Medicine treatment choices with compelling indications

Compelling indications	Drug class
Angina	ß-blocker Calcium channel blocker
Coronary artery disease	ß-blocker ACE inhibitor If ß-blocker contraindicated: verapamil
Post myocardial infarction	ß-blocker ACE inhibitor
Heart failure	ACE inhibitor Carvedilol Spironolactone Hydrochlorothiazide or furosemide
Left ventricular hypertrophy	ACE inhibitor
Stroke	Hydrochlorothiazide ACE inhibitor
Diabetes type 1 or 2 with/without evidence of microalbuminuria or proteinuria	ACE inhibitor, usually in combination with a diuretic.*
Chronic kidney disease	ACE inhibitor, usually in combination with a diuretic.
Isolated systolic hypertension	Hydrochlorothiazide Calcium channel blocker
Pregnancy	See Chapter 6
Prostatism	Alpha-blocker

Caution
Lower BP over a few days.
A sudden drop in BP can be dangerous, especially in the elderly.
BP should be controlled within 1–6 months.

Risk assessment: 10 year risk of MI > 20%:

- HMGCoA reductase inhibitors e.g.:
- Simvastatin, oral, 10 mg daily.
  This therapy requires good initial evaluation, ongoing support for patients and continuous evaluation to ensure compliance.
  Therapy should be initiated together with appropriate lifestyle modification and adherence monitoring.

See section 3.1: Ischaemic heart disease and atherosclerosis, prevention.

REFERRAL

Referral is dynamic and patients can be referred up to a specialist or down to PHC when controlled. Consultation without referral may be all that is necessary.

Referrals are indicated when:

» Patients are compliant with therapy, and the blood pressure is refractory, i.e. >140/90 mmHg, while on drugs from three to four different classes at appropriate dose, one of which is a diuretic.
» All cases where secondary hypertension is suspected.
» Complicated hypertensive urgency e.g. malignant/accelerated hypertension, severe heart failure with hypertension and hypertensive emergency.

3.6.1 HYPERTENSION, SEVERE

DESCRIPTION

These patients have severe hypertension, are asymptomatic and have no evidence of progressive target organ damage.

Keep the patient in the care setting and repeat BP measurement after resting for 1 hour.

If the second measurement is still elevated at the same level, start oral therapy using two drugs together, one of which should be low dose hydrochlorothiazide the second drug is usually a calcium channel blocker, e.g. amlodipine.

Follow up carefully and refer as needed.

3.6.2 HYPERTENSIVE URGENCY

DESCRIPTION

Hypertension is **symptomatic** with evidence of TOD. There are no immediate life threatening neurological or cardiac complications such as are seen in the hypertensive emergencies.

Do not lower BP in acute stroke or use antihypertensive medication unless SBP >220 mmHg or the DBP >120 mmHg, as a rapid fall in BP may aggravate cerebral ischaemia and worsen the stroke.

Treatment may be given orally but in patients unable to swallow, use parenteral drugs.

MEDICINE TREATMENT

Ideally, all patients with hypertensive urgency should be treated in hospital. Commence treatment with two oral agents and aim to lower the DBP to 100 mmHg slowly over 48–72 hours. This BP lowering can be achieved by:

- Long-acting calcium channel blocker.
- ACE inhibitor.
  Avoid if there is severe hyponatraemia, i.e. serum Na < 130 mmol/L.
- β-blocker.

Diuretics may potentiate the effects of the other classes of drugs when added. Furosemide should be used if there is renal insufficiency or signs of pulmonary congestion.

3.6.3 HYPERTENSIVE CRISIS, HYPERTENSIVE EMERGENCY

DESCRIPTION

This is a **life-threatening situation** that requires immediate lowering of BP usually with parenteral therapy. Grade 3-4 hypertensive retinopathy is usually present with impaired renal function and proteinuria.

The true emergency situation should preferably be treated by an appropriate specialist.

Life-threatening complications include:

» Hypertensive encephalopathy, i.e. severe headache, visual disturbances, confusion, seizures and coma that may result in cerebral haemorrhage.
» Unstable angina or myocardial infarction.
» Acute left ventricular failure with severe pulmonary oedema (extreme breathlessness at rest).
» Eclampsia and severe pre-eclampsia.
» Acute kidney failure with encephalopathy.
» Acute aortic dissection.

MEDICINE TREATMENT

Admit the patient to a high-care setting for intravenous drug therapy and close monitoring. Do not lower the BP by >25% within 30 minutes to 2 hours. In the next 2–6 hours, aim to decrease BP to 160/100 mmHg.
This may be achieved by the use of intravenous or oral drugs.

Intravenous therapy

- Labetalol, IV, 2 mg/minute to a total dose of 1–2 mg/kg.
  - Caution in acute pulmonary oedema.

OR

If myocardial ischaemia and CCF:

- Glyceryl trinitrate, IV, 5–10 mcg/minute.

- Furosemide, IV, 40–80 mg.
  - Duration of action: 6 hours.
  - Potentiates all of the above drugs.

Oral therapy

ACE inhibitor, e.g.:

- Enalapril, oral, 2.5 mg as a test dose
  - Increase according to response, to a maximum of 20 mg daily.
  - Monitor renal function.

3.7 RHEUMATIC HEART DISEASE

I09.9

DESCRIPTION

These are chronic sequelae of rheumatic fever consisting of valvular damage, usually involving left heart valves, with progression and complications.

GENERAL MEASURES

Acute stage: bed rest and supportive care.
Patient education.
Intensive health education for prevention of sore throats.

MEDICINE TREATMENT

Acute rheumatic fever

For eradication of streptococci in throat:

- Benzathine benzylpenicillin (depot formulation), IM, 1.2 million units as a single dose.

OR

- Phenoxymethylpenicillin, oral, 500 mg 12 hourly for 10 days.

Penicillin allergy:

- Macrolide, e.g.:
- Erythromycin, oral, 250 mg 6 hourly for 10 days.

Prevention of recurrent rheumatic fever
All patients with confirmed rheumatic fever and **no** rheumatic valvular disease – treat until 21 years of age.
All patients with confirmed rheumatic fever **and** rheumatic valvular disease – treat until 35 years of age.

- Benzathine benzylpenicillin (depot formulation), IM, 1.2 million units every 3–4 weeks.

OR

- Phenoxymethylpenicillin, oral, 250 mg 12 hourly.

Penicillin allergy:

- Erythromycin, oral, 250 mg 12 hourly

Prophylaxis for infective endocarditis
See section 3.5: Endocarditis, infective.

REFERRAL

» Where surgery is contemplated.
» Management of intractable heart failure or other non-responding complications.
» Pregnancy.

CHAPTER 4

DERMATOLOGY

Extemporaneous compounding of some of the preparations listed should only take place at institutions where the competencies and equipment are available.

4.1 ACNE

L70

DESCRIPTION

Acne is an inflammatory condition of the pilosebaceous unit. Secondary changes can lead to scarring and inflammation

GENERAL MEASURES

Do not squeeze lesions.
Avoid greasy or oily topical products such as moisturisers that block the hair follicle openings.
Discourage excessive facial washing.

MEDICINE TREATMENT

- Benzoyl peroxide 5%, gel, apply at night to affected areas as tolerated.
  - Wash off in the morning.
  - If ineffective and tolerated, increase application to 12 hourly.
  - Avoid contact with eyes, mouth, angles of the nose and mucous membranes.

AND/OR

For inflammatory acne:

- Doxycycline, oral, 100 mg daily for 3 months.
  - Review patient after 3 months of treatment.

Topical retinoids

Indicated in non-inflammatory acne and where benzoyl peroxide is ineffective.
The main action is to control comedone formation.
Introduce topical retinoids gradually as a night-time application to limit skin irritant effects, which are worse if used during day (UVL aggravation).

Do not use topical retinoids in pregnant women.

- Tretinoin, topical, apply at night to affected areas for at least 6 weeks.
  - Review patient after 6 weeks' treatment.
  - Minimise exposure to UV light.
  - Acne may worsen during the first few weeks.

4.2 CELLULITIS AND ERYSIPELAS

L03.9/A46

DESCRIPTION

Skin and subcutaneous infections with pain, swelling and erythema usually caused by streptococci, but also staphylococci and occasionally other organisms. Regional lymphadenitis may be present. Erysipelas has a raised demarcated border, whilst the border is indistinct in cellulitis.

The presence of areas of necrosis, haemorrhage or pain out of proportion to the physical signs should raise suspicion of necrotising fasciitis which requires aggressive surgical debridement and broad spectrum antibiotics (e.g. penicillin and metronidazole) as these infections are often polymicrobial.

GENERAL MEASURES

Elevate the affected limb to reduce swelling.

MEDICINE TREATMENT

For pain:

- Ibuprofen, oral, 400 mg 8 hourly after meals.

OR

- Paracetamol, oral, 1 g 4–6 hourly when required to a maximum of 4 doses per 24 hours.

Antibiotic therapy

If intravenous antibiotics are given initially, patients should be switched to oral agents as soon as there is clinical improvement.
Antibiotics should usually be given for 5–10 days depending on clinical response.

- Cloxacillin, IV, 1 g 6 hourly.

When there is clinical improvement, change to:

- Flucloxacillin, oral, 500 mg 6 hourly.

Penicillin allergy:

- Clindamycin, IV, 600 mg 8 hourly.

When there is clinical improvement, change to:
- Clindamycin, oral, 300 mg 8 hourly.

REFERRAL
Urgent
» For debridement if necrotising fasciitis is suspected, i.e. gangrene, gas in the tissues or haemorrhagic bullae.

Non-urgent
» To surgeon for non-response.

4.3 IMPETIGO
L01.0

DESCRIPTION
Superficial skin infection, starting as vesicles with an inflammatory halo. Later a characteristic honey-coloured crust on erythematous base develops which heals without scarring. Usually caused by group A streptococci or staphylococcal infection. Post-streptococcal glomerulonephritis is a potential complication.

GENERAL MEASURES
Good personal and household hygiene to avoid spreading the infection and to reduce carriage of organisms.
Wash and soak sores in soapy water to soften and remove crusts.

MEDICINE TREATMENT
Antibiotic therapy
- Flucloxacillin, oral, 500 mg 6 hourly for 5 days.

Penicillin allergy:
- Macrolide, e.g.:
- Erythromycin, oral, 250 mg 6 hourly for 5 days.

4.4 FURUNCLES AND ABSCESSES
L02.9

DESCRIPTION
Localised bacterial skin infection of hair follicles (furuncle/boil) or dermis (abscess), usually with *S. aureus***.**
The surrounding skin becomes:
» swollen, » red,
» hot , and » tender to touch.

Note:
Boils in diabetic or immunocompromised patients require careful management.
Check blood glucose levels if the boils are recurrent.

GENERAL MEASURES
Drainage of the abscess is the treatment of choice. Perform surgical incision only after the lesion is fluctuant.

MEDICINE TREATMENT
Antibiotic therapy
Systemic antibiotics are seldom necessary, except if there are:
» tender draining lymph nodes,
» fever,
» extensive surrounding cellulitis, and
» facial abscesses.

- Cloxacillin, IV, 1 g 6 hourly.

When there is clinical improvement, change to:
- Flucloxacillin, oral, 500 mg 6 hourly.

Penicillin allergy:
- Clindamycin, IV, 600 mg 8 hourly.

When there is clinical improvement, change to:
- Clindamycin, oral, 300 mg 8 hourly.

4.5 ECZEMA
L30.9

DESCRIPTION
Eczema is an inflammatory skin condition recognised by vesicles, weeping and crusting in the acute phase; and thickened, scaly skin with increased skin markings known as lichenification in the chronic phase. Eczema can be allergic or non-allergic.

GENERAL MEASURES
Avoid exposure to trigger or precipitating factors, where applicable.
Avoid irritants such as strong detergents, antiseptics, foam baths, perfumed soaps and rough occlusive clothing.
Good personal hygiene with regular washing to remove crusts and accretions and avoid secondary infection.

Keep fingernails short to prevent scratching.
Respect patient preference for cream or ointment topical treatment.
Wet wraps may help control eczema and pruritus but should not be used for infected eczema.
Diet modification has no role in atopic eczema treatment unless double blind challenge testing proves food sensitivity.

MEDICINE TREATMENT

To relieve skin dryness:

- Emulsifying ointment (UE), topical, to wash or bath.
- Aqueous cream, topical, applied daily to dry areas as a moisturiser.

Mild eczema

Topical corticosteroids, e.g.:

- Hydrocortisone 1%, topical, applied 12 hourly until control is achieved.
  - Apply sparingly to the face.
  - Use with caution around the eyes.

Severe eczema

Potent topical corticosteroids, e.g.:

- Betamethasone 0.1%, topical, applied 12 hourly for 7 days to the body.
  - Apply sparingly to face, neck and flexures.

<u>If non-responsive</u>

Refer for dermatologist opinion.

- Prednisone, oral. Specialist initiated

Maintenance therapy

Once eczema is controlled, wean to the lowest potency topical corticosteroid that maintains remission.
Apply moisturiser as needed.

- Aqueous cream (UEA) or emulsifying ointment (UE), topical, applied daily.

Infected eczema

This is usually due to staphylococcal infection.

Antibiotic therapy

- Flucloxacillin, oral, 500 mg 6 hourly for 5 days.

<u>Penicillin allergy:</u>

- Clindamycin, oral, 300 mg 8 hourly for 5 days

For sedation and relief of itch:
- Chlorpheniramine, oral, 4 mg at night as needed.

REFERRAL
» Severe, non-responsive or complicated cases (e.g. severe infection including disseminated herpes simplex).

4.6 ERYTHEMA MULTIFORME, STEVENS JOHNSON SYNDROME, TOXIC EPIDERMAL NECROLYSIS
L51.9/L51.1/L51.2

DESCRIPTION
Erythema multiforme
An acute, self-limiting and commonly recurrent inflammatory skin eruption with variable involvement of the mucous membranes and without systemic symptoms.

Symmetrically distributed crops of target lesions (dark centre, an inner, pale ring surrounded by an outer red ring) often involving palms and soles are characteristic. This condition is usually due to an infection, commonly herpes simplex or mycoplasma.

Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis
An acute, systemic condition with vesico-bullous lesions involving the skin and mucous membranes. Non-specific prodromal symptoms, often mistaken as an upper respiratory tract infection, may occur before skin lesions are apparent.

Cutaneous lesions may start as a red morbilliform rash, progressing to purple skin necrosis and blisters which rupture, leaving large areas of denuded skin. The lesions exhibit a positive Nikolsky's sign. Mucous membrane erosions are common and internal organ involvement may be present.

This condition is usually due to medication, e.g. sulphonamides, anti-retrovirals (nevirapine), anti-epileptics (phenytoin, phenobarbitone, carbamazepine, lamotrigine).

Systemic involvement with multi-organ dysfunction is common.
Complications include:
» dehydration,
» sepsis, and
» adhesions and scarring.

Stop all medicines, including complementary, alternative, hormonal contraceptives and self medication.

GENERAL MEASURES

Principles of management

The foundation of management is supportive, good nursing and the prevention of dehydration and sepsis.
Stop all medicines.
Patients usually require care in a high or intensive care unit with dedicated nursing.

Monitoring

Monitor vital organ function.
Examine daily for infection and swab infected lesions. Do blood cultures if septicaemic.

Dressings

Skin hygiene; daily cleansing and bland, non-adherent dressings as needed.

Do not use silver sulfadiazine if condition is thought to be due to cotrimoxazole or other sulphonamide.

Mucous membranes:

Regular supervised oral, genital and eye care to prevent adhesions and scarring.
Two-hourly mouth washes with bland mouth wash, e.g. glycothymol.
Examine daily for ocular lesions and treat 2-hourly with eye care and lubricants and break down adhesions.
Treat genitalia 6 hourly with Sitz baths and encourage movement of opposing eroded surfaces to prevent adhesions.

Fluids:

Oral rehydration is preferred but intravenous fluid therapy may be required in significant dehydration.
Encourage oral fluids to prevent pharyngeal adhesions.
Provide soft, lukewarm food or nasogastric feeds if unable to eat.

Note:

All patients should wear a notification bracelet/necklace.

MEDICINE TREATMENT

Corticosteroids

The practice of using systemic corticosteroids is not supported by evidence and is therefore not recommended.

Antibiotic therapy
Systemic antibiotics may be indicated, depending on results of appropriate cultures.

Analgesia
Appropriate and adequate analgesia for the pain associated with dressing changes, given at least half an hour before dressing change.

4.7 LEG ULCERS, COMPLICATED

L97

DESCRIPTION

A chronic relapsing disorder of the lower limbs, which usually occurs in middle-aged women. It has many causes and is often associated with lipodermatosclerosis (bound-down, fibrosed skin) and eczema. It is mainly associated with vascular, predominantly venous insufficiency and immobility. It is also associated with neuropathy and, occasionally, with infections, neoplasia, trauma or other rare conditions.

GENERAL MEASURES

The aim of management should be to:

» Treat underlying conditions, e.g. Heart failure, diabetes mellitus and stasis.
» Limit the extent of damage.
» Encourage rapid healing to minimise scarring and fibrosis.
» Prevent recurrences.

Avoid all topical irritants and allergens, e.g. lanolin, neomycin, bacitracin, parabens, fusidic acid, clioquinol, antihistamine creams, etc.

If the ulcer is oedema- or stasis-related, rest the leg in an elevated position.

In venous insufficiency, compression (bandages or stockings) is essential to achieve and maintain healing, provided the arterial supply is normal.

In patients with arterial insufficiency, avoid pressure on bony prominences and the toes. Stress meticulous foot care and avoidance of minor trauma.

Walking and exercises are recommended.

Encourage patients with neuropathy not to walk barefoot, to check their shoes for foreign objects, examine their feet daily for trauma and to test bath water before bathing to prevent getting burnt.

Avoid excessive local heat.

Indications for surgical procedures include:
» slough removal,
» surgery for varicose veins,
» arterial insufficiency, and
» skin grafting.

MEDICINE TREATMENT

Antibiotic therapy

Systemic antibiotics are seldom required for ulcers, and should be considered **only if there is surrounding cellulitis.** These infections are typically polymicrobial and broad-spectrum antibiotics are recommended.

- Amoxicillin/clavulanic acid, oral, 875/125 mg 12 hourly for 7 days.

Local wound care

Topical cleansing

Use bland, non-toxic products to clean the ulcer and surrounding skin.

For clean uninfected wounds:
- Sodium chloride 0.9% or sterile water.

