Standard Treatment Guidelines and Essential Medicines List for South Africa

Hospital Level, Adults
2019 Edition

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NOTE:
The information presented in these guidelines conforms to the current medical, nursing and pharmaceutical practice. Contributors and editors cannot be held responsible for errors, individual responses to medicines and other consequences.

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FOREWORD

South Africa has committed to *"achieve universal health coverage including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all"*, one of the 17 Sustainable Development Goals set out by the United Nations. As such, it gives me great pleasure to present the Fifth Edition of the Adult Standard Treatment Guidelines and Essential Medicines List for Hospital Level care, which aims to enable equitable access to safe, effective, and affordable essential medicines at hospital level across South Africa.

It is imperative that the selection decisions are performed in a transparent, objective manner, involving multi-sectoral involvement to build trust and accountability with all internal and external stakeholders. Key to this is good governance together with evidence-based medicine principles.

Extensive stakeholder collaboration and engagement with healthcare workers, professional and clinical societies and organisations and many National Health Programmes has ensued. Further participation from these and other stakeholder groups is encouraged as these guidelines are continuously evolving.

I would like to commend the Adult Hospital Level Expert Review Committee and National Essential Medicines List Committee, together with its co-opted experts, for their unwavering dedication and for going the extra mile to ensure transparency and robustness in guideline development. The Chairpersons of these Committees have exhibited strong leadership. Special mention must be made of the extensive dissemination of selection decisions through journal publications and conference presentations, as well as, the initiation of research to assist decision-making going forward.

The Standard Treatment Guidelines and Essential Medicines List are only as successful as their widespread implementation. As such, the adoption of these guidelines should be closely monitored at the coalface. In preparation for National Health Insurance, the Department of Health remains committed to ensuring equitable access to quality healthcare through the provision of standardised, robust clinical guidance at all levels of care.

DR ZL MKHIZE, MP
MINISTER OF HEALTH
DATE: 18/01/2020

INTRODUCTION

The implementation of National Health Insurance (NHI) is a key enabler for equitable access to quality healthcare for all citizens in achieving South Africa's goal of Universal Health Coverage. Essential medicines and other health technologies have been highlighted in the NHI Bill as informing the healthcare service benefits covered by the NHI fund. Therefore, sound governance and Health Technology Assessments (HTA) principles are followed in the selection of these products.

The Adult Standard Treatment Guidelines and Essential Medicines List for Hospital Level provide a platform for transparency to enable equitable access to safe, effective, and affordable treatment options at hospital level taking into consideration the changing clinical needs of our population and the pragmatic implications of the introducing a new health technology

Health Technology Assessments (HTA), is defined by the World Health Organisation as *"the systematic evaluation of properties, effects, and/or impacts of health technology. It is a multidisciplinary process to evaluate the social, economic, organizational and ethical issues of a health intervention or health technology."* In the development of these guidelines, HTA frameworks for decision-making were piloted and strengthened methods of evidence review and costing analyses were used, involving rigorous internal peer-review processes.

Another new feature of these guidelines include the development of a therapeutic interchange database as a tool to support supply-chain challenges. In addition, coding of diagnostic and procedural healthcare information using the International Classification of Diseases 10th Edition (ICD-10 Code) has been strengthened in accordance with current industry standards. This will, amongst other outcomes, inform more effective analysis of rational medicine use and epidemiological research going forward.

The success of the implementation and further expansion of these guidelines will hinge on the support of all stakeholders involved, including support for implementation, monitoring and evaluation, required research and the further development of systematic reviews and HTAs. There is also a need for increased stakeholder engagement to address unanswered questions that has arisen during the recent review cycle. Leveraging off resources across all sectors and collaboration of internal and external stakeholders is encouraged to realise Universal Health Coverage for all South Africans.

DR T PILLAY
ACTING DIRECTOR-GENERAL: HEALTH
DATE: 06/01/2020

ACKNOWLEDGEMENTS

This edition of the Adult Hospital Level Standard Treatment Guidelines is evidence of the dedication, technical expertise, skills, and considerable time offered up by the Adult Hospital Level Expert Review Committee. The Committee has enthusiastically evolved with the review process, embracing Health Technology Assessment principles as South Africa journeys towards Universal Health Coverage. Collaboration with various stakeholders was strengthened and we thank all for your constructive engagement. We recommend continuous participation in the peer review consultative process and encourage the dissemination and implementation of these guidelines.
In particular, we would like to thank each Committee Member for their valuable contributions, and the Chairpersons of the Adult Hospital Level Expert Review Committee, Dr Black and Dr Dawood, for their unwavering commitment and support during this review process.

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TABLE OF CONTENTS

THE ESSENTIAL MEDICINES CONCEPT

The WHO describes Essential medicines as those that satisfy the priority health care needs of the population. Essential medicines are intended to be available within the context of functioning health systems at all times in adequate quantities, in the appropriate dosage forms, with assured quality and adequate information, and at a price the individual and the community can afford.

The concept of essential medicines is forward-looking. It incorporates the need to regularly update medicines selections to:

» reflect new therapeutic options and changing therapeutic needs;
» the need to ensure medicine quality; and
» the need for continued development of better medicines, medicines for emerging diseases, and medicines to meet changing resistance patterns.

