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REVIEW

Autopsy approach to stroke

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Stroke is a major cause of morbidity and mortality but the brain and other relevant tissues are often examined only cursorily when stroke patients come to autopsy. The pathological findings and clinical implications vary according to the type of stroke and its location and cause. Large ischaemic strokes are usually associated with atherosclerosis of extracranial or major intracranial arteries but can be caused by dissection. Most small cerebral infarcts are caused by arteriosclerosis or, in the elderly, cerebral amyloid angiopathy (CAA). However, vasculitides and coagulopathies can cause a range of different patterns of ischaemic (and, occasionally, haemorrhagic) stroke. Global brain ischaemia, caused by severe hypotension or raised intracranial pressure, produces damage that is accentuated in certain regions and neuronal populations and may be confused with hypoglycaemic injury. The main cause of subarachnoid haemorrhage is a ruptured berry aneurysm but CAA, arteriovenous malformations and infective aneurysms are occasionally responsible. These can also cause parenchymal brain haemorrhage, although this most often complicates hypertensive small vessel disease. Sometimes the haemorrhage arises from a neoplasm. Performing an adequate autopsy in stroke requires proper preparation, awareness of the likely pathological processes, familiarity with intracranial vascular anatomy, careful gross examination and dissection, and appropriate use of histology.

Keywords: brain haemorrhage, brain infarct, brain ischaemia, stroke, thrombophilia, vascular malformation, vasculitis, vasculopathy

Abbreviations: AVM, arteriovenous malformation; CAA, cerebral amyloid angiopathy; CADASIL, cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy; CNS, central nervous system; dAVF, dural arteriovenous fistula; HHT, hereditary haemorrhagic telangiectasia; ICP, intracranial pressure; TTP, thrombotic thrombocytopenic purpura

Introduction

The term stroke describes the sudden loss of neurological function that results from blockage or rupture of a blood vessel supplying the brain or spinal cord. Approximately 80% of strokes are caused by cerebral infarction (see below). Stroke is a major cause of morbidity and mortality. In most parts of the world, it is the second or third commonest cause of death (accounting for 7–10%) after cardiac disease and cancer. Of survivors, about 30% die within 1 year and over 50% within 6 years; in general, most survivors will have impaired vocational capacity, about 30% will need help in caring for themselves and about 15% will require institutional care.

The annual risk of having a stroke more than doubles every decade over the age of 55 years,[1] increasing from about 1–2 per 1000 between 45 and 54 years of age to 11–13 per 1000 in the over-75s. In some groups (e.g. American Indians), the risk is more than double that in the wider population. Although the data indicate that stroke is a major healthcare challenge, it is worth noting that in much of the developed world the incidence has declined over several decades; the reasons are not fully understood but improved

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recognition and control of hypertension, and reductions in cigarette smoking, are probably contributory factors.

Scope of this review

Although stroke is a major cause of death and disability, the brain and other relevant tissues are often examined only cursorily when stroke patients come to autopsy. This is a disservice to their next-of-kin, the clinicians responsible for their assessment and care, and society in general, as findings of genetic or medicolegal relevance are missed, standards of clinicopathological correlation and audit are debased, and opportunities for teaching and research are lost.

The aim of this review is to provide basic guidance to pathologists undertaking the post-mortem examination of stroke patients. It includes an overview of the causes and types of stroke, their pathological features and an approach to their post-mortem investigation. It does not deal with haemorrhagic and hypoxic–ischaemic brain damage in the neonate or with the molecular pathogenesis of ischaemic or haemorrhagic brain damage, complex topics that are extensively covered in reference books and more focused reviews.[1–4] Although the present review refers to some types of vascular pathology that occasionally result from trauma, it does not cover extradural and subdural haemorrhage, which mainly result from trauma and are more appropriately considered in that context. Finally, the main focus of this article is the pathology of cerebrovascular disease and the conduct of the autopsy after stroke-related death; although there is some reference to clinical features and genetic aspects of stroke, these are not described in any detail.

Causes of stroke

VASCULOPATHIES AND VASCULITIDES

The vasculopathies and vasculitides can be broadly subdivided into diseases of large and small vessels (Table 1). These diseases can manifest in several ways, the most common of which is infarction. In the case of thrombosis of a large artery supplying blood to the brain or spinal cord, the infarct typically conforms to the corresponding arterial perfusion territory (Figure 1). Thrombosis of small arteries and arterioles produces small, so-called lacunar infarcts (Figure 2); because most small vessel diseases are generalized or at least multifocal within the central nervous system (CNS), these lacunar infarcts tend to be multiple and to involve multiple arterial perfusion territories.

Large atherosclerotic arteries (usually extracranial) may act as sources of embolism of thrombus or atheromatous material. Less often, thromboembolism complicates arteritis or berry aneurysms. Embolic occlusion typically involves multiple small arteries within the perfusion territory of the originating vessel and causes multifocal infarction, often haemorrhagic.

Two types of small vessel disease, arteriosclerosis/arteriolosclerosis and Aβ cerebral amyloid angiopathy (CAA), are the commonest causes of parenchymal brain haemorrhage. Arteriosclerosis/arteriolosclerosis-related haemorrhage tends to be deep-seated within the brain (involving the basal ganglia, thalamus, pons or cerebellum) and to rupture into the ventricular system. CAA-related haemorrhage tends to occur within the cerebral cortex and superficial white matter, and may extend into (or occur within) the subarachnoid space. In CAA, the risk of haemorrhage is increased by the development of 'vasculopathic' complications, particularly concentric splitting of the vessel wall or fibrinoid necrosis (Figure 3). Rarely, CAA is associated with a surrounding lymphocytic infiltrate[5] or complicated by a vasculitis in which a destructive inflammatory reaction, usually granulomatous, is centred on Aβ deposits in the vessel walls (Aβ-related angiitis).[6] CAA can also be complicated by thrombosis and carries an increased risk of microinfarcts.[7]

Arterial dissection (Figure 4) is largely a disease of large vessels – the carotid artery, its proximal branches and the vertebral arteries – although smaller intracranial arteries can be affected. Most patients have a history of recent blunt trauma or hyperextension of the neck but the 'trauma' may be mild (e.g. chiropractic manipulation of the neck), and vertebral or internal carotid dissection sometimes occurs without an identifiable precipitating event. Extracranial dissections tend to produce arterial occlusion and infarction and intracranial dissections subarachnoid haemorrhage.

The commonest type of aneurysm affecting the CNS is the berry (saccular) aneurysm, which is present in 2–5% of adults. These aneurysms almost always involve branch points of the major intracranial arteries (Figure 5) and the majority involve the anterior part of the circle of Willis (i.e. the proximal branch points or junctions of the internal carotid, middle cerebral, anterior cerebral and anterior communicating arteries). The major clinical complication is rupture and consequent haemorrhage; this is usually into the subarachnoid space and is often associated with retrograde spread of blood into the ventricles, but sometimes the fundus of the aneurysm is partly embedded in the adjacent brain, and rupture produces

Table 1. Major vasculopathies and vasculitides affecting the CNS

Type of vessel	Disease	Risk factors/cause	Major sites (in relation to neurological disease)	Main pathological findings
Large vessel	Atherosclerosis	Age Hypertension Cigarette smoking Diabetes mellitus Family history Dyslipidaemias	Aortic arch Bifurcation of carotid arteries Origin of vertebral arteries Basilar artery Terminal part of internal carotid arteries	Atherosclerosis (as in vessels elsewhere) ± Large (major arterial territory) CNS infarct ± Embolic lesions – multifocal infarcts, often haemorrhagic ± Aneurysmal dilatation, especially in vertebrobasilar region
	Dissection	Blunt craniocervical trauma Neck hyperextension Atherosclerosis Rarely, cystic medial necrosis, fibromuscular dysplasia, arteritis, inherited connective tissue diseases	Extracranial part of internal carotid artery close to skull base Supraclinoid internal carotid artery Intraosseous part of vertebral artery Intracranial part of vertebral artery	Dissection associated with intramural haematoma, usually beneath the external elastic lamina but sometimes in the subintimal region or within the tunica media ± Large (major arterial territory) CNS infarct ± Subarachnoid haemorrhage
	Giant cell arteritis		Ophthalmic artery Carotid artery Vertebral/basilar artery	Segmental chronic intramural inflammation, usually giant cells along the internal elastic lamina with corresponding loss/phagocytosis of elastic; subsequent collagenous scarring ± Large (major arterial territory) CNS infarct
	Fibromuscular dysplasia	α1-antitrypsin deficiency	Upper cervical part of internal carotid artery Intraosseous part of vertebral artery	Segmental collagenous thickening and disorganisation of intima/tunica media/adventitia Usually nonspecific manifestations of intermittent/postural brain stem or hemispheric ischaemia without CNS pathology but can cause major infarcts, or subarachnoid haemorrhage (when complicated by aneurysm formation)
	Takayasu's arteritis	Predominantly Japan	Aorta and its proximal branches	Lymphoplasmacytic inflammation involving tunica media in aortic arch with subsequent collagenous fibrosis Usually nonspecific manifestations of intermittent/postural brain stem or hemispheric ischaemia without CNS pathology May be associated with upper-body or renovascular hypertensive vascular disease (complicating aortic or renal artery stenosis)

Table 1. (*Continued*)