For exudative, infected wounds:
- Povidone-iodine 5% cream, topical apply daily.

4.8 PSORIASIS

L40.9

DESCRIPTION

This is an inflammatory condition of the skin and joints of unknown aetiology. Scaly red, itchy papules and plaques over extensor surfaces and in the scalp are common. The nails and skin folds are often involved. In exceptional cases, it is localised to palms and soles and pustular skin lesions are seen especially following rapid treatment withdrawal, e.g. steroids or systemic agents.

GENERAL MEASURES

Counselling regarding precipitating factors and chronicity.
Encourage sun exposure as tolerated.

MEDICINE TREATMENT

Local plaques

- Coal tar 6% ointment, topical, apply at night.
  - Avoid use on the face, flexures and genitalia.

For flares:

- Betamethasone 0.1%, topical, apply 12 hourly.
  - Decrease according to severity, reduce to hydrocortisone 1%, then stop.

Scalp psoriasis

For maintenance:

- Coal tar 1% ointment, topical, apply at night.

For flares

- Betamethasone 0.1% lotion, topical, apply once daily.

REFERRAL

» No response to treatment.
» Severe disease.

4.9 URTICARIA

L50.9

DESCRIPTION

A transient itchy inflammatory skin and mucosal condition recognised by a wheal and flare reaction. There are many causes. In most chronic cases the precipitant for the urticaria is never found. Lesions due to insect bite are often grouped, show a central bite mark and are on exposed areas of the body. They are often associated with secondary features such as excoriations, vesicles, pigmentary changes and infection.

GENERAL MEASURES

Limit exposure to triggers such as non-immune mast cell degranulators, which aggravate and prolong urticaria, e.g. codeine, NSAIDs, salicylates, alcohol, etc.

MEDICINE TREATMENT

Antihistamines

Regular use is recommended until the urticaria is quiescent. If one antihistamine does not provide relief, change to, or add another class of antihistamine.

For chronic urticaria less sedating antihistamines are preferable.

- Cetirizine, oral, 10 mg daily.

Avoid oral corticosteroids.

4.9.1 PAPULAR URTICARIA

L50.9

DESCRIPTION

Lesions due to insect bite often grouped or in a linear arrangement, show a central bite mark and are on exposed areas of the body.
Initial lesion is a red papule, which may blister, become excoriated, and then heal with hyperpigmentation.
Usually occur in crops over several months.
Chronic, severe, persistent reactions may be seen in immunocompromised patients, e.g. HIV infection, immunosuppressive therapy.

GENERAL MEASURES

Reduce exposure to insects by treating pets, using mosquito nets and fumigating household regularly.
Use of insect repellents may be helpful.
Examine carefully for burrows to rule out scabies.

MEDICINE TREATMENT

New inflamed lesions:

- Betamethasone 0.1%, topical apply daily for 5 days.

For relief of itch and sedation:

- Chlorpheniramine, oral, 4 mg at night as needed in severe cases.

REFERRAL

» Non-responsive and chronic cases.

4.10 FUNGAL INFECTIONS

B35

DESCRIPTION

The skin may be infected by yeasts or fungi and the clinical presentation varies with organism, body site infected and the body's response to the infection. Most infections are due to anthropomorphic species that infect humans primarily. Yeasts such as *Candida* spp (intertrigo, thrush) and *Pityrosporum spp* (tinea/pityriasis vesicolor, folliculitis) are common.

Dermatophyte (tinea) infections are common and do not necessarily imply underlying systemic disease.
Deep fungal infections (mycetomas, sporotrichosis, blastomycosis) occur rarely. Systemic fungal infections (histoplasmosis, cryptococcosis) are increasingly seen in immunocompromised patients and need systemic therapy.

GENERAL MEASURES

Manage predisposing factors, i.e. occlusion, maceration and underlying conditions such as diabetes, eczema, immunocompromise, etc.
Advise patient regarding spread of infection and exposure in communal, shared facilities (dermatophytes).

MEDICINE TREATMENT

Candida

Imidazole, e.g.:

- Clotrimazole 1%, topical, apply 8 hourly until clear of disease.

Pityrosporum

- Selenium sulphide 2.5% suspension, applied once weekly to all affected areas.
  - Allow to dry and leave overnight before rinsing off.
  - Repeat for 3 weeks.

Dermatophytes

Imidazole, e.g.:

- Clotrimazole 1%, topical, apply 8 hourly until clear of disease.

Systemic antifungal therapy

Topical treatment is generally ineffective for hair and nail infections.
Recurrent infections are not uncommon if repeat exposure is not prevented.

- Fluconazole, oral, 200 mg daily for two weeks.
  - In tinea capitis, 200 mg daily for 4 weeks.

REFERRAL

» Non-repsonsive infections.
» Systemic infections.

4.11 VIRAL INFECTIONS

4.11.1 VIRAL WARTS/ANOGENITAL WARTS

B07/A63.0

DESCRIPTION

Superficial muco-cutaneous infection caused by the human papilloma virus.

GENERAL MEASURES

Cryotherapy.
Check patients with anogenital warts for the presence of other STIs.

MEDICINE TREATMENT

Cutaneous warts
Treatment seldom indicated.

Anogenital warts

- Podophyllin 20% in Tinct. Benz. Co., topical.
  - Apply at weekly intervals to lesions by a health care professional until lesions disappear.
  - Apply petroleum jelly to surrounding skin and mucous membrane for protection.
  - Wash the solution off after 4 hours.

  Podophyllin is a cytotoxic agent.
  Avoid systemic absorption.
  Contraindicated in pregnancy. Exclude pregnancy before using podophyllin.

4.11.2 SHINGLES (HERPES ZOSTER)

See section 9.11: Zoster (shingles).

CHAPTER 5
GYNAECOLOGY

5.1 DYSMENORRHOEA
N94.6

DESCRIPTION
Lower abdominal pain that starts with the onset of menstruation, and subsides after menses have ended. It may be primary or secondary. Secondary dysmenorrhoea is associated with chronic pelvic infection, fibroids, endometriosis and adenomyosis.

GENERAL MEASURES
For secondary dysmenorrhoea, investigate and treat the underlying condition.

MEDICINE TREATMENT
Symptomatic relief:
- Paracetamol, oral, 1 g 4–6 hourly when required to a maximum of 4 doses per 24 hours

OR
- Ibuprofen, oral, 400–800 mg 8 hourly depending on severity.

For severe pain:
ADD
- A combined oral contraceptive and review after 3 months.

REFERRAL
» If there is uncertainty about the diagnosis.
» Young women with pain not responding to conventional treatment.
» Older women with persistent pain.

5.2 UTERINE BLEEDING, ABNORMAL
N91–N93

GENERAL MEASURES
Surgical procedures as dictated by the diagnosis.
Perform a transvaginal ultrasound and endometrial sampling in all women over 45 years of age.
Actively exclude organic causes, e.g. fibroids, for abnormal uterine bleeding.

MEDICINE TREATMENT
Dysfunctional uterine bleeding implies that no organic cause is present.

ARREST OF ACUTE HAEMORRHAGE

For excessively heavy anovulatory dysfunctional bleeding:
Progestogen, e.g.:

- Norethisterone, oral, 5 mg 4 hourly for 24–48 hours.

OR

- Tranexamic acid, oral, 1g 6 hourly on days 1–4 of the cycle. Specialist initiated.

After bleeding has stopped, continue with:

- Combined oral contraceptive, oral, 1 tablet 8 hourly for 7 days.
  - Follow with 1 tablet once daily for 3 months.

FOR RESTORING CYCLICITY

For women in the reproductive years:

- Combined oral contraceptive, oral, 1 tablet daily for 6 months.

OR

As alternative to combined oral contraceptives:
Progesterone only:

- Medroxyprogesterone acetate, oral, 30 mg daily from day 5 to day 26 of the cycle.
  - Use for 3–6 cycles.

OR

- Norethisterone, oral, 15 mg daily from day 5 to day 26 of the cycle.
  - Use for 3–6 cycles.

For perimenopausal women, if uterus present, HRT:

- Conjugated oestrogens, oral, 0.625 mg daily for 21 days with the addition of medroxyprogesterone acetate, oral 10 mg daily from day 11 to day 21.
  - Day 22– 28 no treatment.
  - Use for 3–6 cycles.

ADD

For dysmenorrhoea and abnormal bleeding:

- Ibuprofen, oral, 400–800 mg 8 hourly for 2–3 days depending on severity of pain.

5.3 PELVIC INFLAMMATORY DISEASE (PID)

N73.9

DESCRIPTION

PID includes salpingitis with or without oöphoritis and, as precise clinical localisation is often difficult, denotes the spectrum of conditions resulting from infection of the upper genital tract.

Sequelae include:

» recurrent infections if inadequately treated,
» infertility,
» increased probability of ectopic pregnancy, and
» chronic pelvic pain.

Stage	Manifestations
Stage I	» cervical motion tenderness and/or uterine tenderness and/or adnexal tenderness
Stage II	» as stage 1, plus pelvic peritonitis
Stage III	» as stage II, plus » tubo-ovarian complex or abscess
Stage IV	» generalised peritonitis » ruptured tubo-ovarian complex » septicaemia

GENERAL MEASURES

Hospitalise all patients with stage II–IV PID for parenteral antibiotic therapy.
Frequent monitoring of general abdominal and pelvic signs is essential.
Note:
Remove IUCDs.
Test and, if necessary, treat patient for syphilis and offer HIV testing.
Perform a pregnancy test as an ectopic pregnancy forms part of the differential diagnosis.

In stage III, surgery is indicated if:

» the diagnosis is uncertain,
» there is no adequate response after 48 hours of appropriate therapy,
» the patient deteriorates on treatment, or
» after 4–6 weeks there still is a large or symptomatic pelvic mass.

MEDICINE TREATMENT

STAGE I

- Doxycycline, oral, 100 mg 12 hourly for 10 days.

PLUS

- Ceftriaxone, IM, 250 mg as a single dose.

PLUS

- Metronidazole, oral, 400 mg 12 hourly for 10 days.

STAGE II–IV

- Ceftriaxone, IV, 250 mg as a single dose.

Followed by:

- Benzylpenicillin (Penicillin G), IV, 2 million units 6 hourly.

PLUS

- Gentamicin, IV, 6 mg/kg daily.

PLUS

- Metronidazole, IV, 500 mg 8 hourly.

Continue intravenous therapy until there is definite clinical improvement. Thereafter, change to:

- Amoxicillin/clavulanic acid, oral, 875/125 mg 12 hourly to complete 10 days' therapy.

PLUS

To treat chlamydia:

- Doxycycline, oral, 100 mg 12 hourly for 10 days.

Note:

The addition of metronidazole to amoxicillin/clavulanic acid is unnecessary as amoxicillin/clavulanic acid has adequate anaerobic cover.

Penicillin allergy:

- Ceftriaxone 250 mg IV as a single dose.
  If severe penicillin allergy: Ciprofloxacin, oral, 500 mg.

PLUS

- Clindamycin, IV, 600 mg 8 hourly.

PLUS

- Gentamicin, IV, 6 mg/kg daily.

Continue intravenous therapy until there is definite clinical improvement. Thereafter, change to:

- Doxycycline, oral, 100 mg 12 hourly for 10 days.

PLUS

- Metronidazole, oral, 400 mg 8 hourly for 10 days.

REFERRAL

» Stages III and IV should be managed in consultation with a gynaecologist.

5.4 ENDOMETRIOSIS

N80

DESCRIPTION

The presence and proliferation of endometrial tissue outside the uterine cavity, usually within the pelvis. It may manifest as dysmenorrhoea, dyspareunia and chronic pelvic pain. Diagnosis is made by laparoscopy.

GENERAL MEASURES

For women who wish to conceive, referral for surgery.

MEDICINE TREATMENT

- Combined oral contraceptives for 6 months.

OR

- Medroxyprogesterone acetate, oral, 30 mg daily for at least 3 months.

Note:
The recurrence of symptoms is common following cessation of treatment.

REFERRAL

» Women with infertility.
» No response to treatment after 3 months.

5.5 AMENORRHOEA

N91.0/N91.1

DESCRIPTION

Primary amenorrhoea: no menstruation by 14 years of age in the absence of secondary sexual characteristics; or failure to menstruate by 16 years of age.
Secondary amenorrhoea: amenorrhoea for at least 3 months in women with previous normal menses

Investigations

» Body mass index.
» Urine pregnancy test.
» Pelvic ultrasound.
» Serum for TSH, FSH, LH, prolactin.

FSH > 15 units/L in a young woman (< 40 years) suggests premature ovarian failure.
LH/FSH ratio of > 2:1 suggests polycystic ovarian syndrome.

MEDICINE TREATMENT

For treatment of hyperprolactinaemia, hypo- or hyperthyroidism, see Chapter 8: Endocrine System.

If no cause for secondary amenorrhoea is found:
- Medroxyprogesterone acetate, oral, 10 mg daily for 10 days.
  - Anticipate a withdrawal bleed 5–7 days following conclusion of treatment.

REFERRAL
» All cases of primary amenorrhoea.
» Secondary amenorrhoea not responding to medroxyprogesterone acetate.
» Polycystic ovarian syndrome and premature ovarian failure, for further evaluation.

5.6 HIRSUTISM AND VIRILISATION

L68.0/E25

DESCRIPTION
Hirsutism refers to terminal hair growth in amounts that are socially undesirable, typically following a male pattern of distribution. Virilisation refers to the development of male secondary sexual characteristics in a woman.

This condition requires referral to a tertiary hospital for investigation and management.

REFERRAL
» All cases.

5.7 INFERTILITY

N97.9

DESCRIPTION
Inability to conceive after a year of regular sexual intercourse without contraception.

GENERAL MEASURES

Counselling.
Lifestyle modification, e.g. weight optimisation, smoking cessation and regular sexual intercourse.
Investigation of semen analysis and prolactin level.
Mid-luteal (day 21) progesterone assay. > 30 nmol/L suggests adequate ovulation.
Laparoscopy and/or hysterosalpingography (Specialist supervision).

MEDICINE TREATMENT

Treat the underlying disease.

For induction of ovulation:
- Clomifene, oral, 50 mg daily on days 5–9 of the cycle. Specialist only.
  - Monitor the progress of ovulation.

For hyperprolactinaemia after further investigation:
See section 8.15.1: Prolactinoma.

5.8 MISCARRIAGE

O00–O08

Both Manual Vacuum Aspiration (MVA) and medical evacuation are equally effective for miscarriage. However, in the follow settings, MVA is preferred:
» septic miscarriage
» anaemia
» haemodynamic instability
» second trimester miscarriage

5.8.1 SILENT MISCARRIAGE OR EARLY FETAL DEMISE

O02.0

GENERAL MEASURES

Counselling.
Evacuation of the uterus.

MEDICINE TREATMENT

Before MVA, to ripen the cervix:
- Misoprostol, oral/PV, 400 mcg as a single dose.

Medical evacuation:
- Misoprostol, oral/PV, 600 mcg as a single dose.
  - Repeat after 24 hours if necessary.

5.8.2 INCOMPLETE MISCARRIAGE IN THE FIRST TRIMESTER

O02.1

GENERAL MEASURES

Counselling.
Evacuation of the uterus after ripening the cervix.

MEDICINE TREATMENT

Before MVA, to ripen the cervix:
- Misoprostol, oral/PV, 400 mcg as a single dose.

Medical evacuation:
- Misoprostol, oral/PV, 600 mcg as a single dose.
  - Repeat after 24 hours if necessary.

5.8.3 MIDTRIMESTER MISCARRIAGE (FROM 13–22 WEEKS GESTATION)

O03.4

GENERAL MEASURES

Counselling.
Evacuation of the uterus after the fetus has been expelled.

MEDICINE TREATMENT

- Misoprostol, PV, 400 mcg immediately.

Follow with:
- Misoprostol, oral, 400 mcg every 4 hours until expulsion of the products of conception.
  - Duration of treatment must not exceed 24 hours.

Warning
Uterine rupture may occur in women with previous Caesarean sections. Caution for this group and those of high parity: use 200 mcg of misoprostol or alternative methods such as extra-amniotic saline infusion without misoprostol.

If cervical dilatation already present:
- Oxytocin, IV.
  - Dilute 20 units in 1 L sodium chloride 0.9%, i.e. 20 milliunits/mL solution, and infuse at 125 mL/hour.
  - Reduce rate if strong contractions are experienced.

  Note:
  Check serum sodium if used for more than 24 hours because of the danger of dilutional hyponatraemia.

For analgesia:
- Morphine, IV, 10 mg 4 hourly.

If Rh-negative:
- Anti-D immunoglobulin, IM, 100 mcg as a single dose.

REFERRAL
» Uterine abnormalities.
» Recurrent miscarriages (3 consecutive spontaneous miscarriages).
» Suspected cervical incompetence: mid-trimester miscarriage(s) with minimal pain and bleeding.
» Immunological problems.
» Diabetes mellitus.
» Parental genetic defects and SLE or other causes of autoimmune disease.

5.8.4 SEPTIC MISCARRIAGE

O03.87

GENERAL MEASURES
Counselling.
Urgent evacuation of uterus and surgical management of complications.

MEDICINE TREATMENT

- Oxytocin, IV.
  - Dilute 20 units in 1 L sodium chloride 0.9%, i.e. 20 milliunits/mL solution administered at a rate of 125 mL/hour.
  - Reduce rate if strong contractions are experienced.

Antibiotic therapy
- Ampicillin, IV, 1 g immediately, followed by 1 g 6 hourly.

PLUS
- Gentamicin, IV, 6 mg/kg daily.

PLUS
- Metronidazole, IV, 500 mg **or** oral, 400 mg 8 hourly.

Change to oral treatment after clinical improvement:
- Amoxicillin/clavulanic acid, oral, 875/125 mg 12 hourly for 7–10 days.

Note:
The addition of metronidazole to amoxicillin/clavulanic acid is unnecessary as amoxicillin/clavulanic acid has adequate anaerobic cover.

Penicillin allergy:
- Clindamycin, IV, 600 mg 8 hourly.

PLUS
- Gentamicin, IV, 6 mg/kg daily.

Change to oral treatment after improvement:
- Clindamycin, oral, 450 mg 8 hourly for 5 days.

PLUS
- Ciprofloxacin, oral, 500 mg 12 hourly.

If patient has severe sepsis, consider urgent hysterectomy.

REFERRAL
» Evidence of trauma.
» No response to treatment within 48 hours.