Effective health care requires a judicious balance between preventive and curative services. A crucial and often deficient element in curative services is an adequate supply of appropriate medicines. In the health objectives of the National Drug Policy, the government of South Africa clearly outlines its commitment to ensuring availability and accessibility of medicines for all people. These are as follows:

» To ensure the availability and accessibility of essential medicines to all citizens.
» To ensure the safety, efficacy and quality of medicines.
» To ensure good prescribing and dispensing practices.
» To promote the rational use of medicines by prescribers, dispensers and patients through provision of the necessary training, education and information.
» To promote the concept of individual responsibility for health, preventive care and informed decision-making.

Achieving these objectives requires a comprehensive strategy that not only includes improved supply and distribution, but also appropriate and extensive human resource development. The implementation of an Essential Drugs Programme (EDP) forms an integral part of this strategy, with continued rationalisation of the variety of medicines available in the public sector as a first priority. The private sector is encouraged to use these guidelines and medicine list wherever appropriate.

The criteria for the selection of essential medicines for Adult Hospital Level in South Africa were based on the WHO guidelines for drawing up a national EML. Essential medicines are selected with due regard to disease prevalence, evidence on efficacy and safety, and comparative cost.

The implementation of the concept of essential medicines is intended to be flexible and adaptable to many different situations. It remains a national responsibility to determine which medicines are regarded as essential.

HOW TO USE THESE GUIDELINES

Principles

The National Drug Policy[1] makes provision for an Essential Drugs Programme which is a key component in promoting rational medicines use.

The perspective adopted in the Adult Hospital Level Standard Treatment Guidelines (STGs) is that of a competent medical officer practicing in a public sector hospital. The STGs serve as a standard for practice, but do not replace sound clinical judgment. It is important to remember that the treatments recommended are guidelines only and are based on the assumption that prescribers can manage patients with the relevant conditions.
This includes rational prescribing in the elderly and palliative care, as the use of some medicines, especially as people get older or more ill, can cause more harm than good. Optimizing medication through targeted de-prescribing is a vital part of managing chronic conditions, avoiding adverse effects and improving outcomes. The goal of de-prescribing is to reduce pill burden and maintain or improve quality of life.

All reasonable steps were taken to align the STGs with Department of Health guidelines that were available at the time of review. Each treatment guideline in the Adult Hospital Level STGs and Essential Medicines List (EML) was designed as a progression in care from the current Primary Health Care (PHC) STGs and EML. Given that the PHC STGs and EML were reviewed prior to the Adult Hospital Level STGs, the two STGs are not always perfectly aligned. Where referral to a tertiary facility is recommended, the relevant medicines have either been reviewed or included in the tertiary level EML, or are in the process of being reviewed.

Each medicine was included or removed from the EML using an evidence based review of safety and effectiveness, followed by considerations of cost and other relevant practice factors, such as availability and storage requirements. Some recommendations might not be aligned with the SAHPRA registered label/package insert; but are guided by health needs assessment and the best available scientific evidence.

The dosing regimens provide the recommended doses used in usual circumstances. However, the prescribed dose should take into consideration drug-drug interactions and co-morbid states, notably renal or hepatic failure, critical illness, and morbid obesity.

Local formularies

The EML has been developed down to generic or International Non-Propriety Name (INN) level. Each Province is expected to review the EML and prevailing tenders and compile a formulary which:

» lists formulations and pack sizes that will facilitate care in alignment with the STGs and EML;

1 National Drugs Policy, 1996. https://www.gov.za/documents/national-drugs-policy

» selects the preferred member of the therapeutic class based on cost;
» implements formulary restrictions consistent with the local environment; and
» provides information on medicine prices.

Therapeutic classes are designated in the "Medicine treatment" sections of the STGs which provide classes of medicines followed by an example of each class, such as 'HMGCoA reductase inhibitors (statins) e.g. simvastatin'. Therapeutic classes are designated where none of the members of the class offer any significant benefit over the other registered members of the class. It is anticipated that by listing a class rather than a specific medicine there is increased competition and hence an improved chance of obtaining the lowest possible price in the tender process. The designation of medicines into therapeutic classes may also assist with remedial actions to mitigate challenges to security of supply, by providing suggested alternatives which have already been approved by the ministerially appointed National Essential Medicines List Committee (NEMLC)[2].

Where therapeutic classes are listed in the STGs always consult your local formulary to identify the specific medicine that has been approved for use in your facility. A therapeutic interchange database has been developed that lists evidence-based reviewed medicines that have been grouped into each therapeutic class for a specific condition, as outlined in the policy for classifying medicines into therapeutic classes for purposes of therapeutic interchange. The database and policy are available on the National Department of Health website: http://www.health.gov.za/edp.php

Navigating the guidelines

It is important that you become familiar with the contents and layout of these guidelines in order to use the STGs effectively.

The STGs are arranged into chapters according to the organ systems of the body. Conditions and medicines are cross referenced in two separate indexes of these guidelines. In some therapeutic areas that are not easily amenable to the development of a STG, the section is limited to a list of medicines.

