/survival lessons, CPR training, parental supervision of children, using supervised swimming areas, avoiding mixing alcohol and water activities and appropriate water safety equipment. Protective pool fencing, enforcement of water vehicle alcohol laws, and water and safety regulations enforcement for water activity are also important.

Definitions and terminology

Much confusion has been caused in research and management by imprecise definitions. Phrases commonly used have been near-drowning, dry, wet, active, passive or silent, late or secondary drowning, immersion, submersion, suffocation and asphyxia. Most of these were ill defined and confusing.

In 2015, International Liaison Committee on Resuscitation (ILCOR) concurred on the Utstein style definition: drowning is a process resulting in primary respiratory impairment from submersion/immersion in a liquid medium. Implicit in this definition is that a liquid/air interface is present at the entrance of the victim's airway, preventing the victim from breathing air. The victim may live or die after this process, but whatever the outcome, he or she has been involved in a drowning incident.

'Near-drowning' is redundant as drownings are either fatal or non-fatal. Similarly, 'wet' and 'dry' drownings are redundant as all drowning is wet with differing amounts of aspiration. Descriptions by bystanders for activity in drowning are now only described as 'witnessed' and 'unwitnessed' drowning, according to whether or not entry to the water was observed. The term 'secondary drowning' was used to describe both causative problems drowning (e.g. intoxication, illness) or death due to secondary problems (e.g. ARDS, encephalopathy) and was inherently confusing. Therefore precipitating factors or sequelae should be specifically described. Immersion describes any is the inability to maintain a fluid-free airway interface, whereas submersion implies the whole airway is underwater. They are rarely important distinctions for management or epidemiology.

Pathophysiology

The sequential pathophysiology of drowning is well described:

- Initial submersion/immersion leads to voluntary apnoea if drowning is due to initial loss of consciousness (e.g. cardiac arrhythmia or other catastrophic illness). Unless voluntary, most adult victims panic and

struggle, with spitting or expulsion of fluid from nasal and oral cavities with associated increases in blood pressure (BP) and pulse rate (PR). Slow PR may occur secondary to primitive dive reflexes or cold-induced reflex bradycardias, particularly in children or intoxicated adults, in cold water and late on in drownings.

- After an interval dependent on presubmersion oxygenation, intoxication, injuries, illness, fitness and the degree of panic and struggle, synergistic hypercapnia and hypoxia lead to an involuntary breath known as the 'breaking point', normally reached in under a minute. During this stage, large quantities of water are often swallowed/aspirated. If an individual hyperventilates before diving (a highly dangerous activity), plasma CO₂ concentrations may remain so low that hypoxic unconsciousness occurs before the breaking point is reached. This is known as 'shallow water blackout'.
- Fluid inhalation causes sudden increases in airway pressures, bronchoconstriction, pulmonary hypertension and shunting. In 10% to 20%, laryngospasm reduces further aspiration, with a mucus and foam plug forming (previously called 'dry drowning').
- Secondary apnoea occurs, closely followed by unconsciousness.
- Involuntary gasping respirations lead to lungs flooding and alveolar injury, surfactant loss, increased ventilation/perfusion (V/Q) mismatch, shunting and hypoxia. Vomiting of swallowed fluid is common, potentially causing pulmonary aspiration.
- Hypoxia causes marked bradycardia, hypotension and irreversible brain injury within 3 to 10 min (except occasionally in icy water induced rapid hypothermia), culminating in respiratory or cardiorespiratory arrests.

In fatal drownings, the average lung fluid retrieved is 3 to 4 mL/kg, less than 10% of lung volume. However, the effect on the lungs is dramatic. Experimentally, fresh water and sea water cause alveolar injury by different mechanisms. Fresh water denatures surfactant and damages the alveolar cells. Sea water tends to draw in fluid, wash out surfactant and cause foam formation. Aspirated vomitus and/or chemicals may further complicate the clinical picture. Soap and chlorine in water do not appear to affect outcome. Clinically, the type of water inhaled rarely makes a difference, unless grossly polluted. Electrolyte disturbances are normally minimal and transient except in prolonged arrests, owing to the small volumes aspirated (more than 20 mL/kg are required for major disturbances).

Clinical features and organ-specific effects

Airways/lungs

The major features are intense laryngospasm, bronchospasm, pulmonary hypertension and marked V/Q physiological shunts. Even without overt respiratory embarrassment after drowning, shunts of up to 70% may occur and take up to a week to resolve. In the alveoli, there is surfactant loss, formation of protein-rich exudate and alveolar cell injury, often exacerbated by aspiration pneumonitis, chemicals and secondary infection (in up to 15% of intubated patients), leading to ARDS. The importance of the pulmonary insult in determining outcomes is seen by the level of lung involvement and respiratory distress, from arrest, down to cough or asymptomatic patients clearly stratifying death and morbidity (Table 24.5.1).

Table 24.5.1 Grading of drowning severity—pre-hospital based on cardiorespiratory status

Drowning grade	Dead	Grade 6	Grade 5	Grade 4	Grade 3	Grade 2	Grade 1	Rescue
Submersion time	>1 h/ unknown	<1 h						
Signs at scene/ rescue	Clearly dead	No pulse No breaths	Pulse No breaths	Rales—all fields Hypotension	Rales—all fields BP normal	Rales—some BP normal	Cough only	No signs
Mortality rate (%)	100	88–93	31–44	18–22	4–5	1	0	0%
Management	Transport	CPR—ABC resus	Rescue ventilation	O ₂ —prob ETT	O ₂ —poss ETT	O ₂	Check nil other probs	Nil required
Expected level of care	Forensic	ICU	ICU	ICU	HDU—ICU	ED review	Scene first aid	Nil required

CPR, Cardiopulmonary resuscitation; ICU, intensive care unit; HDU, high-dependency unit.