5.8.5 TROPHOBLASTIC NEOPLASIA ('HYDATIDIFORM MOLE')

O01

Misoprostol is not indicated in this condition because of risk of dissemination. Send products of conception for histology.

REFERRAL
» All patients.

5.9 TERMINATION OF PREGNANCY (TOP)

O04

Gestational age is based on the estimated size of the uterus rather than dates. Ultrasound examination is more accurate and of value in identifying ectopic pregnancy, molar pregnancy or twins.

SUMMARY OF CHOICE OF TERMINATION OF PREGNANCY ACT
Women eligible
Up to 13 weeks: on request.
13+ to 20 weeks: If doctor is satisfied that pregnancy was from rape or incest, or there is risk of fetal abnormality or risk to mother's physical or mental health or social or economic circumstances.
More than 20 weeks: Doctor and second doctor or registered midwife are satisfied that there is danger to the mothers' life, severe fetal malformation or risk of fetal injury.

Venue
An accredited facility with staff trained in performing TOP, designated by the Member of Executive Council at provincial level.

Practitioner
Up to 13 weeks: doctor, midwife or registered nurse with appropriate training.
More than 13 weeks: doctor responsible for decision and prescription of medication. Registered nurse/midwife may administer medication according to prescription.

Pre and post termination counselling is essential.
Consent of spouse/partner is not necessary.
Consent for TOP and related procedures e.g. laparotomy may be given by minors.
Minors are encouraged to consult parents or others but consent is not mandatory.

Mentally retarded/unconscious patient
On request from spouse or guardian; doctor and second doctor or registered midwife must agree.
If indicated as for 13+ to 20 weeks (above), spouse/guardian cannot prevent TOP by withholding consent.

5.9.1 GESTATION UP TO 13 WEEKS

O.04

GENERAL MEASURES
Counselling.
Outpatient procedure by nursing staff with specific training.
Manual vacuum aspiration of the uterus.

MEDICINE TREATMENT

Manual vacuum aspiration:

- Misoprostol, PV, 400 mcg 3 hours before routine vacuum aspiration of the uterus.

Routine analgesia for vacuum aspiration

- Pethidine, IM, 100 mg 30 minutes before aspiration procedure.

OR

- Morphine, IM, 10 mg 30 minutes before aspiration procedure.

Do not give intravenous benzodiazepines and parenteral opioid analgesics concurrently.

Alternatively, consider paracervical block.

Oral analgesia as required for 48 hours.

- Paracetamol, oral, 1 g 6 hourly.

AND

- Ibuprofen, oral, 800 mg 8 hourly.

Women who decline MVA:
An alternative is medical TOP with:

- Mifepristone, oral, immediately as a single dose.
  - Up to 9 weeks gestation: 100–200 mg.
  - 9– 13 weeks gestation: 200 mg.

Followed 24–48 hours later by:
- Misoprostol, PV, 800 mcg.
  - If expulsion has not occurred 4 hours after misoprostol administration, a second dose of misoprostol 400 mcg oral/PV may be given.
  - Review with ultrasound on day 7.

Note:
Bleeding may persist for up to 1 week.

After administration of mifepristone, start:
- Paracetamol, oral, 1 g 6 hourly.

ADD
After expulsion is complete:
- Ibuprofen, oral, 800 mg 8 hourly.

5.9.2 GESTATION 13+ TO 20 WEEKS

Inpatient care in facilities with 24-hour service and facilities for general anaesthesia.

GENERAL MEASURES
Manual vacuum aspiration of the uterus, if expulsion of products of conception is not complete.

MEDICINE TREATMENT

The dose of misoprostol decreases with increasing gestational age because of the risk of uterine rupture.

- Mifepristone, oral, 200 mg, oral, immediately as a single dose.

Followed 24–48 hours later by:
- Misoprostol, PV, 400–800 mcg as a single dose.
  - Then, misoprostol, oral, 400 mcg 3 hourly for 4 doses.

If no response after 24 hours, consider adding mechanical cervical ripening.
Pass a Foley catheter with 30 mL bulb through cervix with sterile technique.
Inflate bulb with 50 mL water or sodium chloride 0.9%.
Tape catheter to thigh with light traction on catheter.
Attach sodium chloride 0.9% 1 L with giving set to catheter.
Infuse sodium chloride 0.9% at 50 mL/ hour through catheter into uterus.

Warning
Uterine rupture may occur in women with previous Caesarean sections. Caution for this group and those of high parity: use 200 mcg misoprostol or alternative methods such as extra-amniotic 0.9 % saline infusion without misoprostol.

Analgesia
- Pethidine, IM, 100 mg 4 hourly as needed.

OR
- Morphine, IM, 10 mg 4 hourly as needed.

If Rh-negative:
- Anti-D immunoglobulin, IM, 100 mcg as a single dose.

REFERRAL
» Complicating medical conditions, e.g. cardiac failure, etc.
» Failed procedure.
» Suspected ectopic pregnancy.

5.10 SEXUAL ASSAULT
Y05

INVESTIGATIONS
Urine pregnancy test
Blood for:
» RPR,
» HIV, and
» Hepatitis B if no history of previous Hep B immunisation.

GENERAL MEASURES
Trauma counselling and completion of J88 forms
Examination under anaesthesia may be required for adequate forensic sample collection, or repair of genital tract trauma.

MEDICINE TREATMENT

Emergency contraception:
- Levonorgestrel 1.5 mg, oral, preferably within 24 hours of event.

OR
- Ethinyl estradiol 100 mcg plus norgestrel 1 mg, oral, 12 hourly for 2 doses

Note:
Emergency contraception can be given up to 5 days following an episode of unprotected intercourse.

STI prophylaxis
- Cefixime, oral, 400 mg immediately as a single dose.

PLUS
- Metronidazole, oral, 2 g, immediately as a single dose.

PLUS
- Doxycycline 100 mg 12 hourly for 7 days.
  In pregnancy, use: Amoxicillin, oral, 500 mg 8 hourly for 7 days.

HIV post-exposure prophylaxis (PEP)
See section: 10.5 Post-exposure prophylaxis for penetrative anal or vaginal sexual assault.

5.11 GENITAL PROLAPSE AND URINARY INCONTINENCE
N81.9

Note:
All patients should be referred to a specialist for initial evaluation.
Baseline investigations can, however, be done at lower level.

GENERAL MEASURES
Detrusor overactivity: bladder training, fluid restriction and physiotherapy.
Stress incontinence: pelvic floor exercises.
Surgical procedures as dictated by the diagnosis at specialist care.

MEDICINE TREATMENT
Treat urinary tract infections and underlying conditions, as appropriate.

For detrusor overactivity as demonstrated on urodynamic studies:
- Oxybutynin, oral, 2.5 mg 12 hourly, increasing to 5 mg 6 hourly.
  Specialist initiated.
  Note:
  Dry mouth is a common side effect of treatment.

REFERRAL
» All patients with prolapse.
» Patients not responding to therapy.
» Incontinence:
  > Stress incontinence as surgical repair will be likely.
  > Total incontinence as a fistula has to be excluded.
  > Urge incontinence resistant to 3 months' medicine treatment.
  > Mixed incontinence (both stress and urge incontinence present) as surgery will play a role.

5.12 MENOPAUSE AND PERIMENOPAUSAL SYNDROME

N95.9

GENERAL MEASURES

Counselling.
Stop smoking.
Maintain a balanced diet.
Regular exercise

MEDICINE TREATMENT

Hormone replacement therapy (HRT)

This is not indicated in all postmenopausal women. Symptomatic menopausal women and those with osteoporosis risk factors will benefit most.
The benefits need to be weighed against evidence of potential harm, including the emergence of risks as therapy continues.

Note:

Contraindications to HRT:

» breast cancer,
» endometrial cancer,
» women ≥ 60 years,
» thrombo-embolism,
» coronary heart disease,
» active liver disease,
» porphyria cutanea tarda, and
» women without severe menopausal symptoms.

Intact uterus (no hysterectomy)

HRT can be offered as sequentially opposed or continuous combined preparations. Continuous combined preparations have the advantage of less breakthrough bleeding, but should only be commenced once the woman has been stable on sequentially opposed therapy for a year. Treatment should be planned for 5 years but reviewed annually.

Sequentially opposed therapy:

- Conjugated equine estrogens, oral, 0.3–0.625 mg daily for 21 days.
  - Add medroxyprogesterone acetate, oral, 5–10 mg daily from day 11–21.
  - Followed by no therapy from day 22–28.

OR

- Estradiol valerate, oral, 1–2 mg daily for 11 days.
  - Add medroxyprogesterone acetate, oral, 10 mg daily from day 11–21.
  - Followed by no therapy from day 22–28.

Equivalent doses to medroxyprogesterone acetate:
- Norethisterone acetate, oral, 1 mg daily from day 11–21.
- Cyproterone acetate, oral, 1 mg daily from day 11–21.

Continuous combined therapy, e.g.:
- Conjugated equine estrogens, oral, 0.3–0.625 mg plus medroxyprogesterone acetate, oral, 2.5– 5mg daily.

OR
- Estradiol valerate, oral, 0.5–1 mg plus norethisterone acetate, oral, 0.5–1 mg daily.

Note:
Start at the lowest possible dose to alleviate symptoms. The need to continue HRT should be reviewed annually. A mammogram should be done once a year, and abnormal vaginal bleeding requires specialist consultation/referral
Any unexpected vaginal bleeding is an indication for excluding endometrial carcinoma as with other cases of postmenopausal bleeding. The use of transvaginal ultrasound to measure endometrial thickness plus the taking of an endometrial biopsy are recommended.

Uterus absent (post hysterectomy)
HRT is given as estrogen only. Estrogen supplementation to prevent postmenopausal osteoporosis requires long-term treatment.

- Estradiol valerate, oral, 1–2 mg daily.

OR
- Conjugated equine estrogens, oral, 0.3 mg daily **or** 0.625 mg on alternative days up to a maximum of 1.25 mg daily.

REFERRAL
» Premature menopause, i.e. < 40 years of age.
» Severe complications, particularly severe osteoporosis.
» Management difficulties, e.g. where a contra-indication to oestrogen replacement therapy exists.
» Post menopausal bleeding.

CHAPTER 6

OBSTETRICS

Note:
For medical complications of pregnancy, refer to the relevant chapters. Only common conditions specific to pregnancy, or requiring special management in pregnancy are included in this chapter.

6.1 ANAEMIA IN PREGNANCY

O99.0

DESCRIPTION

Haemoglobin (Hb) <11 g/dL. Anaemia in pregnancy is mostly due to either iron deficiency, folic acid deficiency or a combination of both. Women with iron deficiency may have 'pica', e.g. eating substances such as soil, charcoal, ice, etc.

GENERAL MEASURES

A balanced diet to prevent nutritional deficiency.

MEDICINE TREATMENT

Prophylaxis

- Ferrous sulphate compound BPC, oral, 170 mg daily with a meal.

PLUS

- Folic acid, oral, 5 mg daily.
  - Continue with iron and folic acid supplementation during lactation.
  - Treat other causes of anaemia according to the diagnosis.

Folic acid deficiency

- Folic acid, oral, 5 mg daily.

Identify and treat associated vitamin deficiencies accordingly**.**

Iron deficiency

- Ferrous sulphate compound BPC, oral, 170 mg 8 hourly with meals.
  - Continue for 3–6 months after the Hb reaches normal to replenish iron stores.
  - Hb is expected to rise by at least 1.5 g/dL in two weeks.
  - If Hb does not increase after two weeks, do a full blood count (FBC) to confirm hypochromic microcytic anaemia.
  - When using iron together with calcium supplementation, ensure that iron and calcium are taken at least 4 hours apart from one another.

Parenteral iron

If there is no response to oral iron, review adherence and do a FBC. If iron deficiency is confirmed on FBC and oral iron is not tolerated consider intravenous iron sucrose using the following formula:

Total dose = weight (kg) x [11 g/dL – actual Hb (g/dL)] x 2.4 + 200 mg.
Maximum daily dose: 200 mg.
Administer over 30 minutes in 200 mL sodium chloride 0.9%.
Repeat every second day until the total dose is given.

If delivery is anticipated within 3–5 days, consider blood transfusion in women with a Hb <7 g/dL.

REFERRAL/CONSULTATION

» No response to management.

6.2 DIABETES MELLITUS IN PREGNANCY

O24

This condition should ideally be managed by a specialist.

DESCRIPTION

Established diabetes: Diabetes (type 1 or 2) predating pregnancy.
Gestational diabetes: any degree of carbohydrate intolerance first recognised during pregnancy. It does not exclude the possibility that diabetes preceded the antecedent pregnancy.

Diagnosis of gestational diabetes mellitus

Screen women with the following:

- Glycosuria 1+ on 2 occasions, or 2+ on one occasion.
- Family history of diabetes.
- Previous gestational diabetes.
- Weight > 100 kg or BMI > 40 kg/m^2.
- Previous unexplained stillbirth.
- Previous macrosomic baby (weight > 4 000 g).
- Age > 40 years.
- Polycystic ovarian syndrome.
- Acanthosis nigricans.
- Polyhydramnios in current pregnancy.

Diagnostic criteria

Either a fasting plasma glucose ≥ 5.6 mmol/L **OR** a plasma glucose of ≥ 7.8 mmol/L two hours after a 75 g oral glucose tolerance test.

GENERAL MEASURES

Diet

Diabetic diet of not less than 7 200 kilojoules (1 800 Kcal) unless grossly obese.

» protein 15%,
» fat 25% ,
» high fibre carbohydrate 60%.

Eat 3 meals and 3–4 snacks/day.

Elective delivery at about 38 weeks' gestation.

MEDICINE TREATMENT

The mainstay of therapy is insulin. An initial trial of metformin has a role in the following patients:

» obese women, and
» women with type 2 diabetes.

Even with careful selection, approximately half of patients will require the addition of insulin for adequate glucose control.

- Metformin, oral, 500 mg daily.
  - Increase dose to 500 mg 12 hourly after 7 days.
  - Titrate dose to a maximum of 850 mg 8 hourly according to glucose control.
  - Contra-indications to metformin: liver or renal impairment.
  - If not tolerated change to insulin.

Do six-point blood glucose profiles, i.e. pre- and 1 hour post-breakfast, lunch and supper.

Normal profiles (adequate control)

Preprandial levels < 6 mmol/L and 1 hour postprandial < 7.8 mmol/L, repeat the profiles 2-weekly until 34 weeks and then weekly until delivery.

Abnormal profiles

Start insulin.

Diabetic women should be admitted initially for good control.

When adequate glucose monitoring can be maintained during pregnancy, e.g. home blood glucose monitoring with consultation or long-term admission, the following levels should be aimed for:

» preprandial levels: < 6 mmol/L
» 1-hour postprandial: < 7.8 mmol/L

Insulin requirements may increase with increasing gestation and later readmission may be necessary.

Preferred regimen
Use intermediate acting insulin between 21:00 and 22:00 to maintain preprandial levels and short acting insulin with all 3 meals to maintain the post prandial levels.

Starting dose may be based on previous insulin requirements, if known, or empiric starting dose:
- Insulin, intermediate acting, 10 units.
- Insulin, soluble, short acting, 5 units 30 minutes before main meal.

Adjust insulin dosage daily according to blood glucose profiles, until control is adequate.

Where the above recommended regimen is not feasible
Twice-daily regimen with biphasic insulin.
Empiric starting dose if previous insulin requirements are not known:
- Insulin, biphasic.
  - Daily dose: 0.2 units/kg/day, two-thirds of the dose 30 minutes before breakfast and one-third 30 minutes before supper.
  - Titrate daily to achieve target blood glucose as above.

During labour:
Monitor serum glucose hourly.
Stop subcutaneous insulin.
Administer short acting insulin to maintain physiological blood glucose levels.
- Insulin, short acting, continuous IV infusion, 20 units plus 20 mmol potassium chloride in 1 L dextrose 5% at an infusion rate of 50 mL/hour, i.e. 1 unit of insulin/hour
  - If blood glucose < 4 mmol/L, discontinue insulin.
  - If > 9 mmol/L, increase infusion rate to 100 mL/hour.

Postpartum insulin requirements decrease rapidly.
During the first 48 hours give insulin 4-hourly according to blood glucose levels.
Resume prepregnancy insulin or oral hypoglycaemic regimen once eating a full diet.

The newborn is at risk of:
» hypoglycaemia,
» respiratory distress syndrome,
» hyperbilirubinaemia, and
» congenital abnormalities.

Postpartum contraception
Tubal ligation should be considered.
Consider:
- o Low-dose combined contraceptive in well-controlled cases.
- o Progestogen-only preparation or intra-uterine contraceptive device if blood glucose control is poor.

REFERRAL/CONSULTATION
» Blood glucose not adequately controlled on diet alone.

6.3 HEART DISEASE IN PREGNANCY
O75.4

All women with heart disease require referral for specialist evaluation and risk assessment. The risk is particularly high in women with mechanical valves, Eisenmenger's syndrome or pulmonary hypertension. Termination of pregnancy (TOP) is an option for women with severe heart disease if recommended by a specialist.

GENERAL MEASURES
Consider thyrotoxicosis, anaemia and infection, which may precipitate cardiac failure.
Spontaneous delivery is usually preferable to Caesarean section, unless there are obstetric reasons for surgery.
Nurse in semi-Fowler's position.
Avoid unnecessary intravenous fluids.
Avoid a prolonged second stage of labour by means of assisted delivery with forceps (preferably) or ventouse.
Contraception, including the option of tubal ligation should be discussed after delivery in all women with significant heart disease.
Women who had serious complications during pregnancy should be advised not to become pregnant again.

MEDICINE TREATMENT
Indications for full anticoagulation during pregnancy (high risk):
» valvular disease with atrial fibrillation
» women with prosthetic heart valves

Pregnant women with prosthetic mechanical valves should not receive LMWH unless antifactor Xa levels can be monitored reliably weekly. Pre-dosing level 0.6 units/mL and a 4-hour peak level of 1–1.2 units/mL

First trimester
- Unfractionated heparin, IV, 5 000 units as a bolus.
  - Followed by 1 000–1 200 units/hour as an infusion.

OR
- Unfractionated heparin, SC, 15 000 units 12 hourly.
  - Adjust the dose to achieve a mid-target aPTT at 2–3 x control.

Practise strict infection control if using multi-dose vials, with one vial per patient and use of needle-free adaptor.

Second trimester
- Warfarin, oral, 5 mg daily.
  - Control with INR to keep within the therapeutic range of 2.5–3.5.