Type of vessel	Disease	Risk factors/cause	Major sites (in relation to neurological disease)	Main pathological findings
	Moyamoya syndrome	Commonest in (but not restricted to) Japan	Supraclinoid internal carotid artery Proximal middle/anterior cerebral artery	Marked collagenous thickening of the intima and striking plication of the internal elastic lamina ± evidence of thrombosis and recanalisation Very prominent dilated collateral vessels Multifocal/widespread ischaemic cerebral damage
	Berry aneurysm	Peak detection in late middle age Family history Cigarette smoking Alcohol consumption Hypertension (associated with rupture)	Major artery branch points >85% involve terminal internal carotid/anterior communicating/proximal middle cerebral artery <15% involve vertebrobasilar arteries	Aneurysm is usually obvious once artery is exposed (best done before fixation) Wall shows patchy/complete loss of internal elastic lamina and tunica media May be scanty inflammatory infiltrate in wall, including haemosiderin-laden macrophages Lumen usually contains old thrombus
Small vessel	Arteriosclerosis and arteriolosclerosis	Age Hypertension Diabetes mellitus	Deep cerebral grey matter structures Cerebral white matter Pons	Hyaline collagenous thickening of vessel walls with narrowing of lumina Loss of tunica media Increased vascular tortuosity ± microaneurysmal outpouchings Enlarged perivascular spaces ± Fibrinoid necrosis ± Foci of recent/old haemorrhage, small or large ± Lacunar infarcts ± Deep white matter rarefaction and gliosis
	Cerebral amyloid angiopathy (CAA)	Possession of *APOE* $\varepsilon 4$ is risk factor for commonest form (Aβ-CAA), particularly in Alzheimer's disease Other specific genetic mutations in much rarer forms of CAA	Cerebral cortex and leptomeninges (often most severe in occipital region) Less often cerebellar involvement	Patchy mural deposition of Aβ (mainly $A\beta_{1-40}$), initially in basement membrane along outer aspect of tunica media, then around smooth muscle cells, eventually replacing media and extending through adventitia into surrounding brain parenchyma ± 'Vasculopathic' changes: concentric splitting of vessel wall, fibrinoid necrosis, thrombosis, microaneurysmal dilatation ± Small perivascular haemorrhages in cortex ± Circumscribed lobar parenchymal haematomas ± Subarachnoid haemorrhage ± Lacunar infarcts and ischaemic lesions in cerebral cortex (8)

Table 1. (*Continued*)

Type of vessel	Disease	Risk factors/cause	Major sites (in relation to neurological disease)	Main pathological findings
	Primary angiitis of the CNS (PACNS)	Occasionally related to varicella-zoster virus infection	Small arteries/arterioles in leptomeninges or anywhere in CNS parenchyma	Multifocal segmental chronic inflammation adjacent to and within the vessel walls, often granulomatous, ± fibrinoid necrosis ± Lacunar infarcts ± Small foci of parenchymal brain haemorrhage ± Subarachnoid haemorrhage
	CAA-related inflammation and Aβ-related angiitis (ABRA)	Variant of PACNS in which the inflammation is directed against Aβ in the vessel wall (i.e. a complication of Aβ-CAA)	Cerebral cortex and leptomeninges	Multifocal segmental chronic inflammation adjacent to and within the walls of Aβ-laden vessels, (5) often granulomatous and with fragments of Aβ in some of the macrophages and giant cells, ± fibrinoid necrosis ± Small perivascular haemorrhages in cortex ± Circumscribed lobar parenchymal haematomas ± Lacunar infarcts and ischaemic lesions in cerebral cortex and underlying white matter ± White matter oedema (sometimes marked) ± Occasionally plaque-associated clusters of microglia in cerebral cortex (6)
	Cerebral autosomal dominant arteriopathy with subcortical infarcts and eukoencephalopathy (CADASIL)	*NOTCH3* mutations	Cerebral leptomeninges Cerebral white matter Deep cerebral grey matter structures Brain stem	Small arteries and arterioles in leptomeninges and white matter show fibrosis and loss of the tunica media, which is progressively replaced by deeply eosinophilic, moderately PAS-positive granular material Small arteries and arterioles in other tissue (e.g. skin) show similar but much less marked changes, demonstrable by electron microscopy Multiple lacunar infarcts White matter rarefaction and gliosis
	Infective vasculitis/ aneurysm	Septicaemia Endocarditis Immunodeficiency (especially fungal vasculitis) Meningovascular syphilis	Small arteries and arterioles in leptomeninges and brain parenchyma Occasionally major artery at base of brain	Focal vessel wall necrosis, thrombosis Associated infarcts/abscesses or foci of haemorrhage Bacteria demonstrable by Gram stain (may be difficult to find, especially if patient has received antibiotics) Fungal hyphae usually easy to see, particularly with Grocott silver impregnation or PAS stain Meningovascular syphilis causes infiltration of artery wall by lymphocytes and plasma cells and later marked fibrous thickening and stenosis

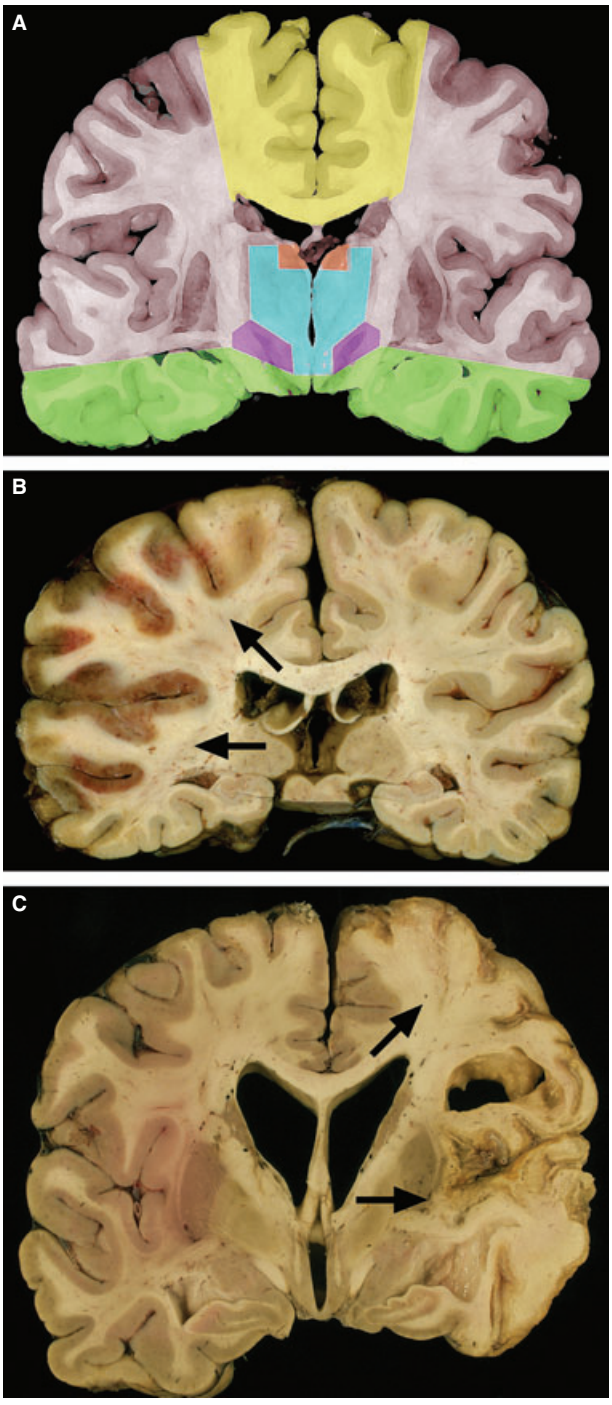

Figure 1. Infarcts associated with large artery occlusion. **A**, In this brain slice in the coronal plane of the thalamus, the shading with different colours gives an approximate indication of the perfusion territories of the anterior cerebral arteries (yellow), middle cerebral arteries (greyish brown), posterior cerebral arteries (green), thalamic perforating arteries (blue), anterior choroidal arteries (purple) and posterior choroidal arteries (orange). **B**, Acute infarct (arrows) caused by occlusion of the left middle cerebral artery. The extent of cortical infarction is clearly indicated by the associated congestion and dusky brown discolouration. The extent of white matter infarction is not yet well defined on macroscopic examination. **C**, Old right middle artery territory infarct (arrows). The infarcted cortex is yellowish brown and markedly thinned. The white matter is partly cavitated, and intact regions have a chalky appearance, reflecting the breakdown of myelin and accumulation of cholesterol esters.

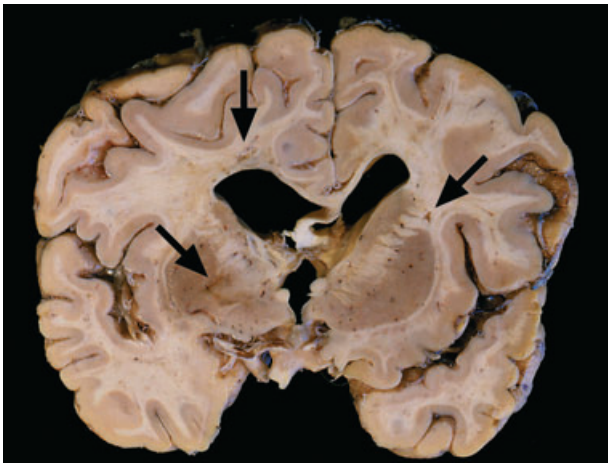

Figure 2. Lacunar infarcts and ischaemic white matter damage. This brain slice is from a patient who had vascular dementia associated with arteriosclerotic small vessel disease. The slice shows several lacunar infarcts (arrows) as well as a mottled pattern of ill-defined yellowish grey discolouration of the white matter (including the corpus callosum). Despite the severity of the small vessel disease, the larger arteries in the brain slice show only mild atheroma.

an intraparenchymal haemorrhage. Atherosclerotic aneurysms are much less common than berry aneurysms and usually occur in the vertebrobasilar region; they may be complicated by thrombosis and/or embolism but rupture is rare. In a minority of patients, atherosclerotic, dissecting or berry aneurysms (see below) present with neurological deficits resulting from compression of adjacent cranial nerves, arteries or brain structures by the abnormally dilated blood vessel.