(Modified with permission from Szpilman D, Bierens JJLM, Handley AJ, Orlowski JP. Drowning. *N Engl J Med*. 2012;366:2102–2110).

24.5 DROWNING

Table 24.5.2 Modell/Conn classification of mental status following drowning

Grade	Description of mental status	Equivalent GCS	Expected Likelihood of good outcome (neurologically intact) (%)
A	Awake/alert	14–15	100
B	Blunted	8–13	100
C	Comatose	6–7	>90
C ₁	Decerebrate	5	>90
C ₂	Decorticate	4	>90
C _{3/4}	Flaccid coma or arrest	3	<20

GCS, Glasgow coma scale.

Brain

The major brain effects are secondary to hypoxic encephalopathy. It is the major cause of death in drownings and a major determinant of survival for drowning arrests (Table 24.5.2). Cerebral oedema, convulsions and persistent vegetative states are observed frequently. Trauma or an underlying medical complaint should be considered in the differential diagnosis in unwitnessed or unexplained events in water resulting in drowning. It is essential to consider this in those drowning involving water transport or motor vehicles, patients with obvious signs of injury involved in shallow pool drownings, patients who are intoxicated and the elderly.

Cardiovascular

Most drowning patients are haemodynamically stable after resuscitation. Most prolonged drownings in arrest will have some degree of hypovolaemia and should have 10 to 20 mL/kg of Nsal. Hypothermic patients may develop any arrhythmia and should be gently handled and aggressively rewarmed (see Chapter 24.2). In older patients, underlying ischaemic heart disease should be considered. Long QT syndrome, and other channelopathies or cardiomyopathies may be associated with arrhythmia in some immersions. Unexplained immersion arrests in patients under 40 should prompt consideration of congenital/familial cardiac syndromes.

Haematological

Haemolysis occurs occasionally in fresh-water drownings.

Renal

Acute tubular necrosis or tubular injury from hypoxia infrequently occur. Electrolyte disturbances are rarely significant.

Gastrointestinal

Vomiting is frequently observed (up to 80% in some series) but may be a marker for better outcomes. It is secondary to ingestion of large volumes of water, potentially aggravated by

poor positioning or use of Heimlich/active lung emptying techniques, with aspiration a significant risk. Diarrhoea is infrequently seen. Hypoxic gut injury may contribute to late multiorgan failure, ARDS and sepsis.

Orthopaedic

Cervical spine injury should always be considered in drownings related to diving into water or with co-existent injuries. Coexistent trauma is more frequent with alcohol, water sports or boating-related drownings.

Treatment

Pre-hospital

Hypoxia (particularly brain hypoxia) is the major cause of early drowning mortality and morbidity, and many late problems. Rapid institution of effective pre-hospital care, particularly early retrieval, supplemented (or exhaled responder) breathing/oxygenation (potentially in water for expert providers, e.g. surf lifesavers) and rapid EMS activation are important factors in determining good outcome following drowning. Early access and activation of EMS is essential. All patients seen alive within 1 hour of removal from cold water (<10°C) should be transported for definitive care. Retrievals by non-expert, untrained bystander swimmers have high rates of retriever drownings (up to 10%) and fatalities. However recreational surfers in some series saved high numbers of distressed swimmers, probably due to their knowledge of local conditions, flotation devices, swimming ability and high rates of first-aid training/experience.

The level of pre-hospital care varies with the clinical severity of the case (see Table 24.5.1), ranging from asymptomatic (the majority) to cardiopulmonary arrest. Initial retrieval from water should be horizontal (avoiding hypovolaemic arrest), and assessment of ABCs may be done with the patient on their side allowing airway fluid drainage if breathing or on their back followed by institution of CPR (with an

ABC emphasis) if respirations or pulse are absent. There is little role for in-water resuscitation, excepting patrolled beach deep water retrievals by properly equipped expert lifesavers who can easily get to shore. Lung drainage procedures (e.g. abdominal compressions) and the Heimlich manoeuvre are dangerous, as they increase gastric aspiration and are contra-indicated. The priority is to re-initiate breathing and, in arrests, A and B are priorities. In particular, rescue breathing (or bagging if available) is obligatory (two breaths if good chest movement), but normally five breaths are required for inadequate chest movements because of poor lung compliance. Victims often vomit upon resumption of spontaneous respiration, and if obtunded, they should be transported on their side (if not intubated) to minimize further aspiration. All symptomatic patients should have supplemental high-flow oxygen. IV fluids for hypovolaemia with 250 to 500 mL boluses of N-Saline are appropriate if IV access is possible and does not delay transport. Wet clothing should be removed gently and the patient dried, wrapped and covered to minimize heat loss. Only if neck trauma is likely should the C-spine be immobilized. People with patient knowledge and/or drowning witnesses should be encouraged to go to the hospital or travel with EMS. A clear rapid history should be taken by EMS and documented.

Emergency department

History

Important factors in the history of arrested drowning include environment of drowning and potential associated factors, such as water temperature/type, submersion duration (or time last seen), time CPR starts, CPR quality and response to first assisted breaths / CPR, time of first spontaneous breath, and/or return of spontaneous cardiac output, initial Glasgow coma scale (GCS) and GCS after resuscitation (Utstein style). A collateral history for health problems (including psychiatric issues), intoxicants, vomiting and potential trauma is also useful.

Initial resuscitation

Initial assessment and resuscitation continue the priorities from pre-hospital being directed towards the assessment and maintenance of ABCs. Monitoring should include oximetry, capnometry, telemetry, BP and core temperature (urinary or rectal probes if obtunded).