After 36 weeks until delivery
- Unfractionated heparin, IV, 5 000 units as a bolus.
  - Followed by 1 000–1 200 units/hour as an infusion.

OR
- Unfractionated heparin, SC, 15 000 units 12 hourly.
  - Adjust dose with aPTT to keep it 2 – 3 x control.
  - Stop heparin on the morning of elective Caesarean section or when in established labour, and re-start 6 hours after vaginal delivery or 12 hours after Caesarean section.

Consider the use of warfarin throughout pregnancy for women with older generation mechanical valves, or valves in the mitral position

Prophylaxis for venous thromboembolism
» More than one previous episode of venous thromboembolism.
» One previous episode without a predisposing factor, or with evidence of thrombophilia.

- Low molecular weight heparin, e.g.: dalteparin, SC, 5000 units daily.

OR
- Unfractionated heparin, SC, 5 000 units 8 hourly.

Antibiotic therapy
See section 3.5: Endocarditis, Infective for indications for prophylaxis against infective endocarditis.

Procedures for which endocarditis prophylaxis is indicated include:
» Vaginal delivery in the presence of suspected infection.
» Caesarean section.
» Assisted vaginal delivery.
» Prelabour rupture of membranes.

See section 3.5: Endocarditis, Infective.

Cardiac failure
Refer to section 3.4: Congestive Cardiac Failure.
Treatment is as for non-pregnant women, except that **ACE-inhibitors** and ARBs are contra-indicated.
If a vasodilator is needed:
- Hydralazine, oral, 25 mg 8 hourly.
  - Maximum dose: 200 mg daily.

PLUS
- Isosorbide dinitrate, oral, 20 mg 12 hourly.
  - Maximum dose: 160 mg daily.

Delivery
Contraction and retraction of the uterus after delivery increases the total peripheral resistance, and causes a relative increase in circulating volume. This may precipitate pulmonary oedema.

In women with NYHA grade II dyspnoea or more, consider the use of furosemide:
- Furosemide, IV, 40 mg with delivery of the baby.
  - Monitor for 48 hours thereafter for pulmonary oedema.

6.4 PRE-ECLAMPSIA
O15.9

DESCRIPTION
Diastolic blood pressure > 90 mmHg on two occasions measured at least 4 hours apart or > 110 mmHg on one occasion, after 20 weeks' gestation.
PLUS
» proteinuria > 300 mg/24 hours, or
» urinary **protein-creatinine ratio** > 0.03 g/mmol
in a woman who is not hypertensive outside pregnancy.

The main pathology is widespread endothelial damage from a placental endotheliotoxin. This affects all systems, particularly arterioles, coagulation, kidneys, liver and CNS.

GENERAL MEASURES
Prevention
Advise adequate dietary calcium (at least 1 000 mg daily).
Bed rest, preferably in hospital.
Lifestyle adjustment and diet.
Monitor BP, urine output, renal and liver function tests, platelet count, proteinuria and fetal condition.
Consider delivery when risks to mother outweigh risks of prematurity to baby.

MEDICINE TREATMENT

Prevention

For women at high risk of pre-eclampsia, e.g. pre-eclampsia in a previous pregnancy, chronic hypertension, diabetes, antiphospholipid syndrome or SLE, from 16 weeks gestation onwards:

- Aspirin, oral, 75–150 mg daily with food.
- Calcium, oral.
  - For high-risk patients: Calcium carbonate, oral, 500 mg 12 hourly (equivalent to 1 g elemental calcium daily).
  - Although the benefit is greatest in high-risk women, consider use of this agent in all pregnant women.
  - When using iron together with calcium supplementation, ensure that iron and calcium are taken at least 4 hours apart from one another.

Treatment

Antihypertensives

Drug treatment will be dictated by blood pressure response.
Monitor progress until a stable result is achieved.
In general, diuretics are contra-indicated for hypertension in pregnant women.
When needed, combine drugs using lower doses of the three agents before increasing the doses to a maximum.

- Methyldopa, oral, 250 mg 8 hourly as a starting dose.
  - Increase to 500 mg 6 hourly, according to response.
  - Maximum dose: 2 g/day.

AND/OR

- Amlodipine, oral, 5 mg daily.
  - Increase to 10 mg daily.

AND/OR

- Hydralazine, oral, 25 mg 8 hourly.
  - Titrate up to 50 mg 6 hourly

Hypertensive emergency

SBP ≥160 mmHg or DBP ≥110 mmHg. Admit to a high-care setting for close monitoring.

Preload with:

- Sodium chloride 0.9%, IV infusion, 200 mL.

- Nifedipine, oral, 10 mg
  - Repeat after an hour if needed until systolic blood pressure <160 mmHg and diastolic blood pressure < 110 mmHg
  - Swallow whole. Do not chew, bite or give sublingually.

OR

- Hydralazine, oral, 25 mg
  - Repeat after an hour if needed until systolic blood pressure < 160 mmHg and diastolic blood pressure < 110 mmHg.

If unable to take oral or inadequate response:

- Labetalol, IV infusion, 2 mg/minute to a total of 1–2 mg/kg.
  - Reconstitute solution as follows:
    Discard 40mL of sodium chloride 0.9% from a 200mL container.
    Add 2 vials (2 x 100 mg) of labetalol (5 mg/mL) to the remaining 160 mL of sodium chloride 0.9% to create a solution of 1 mg/mL.
    Start at 40mL/hour to a maximum of 160 mL/hour.
    Titrate against BP – aim for BP of 140/100 mmHg.

Delivery

- Oxytocin, IV/IM, 10 units as a single bolus after delivery of the baby.

Ergot-containing drugs are contraindicated in hypertensive women, including pre-eclampsia, following delivery of the baby.

Pre-eclamptic and eclamptic women are hypovolaemic, particularly when the haematocrit exceeds 40%, but are also susceptible to pulmonary oedema. Consequently, hypotension is a risk during anaesthesia. Careful infusion of IV fluids is important. Limit blood-loss at Caesarean section.

Both epidural and spinal anaesthesia may be used for operative delivery in hypertensive women, including pre-eclampsia. This should be administered by an experienced person, with meticulous attention to IV fluid management and haemodynamic monitoring.

Epidural analgesia is ideal for labour and delivery, but should only be undertaken by experienced practitioners in a unit properly equipped for resuscitation and with facilities available for urgent operative delivery. Avoid excessive IV fluids as there is no need for IV fluid loading in labour.

6.5 ECLAMPSIA

O15

DESCRIPTION

Eclampsia is diagnosed when a woman with pre-eclampsia has a seizure. Exclude any other obvious cause of the seizure before making the diagnosis. Management will include preventing further seizures, controlling the blood pressure, referral to a high-care unit and delivery of the baby if not already post-delivery.

GENERAL MEASURES

Place patient in left-lateral position.
Clear airway. If necessary, insert oropharyngeal airway.

MEDICINE TREATMENT

If necessary:

- Oxygen via nasal prongs or facial mask to maintain a saturation of >90%.

To prevent eclamptic seizures, magnesium sulphate is recommended for patients with severe pre-eclampsia, including imminent eclampsia. In some cases this allows for delivery to be delayed to improve neonatal outcome. When used for prevention of eclampsia, magnesium sulphate is administered for 24 hours, and then stopped. Women with severe pre-eclampsia should be managed under specialist care.

In high-care setting:

- Magnesium sulphate, IV, 4 g in 200 mL sodium chloride 0.9% over 20 minutes.

Follow with:

- Magnesium sulphate, IV infusion, 1 g/hour until 24 hours after delivery, or after the last convulsion.

Where infusion pumps are not available:

- Magnesium sulphate, IM, 5 g every 4 hours different IM sites, until 24 hours after delivery or following the last convulsion.

Stop magnesium sulphate if knee reflexes absent or if urine output < 100 mL/ 4 hours or respiratory rate <16 breaths/minute.

If respiratory depression occurs:

- Calcium gluconate 10%, IV, 10 mL given slowly at a rate not exceeding 5 mL/minute.

Eclamptic seizure in progress despite magnesium sulphate administration

- Lorazepam, IV/IM, 4 mg.
  - Maximum dose: 8 mg.

OR

- Clonazepam, IV, 2 mg.
  - May be repeated after 5 minutes.
  - Maximum dose: 4 mg.

OR

If above not available:

- Diazepam, IV, 10–20 mg, not faster than 2 mg/minute.

Notify the person who will resuscitate the newborn that a benzodiazepine and/or magnesium has been given to the mother.

REFERRAL

» All cases of eclampsia to a high or intensive care facility.

6.6 HYPERTENSION, CHRONIC

O10.9

GENERAL MEASURES

Lifestyle modification

No alcohol should be taken.
Regular moderate exercise, e.g. 30 minutes brisk walking at least 3 times a week.
Smoking cessation.
Aim to keep BP <150/100 mmHg

Fetal surveillance by symphysis-fundus height (SFH) growth and antepartum fetal heart monitoring from 28 weeks onwards.

Consider labour induction if:

- BP persistently ≥ 160/110 mmHg, or
- pregnancy of ≥37 weeks duration, or
- in the presence of maternal or fetal compromise, e.g. poor SFH growth and oligohydramnios, etc.

MEDICINE TREATMENT

See prevention and treatment of pre-eclampsia.
Switch ACE inhibitors, diuretics and beta blockers to methyldopa. Women should be advised that there's an increased risk of congenital abnormalities if these drugs were taken during pregnancy.

6.7 HIV IN PREGNANCY

O98.7

For comprehensive information on the care of HIV-infected pregnant women, refer to the current National PMTCT Guidelines.

All pregnant women should receive routine counselling and voluntary HIV testing at their very first antenatal visit.
Women who test negative should be offered repeat HIV testing from 32 weeks' gestation onwards.
HIV positive pregnant women upon diagnosis, should be clinically staged, and have a blood sample taken for CD4 cell count on the same day. The result must be obtained within a week.
Decisions about postpartum contraceptive use and method of infant feeding must be made in the antenatal period.

Women with unwanted pregnancies < 20 weeks' gestation should be assisted with access to TOP services.

Pregnant women with CD4 counts < 350 cells/mm^3 must be fast-tracked for access to lifelong antiretroviral therapy (ART). Those with symptoms of tuberculosis (TB) should be investigated and started on TB treatment before ART initiation.
All women with HIV infection should be counselled about the benefits of PMTCT.

MEDICINE TREATMENT
Perform a baseline ALT and creatinine concentration before starting ART.
Women with abnormal ALT should not start nevirapine.
Tenofovir is contra-indicated in women with a calculated creatinine clearance or eGFR of <60 mL/minute
In concurrent TB, use efavirenz in place of nevirapine after first trimester.

Criteria for lifelong ART initiated during pregnancy:
WHO stage 3 or 4 disease OR CD4 < 350 cells/mm^3

CD4 < 250 cells/mm^3:
- Tenofovir, oral, 300 mg daily.

AND
- Lamivudine, oral, 150 mg 12 hourly **or** 300 mg at night.

AND
- Nevirapine, oral, 200 mg daily for two weeks, followed by 200mg 12 hourly.

CD4 ≥ 250 cells/mm^3, only start after the first trimester**:**
- Tenofovir, oral, 300 mg daily.

AND
- Lamivudine, oral, 150 mg 12 hourly **or** 300 mg at night.

AND
- Efavirenz, oral, 600 mg at night.

As attaining an undetectable viral load is important in PMTCT, special attention should be paid to adherence monitoring.

Note:
Women who conceived on efavirenz-based ART and present at or beyond 14 weeks' gestation, should continue with their treatment regimen and, where possible, be referred to a tertiary centre for a fetal anomaly ultrasound scan at 18–22 weeks.

CD4 ≥ 350 cells/ mm^3 **and WHO stage 1 or 2 disease**
From 14 weeks' gestation onwards until the onset of labour:
- Zidovudine, oral, 300mg 12 hourly,

AND
At the onset of labour:
- Nevirapine, oral, 200mg immediately as a single dose

PLUS
- Tenofovir 300mg and emtricitabine 200mg oral, as a single dose

AND
- Zidovudine, oral, 300mg intrapartum every 3 hours until birth

Do a baseline haemoglobin (Hb) antenatally before starting zidovudine and monitor Hb every 4 weeks. If Hb < 8 g/dL, correct the anaemia before re-introducing zidovudine.

Women scheduled for elective Caesarean section:
- Antenatal zidovudine as above

AND
4 hours before surgery:
- Nevirapine, oral, 200 mg as a single dose.

AND
Within a day following Caesarean section:
- Tenofovir 300mg and emtricitabine 200 mg, oral.

For more detail regarding HIV management, see section 10.1 Antiretroviral Therapy.

6.8 SYPHILIS

A53.9

DIAGNOSTIC CRITERIA
Positive syphilis serology (RPR titre > 1:4).

GENERAL MEASURES
Inform contact(s).

MEDICINE TREATMENT
Mother
- Benzathine benzylpenicillin (depot formulation), IM, 2.4 million units weekly for 3 doses.

Note:
If mother has received <3 doses, the baby should be treated for congenital syphilis.

Penicillin allergy

- Erythromycin, oral, 500mg 6 hourly for 28 days.
  Note:
  Erythromycin for syphilis is not sufficient to prevent congenital syphilis. For penicillin sensitive patients, the penicillin desensitisation regimen is an option. If penicillin is not used, the baby must be regarded as inadequately treated and given penicillin after delivery.

Retreat mother with doxycycline once she has stopped breast feeding

- Doxycycline, oral, 100 mg 12 hourly for 28 days.

Asymptomatic, well baby:
Mother seropositive or result unknown, and mother has not been treated or was only partially treated:

- Benzathine benzylpenicillin (depot formulation), IM, 50 000 units/kg as a single dose into the antero-lateral thigh.

Symptomatic baby

- Procaine penicillin, IM, 50 000 units/kg daily for 10 days. (Not for I.V. use).

OR

- Benzylpenicillin (Penicillin G), IV, 50 000 units/kg, 12 hourly for 10 days.

6.9 JAUNDICE IN PREGNANCY

O26.6

DESCRIPTION
The most common causes of jaundice in pregnancy are not pregnancy-specific. They include viral hepatitis, and adverse drug reactions.

Pregnancy-specific causes include:

» intrahepatic cholestasis of pregnancy,
» acute fatty liver of pregnancy (acute yellow atrophy of the liver),
» severe pre-eclampsia or eclampsia, and
» hyperemesis gravidarum.

REFERRAL

» All, as certain causes of jaundice in pregnancy have a high mortality.

6.10 HYPEREMESIS GRAVIDARUM

O21.9

DESCRIPTION

Recurrent vomiting leading to ketosis, generally in the first trimester.

Exclude:

» medical causes, e.g. thyrotoxicosis, and
» molar pregnancy.

GENERAL MEASURES

Counselling.
Frequent small, dry meals.
Avoid fatty and spicy foods.
Restrict oral intake for 24–48 hours, but ensure adequate intravenous hydration.

MEDICINE TREATMENT

Correct electrolyte imbalance with IV fluids.

- Pyridoxine, oral, 25 mg 8 hourly.

PLUS

- Metoclopramide, oral/IV, 10–20 mg 6 hourly as needed.

PLUS

- Vitamin B complex, IV, 10 mL.

In refractory cases:
Administer daily until hyperemesis is controlled:

- Dexamethasone, IM/IV, 4–8 mg daily.

PLUS

- Ondansetron, IV, 4–8 mg over 5 minutes, daily.

6.11 PRETERM LABOUR (PTL) AND PRETERM PRELABOUR RUPTURE OF MEMBRANES (PPROM)

O60/O42

DESCRIPTION

Preterm: <37 weeks gestation.
Most problems occur at <34 weeks' gestation.
Confirm ruptured membranes by sterile vaginal speculum.
Preterm labour confirmed by regular uterine contractions with progressive cervical changes.

GENERAL MEASURES
Assess fetal wellbeing.
Estimate fetal weight.
Deliver if chorio-amnionitis suspected.

MEDICINE TREATMENT
If gestation <34 weeks:
Pre-hydrate before administration of nifedipine:
- Sodium chloride 0.9%, IV, 200 mL.

PLUS
- Nifedipine, oral, 20 mg.
  - If contractions persist, follow with 10 mg after 30 minutes then 10 mg 4 hourly for up to 48 hours.

If gestation <30 weeks and where nifedipine contra-indicated:
- Indomethacin, oral, 50 mg immediately then 25 mg 4 hourly for up to 48 hours.
  Note:
  Indomethacin may cause oligohydramnios, and its use is associated with a risk of premature closure of the ductus arteriosis. Use only if there is intolerance to nifedipine.

To improve fetal lung maturity at 26–34 weeks:
- Betamethasone, IM, 12 mg, 2 doses 24 hours apart.

If not available:
- Dexamethasone, IM, 12 mg, 2 doses 24 hours apart.
  Note:
  Corticosteroids are maximally effective if the complete course is administered at least 24 hours before delivery. Therefore give as soon as possible following diagnosis of PTL or PPROM.

Antibiotic therapy
Indicated routinely for ruptured membranes and selectively for preterm labour with intact membranes at high risk of infection.
- Amoxicillin, oral, 500 mg 8 hourly for 10 days.

PLUS
- Metronidazole, oral, 400 mg 8 hourly for 10 days.

OR

- Erythromycin, oral, 250 mg 6 hourly for 10 days.

PLUS
- Metronidazole, oral, 400 mg 8 hourly for 10 days.

Prepare for appropriate care of preterm infant.

REFERRAL
» Fetus requiring neonatal intensive care: weight < 2 kg or gestation <34 weeks.
» Fetus requiring specialised treatment after birth, e.g. surgery.
» Severely ill mother.

6.12 SUPPRESSION OF LABOUR
O62.9

DESCRIPTION
Tocolysis is useful to treat fetal distress in labour and to suppress labour in women needing transfer or awaiting Caesarean section. Also used prior to external cephalic version.

MEDICINE TREATMENT
- Salbutamol bolus, 250 mcg IV, slowly over 2 minutes.
  - Reconstitute the solution as follows:
    Add 1 mL (i.e. 0.5 mg/mL) salbutamol to 9 mL sodium chloride 0.9% to create a solution of 50 mcg/mL.
    Monitor pulse. Inject 5 mL (250 mcg) over at least 2 minutes. Do not administer if mother has cardiac disease.
    Place the mother in the left lateral position.

6.13 LABOUR INDUCTION
O80

If induction of labour is indicated, for medical reasons, for example pre-eclampsia, diabetes, or post-term pregnancy.