This edition of the Adult Hospital Level STG and EML provides additional information: Appendix III – guidance on the use of certain medicines in pregnancy; and Appendix IV – guidance on extemporaneous preparation of certain medicines using a standardised formula.

Revisions to previous recommendations are accompanied by the level of evidence that is cited and hyperlinked accordingly. All evidence is graded according to the Strength Of Recommendation Taxonomy (SORT) (a patient-centered approach to grading evidence in the medical literature), described in detail on page xli. To further promote transparency of medicine selection decisions, NEMLC reports, medicine reviews and costing reports are available

2 NEMLC is tasked to formulate and revise the Standard Treatment Guidelines (STGs) and Essential Medicines List (EML) using a peer review consultative process.

on the National Department of Health website: http://www.health.gov.za/edp.php

The section on Patient Education in Chronic Conditions aims to assist health workers to improve patient adherence and health, generally. Information on the Central Chronic Medicines Dispensing and Distribution (CCMDD) programme is available at: nhiccmddadmin@health.gov.za

Diagnosis codes from the International Statistical Classification of Diseases and Related Health Problems (ICD-10) are included for each condition to facilitate accurate recording of diagnoses. The primary ICD-10 code may be accompanied by a secondary code that is bracketed to differentiate a secondary manifestation from the primary aetiology. (For example, uncomplicated broncho-pneumonia with severe penicillin allergy would be coded as: J18.0+(Z88.0)). All the rules and guidelines for the use of ICD-10 must be applied as per the World Health Organisation (WHO), the agreed South African Morbidity Coding Standards and Guidelines document, and the South African Master Industry Table (MIT).
Available at: http://www.health.gov.za/index.php/shortcodes/2015-03-29-10-42-47/2015-06-10-09-23-36/2015-06-10-09-26-11

Medicines safety
Provincial and local Pharmaceutical and Therapeutics Committees (PTCs) should develop medicines safety systems to obtain information regarding medication errors, prevalence and importance of adverse medicine events, interactions, and medicines quality. These systems should not only support the regulatory pharmacovigilance plan, but should also provide pharmacoepidemiology data that will be required to inform future essential medicines decisions as well as local interventions to improve safety.

In accordance with SAHPRA's guidance on reporting adverse drug reactions in South Africa, the medical officer with the support of the PTC should report the relevant adverse reactions to the National Adverse Drug Event Monitoring Centre (NADEMC). To facilitate reporting, a copy of the form and guidance on its use has been provided.

Feedback
Comments that aim to improve these treatment guidelines will be appreciated. The submission form and guidance for completing the form are included with these guidelines. Motivations will be accepted from Provincial PTCs only.

THERAPEUTIC DRUG MONITORING (TDM)
Medicines with narrow therapeutic indices and those with variable pharmacokinetics should be monitored regularly to optimise dosing, obtain maximum therapeutic effect, limit toxicity, and assess compliance. Appendix II provides detailed information for specific medicines.
TDM sampling for all drugs is to be done only once steady state has been reached (i.e. after 4–5 half-lives).

Lithium
Measure serum concentrations at about 12 hours after the last dose – i.e.

immediately prior to the next dose. Concentrations should be less than 1 mmol/L and should be monitored 6-monthly while on therapy, with more frequent monitoring in the elderly (see Appendix II for guidance on prescribing lithium).

Aminoglycosides
Peak concentrations will generally be adequate if dosing is adequate (e.g. gentamicin 5 mg/kg/day in a single daily dose) and measuring peak concentrations is not recommended unless the organism has a high minimum inhibitory concentration (MIC) or if the patient is critically ill. Trough concentrations, taken immediately before the next dose, are valuable for identifying potential toxicity. Toxicity may manifest as deafness or renal impairment. Aminoglycosides are relatively contraindicated in renal impairment. Audiology assessment and renal function monitoring is indicated in all patients who develop aminoglycoside toxicity (see Appendix II for guidance on prescribing amikacin and gentamicin).

Anti-epileptics
Measuring concentrations may be helpful to confirm poor adherence or to confirm a clinical suspicion of toxicity. Routine measurement in patients with well-controlled seizures and no clinical evidence of toxicity, is not appropriate. Individual concentrations may be difficult to interpret – if in doubt, seek assistance from a clinical pharmacologist.

PRESCRIPTION WRITING

Prescribers may initiate and/or maintain treatment with medicines as per the STGs in accordance with their scope of practice.

Medicines should be prescribed only when they are necessary for treatment following clear diagnosis. Not all patients or conditions need prescriptions for medication. In certain conditions simple advice and general and supportive measures may be more suitable.

In all cases carefully consider the expected benefit of a prescribed medication against potential risks. This is especially important during pregnancy where the risk to both mother and fetus must be considered.

All prescriptions must:

» be written legibly in ink by the prescriber with the full name, identification number and address of the patient, and signed with the date on the prescription form;
» specify the age and, in the case of children, weight of the patient;
» have prescriber details including contact details i.e. name, qualification, registration number, address and contact telephone number;
» indicate the diagnosis on the prescription, where there patient has provided consent.