Airway management may be just supplemental oxygen or clearing and positioning the airway. Endotracheal intubation is indicated if respiration is ineffective, saturation is poor, lung fields have extensive rales or GCS <8. Patients who cannot maintain PaO₂ of 90 mm Hg on a non-rebreathing mask should be considered for early intubation, although non-invasive ventilation is an alternative in the cooperative patient. Extensive persistent rales suggest a high risk for late respiratory compromise and potential ARDS. Bronchospasm should be treated with nebulized β-agonists, without steroids, unless the patient is a known asthmatic. In the unconscious patient, a nasogastric tube should be placed early after intubation to minimize pulmonary aspiration. All intubated patients require small tidal volume, early positive end-expiratory pressure (PEEP; 10 to 20 cm) and end-tidal CO₂ monitoring.

Most obtunded, arrested patients will require IV fluids, as hypovolaemia is common. Cardiac complications should be managed according to standard treatment regimens, except patients with hypothermia (<33°C). Hypothermic patients (see Chapter 24.2) should be handled gently with antiarrhythmic drugs avoided if possible until rewarming occurs. All rhythms without output require CPR. In general, asystole following drowning has the same dire prognosis as from other causes, particularly if present after adequate pre-hospital resuscitation. Occasional witnessed cold-water (<10°C) arrests in younger patients have had good outcomes after prolonged (60+ min) resuscitations. Hypotension is managed with judicious (e.g. small bolus) fluids and inotropes if unresponsive, with invasive monitoring if persistent, particularly in patients with pulmonary oedema.

The management of hypothermia is described elsewhere in this book (see Chapter 24.2). Where cervical spine injury is a distinct possibility (especially following shallow diving or water vehicle accidents), cervical spine immobilization should be maintained until the C-spine is cleared.

Ongoing management

Intubated patients, especially with obvious chest x-ray infiltrates, should have PEEP and low volume ventilation. Commence with low pressures (5 to 10 cm H₂O) but increase rapidly as tolerated until adequate oxygenation is achieved or hypotension or high airway pressures supervene. Pressure-controlled ventilation may be added but may increase barotrauma and alveolar injury. Use should

be discussed with the ICU providing ongoing care. These modalities improve outcome for near-drowning patients with secondary lung injury. Ventilatory weaning should begin as soon as possible after 24 hours in order to reduce barotrauma. Non-invasive ventilation may be a bridge to intubation or avoiding intubation in some but should always be discussed with ICU. Maintenance of normoglycaemia, normovolaemia, normocarbia, seizure control plus avoiding hyperthermia, hypoxia and hypotension are important for cerebral outcomes. Dehydration and prolonged hyperventilation are dangerous. Induced hypothermia post-arrest from drowning has been an area of some controversy (discussed later). Targeted temperatures between 32°C and 36°C are recommended.

Experimental therapies

A number of other therapeutic modalities have been trialled in an effort to improve the outcome of lung and brain injuries caused by near-drowning. These include the following:

- Induced hypothermia. Popularized by Conn, this therapy offers the theoretical advantage of cerebral protection. Unfortunately, drowning patients were actively excluded from most therapeutic hypothermia trials, ironically because this group was most likely benefitting from environmental hypothermia! Induced hypothermia trials after cardiac arrest from ventricular fibrillation (VF) renewed interest in this area but recent ILCOR recommendations suggest only targeting to a 33°C to 36°C temperature.
- Pharmacological cerebral protection. Barbiturate infusions, steroids, magnesium and chlorpromazine have all been trialled. None has been shown to be of benefit, and all may have deleterious effects.
- Intracranial pressure monitoring. Its use is controversial and lacking in outcome data, and depends on which ICU cares for the patient.
- Prophylactic antibiotics. These are of no value except following drowning in grossly polluted water. In such cases, a second-generation cephalosporin is recommended. Drownings in hot spas and tubs may require anti-pseudomonal cover.
- Hyperbaric oxygen therapy and nitric oxide therapy are of unproven benefit.
- Exogenous surfactant therapy. Has no proven benefit, with some animal research suggesting increased lung injury.
- Extracorporeal oxygenation. Successfully applied in some centres for severe lung injury, particularly hypothermic children. It may be used as a bridge for drowning related ARDS, which should be more reversible than inflammatory ARDS. There are no definitive trials showing benefit.

Clinical investigations

Ordering of investigations in the ED is guided by the clinical status of the patient—in particular, mental and cardiorespiratory status. All symptomatic patients require continuous pulse oximetry and a chest x-ray, which should be repeated at 4 to 6 hours. Using the Modell/Conn classification of mental status (see Table 24.5.2), patients in group A only require a chest x-ray and oximetry. Patients in group B may also require a full blood count, electrolytes and creatinine, blood sugar, arterial blood gases and an ECG. The ECG/rhythm strips should be checked for prolonged QT or ventricular arrhythmias in younger patients with a history of unexpected rapid submersions looking for congenital/familial cardiac problems. Arrhythmias are rare in most drowning patients, excepting bradycardias. If patients do not improve rapidly after ED supplemental oxygen, they should be investigated and managed like group C patients. Patients in group C are recommended to have liver function tests, creatine kinase and troponins, alcohol levels, coagulation profiles, urine dipstick and a computed tomography (CT) head scan if coma persists. Cervical spine x-rays and trauma films are only indicated if trauma is likely. Intracranial pressure monitoring, EEGs, MRI and so on are not normal ED care and should be considered in ICU.

Prognosis

Mortality rates of 15% to 30% and severe neurological disability rates of up to 25% are reported in ICU series (these are highly selected studies). Patients with prolonged (>30 minute) cardiac arrests, poor initial response and no signs of life on ED arrival have almost universal mortality or catastrophic neurological outcomes (see Tables 24.5.1 and 24.5.2). Patients with GCS >8 but persistent hypoxia, early recovery from arrest and/or persistent rales are at high risk of ARDS and multi-organ failure and have relatively high later mortality (persistent rales 4% to 5% to recovered arrest 40%).