Bacterial vasculitis usually occurs in the context of septicaemia with or without endocarditis and septic emboli (Figure 6) and fungal vasculitis in the context of immunodeficiency. Both can involve large basal arteries but more often affect small arteries, arterioles and venules. Infective vasculitis tends to cause thrombosis and infarction but can also cause weakening, aneurysmal dilatation and rupture of the vessel wall, with resulting subarachnoid or parenchymal brain haemorrhage. Because infective aneurysms are mostly small and embedded in thrombus, they can rarely be identified macroscopically; their diagnosis usually requires histological assessment.

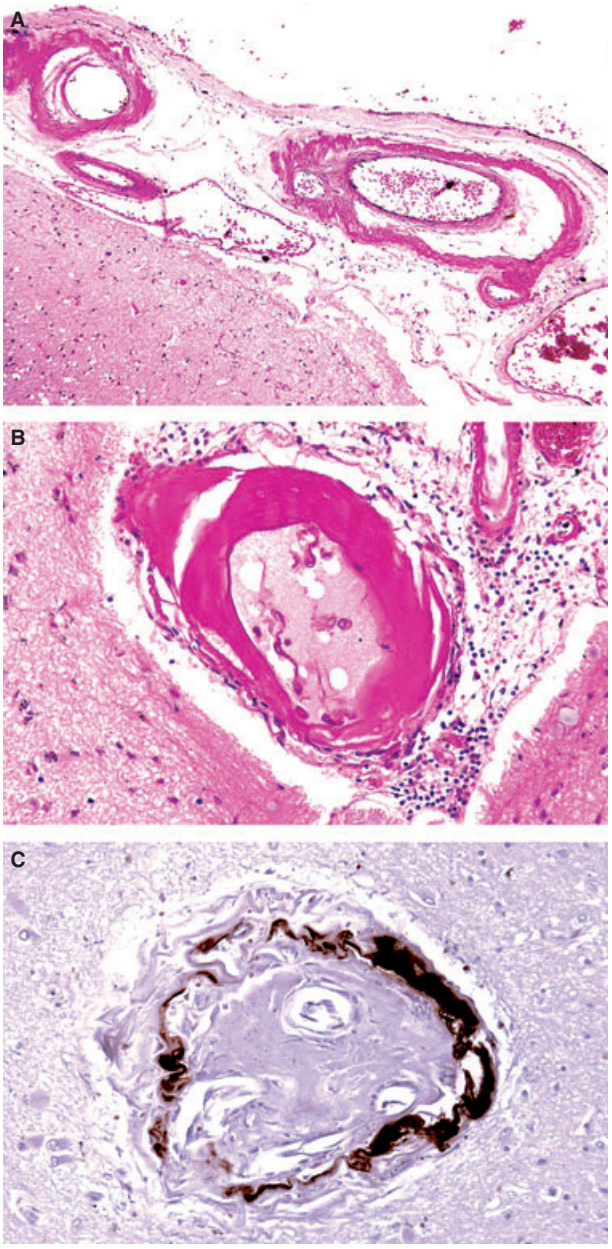

Figure 3. Vasculopathic abnormalities in Aβ cerebral amyloid angiopathy (CAA). **A**, Amyloid-laden vessels in the meninges show concentric splitting of the vessel walls. **B**, Fibrinoid necrosis in CAA. Note also the surrounding lymphocytic infiltrate; when this accompanies CAA, it tends to be associated with seizures or subacute cognitive decline, and marked oedema or rarefaction of the cerebral white matter. **C**, Immunohistochemistry reveals Aβ in the wall of this vessel, which shows evidence of previous thrombosis and recanalization.

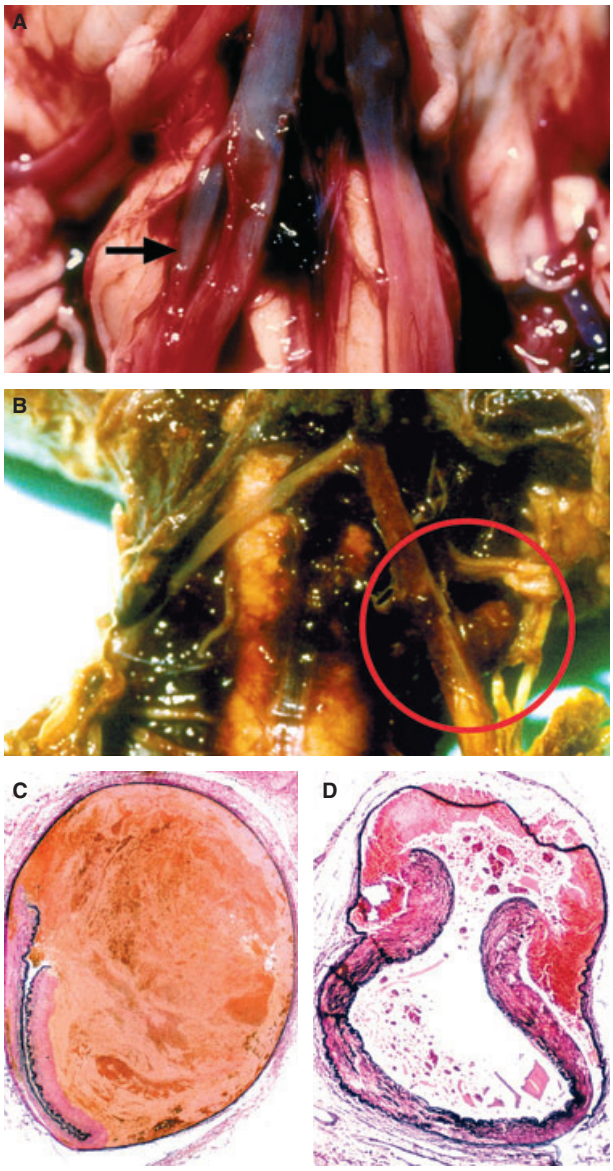

Figure 4. Traumatic arterial damage. **A**, This traumatic tear (arrow) in the right vertebral artery caused massive subarachnoid haemorrhage. **B**, Traumatic dissection of the left vertebral artery produced a false aneurysm (red circle), which eventually ruptured, causing subarachnoid haemorrhage. **C** and **D**, Dissection of the internal carotid (**A**) and vertebral (**D**) arteries complicating craniocervical trauma. The sections have been stained by the elastin van Gieson method, which shows very clearly the breach in the internal elastic lamina.

EMBOLISM

The commonest types of CNS embolism are thrombotic and atheromatous, as described above. Septic emboli are also considered above, in the context of infective vasculitis and aneurysms. Other types of cerebrovascular embolism include fat embolism, therapeutic embolism and a few much rarer entities (e.g. air embolism, embolism of tumour tissue or embolism of intervertebral disc material). In most of these cases, the embolic material occludes multiple arterioles and capillaries in the internal carotid artery distribution,

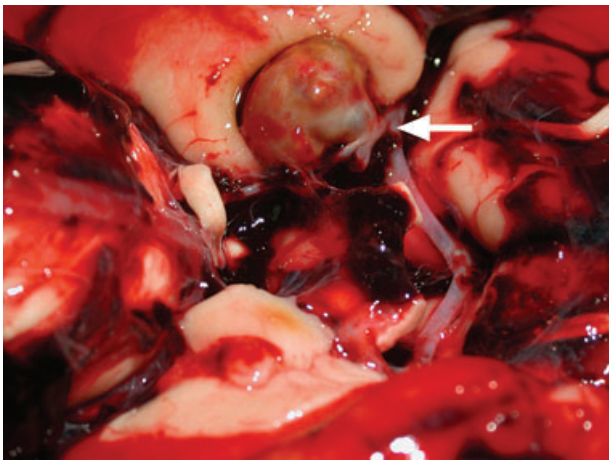

Figure 5. Ruptured berry aneurysm. Some of the blood clot has been washed away to demonstrate the origin of this aneurysm (arrow) from the junction of the right internal carotid and posterior communicating arteries.

and the pathological presentation is with scattered small foci of haemorrhage and infarction, predominantly in the cerebral white matter and centred on small blood vessels that may be necrotic. After a few days, the red blood cells are phagocytosed and removed, and the picture becomes one of scattered microinfarcts, some containing small amounts of haemosiderin. Fat embolism is seen mainly in patients who have sustained multiple traumatic injuries that include fractures of long bones. Patients with cerebral fat embolism usually have clinical, radiological and pathological evidence of pulmonary fat embolism as well but this is not always the case. The lipid remains demonstrable for several days in frozen sections through the affected white matter (Figure 7).

IMPAIRED COAGULATION

Much the most common coagulopathy in stroke patients is the acquired impairment of γ-carboxylation and activation of the coagulation factors II, VII, IX, and X caused by administration of warfarin.[8,9] This accounts for 5–25% of haemorrhagic strokes. About 70% are intracerebral and the remainder are subdural. The risk increases with intensity of anticoagulation, age and a history of previous cerebral ischaemic events. The risk of haemorrhagic stroke is also increased by intravenous tissue plasminogen activator.