In all prescriptions:

» State the treatment regimen in full:
    - medicine name, strength and formulation,
    - dose or dosage,

- dose frequency,
- dose route
- duration of treatment,
- e.g. amoxicillin 250 mg capsules, 8 hourly orally for 5 days.

» Write the name of the medicine/preparation in full using the generic name.
» Avoid abbreviations to reduce the risk of misinterpretation. Avoid the Greek mu (ų): write mcg as an abbreviation for micrograms.
» Avoid unnecessary use of decimal points. If necessary, write a zero in front of the decimal point only, e.g. 2 mg not 2.0 mg; or 0.5 mL not .5 mL.
» Avoid Greek and Roman frequency abbreviations that cause considerable confusion (qid, qod, tds, tid, etc). Instead either state the frequency in terms of hours (e.g. '8 hourly') or times per day in numerals (e.g. '3x/d').
» In the case of "as required", a minimum dose interval should be specified, e.g. 'every 4 hours as required'.
» Most monthly outpatient scripts for chronic medication are for 28 days; check that the patient will be able to access a repeat before the 28 days are completed.
» Prescriptions for schedules 6 medicines are not repeatable, requiring to be issued monthly; and the quantity to be issued should be expressed in words.

After writing a prescription, check that the dose, dose units, route, frequency, and duration for each item is stated. Consider whether the number of items is too great to be practical for the patient, and check that there are no redundant items or potentially important drug interactions. Check that the script is dated, that the patient's name, identification number and diagnosis/diagnostic code are on the prescription form. Only then should you sign the prescription and provide some other way for the pharmacy staff to identify the signature if there are problems (print your name, use a stamp, or use a prescriber number from your institution's pharmacy).

Notes on specific medicines

ACE-inhibitor	Angioedema is a potentially serious complication of ACE-inhibitor treatment and if it occurs it is a contraindication to continued therapy or to re-challenge.
ACE-inhibitors and ARBs	ACE-inhibitors and ARBs can cause or exacerbate hyperkalaemia in chronic kidney disease (eGFR < 60 mL/minute). Check the serum potassium before starting these medicines, and monitor serum potassium on therapy. ACE-inhibitors and ARBs are contra-indicated in pregnancy.
Allopurinol	Contra-indicated in patients with eGFR <30 mL/minute. Do not stop uric acid lowering drugs during an acute attack.
Amitriptyline + citalopram	Concomitant use of amitriptyline and citalopram may increase the risk of serotonin syndrome or neuroleptic malignant syndrome. Furthermore, there is a potential risk for QT-prolongation.

Anti-epileptic medicines	Phenytoin, phenobarbitone, and carbamazepine are potent enzyme inducing agents and should be used with caution with other medicines metabolised by the liver, especially warfarin, antiretrovirals, progestin subdermal implants, and oral contraceptives.
Benzodiazepines	Benzodiazepines can cause respiratory depression. Monitor patients closely as benzodiazepines can exacerbate an abnormal mental state or mask important neurological signs of deterioration. Prolonged treatment with benzodiazepines often leads to tolerance and withdrawal symptoms if the medicine is discontinued abruptly. Combination therapy with more than one benzodiazepine is not indicated.
ß–blockers	ß–blockers should not be used in cocaine poisoning. ß–blockers may cause bronchospasm in asthmatics.
Ciprofloxacin	Irrational use of quinolones contributes to the emergence of XDR-TB and potential masking of active TB.
Clindamycin	Clindamycin has good coverage against Gram positive organisms and anaerobes, so the addition of metronidazole is unnecessary.
Folic acid + vitamin B12	Anaemia megaloblastic: Give vitamin B12 and folic acid together until the test results are available as giving folic acid alone in patients with a B12 deficiency may precipitate a permanent neurological deficit.
Haloperidol	Dosing may vary according to clinical circumstances, e.g. lower doses in the elderly or where HIV infection or HIV-related dementia is known or suspected. In frail and elderly patients, reduce the dose by half.
Lithium	Therapeutic drug monitoring is essential when using lithium. Clinical toxicity may occur even within the therapeutic range. Concomitant use of many medicines e.g. ACE-inhibitors, NSAIDs and diuretics may increase the risk of lithium toxicity.
Loperamide	Contraindicated in dysentery, acute non-inflammatory diarrhoea, antibiotic-associated diarrhoea and amoebic dyssentery; as it may result in toxic megacolon.
Low molecular weight heparin (LMWH)	In morbid obesity dosing of LMWH should be individualised, in discussion with a specialist. In renal failure (eGFR < 30 mL/minute), the recommended dose of LMWH is 1 mg/kg/day. Pregnant women with mechanical prosthetic valves should not receive LMWH unless antifactor Xa levels can be monitored reliably weekly. Therapeutic range is pre-dosing level 0.6 units/mL and a 4-hour peak level of 1–1.2 units/mL.
Metformin	Metformin should be dose adjusted in renal impairment (eGFR: 30-60 mL/minute).
Metronidazole	The addition of metronidazole to amoxicillin/clavulanic acid is unnecessary as amoxicillin/clavulanic acid has adequate anaerobic cover.