Potential prognostic features have been extensively evaluated to try and reduce rates of severely neurologically handicapped survivors, avoid prolonged CPR, and provide staff and relatives with accurate prognostic information. The most useful predictors of neurological outcome relate to the initial resuscitation (field predictors). Factors associated with good outcomes include witnessed drowning, early retrieval times (<10 minutes submersion), good-quality CPR provided within 10 minutes, vomiting, early EMS attendance, a spontaneous breath within 30 min of retrieval and return of spontaneous circulation before ED. Early respiratory efforts post resuscitation are associated with good

24.5 DROWNING

neurological outcome, provided ARDS does not supervene. Pre-hospital factors associated with poor outcome include male sex, cold or fresh water, unwitnessed or prolonged submersion (particularly >25 minutes), prolonged arrests (particularly asystole >30 minutes, almost universally poor outcomes) and long pre-hospital times. Absolute EMS predictors of poor outcome have not been identified, and all drowning patients arriving at ED deserve full assessment and resuscitation efforts, short of clear signs of prolonged death (e.g. lividity, rigor) or clearly unsurvivable combinations of prognostic features. In general, outside of witnessed young, icy water-induced arrests, asystole for longer than 30 minutes can have resuscitation stopped unless trials of ECMO are rapidly available at a nearby hospital.

Emergency department prognostic factors have been identified, although no combination of factors reliably predicts all poor outcome patients. Good ED prognostic features include pupillary response, perfusing cardiac rhythm or any motor response to pain. Asystole, if the only rhythm seen, is predictive of poor outcomes and should lead to consideration of CPR cessation. Hypothermia has been called a favourable prognostic indicator but is highly debatable. Although witnessed ice-cold water immersions are occasionally associated with neural recovery after prolonged resuscitation (probably due to rapid brain cooling), hypothermia normally suggests prolonged submersion and poor prognosis. A recent Dutch series of paediatric patients retrieved from icy waters found all 98 with >30 minute resuscitations died or had severe neurological deficits.

In-hospital factors associated with poor outcome include GCS <5 on transfer to ICU (<20% intact survival; see Table 24.5.2), fixed dilated pupils at 24 hours and any abnormal CT head within 36 hours. A normal CT scan is of minimal prognostic value.

Disposition

All symptomatic drowning victims should be closely observed for 6 hours with pulse oximetry. Any patient with abnormal CXR, widespread rales or hypoxaemia after 6 hours should be admitted to HDU/ICU. Those requiring intubation, persistently obtunded, post-arrest or hypoxaemic require ICU. Truly asymptomatic patients or, non-progressive minor rales with stable adequate oximetry for 6 hours, may be discharged home after observation, but should return if they develop respiratory symptoms.

CONTROVERSIES

- Developing accurate prognostic indicators to decrease persistent severe neurological disability states is important. Most authorities agree that almost all drownings should be aggressively initially resuscitated, but 15% of ICU patients survive in persistent vegetative states, suggesting current resuscitation may be excessively aggressive.
- New treatment modalities for secondary lung injury, including nitrous oxide, artificial surfactant and particularly ECMO, individually or sequentially, is still being studied. Therapeutic hypothermia for the comatose post arrest patient has been de-emphasized, but a temperature should be targeted to below 36°C.
- Use of NIV to avoid intubation in the hypoxic patient with respiratory distress is poorly studied and should occur in discussion with the ICU.

Further reading

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24.6 Electric shock and lightning injury

Daniel M. Fatovich

ESSENTIALS

- 1** Death from electric shock is due to ventricular fibrillation, the lethal arrhythmia occurring at the time of the exposure. Routine admission for ECG monitoring is unnecessary.
- 2** Most deaths are caused by low-voltage (<1000 V) exposures.
- 3** The amount of current passing through the body is determined mainly by tissue resistance, which is dramatically reduced by moisture.
- 4** Electrical injury resembles a crush injury more than a burn. The tissue damage below skin level is invariably more severe than the cutaneous wound would suggest.
- 5** There is a diversity of clinical manifestations seen with electrical injury.
- 6** Lightning injury is different from high-voltage electrical injury and has a unique range of clinical features. The management is predominantly expectant.

ELECTRIC SHOCK

Introduction and epidemiology

Electricity is an integral part of our everyday world and electric shock is common. Patients may present to the emergency department (ED) with resulting injuries that range from trivial to fatal (termed electrocution). Although permanent disability can occur, it is reassuring to note that if the initial exposure is survived, subsequent death is unlikely. For each death caused by electricity, there are 2 serious injuries and 36 reported electric shocks.

There are approximately 20 electrical fatalities each year in Australia. Victims are predominantly male and young. Death is just as likely to occur at home as in the workplace, most often in summer. Electricians and linesmen are most at risk. The ratio of low-to-high-voltage deaths ranges from 3:1 to 7:1. The presence of water is associated with fatality. Electrical burns represent 3% to 5% of admissions to burns units.

Physics of electricity and pathophysiology of electrical injury

Electrical current passing through the body can cause damage in two ways:

- thermal injury
- physiological change.

The threshold for perception of an electrical current is 1 mA, which results in a tingling sensation. Current greater than 10 mA can induce muscular tetany and prevent the patient letting

go of the current source. Paralysis of respiratory muscles occurs at 20 mA. The threshold for ventricular fibrillation is 100 mA (Fig. 24.6.1). Cardiac standstill and internal organ damage occurs at 2 A. The maximum 'safe' current tolerable for 1 s is 50 mA.

Ohm's law is fundamental to the understanding of the physics of electricity. This states that the amount of current passing through the body is directly proportional to voltage and inversely proportional to resistance (current [amperes] = voltage [volts] / resistance [ohms]).

Factors that determine the effects of an electrical current passing through the body are:

- type of current
- voltage
- tissue resistance
- current path
- contact duration.

Type of current

The vast majority of serious electrical injuries result from alternating current (AC), which is approximately three times as dangerous as direct current (DC). Alternating current can produce tetanic contraction of muscle such that the victim may not be able to let go of the current source. This is not a feature of direct current shock.