IMPAIRED PLATELET FUNCTION

Although, in some studies, antiplatelet agents such as aspirin and clopidogrel have been associated with a slightly increased incidence or severity of cerebral haemorrhage, other studies have not confirmed these findings.[8–10]

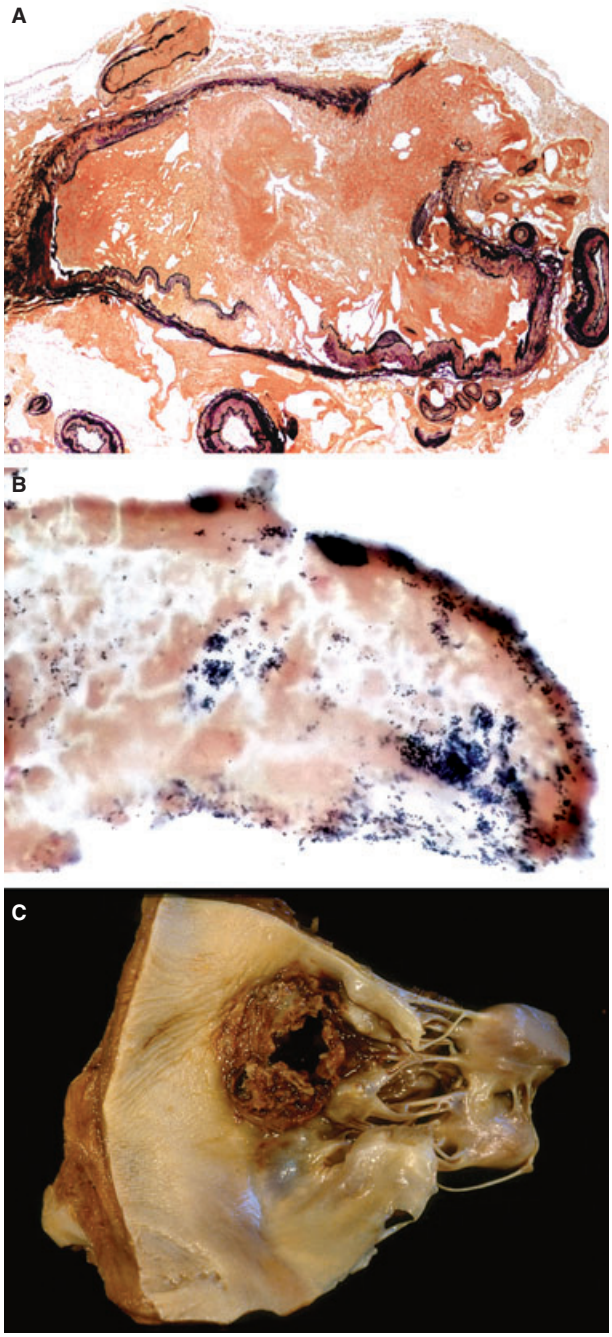

Figure 6. Infective aneurysm, complicating bacterial endocarditis. **A**, Ruptured aneurysm involving the distal part of a middle cerebral artery (elastin van Gieson stain). **B**, High-magnification view of a section through the blood clot stained by Gram's method reveals numerous Gram-positive cocci. **C**, The source of the infection was this large vegetation, which had eroded through the mitral valve.

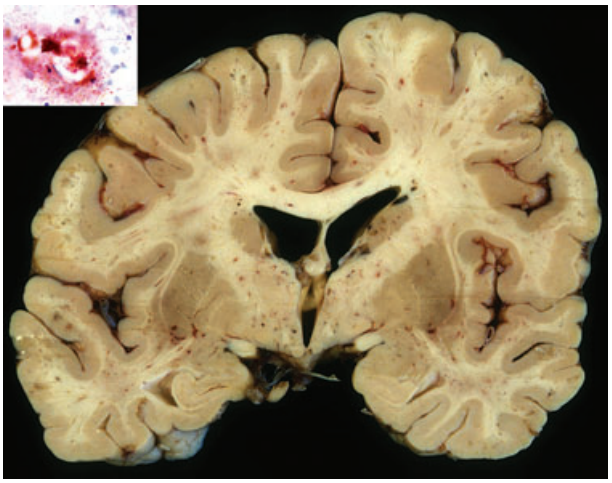

Figure 7. Cerebral fat embolism. This brain slice from a patient who died several days after a motor vehicle collision, during which he sustained multiple fractures of long bones, contains numerous small foci of infarction and some petechial haemorrhages. Staining of cryostat sections with Oil Red O (inset) revealed globules of neutral lipid within many of the small vessels at the centre of the infarcts and petechial haemorrhages.

THROMBOPHILIA

There are multiple acquired and inherited diseases that predispose to clotting of the blood.[11] Most are associated predominantly with venous occlusion but the more severe forms of thrombophilia also cause arterial thrombosis and infarction. The most common of the thrombophilias is the acquired antiphospholipid syndrome,[12] in which patients (most often female) experience episodes of vascular thrombosis and/or unexplained fetal death in association with the presence of medium to high titres of anticardiolipin antibodies. Patients may experience arterial thrombosis, venous thrombosis or a combination of the two, leading to arterial infarcts (usually lacunar) and venous infarcts and haemorrhages.

Thrombotic thrombocytopenic purpura (TTP) is characterized clinically by the combination of thrombocytopenia, neurological abnormalities, microangiopathic haemolytic anaemia, fever, and renal failure. It may be idiopathic (associated with antibody-mediated inhibition of the metalloprotease ADAMTS13, which normally cleaves the prothrombotic von Willebrand factor) or a complication of pregnancy, certain medications and diseases (e.g. human immunodeficiency virus infection). The neurological abnormalities are caused by occlusion of multiple small vessels by platelet and fibrin thrombi (Figure 8).

CEREBRAL VENOUS SINUS THROMBOSIS

This is uncommon but probably also under-diagnosed. Risk factors include a range of local and systemic conditions. The most common local risk factors are infection – involving either the middle ear and mastoid bone or the paranasal sinuses, with spread to the overlying dura – and cranial trauma. Others include local surgical procedures and, rarely, tumours.

Systemic risk factors include pregnancy and the puerperium, antiphospholipid syndrome (see above) and other causes of thrombophilia (protein C or S deficiency, factor V Leiden, antithrombin deficiency, etc.), polycythaemia rubra vera, severe dehydration, nephritic syndrome and Behçet's disease. The risk is slightly increased with oral contraceptive use.

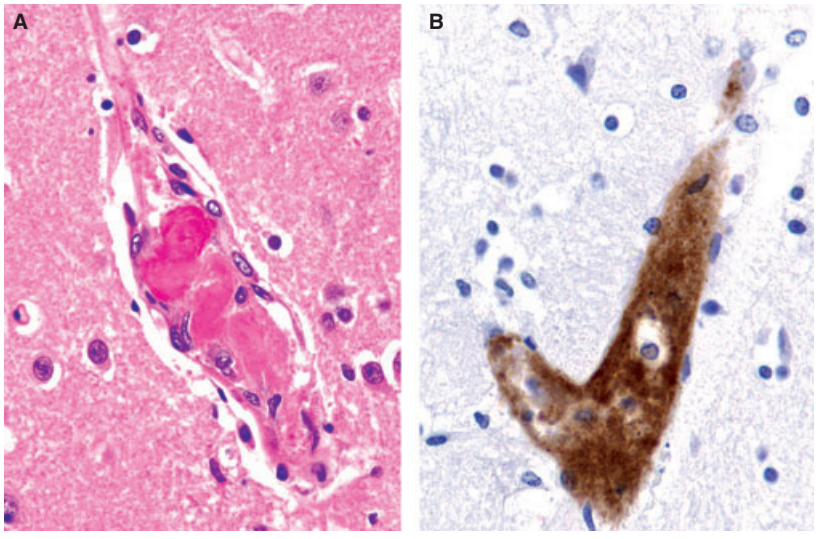

Figure 8. Thrombotic thrombocytopenic purpura. **A**, Platelet and fibrin thrombus in a small blood vessel in the deep grey matter. Note also the hypertrophy of the endothelial cells, a consistent if non-specific finding. **B**, Here, the platelets in another affected blood vessel have been immunolabelled for CD61.

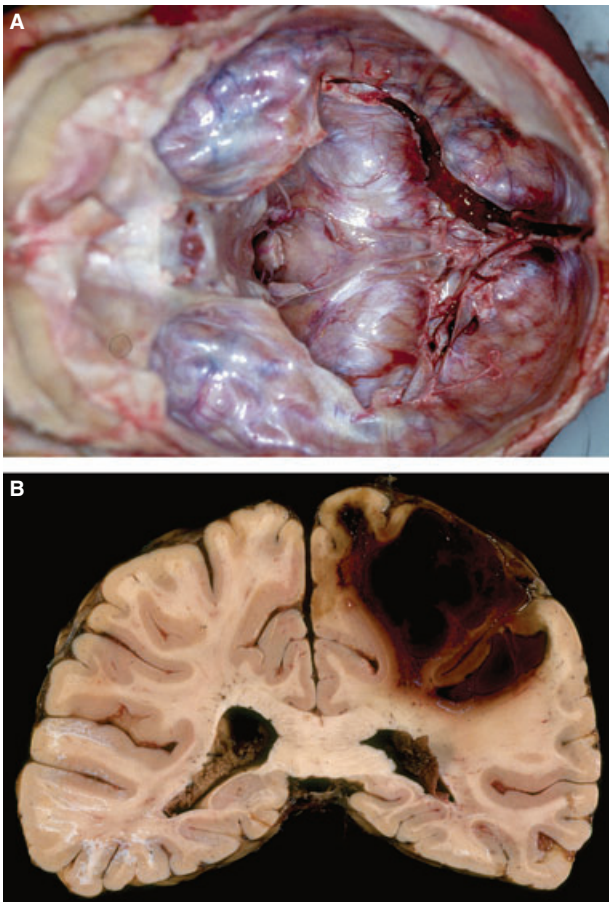

Figure 9. Venous sinus thrombosis and venous infarction. **A**, The right transverse (lateral) sinus is filled by thrombus. In contrast, the left transverse sinus appears normal. **B**, In this patient, the thrombosis involved the superior sagittal sinus as well as major cortical veins over the right cerebral convexity. The coronal slice includes a large region of infarction and haemorrhage in the drainage territory of the affected cortical veins.

The thrombus tends to propagate along the venous sinuses and major veins draining the cerebral convexities and deep grey matter, to produce extensive infarction and haemorrhage in the corresponding venous territories (Figure 9).