GENERAL MEASURES
Counsel the woman about the risks: failed induction or uterine hyperstimulation syndrome, which may require emergency caesarean section.

Cervix favourable and confirmed HIV negative mother
Artificial rupture of the membranes.

Cervix unfavourable
Extra-amniotic saline infusion: recommended if attempts at ripening the cervix with prostaglandins fail.
Pass a Foley catheter with 30 mL bulb through cervix with sterile technique.
Inflate bulb with 50 mL water or sodium chloride 0.9%.
Tape catheter to thigh with light traction.
Attach sodium chloride 0.9% 1 L with giving set to catheter.
Infuse sodium chloride 0.9% at 50 mL/ hour.
Remove after 24 hours if catheter has not fallen out.

MEDICINE TREATMENT

Cervix favourable

Amniotomy (if HIV negative) followed 2 hours later by:

- Oxytocin, IV, 2 units in 200 mL sodium chloride 0.9%
  - Start at an infusion rate of 12 mL/hour (i.e. 2 milliunits /minute)

Time after starting (minutes)	Oxytocin dose (milliunits/minute)	Dilution: 2 units in 200 mL sodium chloride 0.9% (mL/hour)
0	2	12
30	4	24
60	6	36
90	8	48
120	10	60
150	12	72
180	16	96
210	20	120

Note:

Avoid oxytocin in women with previous caesarean section or parity ≥5.
Oxytocin use requires continuous electronic fetal heart rate monitoring.
Aim for adequate uterine contractions (3–5 contractions in 10 minutes).
Most women will experience adequate contractions at a dose of 12 milliunits/minute.
If uterine hyperstimulation syndrome develops (>5 contractions in 10 minutes with fetal heart rate abnormalities), stop the oxytocin infusion and administer salbutamol as above.

Cervix unfavourable

Prostaglandins, e.g.:

- Dinoprostone gel, intravaginally, 1 mg.
  - Repeat after 6 hours.
  - Do not exceed 3 mg.

OR

- Dinoprostone tablets, intravaginally, 1 mg.
  - Repeat after 6 hours.
  - Do not exceed 3 mg.

Note:

Perform a non-stress test (cardiotocography) within an hour of each dinoprostone insertion, to evaluate the fetal condition during labour induction.

OR

- Misoprostol, oral, 20 mcg 2 hourly until in labour, or up to 24 hours.
  Oral misoprostol may be given as freshly made-up solution of one 200 mcg tablet in 200 mL water, i.e. 1 mcg/mL solution. Give 20 mL of this solution 2 hourly.
  Stop misoprostol administration when in established labour.
  Maximum 24 hours.
  If no response, consider extra-amniotic saline infusion.
  Never use oxytocin and misoprostol simultaneously.
  Misoprostol and other prostaglandins are contraindicated in women with previous Caesarean sections and in grand multiparous women.
  Note:
  Misoprostol is not registered for this indication in SA.
  Misoprostol in larger doses than indicated here for labour induction at term, may cause uterine rupture.
  Only to be prescribed by a doctor experienced in Maternal Health.
  A non-stress test to be done 4-hourly during misoprostol administration

6.14 LABOUR PAIN, SEVERE

GENERAL MEASURES

Antenatal counselling.
Psychological support from family member, friend or volunteer 'doula'.
The need for analgesics may be reduced by keeping the woman informed about the progress of labour, providing reassurance and carefully explaining the procedures performed.
Anticipate the need for analgesia rather than waiting for severe distress.

MEDICINE TREATMENT

At the onset of a uterine contraction:

- Morphine, slow IV, 10 mg as a single dose **or** pethidine, slow IV, 100 mg as a single dose.

Follow with:

- Morphine, IM, 10 mg 4 hourly **or** pethidine, IM, 100 mg 4 hourly.

AND

- Promethazine, IM, 25 mg 4 hourly.

Titrate dose and dose frequency according to pain.
Supplement with premixed nitrous oxide 50%/ oxygen 50% in late first stage.
Absorption from intramuscular injections during labour is poor.
The preferred route is IV.

Epidural anaesthesia
Offer this service only at hospitals with anaesthetic staff and equipment for epidural.
- Bupivacaine 0.25%.

OR
- Bupivacaine 0.125% with fentanyl 2 mcg/mL.
  - Do not exceed 2 mg/kg (maximum 150 mg) in any 4-hour period, or 400 mg in 24 hours.

Perineal analgesia:
- Lidocaine, 1 or 2%, infiltration, locally or by a pudendal block.

Postpartum and post-episiotomy pain
- Paracetamol, oral, 1 g 4–6 hourly when required to a maximum of 4 doses per 24 hours.

OR
- Ibuprofen, oral, 400 mg 8 hourly with meals.

OR
- Morphine 10 mg **or** pethidine 100 mg, IM, as appropriate.

6.15 DEHYDRATION/KETOSIS IN LABOUR
E86

DESCRIPTION
Subclinical dehydration is often missed in labour.

GENERAL MEASURES
Encourage adequate oral fluid intake.

MEDICINE TREATMENT
Mild dehydration
Give oral fluids.

Moderate/severe dehydration
Administer intravenous fluids, e.g.:
- Sodium chloride 0.9%, IV, 250 mL/hour.

Re-evaluate hydration hourly.

6.16 POSTPARTUM FEVER
O75.2

DESCRIPTION
During delivery the woman's protective barrier against infections is temporarily reduced and this may lead to infections.

The cause of fever may be a serious complication and is often preventable by attention to aseptic techniques.

GENERAL MEASURES

Prevent deep vein thrombosis.
Complete evacuation of uterine contents.
Hysterectomy may be indicated in severe uterine sepsis.
Attention to breast engorgement.

MEDICINE TREATMENT

Antibiotic treatment, where appropriate, should be guided by the presumed source of infection.

Empiric antibiotic therapy

- Ampicillin, IV, 1 g 6 hourly.

PLUS

- Metronidazole, oral, 400 mg 8 hourly.

PLUS

- Gentamicin, IV, 6 mg/kg daily.

6.17 POSTPARTUM HAEMORRHAGE

O72

DESCRIPTION

Blood loss >500 mL after birth of the baby or any blood loss which is regarded as excessive.

GENERAL MEASURES

Bimanual compression of the uterus.
Ensure delivery of placenta.
Check for local causes of bleeding.
Compress the abdominal aorta in situations where bleeding is not responsive to above measures when transferring or waiting for definitive treatment.

MEDICINE TREATMENT

Prevention

Active management of the 3rd stage of labour:

- Oxytocin, IM, 10 units.

AND

Controlled cord traction.

Treatment
Resuscitate
Put up two IV lines, one line for fluid resuscitation the other for oxytocin infusion.

- Oxytocin, IV, 20 units in 1 L sodium chloride 0.9% at 250 mL/hour.

If necessary:
ADD
- Ergometrine, IM, 0.2–0.5 mg.

OR

- Oxytocin, IM, 5 units.

PLUS
- Ergometrine, IM, 0.5 mg.
  - Repeat ergometrine as needed up to a maximum of 1 mg in 24 hours.
  - Avoid ergometrine in women with hypertension or cardiac disease, except in severe cases where the benefit is considered to outweigh the risk.

For non-responding cases:
- Dinoprost 5 mg/mL, intramyometrial.
  - Dilute 1 mL to 10 mL.
  - Give 2 doses of 1 mL of dilute solution at different sites.

6.18 THE RHESUS NEGATIVE WOMAN
O36.0

GENERAL MEASURES
Maternal serum antibodies absent
Prevention
Test for maternal serum antibodies at 'booking', 28 and 34 weeks' gestation. During pregnancy, give prophylactic anti-D immunoglobulin to the mother within 72 hours of a potentially sensitising event.

MEDICINE TREATMENT
After a termination of pregnancy (TOP), miscarriage, ectopic pregnancy or amniocentesis:
- Anti-D immunoglobulin, IM, 100 mcg.

After external cephalic version:
- Anti-D immunoglobulin, IM, 100 mcg.

At birth, determine the Rh status of the cord blood and request a Coomb's test:
Cord blood Rh negative - no treatment.

Cord blood Rh positive, Coomb's negative:
- Anti-D immunoglobulin, IM, 100 mcg.

If a large feto-maternal transfusion is suspected:
- Anti-D immunoglobulin, IM, 300 mcg for every 30 mL transfusion.
  - Maximum dose: 1 200 mcg.

PLUS
Do a maternal blood Kleihauer test.

Rh positive, Coomb's positive:
In these cases the mother will also have antibodies.
Do not administer anti-D immunoglobulin.

Maternal serum antibodies present
Consult a specialist.

CHAPTER 7

NEPHROLOGICAL/UROLOGICAL DISORDERS

7.1 NEPHROLOGY SECTION

7.1.1 CHRONIC KIDNEY DISEASE (CKD)

N18.9

DESCRIPTION

The presence of CKD should be established, based on:

» the presence of kidney damage e.g. proteinuria/haematuria, or small kidneys on ultrasound for at least 3 months; and/or

» level of kidney function: GFR < 60 mL/minute for at least 3 months with or without kidney damage. GFR is calculated using the Cockcroft and Gault formula in patients with stable renal function:

$$\text{CrCl (mL/minute)} = \frac{(140 - \text{age}) \times \text{weight (kg)}}{0.82 \times \text{serum Cr (micromol/L)}}$$

*in males

* In females, multiply serum Cr by 0.85 instead of 0.82.

The eGFR is an automatic calculation done by the NHLS using the MDRD formula. Results from eGFR may differ slightly from the Cockcroft and Gault equation. Neither the MDRD nor the Cockcroft and Gault formula is reliable in patients with unstable renal function.

Common causes of CKD include:

» hypertension,

» diabetes mellitus,

» glomerular disease (idiopathic, HIV, hepatitis B and C and systemic lupus erythematosus, etc.), and

» polycystic kidney disease.

Chronic kidney disease can be entirely asymptomatic until over 75% of kidney function is lost.
Check all drugs for possible dose adjustment based on eGFR/CrCl.

TREATMENT AND PREVENTION STRATEGIES ACCORDING TO STAGES

Adverse outcomes of CKD can often be prevented or delayed through early detection and treatment of risk factors for CKD.

In patients with CKD, the stage of disease should be assigned based on the level of kidney function according to the classification below, irrespective of diagnosis. All stage 4 and 5 patients require referral/consultation with a specialist.

Staging of kidney disease

Stage/ glomerular filtration rate (mL/minute/1.73m^2)	**Description**	**Action** Includes actions from preceding stages
Stage 0 or GFR > 90	» At increased risk of CKD	» Screening » CKD risk reduction » CVD risk reduction
Stage 1 or GFR > 90	» Kidney damage with normal or ↑ GFR	» Diagnose and treat comorbid conditions » Slow progression » CVD risk reduction
Stage 2 or GFR 60–89	» Kidney damage with mild ↓ GFR	» Estimate progression.
Stage 3 or GFR 30–59	» Moderate ↓ GFR	» Evaluate and treat for complications
Stage 4 or GFR 15–29	» Severe ↓ GFR	» Refer for consideration of renal replacement therapy.
Stage 5 or ESRD or GFR < 15 or on dialysis	» Kidney failure requiring renal replacement therapy » End Stage Renal Disease (ESRD)	» Refer for consideration of renal replacement therapy, i.e. dialysis or transplant if uraemia present.

Note:

A normal decline in GFR is observed with ageing at a rate of 1 mL/minute/year after 45 years so that patients over the age of 60 years may have an eGFR slightly below 60 mL/minute without overt kidney disease.

GENERAL MEASURES

Treat underlying CVD risk factors as appropriate.

Limit salt intake and stop smoking.

Avoid nephrotoxic drugs like NSAIDs.

MEDICINE TREATMENT

The following interventions may delay progression of renal disease.

Proteinuria reduction

Determine the amount of proteinuria with a spot urine specimen.

» If urine dipstick 1+ or greater, request protein creatinine ratio.
» If urine dipstick less than 1+, request albumin creatinine ratio.

The ideal target is: protein creatinine ratio (PCR) < 0.03 g/mmol or albumin creatinine ratio (ACR) < 2.2 mg/mmol. Most benefit is achieved by reducing PCR to < 0.1 g/mmol or ACR < 100 mg/mmol.
Achievement of these targets must be balanced against side-effects such as hypotension and hypoglycaemia.

Start treatment with an ACE inhibitor and titrate up to the maximum tolerated dose.

- ACE inhibitor, e.g.:
- Enalapril, oral, 20 mg 12 hourly.
  - Monitor creatinine and potassium after 1–2 weeks if eGFR < 60 mL/minute and after 4 weeks if eGFR > 60 mL/minute.
  - If creatinine increases by >20% from the baseline, stop ACE inhibitor and consult a specialist.
  - If stable, monitor thereafter at regular clinic visits.

If ACE inhibitor is not tolerated due to intractable cough, consider an angiotensin receptor blocker, e.g.:

- Losartan, oral, 100 mg daily.
  - Angiotensin receptor blockers are contra-indicated following ACE inhibitor-associated angioedema.

Optimise blood pressure control with additional antihypertensive agents, BP control results in a lowering of proteinuria and slower decline in GFR.
Target BP is 130/80 mmHg.

Diabetes mellitus

In diabetics with kidney disease there is an increased risk of hypoglycaemia. Insulin is the preferred medicine to control blood glucose in patients with eGFR <60 mL/minutes.

Note:

Insulin requirements will decrease as renal disease progresses.
Stop glibenclamide when eGFR < 60 mL/minute because of an increased risk of hypoglycaemia.
Stop metformin when eGFR < 45 mL/minute because of the risk of lactic acidosis.

In patients unable to take insulin, consider:
- Gliclazide, oral, 40 mg daily.

Fluid overload and oedema
- Furosemide, oral, 40 mg 12 hourly.

When fluid overloaded and eGFR < 60 mL/minute, start:
- Furosemide, oral, 40 mg 12 hourly.
  - Titrate to a maximum of 500 mg 12 hourly.

Furosemide is ineffective when patients are on dialysis and anuric.

Hypocalcaemia and hyperphosphataemia
The aim is to lower phosphate levels and maintain normal calcium levels to ensure calcium phosphate product (i.e. Ca x PO_4) <4.4 mmol/L, to prevent calcium deposition in vessels and tissue which aggravates vascular disease.

Patients with CKD stage 3–5, not on dialysis:
- Calcium carbonate, oral, equivalent to 500–1500 mg daily of elemental calcium.
  - Take in divided doses with meals.
  - If serum phosphate is low, then take between meals.

In symptomatic patients with CKD stage 5 who are not candidates for renal replacement therapy, the benefits of phosphate binding are unclear.

Patients considered suitable candidates for renal replacement therapy
Monitor Ca^{++} and PO_4 and PTH levels regularly.

For hyperphosphataemia uncontrolled on calcium carbonate:
- Aluminium hydroxide BP, oral, 10 mL 8 hourly. Specialist initiated.
  - To prevent dementia-associated aluminium toxicity, do not use for longer than 3 months.

For hyperparathyroidism, initiate when PTH levels > 2–3 times normal:
- Calcitriol, oral, 0.25–4 mcg daily. Specialist initiated.

Anaemia associated with CKD in patients on dialysis programmes
Patients on chronic haemodialysis or peritoneal dialysis are often anaemic due to iron deficiency and deficiency of erythropoietin.

In CKD, especially CKD stage 4–5:
- Iron, elemental, oral. Specialist initiated.
  - If no response consider parenteral iron.

AND

- Erythropoietin, SC/IV. Specialist initiated.

Definitive treatment, e.g. transplantation, usually improves anaemia. It is important to identify factors likely to aggravate anaemia, e.g. iron deficiency and infection.

Acidosis and hyperkalaemia
See section 7.1.5: Acute Renal Failure (ARF).

REFERRAL/CONSULTATION

» CKD stage 3 and above.
» Unknown cause of kidney failure.
» Rapid deterioration in renal function.
» Resistant hypertension despite appropriate medication and adherence.

7.1.2 GLOMERULAR DISEASE (GN)

N00–N08

REFERRAL

All patients with:

» unexplained haematuria on two consecutive visits,
» protein:creatinine ratio > 0.10 g/mmol for possible kidney biopsy,
» uncontrolled hypertension with CKD,
» severe kidney dysfunction, i.e. reduced eGFR, CKD stage 4 (GFR <30 mL/minute), and
» progressive decline in kidney function.

Where facilities are available, investigation and management is usually done with guidance or referral to a specialist.

7.1.3 GLOMERULAR DISEASE AND NEPHRITIC SYNDROME

N01/N03

DESCRIPTION

Presents clinically as an acute glomerulonephritis with haematuria, an acute decrease in glomerular filtration rate (GFR), sodium retention and water retention with hypertension.

GENERAL MEASURES

» Regulate fluid and electrolyte balance. Monitor weight closely.
» Dietary modification if severe kidney dysfunction, e.g. restrict protein, potassium and phosphate intake.

» Avoid potential nephrotoxins: e.g. NSAIDs, aminoglycosides.
» Treat hypertension adequately to prevent renal failure or worsening of renal failure.

See Section 7.1.1: Chronic Kidney Disease (CKD).

MEDICINE TREATMENT

The management of glomerular disease is individualised and dependent on the type of glomerular disease.
Management should be carried out or guided by a nephrologist according to the biopsy result.

Check all drugs for possible dose adjustments.

See section 7.1.1: Chronic Kidney Disease (CKD).

CONSULTATION/REFERRAL

» All patients.

7.1.4 GLOMERULAR DISEASE AND NEPHROTIC SYNDROME

N04

DESCRIPTION

Glomerular disease characterised by:
» severe proteinuria, i.e.: protein:creatinine ratio >0.25 g/mmol

and

» resultant clinical picture which includes:
  - oedema,
  - hypoalbuminaemia, and
  - hyperlipidaemia.

The cause cannot be determined accurately without a biopsy.

GENERAL MEASURES

Regulate salt and fluid intake. Weigh daily.
Postural blood pressure for monitoring fluid loss and to prevent excessive diuresis.
Evaluate proteinuria with protein creatinine ratio:
» initially – weekly
» when discharged – monthly, until stable

Monitor potassium frequently for patients on ACE inhibitors and/or diuretics.

MEDICINE TREATMENT

Management should be guided by a nephrologist according to the biopsy result.

Note:
These patients are at increased risk of renal and deep vein thrombosis.

CONSULTATION/REFERRAL

» All patients.