Human muscular tissue is sensitive to frequencies between 40 and 150 Hz. As the frequency increases beyond 150 Hz, the response decreases and the current is less dangerous. In Australia, a frequency of 50 Hz is used for household current because this is optimal for the transmission and

use of electricity and also has advantages in terms of generation. As such, household current lies directly within the dangerous frequency range. It also spans the vulnerable period of the cardiac electrical potential and is thus capable of causing ventricular fibrillation.

Voltage

Voltage is the electromotive force in the system. In general terms, the greater the voltage, the more extensive the injury, but it must be remembered that the amount of current passing through the body will also be determined by resistance (Ohm's law). High voltage is defined as greater than 1000 V. Household voltage in Australia is 240 V. Voltages less than 50 V (50 Hz) have not been proved hazardous. Survival has been reported following shocks of greater than 50,000 V.

Resistance

Different tissues provide differing resistances to the passage of electrical current. Bone has the highest resistance, followed by, in decreasing

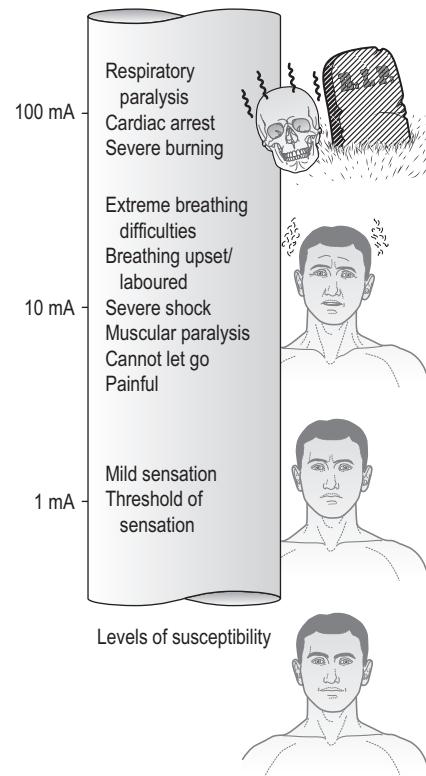


FIG. 24.6.1 The levels of electric shock and their effects.

24.6 ELECTRIC SHOCK AND LIGHTNING INJURY

order, fat, tendon, skin, muscle, blood vessels and nerves. Skin resistance varies greatly according to moisture, cleanliness, thickness and vascularity. Moist skin may have a resistance of $1000\ \Omega$, and dry, thick, calloused skin may have a resistance of $100,000\ \Omega$. By Ohm's law, dry skin resistance to a contact with a $240\ V$ potential results in a current of about $2.4\ mA$, which is just above the threshold for perception. However, the resistance of wet or sweat-soaked skin drops to $1000\ \Omega$, increasing the current flow to $240\ mA$, which is easily enough to induce ventricular fibrillation. Not surprisingly, moisture has been identified as a key factor in over half of electrocutions.

Current path

Prediction of injuries from knowledge of the current path is unreliable. Mortalities of 60% for hand-to-hand (transthoracic) and 20% for head-to-foot passage of current are quoted, but have not been verified. When current passes hand-to-hand (or hand-to-foot), only about 5% of the total current passes through the heart. If current passes leg-to-leg, no current traverses the heart.

Contact duration

The longer the duration of contact, the greater the potential for injury. Fortunately, most contacts are brief and frequently result in the victim being thrown back from the current source. This may result in a secondary injury, especially if the victim falls from a height.

Unfortunately, exposures to more than $10\ mA$ of alternating current can induce sweating. Moisture decreases skin resistance and increases current flow, thereby reducing the ability to release the current source. This can progress to a fatal exposure.

Prevention

All members of the community must be encouraged to treat electricity with respect and to practise electrical safety. Licensed electrical contractors should be used to carry out any electrical repairs or installations. Water and electricity should never be mixed.

Residual current devices are useful in providing an additional level of personal protection from electric shock. These devices continuously compare current flow in both active and neutral conductors of an electrical circuit. If current flow becomes sufficiently unbalanced, then some of the current in the active conductor is not returned through the neutral conductor and leaks to earth. These devices operate within 10 to $50\ ms$ and disconnect the electricity supply when they sense harmful leakage, typically $30\ mA$.

Clinical features

Electrical injury resembles a crush injury more than a burn. Invariably, the damage below skin level is more severe than the cutaneous wound suggests. The current passing through low-resistance structures produces massive necrosis of muscles, vessels, nerves and subcutaneous tissues.

The clinical manifestations differ from thermal burns in the following ways:

- There are direct effects on the heart and nervous system.
- Electrical injury classically involves deep structures.
- The small entry and exit wounds do not accurately indicate the extent or depth of tissue damage.
- A diversity of clinical manifestations is seen with electrical injury.

Burns

As electricity traverses the skin, energy is converted to heat. The smaller the area of contact, the greater the current density, heat production and the consequent skin and adjacent tissue destruction.

Electrothermal burns are best characterized by arc burns, which result from the external passage of current from the contact point to the ground. These may be associated with extensive damage to skin and underlying tissue. Secondary flame burns may occur when the current arc ignites clothing or nearby combustibles.

Electrical burns may range from first degree to third degree. The typical appearance is of a central depressed charred black area surrounded by oedema and erythema. Single or multiple exit wounds may be present.

Cardiac

Ventricular fibrillation is the usual cause of immediate death from electric shock and occurs at the time of the shock. Delayed arrhythmia resulting in death is exceptionally rare. Sinus tachycardia is common and non-specific ST- and T-wave changes may be observed. Atrial fibrillation occurs infrequently and usually resolves spontaneously. Acute myocardial infarction following electric shock has been reported.