VASCULAR MALFORMATIONS

Arteriovenous malformations (AVMs)

AVMs are present in 15–20 per 100 000 adults[13,14] and carry a risk of rupture and symptomatic haemorrhage of about 2–6% per annum,[15,16] depending on size, whether or not the AVM has bled previously, and ethnic factors (for example, in a Californian study the risk was higher in Hispanics than in other ethnic groups).[16] An AVM consist of an interconnected

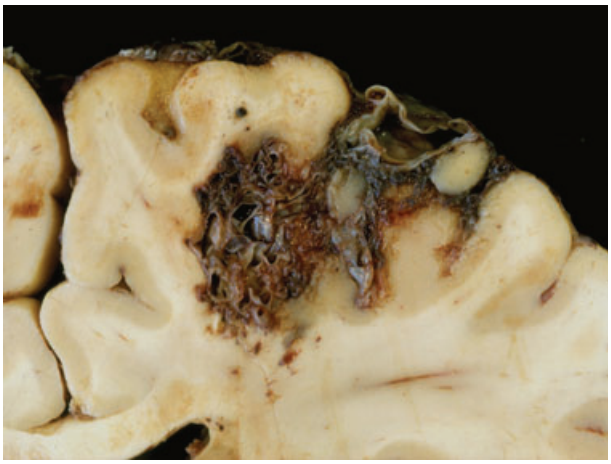

Figure 10. Arteriovenous malformation. This malformation extends through the frontal white matter and cortex into the overlying subarachnoid space. Note the large calibre and irregular contour of many of the venous channels.

network of arteries, veins and abnormal blood vessels (Figure 10), including large veins with irregularly thickened, fibrotic walls and ectatic thin-walled vascular channels that have a prominent internal elastic lamina but little or no tunica media. Some vessels may be thrombosed or calcified. The vessels are partly separated by brain parenchyma, which is often gliotic and may show evidence of previous haemorrhage or ischaemic damage. Many AVMs involve the leptomeninges as well as the underlying brain tissue. In 5–10% of patients with AVMs, saccular aneurysms develop on the feeding arteries. Arterial aneurysms can also occur within the AVM itself.

In infants, a distinct subtype of AVM occasionally occurs, in which there is shunting between one or more enlarged choroidal or thalamic arteries and the great vein of Galen. Because the affected blood vessels usually dilate markedly, the AVM is sometimes called an 'aneurysm' of the vein of Galen. The massive shunting of cardiac output that tends to occur through these AVMs can cause high-output cardiac failure. Other complications include obstructive hydrocephalus, intracranial haemorrhage and ischaemic brain damage.

In hereditary haemorrhagic telangiectasia (HHT; Osler–Weber–Rendu disease), capillary telangiectases involving the skin and mucosae are associated with AVMs of internal organs, including the CNS (affected in ~10% of patients).[17] At least five genetic subtypes exist (including HHT associated with juvenile polyposis), all of which are autosomal dominant. Neurological complications include haemorrhage from cerebral AVMs

and consequences of pulmonary AVMs (embolism, ischaemic stroke and cerebral abscess).

Dural arteriovenous fistula (dAVF) (including Foix–Alajouanine syndrome)

dAVFs most often occur within nerve root sleeves, between thoracic or upper lumbar spinal radicular arteries and veins communicating with the paraspinal valveless venous plexus.[18] Cervical dAVFs are much less common and intracranial dAVFs are rare. Typically, spinal dAVFs present in adulthood, with slowly progressive myelopathy accompanied by striking dilatation and tortuosity of the venous plexus over the dorsum of the cord. The walls of the veins become markedly thickened and fibrotic (Figure 11). Small vessels within the cord also show fibrous thickening of their walls (sometimes to the extent of obliteration of the central lumen) and over time the surrounding parenchyma becomes depleted of neurons, gliotic and cavitated.

Cavernous haemangioma (cavernoma)

Cavernous haemagiomas are present in about 0.5% of people[19] and are composed of numerous thin-walled vascular channels, lined by endothelium surrounded by collagenous connective tissue, with no internal elastic lamina or tunica media (Figure 12). Most of the channels abut one another with no intervening brain parenchyma. About 75% are supratentorial and 25% infratentorial. Many cavernomas remain asymptomatic, but over half eventually manifest with headaches, seizures, neurological deficits or brain haemorrhage. About 20% of cases of cavernoma are familial, with autosomal dominant transmission.[20,21] The proportion of familial cases is higher in Hispanic Americans of Mexican descent.[22] To date, four genetic loci for cavernoma have been identified (one is not yet fully characterized). Over 50% of patients with familial cavernomas have multiple lesions, but fewer than 20% of those with sporadic cavernomas.[19]

Venous angioma

Venous angioma (or developmental venous anomaly) is the most common cerebrovascular malformation.[23] It consists of clusters of enlarged venous channels, usually separated by normal brain tissue. They are usually asymptomatic but venous infarction, haemorrhage and seizures are rare complications. About 25% occur in the vicinity of a cavernous haemangioma (see above), and a smaller proportion involve the venous drainage of AVMs (see above); these two forms of associated vascular malformation may be the true source of many of the clinical manifestations attributed to venous angiomas.[23]

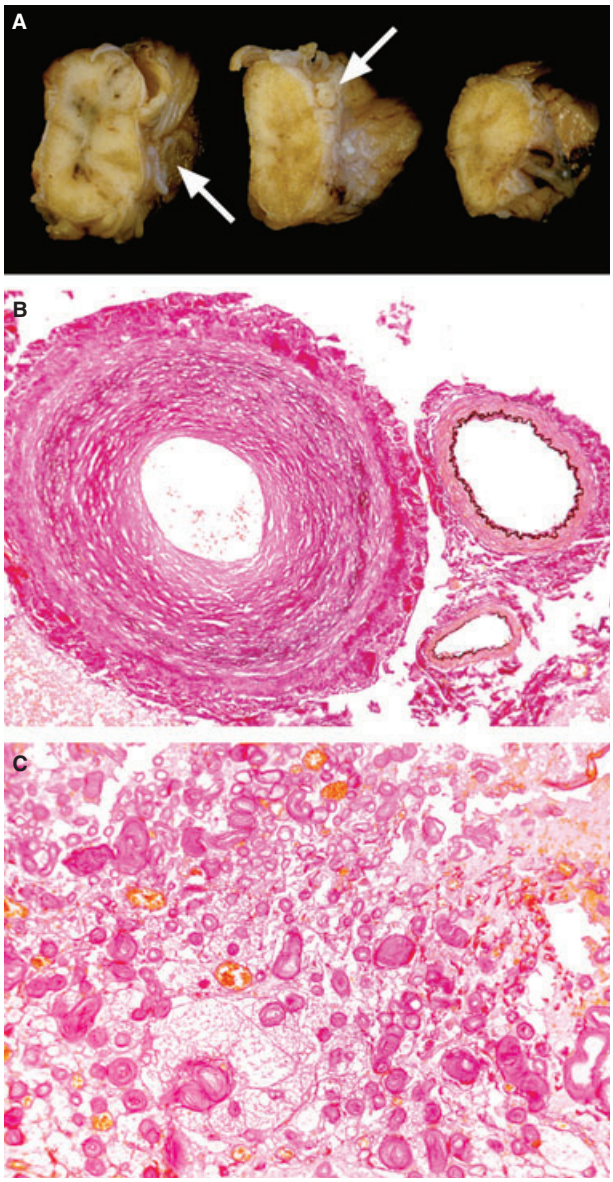

Figure 11. Foix–Alajouanine syndrome. **A**, Transverse sections through the thoracic and upper lumbar spinal cord in a case of Foix–Alajouanine syndrome. There is patchy softening and yellow discolouration of the cord parenchyma, and multiple thick-walled vessels are present over the dorsum of the cord (arrows). **B**, Large vein with a markedly thickened fibrotic wall. For comparison, see the two adjacent normal arteries (elastin van Gieson). **C**, Marked collagenous thickening of small vessels within the cord. The intervening grey matter has been replaced by a loose meshwork of astrocytic processes (elastin van Gieson).

Capillary telangiectasia

This comprises clusters of dilated capillaries with normal intervening tissue. Capillary telangiectases most often involve the pons but can occur in any part of the brain; their prevalence is similar to that

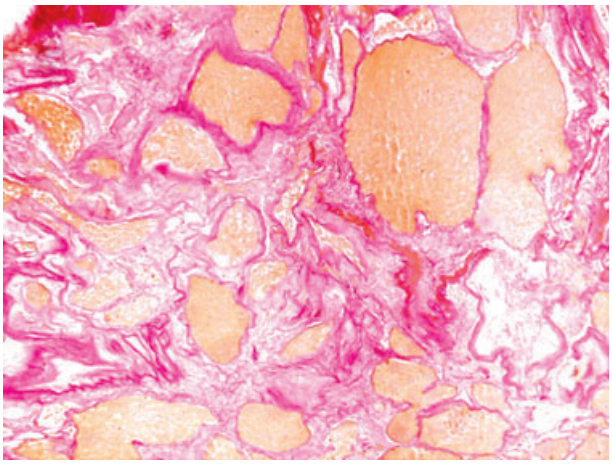

Figure 12. Cavernous haemangioma. This consists of numerous, abutting thin-walled vascular channels, lined by endothelium surrounded by collagenous connective tissue, with no internal elastic lamina or tunica media (elastin van Gieson).

of cavernous haemangiomas but they hardly ever manifest clinically.

Neuropathological findings: brain ischaemia

DISEASE OF LARGE ARTERIES

Atherothrombotic narrowing or occlusion of major intracranial or extracranial cerebral arteries accounts for 10–30% of symptomatic cerebral infarcts (the figure varies with ethnicity).[24–26] The infarct is usually of large volume, occupying much of the perfusion territory of the affected artery (Figure 1). However, depending on the extent of collateral supply of blood from adjacent arteries, the infarct may be predominantly subpial, deep or even sited along part of the boundary zone of the perfusion territory of the affected artery.[27]

DISEASE OF SMALL ARTERIES

Occlusion of small arteries and arterioles is the main cause of lacunar infarcts (infarcts measuring up to about 10 mm in diameter). Pathological examination reveals multiple small foci of cavitated infarction and ischaemic damage (see 'Selective loss of neurons after ischaemia', below) involving multiple arterial territories (Figure 2). These are usually associated with widespread arteriosclerosis and arteriolosclerosis, particularly in the cerebral white matter and deep grey matter structures; enlargement of perivascular spaces in these regions; tortuosity and occasional microaneurysmal dilatation of arterioles; and very occasional fibrinoid necrosis or thrombosis. Some of the infarcts may contain haemosiderin-laden macrophages, and in practice it is sometimes difficult to distinguish lacunar infarcts from old microhaemorrhages.