7.1.5 ACUTE RENAL FAILURE (ARF)

N17

DESCRIPTION

This is reversible kidney failure, most commonly as a result of:

» prerenal ARF, e.g. dehydration and fluid loss,
» intrarenal ARF, e.g. acute tubular necrosis or acute glomerulonephritis, and
» postrenal ARF, e.g. cervical cancer, ureteric obstruction and prostatic hypertrophy.

Often combinations of the above occur, i.e. dehydration with prerenal ARF and resultant ischaemia causing intrarenal ARF from acute tubular necrosis (ATN).

Common causes of acute renal failure:

» nephrotoxic drugs, e.g. NSAIDs, aminoglycosides, contrast agents and tenofovir,
» sepsis,
» shock, and
» dehydration.

Predisposing factors for acute renal failure include:

» HIV,
» diabetes,
» heart failure, and
» advanced age.

Common complications of acute renal failure include:

» fluid overload and pulmonary oedema,
» hyperkalaemia,
» bleeding,
» acidosis, and
» encephalopathy.

GENERAL MEASURES

A detailed history and good clinical examination is necessary to identify potentially reversible causes.
Judicious fluid replacement for dehydrated patients.
Check all drugs for possible dose adjustments.

Early consultation with expert/experienced clinician is required.

MEDICINE TREATMENT

Short trial of furosemide only after adequate fluid replacement, if volume status and BP is satisfactory:

- Furosemide, IV, 250 mg in 50 mL dextrose 5% infused over 30 minutes.

Acute dialysis

Discuss all cases with the referral centre.
Common indications:

» Pulmonary oedema and anuria.
» Intractable metabolic acidosis and severe hyperkalaemia (> 7 mmol/L).
» Uraemic complications, e.g. pericarditis, encephalopathy and bleeding.
» Drug overdose only if due to dialysable toxin. See section 19: Exposure to poisonous substances.

Note:
HIV infection is not a contra-indication for dialysis. Peritoneal dialysis fluid should be considered potentially infectious for HIV and viral hepatitis.

Both haemodialysis and peritoneal dialysis are acceptable modalities of therapy in the acute setting.

Acidosis

If pH <7.25 and HCO_3 <15 mmol/L and the patient is stable and not dehydrated, refer for dialysis. If dehydrated, administer fluid.

CAUTION
Avoid fluid overload.

If associated acidosis, see fluid preference below.

Hyperkalaemia

Serum K^+ >6.5 mmol/L.
Beware of spurious hyperkalaemia due to haemolysis during venipuncture.

Emergency measures

- Calcium gluconate 10%, slow IV bolus, 10 mL.
  - Maximum dose: 40 mL.

- Dextrose 50%, continuous IV infusion, 100 mL with soluble insulin, 10 units administered over 15–30 minutes.
  - Monitor blood glucose levels hourly.

AND

- Salbutamol 0.5%, solution, nebulised over 3 minutes preferably driven by oxygen.
  - Dilute 1 mL in 3 mL of sodium chloride 0.9%.

If there is no response, patients will require dialysis.

For long-term or chronic, non-urgent need for potassium removal:
- Sodium polystyrene sulfonate, oral, 15 g with 15 mL lactulose, 6 hourly.

OR
- Sodium polystyrene sulfonate, rectal, 30–60 g as an enema.
  - After 8 hours, wash out with phosphate enema.

  Note:
  Rectal administration is less effective.

Treat acidosis to prevent cardiac instability.
Furosemide may also be of benefit.
Monitor ECG and measure serum K^+ frequently.

If the above treatment fails, urgent dialysis is required.

Hyperphosphataemia
To decrease absorption of phosphate in acute renal failure:
- Aluminium hydroxide 300 mg/5 mL, oral, 10 mL 8 hourly.

Do not administer aluminium hydroxide and sodium polystyrene sulfonate simultaneously as this may potentiate aluminium toxicity.

Acute renal failure may complicate chronic renal failure.
A small percentage of patients do not recover kidney function and should be treated as CKD.

REFERRAL/CONSULTATION
» Severe fluid overload.
» Suspected glomerular disease or cause of ARF is unknown.
» Failure to recover kidney function after 3 weeks on dialysis or after suspected cause has been treated or withdrawn.

7.1.6 END STAGE RENAL DISEASE (ESRD) - CKD STAGE 5
N18.5

DESCRIPTION
A permanent and usually irreversible stage of kidney failure caused by a variety of diseases (See section 7.1.1: Chronic Kidney Disease), which requires dialysis or transplantation for the patient to survive.
Note:
These patients are best managed at a specialist centre and by specialists.

GENERAL MEASURES

Appropriate dietary control of metabolic needs, electrolyte, fluid status and serum phosphate and calcium.
Restrict salt, phosphate and potassium.

MEDICINE TREATMENT

Avoid magnesium and aluminium containing substances.
Manage fluid balance on an individual basis.
Review all drug doses and adjust for the level of renal function, most will be GFR < 10 mL/minute.

REFERRAL/CONSULTATION

» All ESRD patients who may qualify for long term dialysis programs. See section 7.1.7: Renal replacement therapy.
» Patients with potentially reversible factors.

7.1.7 RENAL REPLACEMENT THERAPY

PATIENT SELECTION

The final decision for selection of patients for renal replacement therapy should be made at the tertiary level hospital or by a nephrologist.
The ideal patient for renal replacement therapy is a patient with uncomplicated CKD stage 5 (ESRD), who is a suitable candidate for renal transplantation.
Referral may be most useful in identifying the conditions outlined earlier.

Individual renal units have their own criteria for acceptance and these may include:
» considerations of presence of systemic illnesses,
» age,
» BMI, and
» psychosocial factors.
Obtain these guidelines from the referral centre.

7.1.8 URINARY TRACT INFECTION (UTI)

N39.0

DESCRIPTION

Infection, which, because of the anatomical continuity of the system, involve part or all of the urinary tract. Uncomplicated cystitis is a lower UTI in a non-pregnant woman of reproductive age who has a normal urinary tract.
All other UTIs are regarded as complicated.

An upper UTI is a more serious condition and requiring longer and sometimes intravenous treatment.

Features of upper UTI include:
» flank pain/tenderness,
» temperature ≥38°c or higher,
» other features of sepsis, i.e. tachypnoea, tachycardia, confusion and hypotension, or
» vomiting.

In complicated, recurrent or upper UTIs, urine should be sent for microscopy, culture and sensitivity.

MEDICINE TREATMENT

Empirical treatment is indicated only if:
» positive leucocytes and nitrites on urine test strips, or
» leucocytes or nitrites with symptoms of UTI, or
» systemic signs and symptoms.

Alkalinising agents are not advised as many antibiotics require a lower urinary pH.

Uncomplicated cystitis
- Ciprofloxacin, oral, 500 mg as single dose.

Complicated cystitis
- Ciprofloxacin, oral, 500 mg 12 hourly for 7 days.

For pregnant women:
- Amoxicillin/clavulanic acid, oral, 875/125 mg 12 hourly for 7 days.

Acute pyelonephritis
Admit all patients with vomiting, sepsis or diabetes.
Ensure adequate hydration with intravenous fluids.
If there is a poor response, perform an ultrasound on all hospitalised patients urgently as in-patients or electively as out-patients.

Adjust antibiotic according to sensitivity.
Duration of antibiotic therapy:
» fluoroquinolones 7 days
» other antibiotics 14 days.
Longer courses of therapy, 2–3 weeks, should be given for complicated pyelonephritis.

If normal renal function:
- Gentamicin, IV, 6 mg/kg daily.

Switch to oral therapy as soon as the patient is able to take oral fluids:
- Ciprofloxacin, oral, 500 mg 12 hourly for 7 days.

If impaired renal function:
- Ceftriaxone, IV, 1 g daily.

Switch to oral therapy as soon as the patient is able to take oral fluids:
- Ciprofloxacin, oral, 500 mg 12 hourly for 7 days.
  - CrCl: < 10 mL/minute 50% of normal dose

Refer to a urologist if there is failure to resolve.

7.1.9 RECURRENT UTI

DESCRIPTION
Recurrence of a UTI more than 3 times within a one-year period.

Two types occur:
» Relapse or recurrence of bacteriuria with the same organism within 3 weeks of completing treatment. This may be due to:
  > antibiotic resistance,
  > inadequate duration of therapy, e.g. prostatitis, or
  > underlying structural abnormality, e.g. benign prostatic hyperplasia with bladder outflow obstruction, renal cysts and pyogenic abscess.
» Re-infection, i.e. eradication of bacteriuria by appropriate treatment, followed by infection with a different organism. This constitutes 80% of recurrent infections.

Send urine for microscopy, culture and sensitivity as treatment is determined by the results.

GENERAL MEASURES
Women should void soon after intercourse.
Identify and treat hormone-deficient atrophic vulvo-vaginitis in the elderly.
Patients with impaired bladder emptying require careful urological examination to establish whether surgical treatment is required.
Patients with ileal conduits or long-term indwelling catheters should not receive antibiotics unless there is invasive upper UTI. In this setting, treatment with a short, intensive course of antibiotic is appropriate.

MEDICINE TREATMENT
Prophylaxis
To reduce risk of recurrence in patients with >3 infections/year requires continuous prophylaxis for at least 6 months:
- Cotrimoxazole 80/400 mg, oral, 1 tablet at night.

OR
- Nitrofurantoin, oral, 100 mg at night.
  - Beware of pulmonary fibrosis.
  - Limit to 6 months only.

2–3 infections/year:
- Ciprofloxacin, oral, 500 mg as single dose for symptomatic infections (self treatment).

UTI in relation to sexual activity:
- Ciprofloxacin, oral, 500 mg as single dose.

Treatment
Treat according to microscopy, culture and sensitivity.

REFERRAL
» Septicaemia not responding to treatment.
» Uncertain diagnosis.
» Recurrent infections where no facilities exist for adequate culture of urine.
» Further investigation in women with relapses, especially outside pregnancy.
» All men with recurrent UTI.

7.1.10 PROSTATITIS
N41.0/N41.1

DESCRIPTION
This is an infection of the prostate caused by uropathogens.
Clinical features include:
» pyrexia,
» acute pain in the pelvis and perineum,
» urinary retention or difficulty, and
» acutely tender prostate on rectal examination.

Chronic non-bacterial prostatitis
This is a diagnosis of exclusion, i.e. failure to respond to antibiotics. It is associated with perineal, suprapubic, penile and testicular pain.

MEDICINE TREATMENT
Acute bacterial prostatitis
In men < 35 years old:
- Cefixime, oral, 400 mg as single dose.

Follow with:
- Doxycycline, oral, 100 mg 12 hourly for 7 days.

In men > 35 years old:
- Ciprofloxacin, oral, 500 mg 12 hourly for 14 days.

Chronic/relapse/persistent infection:
- Ciprofloxacin, oral, 500 mg 12 hourly for 28 days.

REFERRAL
» To a urologist if no response to treatment.

7.2 UROLOGY SECTION

7.2.1 HAEMATURIA
R31

DESCRIPTION
Bleeding from the urinary tract, which can be from the kidneys, collecting system, bladder, prostate and urethra.
Proteinuria and casts on routine microscopy suggest glomerular disease.
Schistosomiasis (bilharzias) is a common cause of haematuria.

GENERAL MEASURES
All patients must have a urine microscopy evaluation to determine the origin of the haematuria.

Isomorphic red cells: suggests urinary tract below the kidney i.e. pelvis to urethra.
Dysmorphic red cells: suggests intrarenal and glomerular origin.

Exclude schistosomiasis.

Note:
The presence of blood on urine test strips does not indicate infection and should be investigated as above.

MEDICINE TREATMENT
Only if evidence of associated urinary tract infection, i.e. positive leucocytes or nitrites on urine test strips.
See section 7.1.8: Urinary Tract Infection (UTI) and see section 7.1.2: Glomerular Disease.

REFERRAL
» All cases not responding to specific drug treatment.
» Suspected glomerular disease.
» Gross macroscopic haematuria with no response to primary therapy and with a drop in haemoglobin.

7.2.2 BENIGN PROSTATIC HYPERPLASIA

N40

DESCRIPTION

Benign prostatic hyperplasia is a noncancerous (benign) growth of the prostate gland. It usually occurs in men over 50 years of age. The cause is unknown and believed to be due to changes in hormone levels associated with ageing.

GENERAL MEASURES

Annual follow-up with digital rectal examination (DRE).
For patients presenting with urinary retention, insert a urethral catheter as a temporary measure while the patient is transferred for referral.
Surgical reduction of the prostate is the preferred treatment, e.g. minimally invasive transrectal procedures or radical prostatectomy.
Remove drugs that prevent urinary outflow e.g. tricyclics and neuroleptics.

MEDICINE TREATMENT

When surgery is not feasible or deferred:

- Doxazosin, oral, 4 mg daily.

REFERRAL

» Renal failure.
» For biopsy if associated constitutional symptoms or weight loss.
» Hydronephrosis.
» Recurrent urinary tract infections.
» Urinary retention.
» Urge incontinence.
» Suspected prostate cancer on digital rectal examination.
» Suspected TB of prostate gland on biopsy.
» Haematuria.
» Bladder calculi.

7.2.3 OVERACTIVE BLADDER

N39.4

DESCRIPTION

Hyperactivity or hyperplasia of the detrusor muscle, or failure of the detrusor muscle to contract.

GENERAL MEASURES

Health education.
Clean intermittent self-catheterisation (CISC).
Indwelling catheter, suprapubic or transurethral.

Surgical therapy, where indicated: e.g. enterocystoplasty, urinary diversion, or continence surgery as decided by the surgeon.

MEDICINE TREATMENT

For detrusor hyperactivity demonstrated on urodynamic studies:

- Oxybutynin, oral, 2.5–5 mg 8 hourly. Specialist initiated.

REFERRAL

» For confirmation of diagnosis.
» Complications.

7.2.4 IMPOTENCE

N48.4/F52.2

DESCRIPTION

The inability to attain and maintain an erect penis with sufficient rigidity for vaginal penetration. Organic causes include neurogenic, vasculogenic or endocrinological causes as well as many systemic diseases and certain drugs.

GENERAL MEASURES

Thorough medical and psychosexual history
Examination should exclude gynaecomastia, testicular atrophy or penile abnormalities.
Consider the removal of drugs that may be associated with the problem.
A change in lifestyle or drugs may resolve the problem.

MEDICINE TREATMENT

Treat the underlying condition.

In patients with proven testosterone deficiency:

- Testosterone. Specialist initiated.

See section 8.3: Androgen deficiency.

REFERRAL

» Where an organic disease or medical condition is suspected as a cause.
» To a urologist or appropriate specialist if surgical intervention is needed, e.g. penile prostheses, vascular surgery and pelvic fractures.

7.2.5 RENAL CALCULI

N20.2

DESCRIPTION

A kidney stone or calculus which has formed in the renal tract, i.e. pelvis, ureters or bladder, as a result of urine which is supersaturated with respect to a stone-forming salt.

Collect the stones and send to the laboratory for analysis.

GENERAL MEASURES

Acute stage

Oral fluids administered liberally.
Intravenous fluids to ensure adequate hydration and urine flow.
Surgical procedures, if required.

Maintenance therapy, for the prevention of recurrence

Fluid intake of at least 2.5–3.5 L daily, especially in warm climates.

MEDICINE TREATMENT

Analgesia for pain, if needed:

- Morphine, IM/slow IV, 10–15 mg.

For hypocitraturia:

- Potassium citrate mixture BP, oral, 10–15 mL 8 hourly for 10 days.
  - Dilute in a glass of water.
  - Repeat as necessary.

For uric acid stones:

- Potassium citrate mixture BP, oral, 10–15 mL 8 hourly for 10 days.
  - Dilute in a glass of water.
  - Repeat as necessary.

PLUS

- Allopurinol, oral, daily.
  - Starting dose: 100 mg
  - Titrate up to 300 mg.

The treatment is long-term to prevent recurrence.

For mild metabolic hyperoxaluria:

- Pyridoxine, oral, 25–75 mg daily.

PLUS

- Calcium carbonate, oral, equivalent to 500–1 000 mg/day of elemental calcium.
  - Take 8 hourly with meals for 4 weeks.

For renal hypercalciuria (absorptive type):

- Hydrochlorothiazide, oral, 50 mg daily for 1 month.
  - May be repeated.

REFERRAL

» In acute setting for suspected or diagnosed obstruction and/or ongoing pain.
» Complicating urinary tract sepsis.
» Renal damage or insufficiency, i.e. presence of CKD at the time of diagnosis or afterwards.
» Recurrent calculi.
» If medical problem is suspected to be the cause e.g. chronic UTI and Crohn's disease and unable to make the diagnosis at secondary hospital level.

CHAPTER 8

ENDOCRINE SYSTEM

8.1 ACROMEGALY

E22.0

This condition should be managed at a tertiary centre.
Transsphenoidal hypophysectomy is the accepted form of therapy.
Radiotherapy post operatively is required in most cases (with large tumours).

REFERRAL

» All patients to a hospital with endocrine and neurosurgery facilities.

8.2 ADRENAL INSUFFICIENCY (ADDISON'S DISEASE)

E27.1

DESCRIPTION

Primary adrenocortical insufficiency.

Clinical presentation

Acute crisis:

- hypotensive shock
- fever
- GIT disturbances
- dehydration
- weakness
- depressed mentation
- hypoglycaemia
- hyponatremia
- hyperkalaemia
- acidosis

Chronic:

- hyperpigmentation
- weakness and fatigue
- loss of weight
- postural dizziness
- GIT disturbances
- hypotension
- hypoglycaemia
- hyponatraemia

Always consider this diagnosis in a thin, hypotensive, hypoglycaemia patient, or during stress e.g. sepsis.

Investigations

08h00 serum cortisol level (or at time of presentation in acute crisis):
> 550 nmol/L: virtually excludes the diagnosis
< 100 nmol/L: highly suggestive of hypoadrenalism

100–550 nmol/L is indeterminate and may require an adrenocorticotropic hormone (ACTH) stimulation test:

- ACTH depot, IM, 1 mg with blood sampling at 60 minutes.
  - Post ACTH, serum cortisol level normal value: > 550 nmol/L or double the pre-test level.

GENERAL MEASURES

All patients should wear a notification bracelet.

MEDICINE TREATMENT

Acute crisis

Exclude sepsis.

- Hydrocortisone, IV, 200 mg 6 hourly.

Change to oral maintenance therapy once stable.

To maintain adequate intravascular volume guided by blood pressure:

- Sodium chloride 0.9%, IV.

The fluid deficit is often several litres.

Monitor glucose levels closely and treat hypoglycaemia if present.