Nervous system

Both acute and delayed neurological sequelae have been described following electric shock. Acute complications include respiratory arrest, seizures, altered mental state, amnesia, coma, expressive dysphasia and motor deficits. Reported delayed complications include spinal cord injury (myelopathy) with local amyotrophy and long tract signs, and reflex sympathetic dystrophy.

Peripheral nerve injury is usually associated with significant soft-tissue injury. It has also been reported in the absence of soft-tissue injury, and such cases appear to have a good prognosis.

Renal

Acute renal failure may occur secondary to myoglobinuria. Electric shock results in disruption of muscle cells with the release of myoglobin and creatine phosphokinase, similar to a crush injury. Transient oliguria, albuminuria, haemoglobinuria and renal casts are common, and there have been reports of high-output renal failure.

Vascular

Large and small vessel arterial and venous thrombosis are responsible for the tissue damage in electrical injury. Vascular complications have included immediate and delayed major vessel haemorrhage, arterial thrombosis and deep vein thrombosis.

Musculoskeletal

Tetanic muscle contractures can result in compression fractures of vertebral bodies, fractures of long bones and dislocations of joints. Injuries may also result from a secondary fall, rather than from the electric shock.

Other

Numerous complications involving other systems, including the eye (especially cataracts), have been reported.

Electric shock in pregnancy

Reports of electric shock in pregnancy are rare and the true incidence is unknown. A high mortality has been reported in the literature. However, this may represent publication bias and a prospective cohort study concluded that in most cases, accidental electric shocks during pregnancy do not pose a major foetal risk.

If there was an immediate problem, the mother may notice a sudden cessation of foetal movements. However, there is no preventative action possible in the ED. Other reported foetal complications of electric shock include intrauterine growth retardation, oligohydramnios and abortion.

Fortunately, therapeutic electric shocks, such as DC cardioversion and electroconvulsive therapy, are known to be safe in pregnancy. The critical factor is current path: accidental electric shocks include the uterus, whereas therapeutic shocks do not.

Treatment

Pre-hospital

Everyone should be aware of the pre-hospital management of electric shock. Most importantly,

the rescuer should avoid becoming a further victim. The victim can be separated from the electrical source by using rubber, a wooden handle, a mat or any other non-conductive substance or, if possible, by turning off the electricity supply. Cardiopulmonary resuscitation (CPR) should begin immediately, if indicated, and help summoned. CPR may need to be prolonged. Ventricular fibrillation is the most common lethal arrhythmia after electric shock, and early defibrillation provides the greatest chance for survival.

Emergency department

The majority of patients who present to the ED after electric shock are well. Following appropriate assessment to exclude primary or secondary injury, an ECG should be performed. Cardiac monitoring is not indicated if the patient is asymptomatic and has a normal ECG. Most patients can be reassured and discharged directly from the ED. Routine measurement of creatine phosphokinase levels or troponin is not required. It should be acknowledged that exposure to an electric shock is an unpleasant experience. Tetanus status should be checked.

Many patients have a degree of muscle pain following electric shock owing to the tetanic nature of alternating current. Simple analgesia is appropriate. Any secondary injury, such as fractures or loss of consciousness, should be treated as dictated by the injury.

If an arrhythmia is present, it will usually resolve spontaneously and not require specific treatment. Delayed lethal arrhythmias have not been reported in patients without initial arrhythmias.

Severe electrical injury with extensive soft-tissue damage should be managed as a crush injury. This is more likely following high-voltage exposure, which results in a large exudation and sequestration of fluids in the damaged area. Emergency management includes adequate volume replacement and treatment of acidosis and myoglobinuria.

Emergency physicians should be aware of the low potential for foetal harm following electric shock in pregnancy. It would be prudent to adopt a conservative approach of performing a foetal heart Doppler assessment with obstetric follow-up, including ultrasound.

Prognosis

The prognosis for the majority of patients surviving the initial shock is excellent. Those with significant soft-tissue injury or secondary injury may be left with long-term deficits.

Disposition

The majority of patients presenting to the ED following an electric shock will be suitable for

discharge following assessment and reassurance, as detailed previously. Those suffering muscle pain secondary to tetanic contractions should be given simple analgesia and instructed to follow up with their general practitioner.

Patients with cardiac arrhythmias require admission for observation until the arrhythmia resolves. Those with evidence of neuropathy should be referred to a neurologist, as nerve conduction studies may be required.

Severe electrical injuries with extensive soft-tissue damage require admission to hospital and, sometimes, to an intensive care unit. All patients with electrical burns should be reviewed by a burns specialist, and referral to a specialist burns unit may be indicated. Minor burns may be suitable for elective review.

Secondary injuries, such as loss of consciousness or fractures, should be admitted or referred on their merits.

The Taser

The Taser is a development of the stun gun. It is used by police to fill the operational gap between the baton and the gun for controlling potentially dangerous and violent suspects. 'Tasered' victims are occasionally brought to the ED for assessment.

The device is a battery-operated unit resembling a handgun that fires two barbed electrodes on 7 m long copper wires at 60 m/s. The barbs attach to the subject's skin or clothing and deliver up to 50,000 V of electricity in rapid pulses over 5 s. The current can cross up to 5 cm of clothing.

Electricity delivered by a Taser is neither pure AC nor pure DC and is probably akin to rapid-fire low-amplitude DC shocks. The output is believed to stay near the surface of the body in the skin and muscles and does not penetrate into the internal organs. There is no evidence to date that this form of electrical delivery interfered with cardiac or neurological function in the 30,000 volunteers or in the reported operational uses.

One author concluded that the pre-existing injuries and toxic conditions leading to the patient being tasered are the most important problems requiring medical treatment after Taser use. It seems that the device is essentially safe on healthy people. However, there is limited evidence to base recommendations for the assessment and management of patients that are brought to the ED after being 'tasered'. Suggestions for management include:

- Most healthy subjects may be safely discharged after barb removal and a clinical assessment.
- High-risk patients are those with known cardiac disease including implanted pacemaker or defibrillator, pregnancy, drug or

alcohol intoxication, bizarre behaviour at the time of arrest, other psychiatric disturbance or coincidental medical problems. Often the coexistent condition (e.g. intoxication or mental health issue) will need to be addressed.