Small lacunar infarcts may also complicate CAA and vasculitis. A further, rare cause of lacunar infarcts and ischaemic degeneration of the white matter and deep grey matter is cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL), caused by mutations of *NOTCH3* and associated with extracellular accumulation of granular material along the plasmalemma of vascular smooth muscle cells (which eventually degenerate), particularly in the brain (Figure 13).

CHANGES IN INFARCTED BRAIN TISSUE OVER TIME

The macroscopic and histological changes that infarcts undergo with time have been extensively described in many reference texts on neuropathology[1,28] and will be summarized here only briefly. Over the first 24 h, the infarcted grey matter becomes increasingly congested, changing from a light greyish tan colour to a dusky reddish brown (Figure 1). It may include foci of

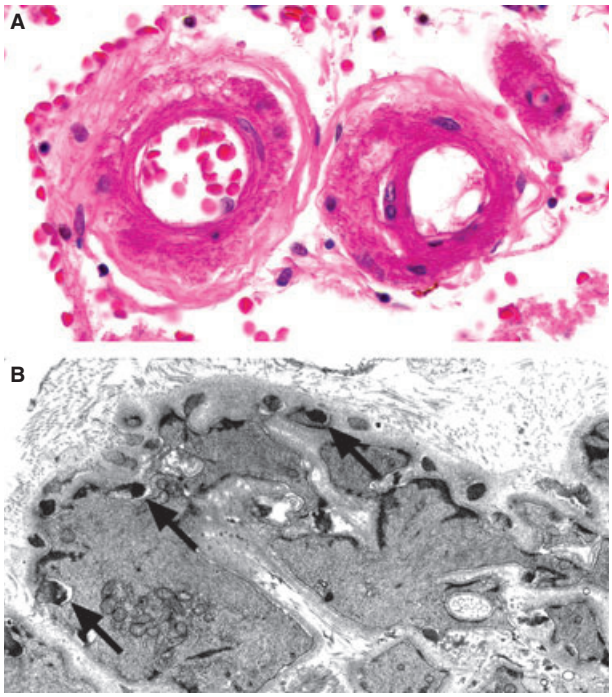

Figure 13. Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL). **A**, The tunica media of these meningeal arterioles in CADASIL is replaced by granular eosinophilic material. **B**, Electron microscopic examination of a dermal arteriole reveals accumulations of granular osmiophilic material (GOMs) in caveolar indentations in the plasmalemma of vascular smooth muscle cells. The GOMs tend to be most prominent along the abluminal surface of the smooth muscle cells (arrows).

petechial haemorrhage. The white matter also darkens and becomes congested but the changes are usually quite subtle and it is difficult to discern the edges of the infarct clearly until after about 2 days. By this time, the infarcted tissue is obviously softer than the adjacent parenchyma, and at 2–3 days may separate from it during post-mortem handling of the brain ('cracking artefact'). Over subsequent days and weeks the infarct undergoes liquefactive necrosis and then cavitation.

Histology reveals a fairly stereotyped sequence of morphological changes in neurons and glia.[29] By 4–6 h, many neurons in the infarcted tissue appear shrunken with pyknotic nuclei, perineuronal glia have swollen, clear cytoplasm, and there may be diffuse microvacuolation of the neuropil (Figure 14). Between 6 and 48 h, more and more of the neurons develop cytoplasmic hypereosinophilia. Their nuclei become less pyknotic and increasingly amphophilic or eosinophilic, and by 2–3 days, although neuronal outlines are still well defined, many of the nuclei are difficult to distinguish from the surrounding cytoplasm. Glia too, particularly oligodendrocytes in the white matter and perineuronal satellite cells in the grey matter, show initial nuclear pyknosis but over the next 2–3 days many undergo apoptosis rather than necrosis, and clusters of apoptotic bodies may be seen in the infarcted tissue, away from blood vessels, sometimes abutting neurons. Vascular endothelial cells initially swell but those in the central region of the infarct later show nuclear pyknosis and undergo apoptosis.

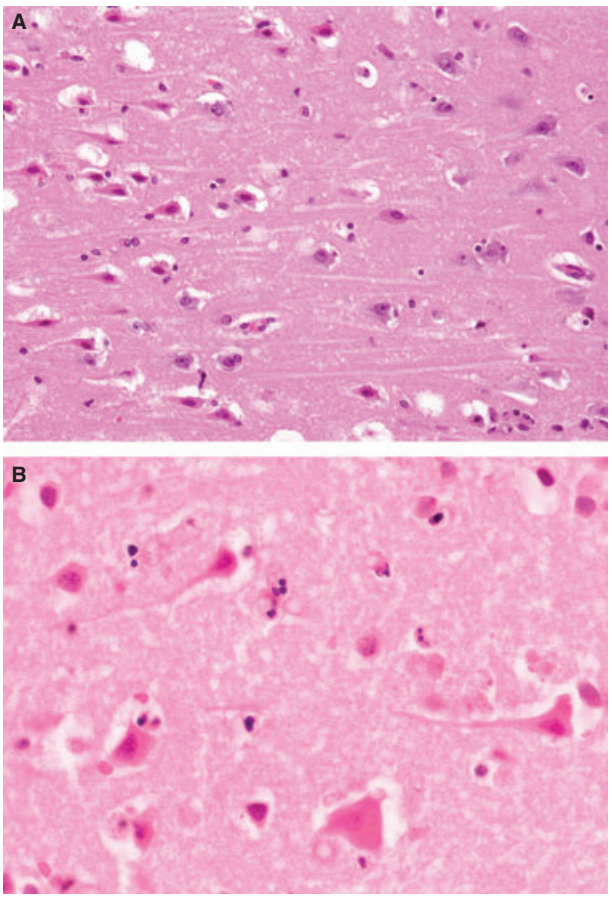

Figure 14. Histological changes in an acute infarct. **A**, Compare the infarcted cortex to the left of the panel with the preserved cortex to the right, at 4–5 h. The infarcted neurons appear shrunken with pyknotic nuclei. Perineuronal glia have swollen, clear cytoplasm, and there is fine microvacuolation of the neuropil. **B**, After 2 days, most of the neuronal nuclei have become amphophilic or eosinophilic, making them increasingly difficult to distinguish from the surrounding cytoplasm. The section includes sparsely scattered apoptotic cells that are glial or inflammatory.

By 6–12 h, blood vessels towards the edge of the infarcted tissue are marginated by neutrophils and scattered neutrophils are visible in the surrounding tissue. Between 1 and 2 days, the inflammatory infiltrate increases but mononuclear cells predominate. Foamy macrophages accumulate within the tissue and around blood vessels. Endothelial cells proliferate in the vessels along the edge of the infarct and vascular buds grow into the necrotic tissue. Fibroblasts may also be identified but are not nearly as prominent as in organizing infarcts outside of the CNS. After several months, the infarct has been transformed into a cavity containing sparse strands of glial and vascular tissue and some remaining foamy macrophages. The surrounding parenchyma contains numerous reactive and fibrous astrocytes and scattered macrophages that contain lipid debris. Some may contain haemosiderin pigment.

SELECTIVE LOSS OF NEURONS AFTER ISCHAEMIA

Neurons are more susceptible to ischaemia than are glia or blood vessels. Focal ischaemia that is brief or incomplete can cause selective death of neurons with relative preservation of other tissue elements. In such cases, the ischaemic damage is marked by focal loss of neurons and reactive astrocytosis, only modest infiltration by macrophages and an absence of cavitation.

GLOBAL BRAIN ISCHAEMIA

A global reduction in the supply of oxygenated blood to the brain most often occurs in the context of severe hypotension or raised intracranial pressure (ICP). The hypotension may be of cardiogenic (e.g. cardiac infarction, arrhythmia or tamponade) or peripheral vascular (e.g. marked blood loss or septicaemic shock) origin. The raised ICP may be caused by a wide range of

conditions, including space-occupying lesions (such as haematomas or tumours), cranial trauma, metabolic disease, intracranial infection or inflammation, hydrocephalus and venous obstruction. Global brain ischaemia is itself a cause of brain swelling and raised ICP. When the cerebral perfusion pressure (the difference between mean arterial pressure and intracranial pressure) falls below ~50 mmHg, the normal autoregulatory mechanisms that maintain cerebral blood flow at ~50 ml/100 g fail, and cell death occurs if the blood flow falls below 10–20 ml/100 g.

Susceptibility to ischaemic damage varies not only between neurons and glia but also among different populations of neurons. Particularly vulnerable are the pyramidal neurons in the hippocampus – of these, neurons in the CA1 field are most vulnerable and those in the CA2 field least so. Other vulnerable neuronal populations are the pyramidal neurons of laminae 3 and 5 in the neocortex. Neurons in the depths of the sulci are more likely to be affected than those over the crests of the gyri. A common finding after global brain ischaemia is laminar necrosis: patchy or extensive loss of neurons from neocortical laminae 3 and 5, particularly towards the depths of sulci, associated with marked astrocytosis and, in longer-surviving cases, neovascularization. Other neurons that are particularly susceptible to ischaemia are the Purkinje cells in the cerebellum.

The distribution of damage also varies with the extent of reduction and duration of global ischaemia. If the reduction in cerebral blood flow has been severe or prolonged, neuronal loss is likely to be widespread. In many cases, however, blood flow is better preserved in the central than the peripheral parts of the major arterial perfusion territories. The result is ischaemic damage that is accentuated in the watershed regions between the perfusion territories.