Misoprostol (for TOP)	Misoprostol can cause uterine rupture in women with previous Caesarean sections and those of high parity. In these women use 200 mcg of misoprostol or alternative methods such as extra-amniotic saline infusion without misoprostol. The dose of misoprostol, PV, decreases with increasing gestational age because of the risk of uterine rupture.
NSAIDs	Concomitant use of more than one NSAID has no additional clinical benefit and only increases toxicity. Chronic use of all NSAIDs is associated with varying degrees of gastrointestinal, renal, and cardiovascular risks. Long-term use of NSAIDs should weigh potential benefits against these risks.
Oral diabetic agents	Oral diabetic agents should not be used in type 1 diabetes and used with caution in liver and renal impairment.
Insulin in the treatment of DKA	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.
Antivenom	Never administer antivenom without being fully prepared to manage acute anaphylaxis.
Sodium chloride	Rapid correction of sodium, in hyponatraemia, may lead to central pontine myelinolysis, which is often irreversible. Sodium should be frequently monitored and increases should be <9 mmol/L per day.
Spironolactone	Monitoring of sodium, potassium and renal function is essential in patients taking spironolactone. Avoid if eGFR < 30 mL/minute.
SSRIs	Adolescents with depression may have an increased risk of suicidal ideation when initiated on SSRIs.
Streptokinase	Do not use heparin if streptokinase is given.
Sulphonylureas	Hypoglycaemia caused by a sulphonylurea can be prolonged. The patient should be hospitalised with an intravenous glucose infusion, and observed for at least 12 hours after glucose infusion has stopped.
Tricyclic antidepressants	Avoid in patients with cardiac disease and a high risk of overdose.
Testosterone	Screen hypogonadal men for prostate cancer before beginning testosterone replacement.
Unfractionated heparin	Evidence indicates that PTT monitoring is not necessary with weight based dosing of unfractionated heparin. However, in patients with morbid obesity and renal failure (eGFR < 30 mL/minute) unfractionated heparin should be used with PTT monitoring to maintain the PTT at 1.5 to 2.5 times the control. Blood for measurement of PTT should be taken 4 hours after SC dose.
Verapamil	Never give verapamil or adenosine IV to patients with a wide QRS tachycardia as this may precipitate ventricular fibrillation. In atrial flutter, do not use verapamil as it will not convert flutter to sinus rhythm and may cause serious hypotension.
Warfarin	Warfarin use requires regular INR monitoring and dose adjustment according to measured INR. See appendix II.

PENICILLIN DESENSITISATION

This has been included for information only.
Perform only in an ICU setting.
Discontinue all ß-adrenergic antagonists. Have an IV line, ECG monitor and spirometer in place. Once desensitised, treatment must not lapse as risk of subsequent allergy increases.
A history of Stevens-Johnson's syndrome, exfoliative dermatitis, erythroderma are absolute contra-indications to desensitisation (use only as an approach to IgE sensitivity).

Oral route is preferred. 1/3 of patients develop a transient reaction during desensitisation or treatment, which is usually mild.

<table>
<tr><td colspan="3">A: Reconstitute phenoxymethylpenicillin 250 mg/ 5mL</td></tr>
<tr><td>Step</td><td>Medicine mg/mL</td><td>Amount to administer (mL)</td></tr>
<tr><td>Strictly every 15 minutes</td><td colspan="2">B: To make 0.5 mg/mL solution:
Dilute 0.5 mL of reconstituted phenoxymethylpenicillin solution in 49.5 mL water.</td></tr>
<tr><td>1</td><td rowspan="7">0.5 mg/mL solution
(1000 units/mL)</td><td>0.1 mL</td></tr>
<tr><td>2</td><td>0.2 mL</td></tr>
<tr><td>3</td><td>0.4 mL</td></tr>
<tr><td>4</td><td>0.8 mL</td></tr>
<tr><td>5</td><td>1.6 mL</td></tr>
<tr><td>6</td><td>3.2 mL</td></tr>
<tr><td>7</td><td>6.4 mL</td></tr>
<tr><td></td><td colspan="2">C: To make 05 mg/mL solution:
Dilute 1 mL of reconstituted phenoxymethylpenicillin solution in 9 mL water.</td></tr>
<tr><td>8</td><td rowspan="3">5 mg/mL solution
(10000 units/mL)</td><td>1.2 mL</td></tr>
<tr><td>9</td><td>2.4 mL</td></tr>
<tr><td>10</td><td>4.8 mL</td></tr>
<tr><td></td><td colspan="2">D: Reconstituted phenoxymethylpenicillin
250mg/ 5mL = 50 mg/mL</td></tr>
<tr><td>11</td><td rowspan="4">50 mg/mL
(80000 units/mL)</td><td>1.0 mL</td></tr>
<tr><td>12</td><td>2.0 mL</td></tr>
<tr><td>13</td><td>4.0 mL</td></tr>
<tr><td>14</td><td>8.0 mL</td></tr>
</table>

After step 14, observe for 30 minutes, then give 1.0 g IV.
Interval between doses: 15 minutes.