- Any patient with chest pain or abnormal ECG should be assessed as per routine clinical practice.
- Pregnant women >24 weeks' gestation should be considered for cardiotocographic monitoring.
- Look closely for direct injury from the barbs or indirect injury from falls. Barb injuries should be approached as a potential penetrating injury and managed accordingly. There are likely to be small puncture wounds and minor burns at the barb sites. On occasion, medical intervention will be required if the barbs are not easily removed, if the barb tip breaks off in the skin or if the barbs have struck vulnerable areas (e.g. mouth, eyes, neck and groin).
- Most patients will complain of muscle aches and anxiety.
- It is clear that, when properly used as a method of restraining violent people, Tasers are less likely than guns to cause injury and death of the target (and of the police officer). They are also generally more effective than other methods of restraint. The deaths that have followed Taser use have occurred in people who were out of control and who had taken potentially fatal drugs. It is likely that the deaths would have occurred whether or not the Taser was used. However, the medical effects of multiple shocks on such persons are unknown.

LIGHTNING INJURY

Introduction and epidemiology

There are several deaths each year in Australia from lightning. For each death, there are five injuries. These events are always prominent, and emergency physicians should be familiar with the pathophysiology.

Many myths surround lightning injury; they include:

- Lightning strike is invariably fatal. In fact, the mortality is 30%. In addition, the probability of long-term impairment after recovery is low.
- A victim of lightning is charged and dangerous to touch. This false notion has led to the withholding of CPR, with fatal results.
- Lightning should be treated in the same way as high-voltage electrical injury. This is incorrect.

24.6 ELECTRIC SHOCK AND LIGHTNING INJURY

Table 24.6.1 Lightning versus high-voltage injury

Factor	Lightning	High voltage
Time of exposure	Brief instantaneous	Prolonged tetanic
Energy level	100 million V 200,000 A	Usually much lower
Type of current	Direct	Alternating
Shock wave	Yes	No
Flashover	Yes	No

(Adapted from Cooper MA. Lightning injuries. In: Auerbach PS, Geehr EC, eds. *Management of Wilderness and Environmental Emergencies*. New York: Macmillan; 1983:500–521.)

Physics

Lightning occurs most commonly during thunderstorms. Particles moving up and down in a thunderstorm create static electricity, with a large negative charge building up at the bottom of clouds. Electrical discharge (lightning) occurs as a result of the great charge difference between the negatively charged thundercloud underside and the positively charged ground. The duration of the lightning stroke is between 1 and 100 ms.

Lightning strike is very different from high-voltage electric shock (Table 24.6.1) and produces different clinical effects, requiring a different management approach.

An interesting phenomenon called 'flashover' seems to save many victims from death by lightning. Current passes around and over, but not through, the body. The victim's clothing and shoes may be blasted apart. Only cutaneous flame-type burns result.

Clinical features

Immediate

- Asystolic cardiac arrest, as opposed to the ventricular fibrillation of electric shocks. The heart is thought to undergo massive depolarization. Although primary lightning-induced arrest may revert quickly, it can be followed by secondary hypoxic arrest.
- Chest pain and muscle aches.
- Neurological deficits. A person struck by lightning may be rendered unconscious. On first regaining consciousness, they may be mute and unable to move. This is transient and usually resolves within minutes, but may take up to 24 h.
- Contusions from shock waves.
- Tympanic membrane rupture.

Delayed

- Keraunoparalysis. Lightning-induced limb paralysis is extremely common. Flaccidity

and complete loss of sensation of the affected limb are observed. Peripheral pulses are generally impalpable, and the affected limb takes on a mottled, pale, blue appearance. The mechanism is unclear, but may be lightning-induced vasospasm. The condition is self-limiting and resolves within 1 to 6 hours.

- 'Feathery' cutaneous burns (Lichtenberg flowers). These burns, pathognomonic of lightning injury, may appear immediately but more often become visible a few hours after injury. Burns may be severe but heal remarkably easily.
- Cataracts. Occur more commonly than following electrical injuries.
- Myoglobinuria and haemoglobinuria are rare.

Other

- Sensorineural deafness
- Vestibular dysfunction
- Retinal detachment
- Optic nerve damage

Reports of lightning strike in pregnancy reveal a high rate of foetal death *in utero*, despite maternal survival.

Treatment

Pre-hospital

The important principle is that those who appear dead should be resuscitated first. Immediate institution of CPR in the field for those in asystole prevents secondary hypoxic cardiac arrest during the interval until cardiac function resumes spontaneously. Fixed dilated pupils should not be taken as an indicator of death after lightning strike.

Emergency department

Most lightning strikes are unwitnessed, and diagnosis may be difficult in the unconscious or confused patient. The diagnosis should be considered where such patients were found outdoors in stormy weather. The presence of multiple victims, exploded clothing, linear or

punctate burns, keraunic markings or tympanic membrane rupture all add weight to the diagnosis. The differential diagnosis includes cerebrovascular event, seizure disorder, spinal cord injury, closed-head injury, Stokes–Adams attack, myocardial infarction and toxin effects.

Standard trauma resuscitation measures should be adopted. Examination of the ears for tympanic rupture and eyes for lens/corneal defects, retinal detachment and optic nerve injury is especially important. If the conscious state deteriorates after arrival, cranial computed tomography scan is indicated. Examination of the cardiovascular system should include an ECG.

Burns are rarely more than superficial and are managed expectantly using standard treatments. Tetanus prophylaxis should be arranged.

Treatment of lightning-induced limb paralysis is expectant. If it does not resolve within a few hours, other causes should be considered. Fasciotomy is unnecessary.