ISCHAEMIA, HYPOXIA AND HYPOGLYCAEMIA

Although cerebral infarction is most often caused by ischaemia (ischaemic hypoxia, also known as stagnant hypoxia), it can also result from reduced oxygen in the blood without a reduction in cerebral perfusion (hypoxic hypoxia or anaemic hypoxia) or from toxins that impair the ability of the cells to use the oxygen for respiration (histotoxic hypoxia). The causes of hypoxic hypoxia include severe pulmonary disease, right-to-left shunting of blood and respiratory arrest. The main causes of infarction resulting from anaemic and histotoxic hypoxia are carbon monoxide and cyanide poisoning respectively. For reasons that are not entirely clear, the brunt of the damage in carbon monoxide toxicity is usually borne by the dorsomedial part of the globus pallidum, which undergoes haemorrhagic infarction. Ischaemic white matter damage may be prominent in longer-term survivors.

Because neurons not only have minimal capacity for anaerobic metabolism but also store hardly any glycogen, they depend for respiration on a continuous supply of glucose as well as oxygen. The brain is therefore very vulnerable to the effects of hypoglycaemia. The most frequent cause is accidental or deliberate over-dosage with insulin or oral hypoglycaemic agents. The pathological consequences are very similar to those of global brain ischaemia in terms of the cellular changes and distribution of damage. One useful distinguishing feature is the relative preservation of Purkinje cells in hypoglycaemic as compared with ischaemic damage.

Vascular dementia

A post-mortem diagnosis of vascular dementia is most readily made largely by exclusion, when examination of the brain from someone who had a clinical history of dementia reveals no more than occasional neuritic plaques and neurofibrillary tangles, largely confined to the hippocampus and inferomedial temporal neocortex; multiple infarcts and ischaemic lesions; moderate to severe arteriolosclerosis, often associated with atherosclerosis; and an absence of histopathological evidence of other disease likely to cause dementia. The ischaemic lesions most consistently associated with dementia are multiple lacunar infarcts in combination with ischaemic white matter degeneration (Figure 2) but occasionally the principal finding is larger infarcts in critical grey matter structures (e.g. bilateral thalamic or hippocampal infarcts). Much more difficult to assess is the significance of ischaemic vascular disease in a patient who also had evidence of another dementing illness, e.g. extensive plaques and neurofibrillary tangles or neocortical Lewy bodies. In this case, the diagnosis is usually expressed in terms of the likelihood that the vascular disease (or other neurodegenerative process) may have contributed to the patient's dementia.

Neuropathological findings: haemorrhagic stroke

SUBARACHNOID HAEMORRHAGE

The vasculopathies responsible for subarachnoid haemorrhage are described above and in Table 1. The most common cause of subarachnoid haemorrhage is

rupture of a berry aneurysm (Figure 5) but cerebral amyloid angiopathy is an important cause, particularly in the elderly. Rarer causes include arteriovenous malformation, infective aneurysms and vasculitides. Cerebral contusions and lacerations are often associated with mild subarachnoid haemorrhage but major subarachnoid haemorrhage is unusual in cranial trauma; among the causes to consider are vertebral artery tear or dissection near the point of entry of the artery into the posterior fossa (Figure 4), dissection of the carotid artery and tearing of the brainstem at the junction of the pons and medulla (a pontomedullary rent).

The distribution of the subarachnoid blood may provide a clue as to the source of the haemorrhage but can be misleading, particularly in the case of a ruptured berry aneurysm. Retrograde flow of blood into the ventricles is common after subarachnoid haemorrhage. However, particularly after cranial trauma, the possibility should always be considered that the blood may have originated within the periventricular tissue or choroid plexus and spread into the subarachnoid space rather than vice versa.

PARENCHYMAL BRAIN HAEMORRHAGE

The most common context in which parenchymal brain haemorrhage occurs is small artery disease associated with hypertension. The changes to the vessels themselves are similar to those associated with lacunar infarcts (collagenous thickening of the vessel walls, enlargement of perivascular spaces, tortuosity and occasional microaneurysmal dilatation of arterioles, and very occasional fibrinoid necrosis). The haematoma is usually large and deep-seated within the brain, causing disruption of the basal ganglia, thalamus and internal capsule, often with rupture into the ventricles. Other sites of predilection include the base of the pons and deep cerebellar tissue (in both cases, usually associated with rupture into the fourth ventricle).

Other common causes of parenchymal brain haemorrhage are thromboembolism, CAA (mainly in the elderly), vascular malformations, coagulopathies, trauma and neoplasms. Rarer causes include vasculitides affecting small vessels. Much the most frequent coagulopathy associated with brain haemorrhage is that resulting from warfarin but this rarely occurs unless the international normalized ratio is above 3. Thrombolytic agents such as tissue plasminogen activator are also sometimes responsible for brain haemorrhage. Haemorrhage may arise from glial or metastatic tumours, the glial tumours most commonly implicated being glioblastomas (Figure 15) and oligodendrogliomas, and the metastatic tumours being melanomas, renal cell carcinomas and choriocarcinomas.

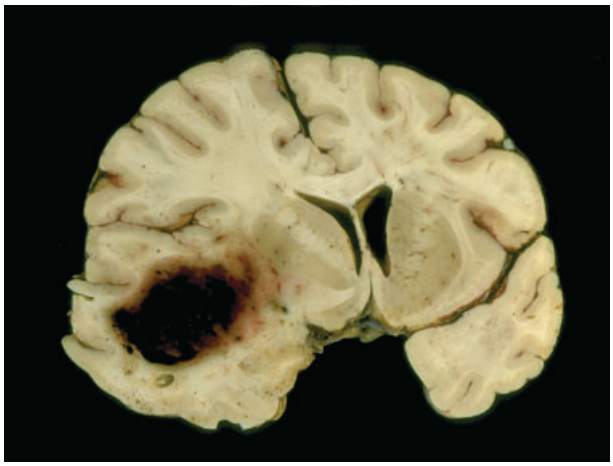

Figure 15. Haemorrhage into a tumour. A bleed was the presenting manifestation of this glioblastoma. Note the rather ill-defined margins of the haematoma and the poor definition of grey and white matter structures in the inferior part of the left temporal lobe.

Although the rupture of a berry aneurysm usually produces subarachnoid haemorrhage, if the fundus of the aneurysm is embedded within the brain itself, parenchymal haemorrhage may result; the responsible aneurysm is most often at the first branch point of the middle cerebral artery or the junction between the anterior and anterior communicating arteries, and the haematoma involves the medial part of the temporal lobes or the anterior inferomedial part of the frontal lobes.

In the event that the haemorrhage is not fatal, the blood clot is removed by macrophages over weeks to months, leaving a cavity containing residual haemosiderin-laden macrophages. The surrounding tissue is gliotic and contains newly formed blood vessels and macrophages. At later time points, it may not be possible to distinguish with certainty between an old haematoma cavity and an old haemorrhagic infarct.

Autopsy in cases of stroke

PREPARATION

It is important to be clear as to the role of each individual autopsy, the scope of the authorization or consent and the expectations of the interested parties. These will vary with the context in which the autopsy is performed. The family may want to know why the death occurred and whether it might have been prevented or treated more effectively. They may also

be concerned about potential genetic implications for other members of the family. The clinicians are likely to share these concerns but will also be interested in correlating the pathological findings with the clinical manifestations and the results of diagnostic tests. The coroner is concerned not only with when and where the death occurred but also with how it occurred – as a consequence of natural disease, or as a result of intervention (e.g. suicide or unlawful killing) or exposure to unnatural conditions (e.g. an occupational hazard). The police, Crown Prosecution Service and insurance companies may also be interested in how the death occurred, particularly in the event that it was not a consequence of natural disease. Last, but not least, the autopsy may be performed to support teaching or research.

For death related to cerebrovascular disease, as for any other autopsy, it is important to review the clinical notes, speak to the clinicians involved in looking after the patient and consider carefully the key questions requiring clinicopathological correlation. These will include the possible sites and systems involved in the disease process and the nature of the pathological abnormalities that might account for the clinical findings. Particularly in the case of cerebrovascular disease, review of the neuroradiological studies is often essential if the critical lesions are not to be missed.

EXTRACRANIAL EXAMINATION

This should include careful inspection of the heart and great vessels, the cervical part of the internal carotid artery and, if relevant, the intraosseous segments of the vertebral arteries. The intraosseous segments of the vertebral arteries can be exposed *in situ* by identification of the lower point of entry of each vertebral artery into the vertebral canal and subsequent use of bone nibblers to remove the anterior bony covering of the canal. The dissection is easier if the bodies of the cervical vertebrae are first removed by sawing parasagittally through the pedicles but this should be done with the saw blade close to the vertebral bodies themselves, as otherwise the blade is likely to traverse the vertebral canal and traumatize the arteries.

INTRACRANIAL EXAMINATION

In cases of subarachnoid haemorrhage, it is best to try to identify the source of the bleeding prior to fixation. Wash away blood and remove blood clot to expose the arteries over the base of the brain. Gently prise apart the two frontal lobes inferiorly and depress the optic chiasm slightly to expose the anterior cerebral and communicating arteries, trace the middle arteries for 3–4 cm along the inferior part of the Sylvian fissures, and expose the upper end of the basilar arteries and the proximal parts of the posterior cerebral and superior cerebellar arteries, and the anterior inferior and posterior inferior cerebellar arteries.

In cases of subarachnoid haemorrhage associated with cranial trauma, it is particularly important to examine the vertebral arteries within the vertebral canals and where they penetrate the dura to enter the posterior fossa. Also, pay close attention to the internal carotid arteries for evidence of dissection; this is much easier to identify before than after fixation, although the confirmation of the nature of the pathological process usually requires fixation and histology.