Chronic

As maintenance therapy:

- Hydrocortisone, oral.
  - Start with 10 mg in the morning and 5 mg at night.
  - Increase the dose according to clinical response up to 20 mg in the morning and 10 mg at night.

OR

- Prednisone, oral.
  - Start with 5 mg daily.
  - Increase to maximum of 7.5 mg daily, if necessary.

For patients who remain symptomatically hypotensive:

- Fludrocortisone, oral, 50–100 mcg daily.

Monitor response to therapy with:

- Symptoms: improvement in fatigue and GIT disturbances.
- Blood pressure: normotensive and no postural drop.
- Electrolytes: normal Na+ and K+.

During times of severe “stress” i.e. acute illness, surgery, trauma, etc.:

- Hydrocortisone, IV, 100 mg 6 hourly.

With minor stress maintenance therapy should be doubled for the duration of illness and gradually tapered to usual dose.

REFERRAL
» All suspected cases for full evaluation.

8.3 ANDROGEN DEFICIENCY
E29.1

DESCRIPTION
Reduced testosterone due to hypothalamic/pituitary hypofunction or primary testicular failure.

Investigations
Morning (08h00–09h00) serum total testosterone.
LH and FSH

	Serum testosterone	LH and FSH
Primary testicular failure	below normal	above normal
Secondary (hypothalamic/pituitary) hypogonadism	subnormal	subnormal

Note:
If the serum total testosterone concentration is borderline low repeat the test before replacement therapy is initiated.
Prolactin
Sperm count, if infertility is a consideration.
Further investigations to determine cause to be undertaken after referral.
Consult a specialist.

MEDICINE TREATMENT
Screen hypogonadal men for prostate cancer before beginning testosterone replacement.
Individualise dosage and review doses based on clinical response.

- Testosterone cyprionate, deep IM, 200–300 mg every 2–4 weeks.

Monitor patients for prostate cancer during treatment as normal.

8.4 CUSHING'S SYNDROME
E24.9

DESCRIPTION
Cushing's syndrome is an illness resulting from excess cortisol secretion or exogenous glucocorticoid administration. Cushing's disease is hypercortisolism secondary to an ACTH-secreting pituitary tumour.

Investigations
Screening tests for Cushing's syndrome: 24 hour urinary free cortisol.
Low dose betamethasone (equivalent to dexamethasone) suppression test:
- Betamethasone, oral, 1 mg.
  - Administer close to midnight.
  - Measure plasma cortisol 8 hours later.
  - In normal people morning cortisol will be suppressed to <50 nmol/L.
  - Refer if levels not suppressed.

GENERAL MEASURES
Check for hypertension and diabetes and treat accordingly.
Check potassium.

REFERRAL
» All cases for investigation of aetiology and appropriate management.

8.5 DIABETES MELLITUS

DESCRIPTION
Types of diabetes:
» Type I
» Type 2
» Pancreatic diabetes mellitus
» Gestational diabetes mellitus – See Section 6.2: Diabetes Mellitus in Pregnancy.

GENERAL MEASURES
All patients require lifestyle modification.
In patients with type 2 diabetes mellitus, appropriate weight loss if weight exceeds ideal weight.
Correct meal/energy distribution in type 1 diabetes mellitus.
Moderate or no alcohol intake.
Discourage smoking.
Increased physical activity, aim for 30 minutes 5 times a week.
Education about foot care is essential.

Monitoring
At every visit:
» blood glucose,
» weight, and
» blood pressure.
Measure HbA1c:
» annually in patients who meet treatment goals, and
» 3–6 monthly in patients whose therapy has changed until stable.

Annually:
» potassium,
» creatinine,
» urine albumin creatinine ratio,
» lipids (fasting triglycerides and cholesterol), and
» eye examination to look for retinopathy.

Parameter	**Optimal** Target for control	**Acceptable**	Additional action suggested
Capillary blood glucose values (finger-prick)			
fasting (mmol/L)	4–7	≤8	> 8
2-hour post-prandial (mmol/L)	5–8	8–10	> 10
(HbA1c) (%)	< 7	7–8	> 8
BMI (kg/m^2)	18.5 – 25		> 25
Waist circumference Male Female	< 94 cm < 80 cm		
Blood Pressure Systolic Diastolic	< 140 mmHg < 80 mmHg		

In the elderly, the increased risk of hypoglycaemia must be weighed against the potential benefit of reducing microvascular and macrovascular complications.
In patients with severe target organ damage, therapy should be tailored on an individual patient basis and should focus on avoiding hypoglycaemia.

REFERRAL
» Inability to achieve optimal metabolic control.
» Complications that cannot be managed on site, especially ophthalmic, e.g. cataracts and proliferative retinopathy.

8.5.1 DIABETES MELLITUS TYPE 2
E11

Management includes:
» Treatment of hyperglycaemia.
» Treatment of hypertension and dyslipidaemia after risk-assessment. See section 3.6: Hypertension.
» Prevention and treatment of microvascular complications.
» Prevention and treatment of macrovascular complications.

MEDICINE TREATMENT

Oral blood glucose lowering drugs

Metformin is added to the combination of dietary modifications and physical activity/exercise.

Combination therapy with metformin plus a sulphonylurea is indicated if therapy with metformin alone (together with dietary modifications and physical activity/exercise) has not achieved the HbA_{1c} target.

For persisting HbA_{1c} above acceptable levels and despite adequate adherence to oral hypoglycaemic agents, add insulin and withdraw sulphonylurea.

Note:

Secondary failure of oral agents occurs in about 5–10% of patients annually.

Metformin

- Metformin, oral, 500 mg daily with meals.
  - Titrate dose slowly depending on HbA_{1c} and/or fasting blood glucose levels to a maximum dose of 850 mg 8 hourly.

  Contra-indicated in:
  - renal impairment i.e. eGFR < 50 mL/minute,
  - uncontrolled congestive cardiac failure,
  - severe liver disease, or
  - patients with significant respiratory compromise.

Sulphonylurea derivatives: gliclazide or glibenclamide.

- Gliclazide, oral, 40 mg daily 30 minutes before breakfast.
  - Titrate dose slowly depending on HbA_{1c} and/or fasting blood glucose levels to a maximum dose of 160 mg 12 hourly.
  - When ≥ 80 mg per day is needed, divide the total daily dose into 2.
  - Preferred in the elderly.

OR

- Glibenclamide, oral, 2.5 mg daily 30 minutes before breakfast.
  - Titrate dose slowly depending on HbA_{1c} and/or fasting blood glucose levels to 15 mg daily.
  - When ≥7.5 mg per day is needed, divide the total daily dose into 2, with the larger dose in the morning.
  - Avoid in the elderly and patients with renal impairment.

Oral agents should not be used in type 1 diabetes, renal impairment or clinical liver failure.

Monitor serum creatinine and estimated GFR in kidney disease.

Insulin therapy in type 2 diabetes

Indications for insulin therapy:

» Inability to control blood glucose with oral drugs, i.e. combination/substitution insulin therapy.
» Temporary use for major stress, e.g. surgery, medical illness.
» Severe kidney or liver failure.
» Pregnancy.

Note:

At initiation of insulin therapy, give appropriate advice on self-blood glucose monitoring (SBGM) and diet.

It is advisable to maintain all patients on metformin once therapy with insulin has been initiated.

Insulin type	Starting dose	Increment	Maximum daily dose
Add on therapy: • Intermediate to long-acting insulin	10 units in the evening before bedtime, but not after 22h00.	If 10 units not effective increase gradually to 20 units (2–4 units increase each week).	40units Refer if > 40 units are needed.
Substitution therapy: • Biphasic insulin	Twice daily. Total daily dose: 15 units divided as follows: • 2/3 of total daily dose, i.e. 10 units, 30 minutes before breakfast. • 1/3 of total daily dose, i.e. 5 units, 30 minutes before supper.	4 units weekly. First increment is added to dose before breakfast Second increment is added to dose before supper.	50 units. Refer if > 50 units are needed.

Also see insulin protocols as in type 1 diabetes mellitus below.

Note:

Insulin requirements decrease in patients with chronic renal impairment. In these situations, blood glucose monitoring must be done regularly (at least daily) in order to reduce the dose appropriately, reducing the risk of hypoglycaemia.

To reduce cardiovascular risk

All patients > 40 years of age should receive a statin e.g.:

• Simvastatin, oral, 10 mg daily.

In patients < 40 years, risk assess as for dyslipidaemia. See section 8.8: Dyslipidaemia.

If urine albumin:creatinine ratio is > 2.5 mg/mmol, consider ACE inhibitor, e.g.:
- Enalapril, oral, 10 mg daily.

See section 7.1.1: Chronic Kidney Disease (CKD).

8.5.2 DIABETES MELLITUS TYPE 1

E10

Management includes:
» Maintenance of glycaemic control within acceptable limits.
» Prevention of chronic complications.
» Prevention of acute complications, e.g. hyperglycaemic and hypoglycaemic coma.

Insulin protocols

- Insulin, short acting, SC, three times daily, 30 minutes before meals:
  Regular human insulin.
  Onset of action: 30 minutes.
  Peak action: 2–5 hours.
  Duration of action: 5–8 hours.

- Insulin, intermediate acting, SC, once or twice daily, usually at night.
  Neutral Protamine Hagedorn (NPH) insulin.
  Onset of action: 1–3 hours.
  Peak action: 6–12 hours.
  Duration of action: 16–24 hours.

- Insulin, biphasic, SC, once or twice daily.
  Mixtures of regular human insulin and NPH insulin in different proportions, e.g. $^{30}/_{70}$.
  Onset of action: 30 minutes.
  Peak action: 2–12 hours.
  Duration of action: 16–24 hours.

Selection of insulin

Basal bolus regimen

All type 1 diabetics should preferentially be managed with combined intermediate-acting (basal) and short-acting insulin (bolus), the so-called basal bolus regimen. This consists of pre-meal short-acting insulin and bedtime intermediate-acting insulin not later than 22h00.

The initial total daily insulin dose:
- 0.6 units/kg body weight.

The total dose is divided into:
- 40–50% basal insulin
- the rest as bolus insulin split equally before each meal.

Adjust dose on an individual basis.

Pre-mixed insulin

Twice daily pre-mixed insulin, i.e. a mixture of intermediate- or short- acting insulin provides adequate control, when used with at least daily blood glucose monitoring. It is a practical option for patients who cannot monitor blood glucose frequently.

Insulin delivery devices

In visually impaired patients, prefilled syringes may be used.

Home glucose monitoring

Patients on basal/bolus insulin should measure glucose at least twice daily
All patients with type 2 diabetes on insulin should be given test strips for home glucose monitoring appropriate for their care plan.

Glucagon

Type 1 diabetics, who are judged to be at high risk of hypoglycaemia should have a glucagon hypoglycaemia kit and both the patient and their family should be trained to use this emergency therapy.

8.6 DIABETIC EMERGENCIES

8.6.1 HYPOGLYCAEMIA

E10.64/E11.65

Diagnosis: Clinical

Symptoms:
- Anxiety
- Palpitations
- Headaches
- Sweating
- Hunger
- Behavioural changes

Signs:
- Sweating
- Tachycardia
- Tremor
- Bizarre neurological signs
- Confusion
- Seizures
- Coma

Biochemical
Act on finger prick blood glucose. Confirm with laboratory measurements if uncertain.

TREATMENT
Start immediately.

At home:
Oral sugary drinks or paste, if able to swallow. If not, family members should administer glucagon.

In hospital:
- Dextrose 50%, rapid IV injection, 50 mL.

Assess clinical status and finger prick glucose level over the next 5–10 minutes.

Establish a large bore intravenous line and keep open with:
- Dextrose 10%, IV.

If no clinical response, give a second injection of:
- Dextrose 50%, IV, 50 mL.

To prevent recurrent hypoglycaemia, continue infusion with:
- Dextrose 10%, IV infusion, at a rate of ± 1 L 6 hourly.

Once blood glucose is normal or elevated, and the patient is awake, check blood glucose hourly for several hours, and check serum potassium for hypokalaemia.

If intravenous glucose cannot be given, for any reason, give:
- Glucagon, IM, 1 mg.
  - Blood glucose will take 10–15 minutes to rise.
  - May cause nausea and vomiting.

If the patient has not regained consciousness after 30 minutes with a normal or elevated blood glucose, look for other causes of coma.

Once the patient is awake, give a snack if possible, and **admit** for observation and education etc., to prevent further hypoglycaemic episodes.

> If hypoglycaemia was caused by a sulphonylurea, the patient will require hospitalisation and a prolonged intravenous glucose infusion.
>
> Observe patient for at least 12 hours after glucose infusion has stopped.

Recurrent hypoglycaemia
In cases ofrecurrent hypoglycaemia consider:
» inappropriate management, e.g. too much insulin or too high dose of sulponylurea,
» poor adherence,
» alcohol abuse,
» factitious administration of insulin,
» the “honeymoon” period of type 1 diabetes,
» the advent of renal failure,
» hypoglycaemic unawareness, or
» pancreatic diabetes/malabsorption.

Other causes of hypoglycaemia should also be considered e.g. associated Addison’s disease or hypopituitarism.
Recurrent hypoglycaemia may be the cause of hypoglycaemic unawareness, which occurs frequently in type 1 diabetic patients. The loss of warning symptoms can lead to severe hypoglycaemia. In some cases this situation can be restored to normal with avoidance of any hypoglycaemia for at least 2–4 weeks.

8.6.2 DIABETIC KETOACIDOSIS (DKA) AND HYPEROSMOLAR NONKETOTIC DIABETIC COMA (HONK)

E10.0

Diabetic comas – recognition and clinical profiles
DKA often occurs in younger patients and develops over hours to days. There may be vomiting, abdominal pain and acidotic breathing.
» blood glucose usually < 40 mmol/L
» blood ketones are positive
» serum osmolality < 350 mOsm/L.

Hyperglycaemic hyperosmolar state is a syndrome characterised by impaired consciousness, sometimes accompanied by seizures, extreme dehydration and severe hyperglycaemia, that is not accompanied by severe ketoacidosis (pH usually >7.2). It usually occurs in the elderly type 2 diabetic and develops over days to weeks.
» Blood glucose usually > 40 mmol/L.
» Blood ketones usually negative to moderately elevated.
» Urine ketones often positive.
» Serum osmolality is > 320 mOsm/L.

Anion gap = Na – (Cl + HCO_3) (Normal = ± 12 : DKA > 20)
Calculated serum osmolarity = 2 (Na + K) + glucose + urea (N = 275–285 mOsm/L)

GENERAL MEASURES

All patients:

» Set up an intravenous line.
» Protect airway and insert a nasogastric tube, if unconscious.
» Monitor urine output.
» Monitor plasma glucose, ketones, urine and electrolytes and venous blood gas.
» Look for precipitating causes, e.g. infection and MI.

MEDICINE TREATMENT

Fluids

Average deficit 6 L, may be as much as 12 L.
If renal or cardiac disease is present, monitor with central venous pressure.
In the absence of renal or cardiac compromise:

- Sodium chloride 0.9%, IV, 15–20 mL/kg in the first hour.
  - For patients < 20 years of age, initial volume: 10–20 mL/kg in the first hour.
  - Subsequent infusion rate varies from 5–15 mL/kg/hour depending on the clinical condition.
  - Correction of estimated deficits should take place over 24 hours.
  - The volume infused in the first 4 hours should not exceed 50 mL/kg.
  - Fluid therapy thereafter is calculated to replace the estimated deficit in 48 hours, ± 5 mL/kg/hour.
  - Reduction in serum osmolality should not exceed 3 mOsm/kg/hour.

Correct plasma sodium value for blood glucose.

[Rough guide: divide glucose by 3 and add to sodium value.]

If plasma Na^+ > 140 mmol/L:

- Sodium chloride 0.45%, IV.

If plasma Na^+ < 140 mmol/L:

- Sodium chloride 0.9%, IV.

If plasma glucose < 12 mmol/L, but ketones still present:

- Dextrose 5% **or** dextrose 5% in sodium chloride 0.9%, IV.

Note:

Adjust fluid volumes according to clinical criteria.
If hypotension is still present after 2 hours, give 2 units of colloid.
Cerebral oedema may occur with over-aggressive fluid replacement or rapid sodium change.

Potassium

> Potassium will fall on insulin treatment and patients with DKA have potassium depletion even if initial potassium is normal or high.
>
> It is therefore essential to monitor and replace potassium.

Total body deficit 300–1 000 mmol.
(1 ampoule = 20 mmol = 10 mL)

- Potassium chloride, IV, added to 1 L of fluid.
  - potassium < 3.5 mmol/L: add 40 mmol (2 ampoules)
  - potassium 3.5–5.5 mmol/L: add 20 mmol (1 ampoule)
  - potassium > 5.5 mmol/L: do not add any potassium

  Maximum potassium dose: 40 mmol/hour.
  Monitor potassium hourly initially, then 2 hourly when stabilised.

If serum potassium results are not readily available:

- Potassium chloride, IV, 20 mmol (1 ampoule) added to 1 L of fluid as soon as **the patient has established adequate urinary output.**

Bicarbonate

There is no proven role for the use of intravenous sodium bicarbonate and it could potentially cause harm.

Insulin therapy

Patients should be preferentially managed with protocol 1 (see below) in a high care ward, with appropriate monitoring.

Note:

Ketonaemia takes longer to clear than hyperglycaemia and combined insulin and glucose (and K^+) are needed to ensure clearance of ketonaemia.
Avoid focusing on glucose control alone!
Continue insulin until ketosis and acidosis have resolved.

Protocol 1: continuous intravenous infusion

- Insulin, short-acting, IV infusion, 50 units in 200 mL sodium chloride 0.9%.
  - 4 mL solution = 1 unit insulin.
  - Initial infusion: 0.1 unit/kg/hour.
  - Usually 5–7 units/hour: 20–28 mL/hour.
  - If plasma glucose does not fall by 3 mmol/L in the first hour, double the insulin infusion (hourly) until a steady reduction of plasma glucose is achieved, i.e. at least 3–4 mmol/L per hour.
  - If plasma glucose < 14 mmol/L, reduce the insulin infusion rate to 0.05–0.1 units/hour and adjust subsequently according to hourly bedside capillary glucose level measured with glucose test strips.