Parenteral route

Step	Medicine mg/mL	Amount to administer (mL)
Strictly every 15 minutes:		
1	0.1 mg/mL	0.1 mL
2		0.2 mL
3		0.4 mL
4		0.8 mL
5	1 mg/mL	0.16 mL
6		0.32 mL
7		0.64 mL
8	10 mg/mL	0.12 mL
9		0.24 mL
10		0.48 mL
11	100 mg/mL	0.1 mL
12		0.2 mL
13		0.4 mL
14		0.8 mL
15		0.16 mL
16		0.32 mL
17		0.64 mL

After step 17, observe for 30 minutes, then give 1.0 g IV.
Interval between doses: 15 minutes.

COTRIMOXAZOLE DESENSITISATION

Attempt desensitisation in patients with a history of cotrimoxazole intolerance, unless this was life-threatening, e.g.: Stevens-Johnson syndrome. (See section 4.6: Erythema Multiforme, Stevens Johnson Syndrome, Toxic Epidermal Necrolysis). Unless the rash is severe or associated with systemic symptoms, continue treatment with careful observation for deterioration.
Desensitisation should be attempted using cotrimoxazole suspension 240 mg/5mL. Dilute the suspension appropriately and consult with your pharmacist if necessary.

Note: Do not administer antihistamines or steroids with this regimen.

Time (hours)	Cotrimoxazole dose (mL of 240mg/5mL suspension
0	0.0005
1	0.005
2	0.05
3	0.5
4	5
5	Two single strength tablets (each tablet = 80/400 mg) followed by full dose

A GUIDE TO PATIENT ADHERENCE IN CHRONIC CONDITIONS

Achieving health goals for chronic conditions such as asthma, diabetes, HIV and AIDS, epilepsy, hypertension, mental health disorders and TB requires attention to:

» Adherence to long term pharmacotherapy – incomplete or non-adherence can lead to failure of an otherwise sound pharmacotherapeutic regimen.
» Organisation of health care services, which includes consideration of access to medicines and continuity of care.

Patient Adherence

Adherence is the extent to which a person's behaviour – taking medication, following a diet and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider.

Poor adherence results in less than optimal management and control of the illness and is often the primary reason for suboptimal clinical benefit. It can result in medical and psychosocial complications of disease, reduced quality of life of patients, and wasted health care resources.

Poor adherence can fall into one of the following patterns where the patient:

» takes the medication very rarely (once a week or once a month);
» alternates between long periods of taking and not taking their medication e.g. after a seizure or BP reading;
» skips entire days of medication;
» skips doses of the medication;
» skips one type of medication;
» takes the medication several hours late;
» does not stick to the eating or drinking requirements of the medication;
» adheres to a purposely modified regimen; and
» adheres to an unknowingly incorrect regimen.

Adherence should be assessed on a regular basis. Although there is no gold standard, the current consensus is that a multi method approach that includes self-report be adopted such as that below.

Barriers that contribute toward poor adherence:

BARRIER	RECOMMENDED SUPPORT
Life style	
» It is often difficult to take multiple medications.	» Create a treatment plan with information on how and when to take the medications.
» A busy schedule makes it difficult to remember to take the medication.	» Use reminders such as cues that form part of the daily routine.
Attitudes and beliefs	
» The condition is misunderstood or denied.	» Remind patients that they have a long term illness that requires their involvement.
» Treatment may not seem to be necessary.	» Use change techniques such as motivational interviewing.
» May have low expectations about treatment.	» Identify goals to demonstrate improvement/stabilisation.
Social and economic	
» May lack support at home or in the community	» Encourage participation in treatment support programs.
» May not have the economic resources to attend appointments.	» Consider down referral or reschedule appointment to fit in with other commitments.
Healthcare team related	
» Little or no time during the visit to provide information.	» Encourage patient to ask questions.
» Information may be provided in a way that is not understood.	» Use patient literacy materials in the patient's language of choice.
» Relationship with the patient may not promote understanding and self-management.	» Engage active listening.
Treatment related	
» Complex medication regimens (multiple medications and doses) can be hard to follow.	» If possible reduce treatment complexity
» May be discouraged if they don't feel better right away.	» Help the patient understand the condition and the role of their medication
» May be concerned about adverse effects.	» Discuss treatment goals in relation to potential adverse effects.

Although many of these recommendations require longer consultation time, this investment is rewarded many times over during the subsequent years of management.

For a patient to consistently adhere to long term pharmacotherapy requires integration of the regimen into his or her daily life style. The successful integration of the regimen is informed by the extent to which the regimen differs from his or her established daily routine. Where the pharmacological proprieties

of the medication permits it, the pharmacotherapy dosing regimen should be adapted to the patient's daily routine. For example, a shift worker may need to take a sedating medicine in the morning when working night shifts, and at night, when working day shifts. If the intrusion into life style is too great alternative agents should be considered if they are available. This would include situations such as a lunchtime dose in a school-going child who remains at school for extramural activity and is unlikely to adhere to a three times a regimen but may very well succeed with a twice daily regimen.

Towards concordance when prescribing

Establish the patient's:

» occupation,
» daily routine,
» recreational activities,
» past experiences with other medicines, and
» expectations of therapeutic outcome.

Balance these against the therapeutic alternatives identified based on clinical findings. Any clashes between the established routine and life style with the chosen therapy should be discussed with the patient in such a manner that the patient will be motivated to change their lifestyle.