For later demonstration of an aneurysm, it is sometimes helpful to dissect the basal arteries away from the brain and to preserve them in formalin in a sealed bag or container. Carefully dissect the vertebral and basilar arteries away from the medulla, pons and midbrain, cutting through the cerebellar and perforating arteries as the larger vessels are peeled away from brainstem. Cut the posterior cerebral arteries near the back of the midbrain, the middle cerebral arteries well beyond their first trifurcation and the anterior cerebral arteries about 1 cm beyond their junction with the anterior communicating artery, and carefully separate these and the posterior communicating arteries from the base of the brain, taking care to cut the small perforating arteries that pass from the larger vessels into the brain.

Remember to open the venous sinuses and to examine the cortical veins for thrombosis. In the event of venous sinus thrombosis, it is important to look for adjacent infection (e.g. look for middle ear infection and mastoiditis in a patient with lateral sinus thrombosis).

If identification of a microbial pathogen is relevant, e.g. in venous sinus thrombosis associated with infection or haemorrhage associated with an infective aneurysm, small samples of the abnormal tissue should be removed with a sterile scalpel and placed in tissue culture medium (or placed in a sterile universal container and taken to a microbiology laboratory as soon as possible). It may be helpful to culture cerebrospinal fluid, which can be obtained from the interpeduncular fossa, cistern magna or a lateral ventricle (by separating the cerebral hemispheres, inserting the needle of a syringe about 30° to the vertical through the corpus callosum and applying slight negative pressure while slowly withdrawing the needle).

Major vascular malformations, foci of haemorrhage and large established infarcts within the brain can

usually be identified on slicing of the unfixed tissue. However, identification of more subtle abnormalities, such as acute infarcts, ischaemic white matter damage, small vascular malformations, vasculitides and cerebral amyloid angiopathy, requires fixation of the brain (or at least of the affected tissue) and histology.

SAMPLING FOR HISTOLOGY

The sampling will depend on the clinical context and macroscopic findings. For assessment of ischaemic brain damage, it should include the main watershed regions in the cerebrum and cerebellum, the hippo-

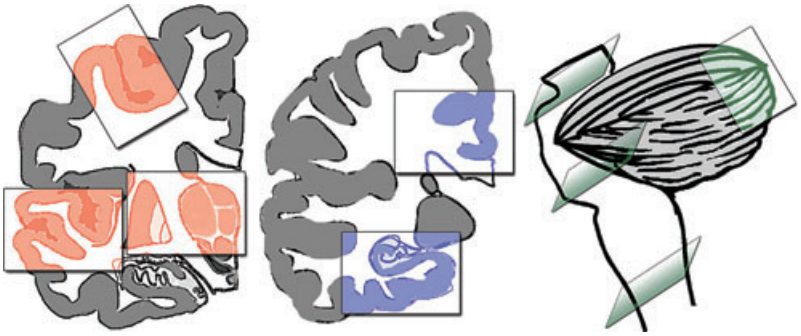

Figure 16. Sampling for histology. The orange, blue and green shaded areas indicate a typical set of blocks for assessment of ischaemic brain damage. Any regions of macroscopic abnormality should also be sampled.

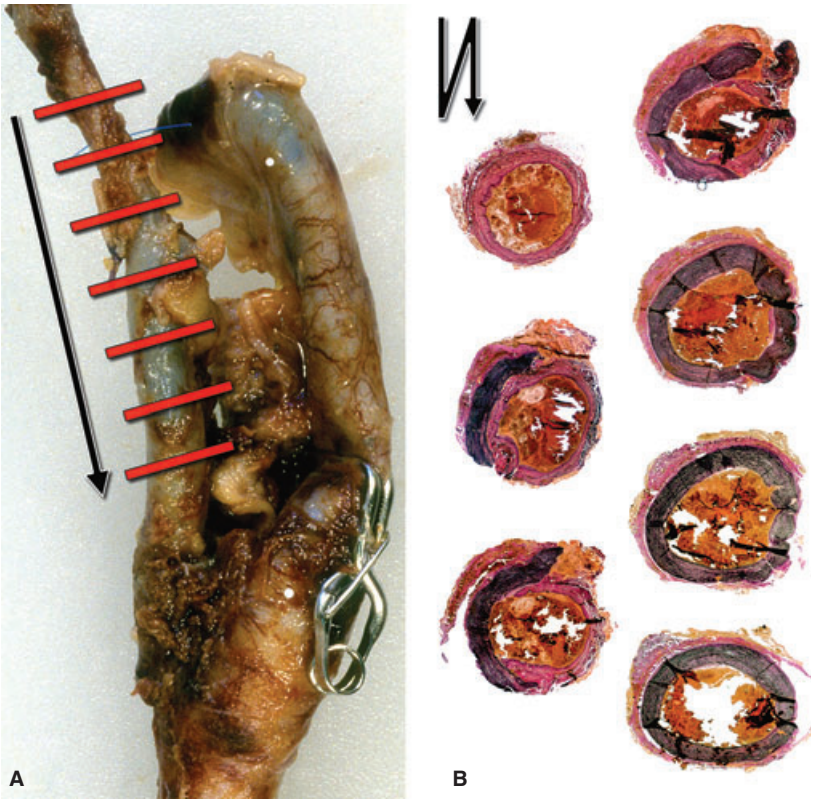

Figure 17. Serial block embedding. **A**, Bifurcation of the right external carotid artery. A clip had been placed across the origin of the internal carotid artery, to cut off the blood flow to a large, inoperable aneurysm in the cavernous sinus, and an extracranial–intracranial bypass saphenous vein graft had been inserted between the external carotid artery and the right middle cerebral artery. Unfortunately, the graft thrombosed and the patient died. A particular concern of the surgeon was the integrity of the proximal arteriovenous anastomosis. A length of vessel across the anastomosis (arrow) was embedded intact in paraffin wax, removed from the wax bath and cut transversely at 3-mm intervals (red bars). **B**, The 3-mm slices were placed face-down, in order (zigzag arrow), in a steel base mould, and embedded in a single paraffin block. This section shows a sequential series of levels through the anastomosis between the elastic-poor vein and the elastic-rich artery. There is a post-mortem blood clot in the lumen but the anastomosis is intact (elastin van Gieson).

campi, deep grey matter structures and brainstem (Figure 16). Ideally, the brain should be fixed by suspension in formalin before it is sliced and blocks are taken for histology. In the event that this is not possible, it is better to take blocks slightly larger than required and to wait until after fixation before trimming them to a size suitable for paraffin embedding and histology; this minimizes artefactual distortion and leads to better-quality sections.

A useful technique for histological assessment of larger blood vessels is the preparation of serial transverse blocks (Figure 17), as originally described by Beesley and Daniel.[30] A length of vessel of up to about 2 cm is embedded intact in paraffin wax. It is removed from the final wax bath, allowed to cool and then sliced transversely with a razor blade at intervals of 2–3 mm. As the slices are cut, they are placed face-down, in order, in a steel base mould into which a thin layer of wax has been poured. When all of the slices have been placed in the mould, it is briefly warmed and then allowed to cool slightly again, fixing the slices in position. The mould is then filled with molten wax, and the block is allowed to harden. Each section cut from the block displays a sequential series of levels through the vessel, enabling it to be sampled extensively in far fewer blocks and sections than would otherwise be needed.

It may be relevant to examine the middle ear (e.g. in cases of venous sinus thrombosis) or the vessels within the base of the skull [e.g. to identify an aneurysm (Figure 18), fistula or site of dissection]. Other organs and tissues often need to be examined histologically to establish the nature of a vasculitic, vasculopathic or embolic process. Particular attention should be given to heart, lungs, kidneys and skin.

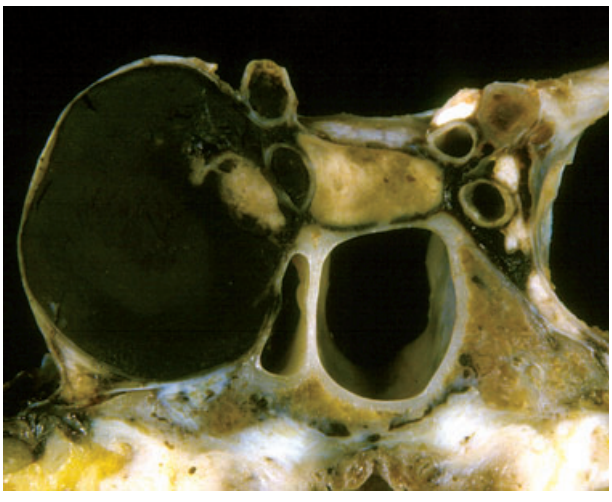

Figure 18. Giant aneurysm of the internal carotid artery within the cavernous sinus. This expanding aneurysm was compressing multiple cranial nerves and pushing into the pituitary fossa, and a decision was made to insert the extracranial–intracranial bypass graft described in the legend to Figure 17.

Most pathological abnormalities in cerebrovascular disease are obvious in sections stained with haematoxylin and eosin. Whether additional stains are needed will depend on the nature of the pathological process. Fat emboli are readily detected in cryostat sections of formalin-fixed brain tissue, by staining with Oil Red O. Elastin/van Gieson stain is helpful for assessment of the integrity of the internal elastic lamina of arteries and arterioles. Fibrinoid vascular necrosis can be demonstrated with phosphotungstic acid and haematoxylin, or Martius Scarlet Blue. Immunostains for the specific peptide or protein constituent of vascular amyloid (usually Aβ) are much more sensitive than tinctorial stains such as Congo Red or Sirius Red. There are several immunohistochemical markers of platelets (e.g. antibody to CD61) that are useful for demonstrating platelet and fibrin thrombi (e.g. in TTP) (Figure 8). Electron microscopy is helpful, even on post-mortem tissue, for diagnosis of CADASIL (Figure 13).

Conclusion

It is not difficult to perform an adequate autopsy in the case of stroke. The requirements are simply an awareness of the possible causes and manifestations, a reasonable knowledge of the vascular anatomy, an informed and careful approach to the gross examination and histology, and an appreciation of the potential value of the procedure to next-of-kin, clinicians and society in general.

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