Protocol 2: hourly intramuscular bolus injections
Where intravenous infusion cannot be safely administered:

- Insulin, short acting
  - Dilute 100 units with sodium chloride 0.9% to 10 mL i.e. 10 units/mL.
  - Loading dose: 0.5 units/kg body weight.
  - Administer half the dose as an intravenous bolus injection and the other half IM. Do not administer with an insulin syringe and needle.
  - Subsequent hourly doses: ± 5–10 units IM every hour (i.e. 0.1 units/kg/hr) and titrated against the bedside capillary glucose level.

Progress management
Continue protocols 1 or 2 until the acidosis has resolved and:

- the patient is able to eat, and
- subcutaneous insulin therapy is instituted either at previous doses or, for newly diagnosed diabetes at 0.5–1 unit/kg total daily dose divided into at least 2 doses with mixed short and long acting insulin (biphasic insulin $^{2}/_{3}$ in the morning and $^{1}/_{3}$ at night).

Infusion must overlap with subcutaneous regimen for 1–2 hour to avoid reversion to keto-acidosis.

Heparin.
For all patients**:**

- Unfractionated heparin, SC, 5 000 units 12 hourly.

8.7 COMPLICATIONS OF DIABETES

Secondary prevention
Diabetic patients with a history of myocardial infarction, vascular bypass, stroke or transient ischemic attack, peripheral vascular disease, claudication, or angina.

Hypertension
See section 3.6: Hypertension.

Dyslipidaemia
See section 8.8: Dyslipidaemia.

8.7.1 DIABETIC NEUROPATHIES

Type 1:E10.4/Type2:E11.4

DESCRIPTION

Neuropathies are a common complication of diabetes. They play an important role in the morbidity and mortality suffered by people with diabetes.

There are three major categories:
» peripheral neuropathy,
» autonomic neuropathy, and
» acute onset neuropathies.

MEDICINE TREATMENT

Ensure appropriate glycaemic control.
Exclude or treat other contributory factors e.g.:
» alcohol excess,
» vitamin B_{12} deficiency, if suspected,
» uraemia,and
» HIV infection.

Pain

- Amitriptyline, oral, 10–25 mg at night increasing to 100 mg, if necessary.

AND/OR

- Paracetamol, oral, 1 g 6 hourly as needed.

If ineffective consider adding:

- Carbamazepine, oral, 100 mg daily.
  - Increase dose to 200 mg 12 hourly, if necessary.
  - Maximum dose: 1200 mg daily.

Gastroparesis

- Metoclopramide, oral, 10 mg 8 hourly before meals.

If ineffective consult a specialist.

8.7.2 DIABETIC KIDNEY DISEASE

N18

See section 7.1.1: Chronic Kidney Disease (CKD).

8.7.3 DIABETIC FOOT ULCERS

L97

GENERAL MEASURES

Metabolic control.
Treat underlying comorbidity.
Relieve pressure: non-weight bearing is essential.
Smoking cessation is essential.

Deep (limb-threatening) infection

X-ray of affected limb.
Surgical drainage as soon as possible with removal of necrotic or poorly vascularised tissue, including infected bone – **refer urgently.**
Revascularisation, if necessary

Local wound care

Frequent wound debridement with scalpel, e.g. once a week.
Frequent wound inspection.
Absorbent, non-adhesive, non-occlusive dressings.

MEDICINE TREATMENT

Superficial ulcer with extensive infection

Debridement with removal of all necrotic tissue.

Antibiotic therapy

For polymicrobial infection:

- Topical antibiotics are not indicated.

- Amoxicillin/clavulanic acid, oral, 875/125 mg 12 hourly for 10 days.
  - Longer course of therapy may be necessary.

Severe infection

- Cloxacillin, IV, 2 g 6 hourly.

PLUS

- Metronidazole, oral, 400 mg 8 hourly.

PLUS

- Gentamicin, IV, 6 mg/kg daily.

Renal impairment

Replace gentamicin plus cloxacillin with 3rd generation cephalosporin, e.g.:

- Ceftriaxone, IV, 2 g daily.

PLUS

- Metronidazole, oral, 400 mg, 8 hourly.

Penicillin allergy
- Clindamycin, oral, 150 mg 8 hourly.

PLUS
- Gentamicin, IV, 6 mg/kg daily

REFERRAL
» Arterial revascularisation procedures.

8.8 DYSLIPIDAEMIA
E78

DESCRIPTION
Non-pharmacological therapy plays a vital role in the management of dyslipidaemia. Many patients with mild or moderate dyslipidaemia will be able to achieve optimum lipid levels with lifestyle modification alone and may not require lifelong lipid modifying therapy.

Accompanying modifiable risk factors for coronary artery disease (CAD) e.g. hypertension, smoking, diabetes, must be sought and treated.
Underlying causes of secondary dyslipidaemia, e.g. excess alcohol intake, hypothyroidism, should be identified and corrected.
The goal of treatment should be explained clearly to the patient and the risks of untreated dyslipidaemia should be emphasised.

GENERAL MEASURES
Lifestyle modification
Dietary strategies are effective.
» Replace saturated fats with unsaturated fats (mono-and polyunsaturated fats) without increasing calories from fats.
» Consume a diet high in fruits, vegetables, nuts and whole unrefined grains.

Smoking cessation.
Increase physical activity.
Maintain ideal body weight.

MEDICINE TREATMENT

Indication for drug therapy
Cardiovascular
The main indication for lipid-modifying medication is to reduce the risk of a cardiovascular event. Drug therapy should be considered when non-pharmacological means have failed to reduce the lipid levels to within the target range. When lipid-lowering drugs are used, this is **always** in conjunction with ongoing lifestyle modification.

Patients with clinically manifest vascular disease require lipid-lowering drug therapy with a HMGCoA reductase inhibitor, irrespective of cholesterol levels:

» confirmed ischaemic heart disease,
» peripheral vascular disease,
» atherothrombotic stroke, and
» type 2 diabetics over the age of 40 years.

Such high-risk patients will benefit from lipid lowering (statin) therapy irrespective of their baseline LDL-C levels.

Patients without established vascular disease, with a risk of MI of greater than 20% in 10 years, and who have not achieved lipid goals within 3 months – See section 3.1: Ischaemic heart disease and atherosclerosis, prevention.

Non-cardiovascular

The most serious non-cardiovascular complication of dyslipidaemia is the development of acute pancreatitis. This is seen in patients with severe hypertriglyceridaemia (fasting triglycerides >15 mmol/L). Ideally such patients should be referred to a lipid specialist.

Fibrates are the drugs of choice for severe hypertriglyceridaemia.

Choice of drug

Depends on the type of lipid disturbance:

» predominant hypercholesterolaemia: statin
» mixed hyperlipidaemia: statin or fibrate
» predominant hypertriglyceridaemia: fibrate

- HMGCoA reductase inhibitors (statins) that lowers LDL by at least 25%, e.g.:
- Simvastatin, oral, 10 mg daily.

OR

For patients with moderate to severe fasting hypertriglyceridaemia and for patients on ARV therapy i.e. triglycerides > 10 mmol/L:

- Fibric acid derivatives e.g.:
- Bezafibrate, oral, 400 mg daily.

Dyslipidaemia in HIV infected patients: See section 10.1.1: Management of selected antiretroviral adverse drug reactions.

REFERRAL

» Patients with familial hypercholesterolaemia (FH)
» Suspected severe familial dyslipidaemias.

8.9 HYPERCALCAEMIA, INCLUDING PRIMARY HYPERPARATHYROIDISM

E83.50/E21.0

DESCRIPTION

When serum calcium (corrected for albumin) concentrations exceed the upper limit of normal.

Aetiology

» Ambulatory patients: hyperparathyroidism is the most common cause (> 90% of cases).
» Hospitalised patients: malignancies are the most common cause (65% of cases). Hyperparathyroidism accounts for another 25%.
» Granulomatous disease (sarcoid).
» Immobilisation in those with high bone turnover.

Investigations

Draw blood for parathyroid hormone (PTH) and simultaneous calcium and albumin concentrations.
A detectable PTH in the presence of hypercalcaemia indicates primary hyperparathyroidism.

MEDICINE TREATMENT

Hypercalcaemia

Patients with moderate/severe hypercalcaemia should be kept well hydrated and may need several litres of fluid.

Avoid thiazide diuretics as they increase serum calcium concentration.
The addition of furosemide has not been shown to be of benefit.

For symptomatic hypercalcaemia:

- Sodium chloride solution 0.9%, IV infusion, 4–6 L in 24 hours.
  - Monitor urine output.

If still symptomatic after 24 hours and adequate hydration, **or** if initial serum calcium is > 3 mmol/L:

ADD

- Bisphosphonates (specialist initiated) e.g.:
- Pamidronic acid, IV infusion, 15–30 mg over 4 hours according to plasma calcium concentration.
  - Dilute each 15 mg in 125 mL sodium chloride solution 0.9% and administer over 1 hour.
  - Doses should not be repeated until after 7 days.
  - A response is noted within 48 hours and trough reached in 5–7 days.

In patients with granulomatous disease and haematological malignancies:
- Prednisone, oral, 40 mg daily.

REFERRAL
» When a diagnosis of hyperparathyroidism is confirmed or other cause is not obvious.

8.10 HYPOCALCAEMIA
E83.5

DESCRIPTION
When serum calcium (corrected for albumin) falls below the lower limit of normal.

Causes
» Renal failure.
» Hypoparathyroidism:
  > post neck surgery,
  > radiotherapy, or
  > idiopathic.
» Vitamin D related, (deficient intake, activation or action).
» Hypomagnesaemia.
» Malabsorption syndrome.

Investigations
Laboratory: blood calcium, albumin, phosphate, urea, creatinine, magnesium and PTH.

MEDICINE TREATMENT
Therapy is aimed at treating the underlying cause.

For acute hypocalcaemia with neurological problems:
- Calcium gluconate 10%, IV, 10 mL given over 15–30 minutes, with ECG monitoring.
  - This may be repeated.

AND/OR
- Calcium gluconate 10%, 20–30 mL in 1 L dextrose 5% and given over 12–24 hours.

For hypoparathyroidism:
- Calcium, elemental, oral, 500–1 500 mg daily in divided doses.

AND
- Alfacalcidol, oral, 1–3 mcg daily.

Correct magnesium deficiency if present.

Renal failure:
See Section: 7.1.1 Chronic Kidney Disease (CKD).

REFERRAL
» If cause is uncertain.
» If hypoparathyroidism suspected and PTH analysis required as above.

8.11 HYPOTHYROIDISM
E03.9

DESCRIPTION
Causes
Common causes of primary hypothyroidism are:
» thyroiditis,
» post surgery, and
» post radio-active iodine.
Secondary hypothyroidism (less than 1% of cases) may be due to any cause of anterior hypopituitarism.

Investigations
Thyroid stimulating hormone (TSH) and thyroxine (T_4) initially.

MEDICINE TREATMENT
If TSH is normal or slightly elevated and T_4 is low this suggests hypopituitarism. Take blood for cortisol and ACTH and then give hydrocortisone replacement before starting levothyroxine and investigate for hypopituitarism.

- Levothyroxine, oral, 100 mcg daily.
  - If there is a risk of ischaemic heart disease, start at 25 mcg daily and increase by 25 mcg every 4 weeks.

Check TSH and T_4 after 2–3 months and adjust dose if required.
TSH levels will take several weeks to stabilise. Once stable check T_4 and TSH annually.

Hypothyroidism in pregnancy
About 60% of hypothyroid pregnant women need an increase in levothyroxine therapy in the second and third trimesters. Check TSH monthly and increase levothyroxine doses to keep serum TSH levels low normal and free T_4 levels in the high-normal range. After delivery, revert to pre-conception doses.

8.12 OSTEOPOROSIS

M81.9

DESCRIPTION

A disease characterised by low bone mass and micro-architectural bone deterioration leading to bone fragility and increase in fracture risk.

GENERAL MEASURES

Prevention

Adequate energy and protein intake.
Adequate dietary calcium intake (>1 g/day) particularly in the young, in breastfeeding mothers and in the elderly.
Weight bearing exercises, e.g. brisk 30 minutes walk 3 times a week.
Smoking cessation.
Ensure alcohol intake is < 10 units /week.
Avoid falls.

MEDICINE TREATMENT

Routine supplementation with calcium and vitamin D marginally increases the risk of myocardial infarction and stroke. Therefore, it is only recommended for use in the institutionalised frail elderly patients, where it may reduce the incidence of hip fractures.

In institutionalised frail elderly patients:

- Calcium, elemental, oral, 1 000 mg daily.

PLUS

- Vitamin D, oral, 800 units daily.

Secondary prevention of osteoporotic fracture, including patients on long- term corticosteroids

In severe osteoporosis, i.e. patients who have a T-score of –2.5 (severe osteoporosis) plus an osteoporotic fracture:

- Alendronate, oral, 10 mg daily for a maximum duration of 5 years.

This should be given with:

- Calcium, elemental, oral, 1 000 mg daily.

PLUS

- Vitamin D, oral, 800 units daily.

Hormone replacement therapy

See Section 5.12: Menopause and Perimenopausal Syndrome.
Only indicated early in menopause, if vasomotor symptoms are significant.
Review contra-indications before initiating therapy.

REFERRAL
» To establish diagnosis (bone densitometry).
» For initial assessment.
» Initiation and monitoring response to therapy and 18–24 monthly bone mineral density (BMD).
» Fractures suspected to be due to osteoporosis for consideration for alendronate.

8.13 OSTEOMALACIA/RICKETS
M83.9

DESCRIPTION
A disorder of mineralisation of newly synthesised bone matrix.

REFERRAL
» All

8.14 PAGET'S DISEASE
M88.9

DESCRIPTION
Bone disease characterised by localised uncontrolled formation of highly active osteoclasts leading to an increase in bone resorption followed by chaotic increase in bone formation.

GENERAL MEASURES
Most cases are mild and asymptomatic and no treatment is required.
Avoid high calcium diet when immobile as hypercalcaemia may occur with immobilisation.

Differentiate bone pain of Paget's, especially at night, from arthritic pain in joints near deformed bone, e.g. hip and knee joints, as well as pain resulting from fracture or complicating osteosarcoma.

MEDICINE TREATMENT
For pain:
- Ibuprofen, oral, 400 mg 8 hourly with meals.

REFERRAL
» All

8.15 PITUITARY DISORDERS

8.15.1 PROLACTINOMA

D35.2

DESCRIPTION

Prolactinoma is the most common functioning pituitary tumour.

Investigations

Serum prolactin.

Note:

There are numerous causes of hyperprolactinaemia other than a prolactinoma, e.g. drugs, physiological, hypothyroidism, chronic renal failure and tumours.

Serum prolactin levels are usually elevated ≥ 4 times the upper limit of the normal reference range for the laboratory method used and may also be found in other pituitary tumours and hypothalamic-pituitary lesions with stalk compression

MEDICINE TREATMENT

Dopamine agonist therapy is the treatment of choice.

- Bromocriptine, oral, 1.25 mg at bedtime with a snack.
  - Initial maintenance dose: increase dose to 2.5 mg 12 hourly with food and check prolactin 4 weeks later.
  - Higher doses may be needed.
  - GIT side effects are minimised by giving doses with food.
  - If total dose of 10 mg does not normalise prolactin, refer.

REFERRAL

» All tumours, once causes of secondary hyperprolactinaemia have been sought and excluded.
» Intolerance to bromocriptine.

Urgent

» Compression of optic chiasm.
» Pituitary apoplexy.

8.15.2 ANTERIOR HYPOPITUITARISM

E23.0

DESCRIPTION

Absent or diminished secretion of one or more anterior pituitary hormones due to primary damage of the anterior pituitary gland or secondary to hypothalamic dysfunction, which may result in hypothyroidism and/or hypoadrenalism and/or hypogonadism or growth retardation in children.

GENERAL MEASURES

Surgery is required for large tumours, pituitary apoplexy, and hormone secreting tumours (prolactinoma excluded). Radiotherapy may be required in selected patients
A notification bracelet is needed.

MEDICINE TREATMENT

Acute crisis
Treat as for Acute crisis in Section 8.2: Adrenal Insufficiency (Addison's Disease)

Chronic
See section 8.2: Adrenal Insufficiency (Addison's Disease)

Hypoadrenalism
See sections 8.2: Adrenal Insufficiency (Addison's disease) and
8.11: Hypothyroidism.

Hypothyroidism
See section 8.11: Hypothyroidism.

Hypogonadism
Individualise dosage and need for replacement according to age, symptoms, etc.

Women:
As for postmenopausal HRT: See section 5.4.

Men:
- Testosterone, IM, 200–300 mg every 3–4 weeks

See section 8.3: Androgen deficiency

REFERRAL

» All diagnosed patients for initial assessment.

8.15.3 DIABETES INSIPIDUS (POSTERIOR HYPOPITUITARISM)

E23.2

DESCRIPTION

Damage to the posterior pituitary leading to deficient production of antidiuretic hormone. Characterised by the passage of copious amounts of very dilute urine.
Causes include head trauma and neurosurgery but most cases are idiopathic.

GENERAL MEASURES
Rehydration with water or hypotonic fluids.

MEDICINE TREATMENT
Replacement therapy
- Desmopression, oral, 0.2–1.2 mg daily.
  - Optimal dose: 0.1–0.2 mg 8 hourly.

Acute management
Post operatively:
- Desmopressin, nasal spray, 10–20 mcg 12–24 hourly.

OR
- Desmopressin, oral, 0.1 mg 8 hourly.
  - Adjust dose according to response to a maximum of 1.2 mg per day in divided doses.
  - Larger doses can lead to water overload and hyponatraemia.

REFERRAL
» Water deprivation is necessary to confirm the diagnosis. Careful monitoring of electrolytes and exclusion of fluid overload while on therapy is essential to determine the appropriate dose.

8.16 PHAEOCHROMOCYTOMA
C74.9

DESCRIPTION
Catecholamine-secreting tumour of the adrenal medulla.

Clinical presentation
Always consider in hypertensive patients who have paroxysmal symptoms:
- » headaches,
- » GIT symptoms,
- » palpitations,
- » anxiety.
- » tremor,
- » recurrent chest discomfort,
- » sweating, and

There is marked inter-individual variation in symptoms.
These hypertensive patients may also have orthostatic changes in blood pressure.

Diagnosis
24 hour urine acidified with HCl: normetanephrine (NMA), vanillylmandelic acid (VMA), should be ≥ twice normal for a definite diagnosis. Test is best done during a paroxysm, if possible, using at least 2 samples.
There are many drugs, foods and diseases that can falsely elevate or lower NMA/VMA levels; therefore the clinician must interpret the results in the light of the clinical context and after having taken an accurate history.