Note: Education that focuses on these identified problems is more likely to be successful than a generic approach toward the condition/medicine.

Education points to consider

» Focus on the positive aspects of therapy, but be supportive regarding negative aspects and offer guidance on how to manage this, if present.
» Provide realistic expectations regarding:
  – normal progression of the illness - especially important in those diseases where therapy merely controls the progression and those that are asymptomatic;
  – the improvement that therapy and non-medicinal treatment can add to the quality of life.
» Establish therapeutic goals and discuss them openly with the patient.
» Any action to be taken with loss of control or when side effects develop.
» In conditions that are asymptomatic or where symptoms have been controlled, reassure the patient that this reflects therapeutic success, and not that the condition has resolved.
» Where a patient raises concern regarding anticipated side effects, attempt to place this in context with respect to incidence, the risks vs. the benefits, and whether or not the side effects will disappear after continued use.

Note: Some patient's lifestyles make certain adverse responses acceptable which others may find intolerable. Sedation is unlikely to be acceptable to a student, but an older patient with insomnia may welcome this side effect. This is where concordance plays a vital role.

Notes on prescribing in chronic conditions.

» Do not change doses without good reason.
» Never blame anyone or anything for non-adherence before fully investigating

the cause.

» If the clinical outcome is unsatisfactory - investigate adherence (note that side effects may be an issue).
» Always think about side effects and screen for them from time to time.
» When prescribing a new medicine for an additional health related problem ask yourself whether or not this medicine is being used to manage a side effect.
» Adherence with a once daily dose is best. Twice daily regimens show agreeable adherence. However, adherence decreases as the number of administration interval increases.
» Keep the total number of tablets to an absolute minimum as too many may lead to medication dosing errors and may influence adherence.

Improving Continuity of Therapy

» Make clear and concise records.
» Involvement the patient in the care plan.
» Every patient on chronic therapy should know:
  – his/her diagnosis
  – the name of every medicine
  – the dose and interval of the regimen
  – his/her BP or other readings

  Note: The prescriber should reinforce this only once management of the condition has been established.
» When the patient seeks medical attention for any other complaints such as a cold or headache he/she must inform that person about any other condition/disease and its management.
» If a patient indicates that he/she is unable to comply with a prescribed regimen, consider an alternative - not to treat might be one option, but be aware of the consequences e.g. ethical.

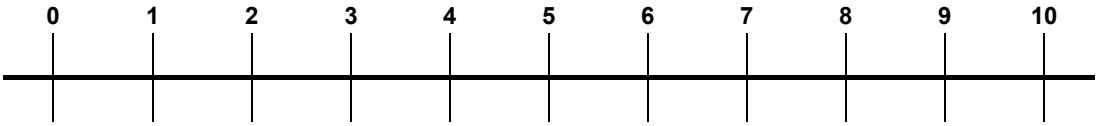
Patient Adherence Record

Folder No.	Date (dd/mm/yyyy) / /

Self-Reporting

Question	**Yes**	**No**
Do you sometimes find it difficult to remember to take your medicine?		
When you feel better, do you sometimes stop taking your medication?		
Thinking back over the past four days, have you missed any of your doses?		
Sometimes if you feel worse when you take the medicine, do you stop taking it?		

Visual Analogue Scale (VAS)



Score ____%

Pill Identification Test (PIT)

Medication	Knows the name (Y/N)	Knows the number of pills per dose (Y/N)	Time the medication is taken			Knows any additional instruction
			Morning (hour)	Evening (hour)	Considered Acceptable (Y/N)	

Pill Count

Did the client return the medication containers? Yes* No

***If yes,** check that the client only used medication from this container since the date of their last visit. If leftover medication had been used or an emergency prescription obtained, then the calculation will be invalid – skip to adherence assessment.

$$\text{\% Adherence} = \frac{\text{Dispensed} - \text{Returned}}{\text{Expected to be taken}} \times 100 = \frac{\square - \square}{\square} \times 100 = \square\ \%$$

Adherence Assessment

Self-reporting	Answered 'No' to all questions	Answered 'Yes' to 1 question	Answered 'Yes' to 2 or more questions
VAS	≥ 95%	75–94%	Less than 75%
PIT—*Client knows the…*	Dose, Time, and Instructions	Dose and Time	Dose only or confused
Pill count	≥ 95%	75–94%	Less than 75%
Overall Adherence	High	Moderate	Low

CENTRAL CHRONIC MEDICINE DISPENSING AND DISTRIBUTION (CCMDD)

The Central Chronic Medicines Dispensing and Distribution programme (CCMDD) has been implemented to improve access to medicines for stable patients with chronic conditions. It enables patients to collect their repeat medicines for one or two month`s supply at a pick-up point nearer to home or place of work and it is thus no longer necessary to wait in long queues at health facilities just to collect repeat medicines.

Each province provides a list of medicines aligned to the EML and STGs including prescriber levels that can be utilised for recruitment of patients on the programme. Prescriptions for patients enrolled on CCMDD not meeting legal requirements and compliance to EML and STGs are rejected. The ultimate goal of the CCMDD programme is to improve adherence and better health outcomes.