Standard therapy for ocular complications, such as retinal detachment or cataracts, is indicated. Baseline visual acuity should be documented for future reference.

Prognosis and disposition

For survivors of the initial strike the prognosis is excellent unless significant secondary injury has occurred. Admission for observation is indicated for those with abnormal mental status or ECG, or with significant burns or traumatic complications. The burns usually heal well, and grafting is rarely required. For those with ocular complications, long-term ophthalmic follow-up is necessary.

Further reading

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24.7 Altitude illness

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ESSENTIALS

- 1** The high-altitude syndromes—acute mountain sickness (AMS), high-altitude cerebral oedema (HACE) and high-altitude pulmonary oedema (HAPE)—are all clinical diagnoses, where management may need to be undertaken without access to diagnostic testing.
- 2** AMS and HACE represent stages along a continuum owing to cerebral vasodilatation and cerebral oedema, while in HAPE the oedema manifests in the lungs.
- 3** Descent is the single best treatment for AMS, HACE and HAPE; however, milder cases in selected settings may be able to be managed with rest and/or oxygen.
- 4** Additional drug treatments may be used in the treatment of established altitude illness. The most often employed therapies are dexamethasone for AMS/HACE and nifedipine for HAPE.
- 5** Prevention is best achieved by controlled ascent, with adequate time for acclimatization.
- 6** Low-dose acetazolamide provides effective prophylaxis against AMS.

Introduction

Altitude illness comprises a number of syndromes that can occur on exposure to the hypobaric hypoxic environment of high altitude. At any altitude, the partial pressure of inspired oxygen (P_O_2) is equal to 0.21 times the barometric pressure minus water vapour pressure of 47 mm Hg. At an altitude of 5500 m, barometric pressure is halved. On the summit of Mount Everest (8850 m), the P_O_2 is only 43 mm Hg, and a typical climber without oxygen can be expected to have a PaO_2 of <30 mm Hg and a $PaCO_2$ of about 13 mm Hg.¹ In addition to the hypoxic stress of altitude, a subject may also be exposed to cold, low humidity, fatigue, poor diet and increased ultraviolet radiation. For the emergency physician, the unique feature of altitude illness is that it requires recognition and treatment in the field, frequently without access to sophisticated diagnostic and imaging techniques, and often without access to rapid evacuation.

Epidemiology and pathophysiology

The human body has the capacity to acclimatize to hypoxic environments. This is principally achieved by increasing ventilation (the hypoxic ventilatory response effected by the carotid body), increasing numbers of red blood cells (via stimulation of erythropoietin), increasing the diffusing capacity of the lungs (resulting from

increased lung volume and pulmonary capillary blood volume), increasing vascularity of the tissues, and increasing the tissues' ability to use oxygen (possibly owing to increased numbers of mitochondria and oxidative enzyme systems).

In some individuals, exposure to low PO_2 initiates a sequence of pathophysiological changes, which result in oedema formation in the brain and lungs. The altitude illness syndromes, acute mountain sickness (AMS), high-altitude cerebral oedema (HACE) and high-altitude pulmonary oedema (HAPE), are the result of this oedema formation. The exact mechanism of these pathophysiological changes is still debated, but vasodilatation is a key part.

In the brain, the development of oedema causes intracranial pressure (ICP) to rise. Initially, this is partially compensated for by displacement of cerebrospinal fluid (CSF) into the spinal space, and adjustment of the balance between production and absorption of CSF. However, once these compensatory mechanisms are overwhelmed, ICP can rise beyond the cerebral perfusion pressure. Without intervention, cerebral blood flow ceases and the patient dies.

In the lung, non-cardiogenic pulmonary oedema develops. A significant rise in pulmonary artery pressure appears to be a crucial pathophysiological factor.² Impaired sodium driven clearance of alveolar fluid may contribute to HAPE.³ It has been postulated that uneven pulmonary vasoconstriction increases the filtration pressure

in non-vasoconstricted lung areas, worsening the interstitial and alveolar oedema.

The tendency to develop altitude illness is idiosyncratic. The major predisposing factors are the rate of ascent and the altitude reached. It is not related to physical fitness or gender. Individuals vary in their ability to compensate for changes in ICP, and in their pressor responses to hypoxia. This may explain the reproducibility of AMS, HACE and HAPE in susceptible individuals, and why some, and not others, develop symptoms at the same altitude. The risk is higher in those who have an impaired ventilatory response to hypoxia in normobaric conditions, and with dehydration, vigorous exercise and the use of depressant drugs.

Prevention

The best form of prevention is gradual ascent to allow sufficient time for acclimatization.⁴ Although individuals vary in how quickly they acclimatize, a sensible recommendation is sleeping no more than 500 m higher than the previous day once above 2500 m. Keeping warm, avoiding alcohol, maintaining hydration and eating a high-carbohydrate diet to improve the respiratory quotient may all decrease the incidence of altitude illness. Modest exercise on acclimatization days should be encouraged.

Acclimatization is not always practical or possible, and so pharmacological agents may be required.⁴ Acetazolamide reduces the incidence and severity of AMS/HACE when used prophylactically in subjects experiencing rapid ascent.⁵ Doses recommended have decreased as a result of ongoing research.⁶ Chemoprophylaxis can be achieved with 125 mg bd, starting the day before ascent and continued for 2 days after reaching high altitude. Dexamethasone 4 mg bd may be equally effective, and may be more so when a rapid onset is required, such as in unacclimatized personnel involved in high-altitude rescue missions. Ibuprofen has more recently been suggested as chemoprophylaxis for AMS. Whether it simply masks symptoms or speeds acclimatization is debatable.⁷

Nifedipine 20 mg slow-release tds or 30 mg bd provides protection against HAPE in susceptible individuals. More recent research suggests that other drugs such as sildenafil, tadalafil and salmeterol may have a role in HAPE prevention, but it is generally advised that vasodilators not be combined.