CCMDD Benefits:

Improved **access** to chronic medicines;

Reduced **workload** for public health facilities and health workers;

Reduced patient **waiting times** and better time management;

Improved **quality** of care and service delivery;

Improved **patient experience** in collection of chronic medication;

Decongestion of health facilities through the use of alternative Pick up Points;

Improved **patient satisfaction** and knowledge of care.

Improved treatment **adherence**;

Decreased **stigma** for HIV patients;

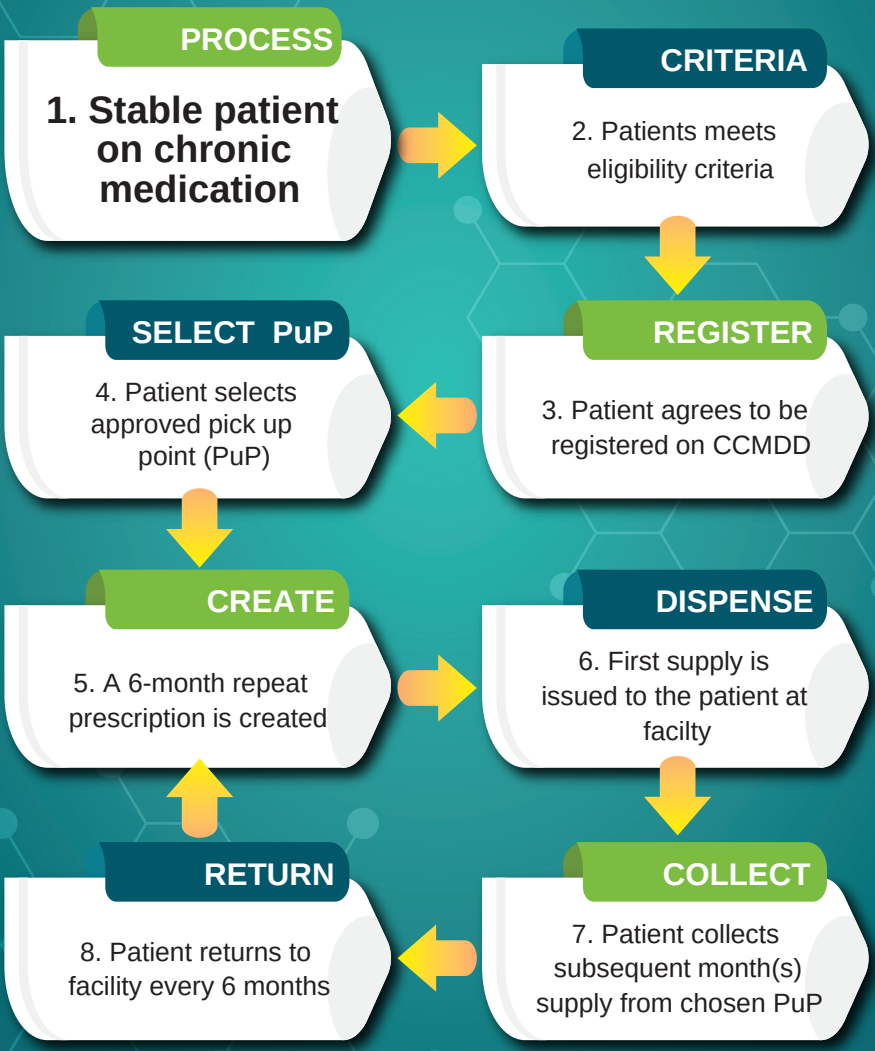
Improved availability of reliable **data** to inform decision-making at Facilities, SPs, PuPs;

Improved **supply chain** processes.

CCMDD is a proven, successful, patient centric approach to service patients in a manner that is beneficial to patients, Departments of Health, communities and creates lasting partnerships with the private sector.

Detailed information regarding the CCMDD process can be accessed at: www.health.gov.za/

Central Chronic Medicine Dispensing and Distribution (CCMDD)



ALIMENTARY TRACT

1.1 GASTROINTESTINAL DISORDERS

1.1.1 BOWEL PREPARATIONS

Bowel preparation is essential for colonoscopy.
Split-dose (half the dose the night before and half the dose on the day of colonoscopy) bowel cleanser and no dietary restriction seems to provide better quality colon cleansing than single doses with a liquid diet on the day preceding colonoscopy.

GENERAL MEASURES

Health care professionals should provide both oral and written patient education instructions and emphasise the importance of adherence to the bowel preparation.

MEDICINE TREATMENT

Preparations containing ingredients such as polyethylene glycol (PEG), and sodium sulphate are adequate for bowel cleansing. *LoE:II*[i]

- PEG/sodium sulfate, oral, solution.
  - 2 litres the night before the procedure and 2 litres the following morning within two hours of the procedure. *LoE:I*[ii]

Routine use of adjunctive agents (e.g. bisacodyl, senna, prokinetics) for bowel cleansing before colonoscopy is not recommended. *LoE:III*[iii]

1.1.2 DIVERTICULOSIS

K57.0-5/K57.8-9

DESCRIPTION

Colonic diverticulosis becomes increasingly common with age. Acute diverticulitis is suspected in patients with lower abdominal pain (typically in the left lower quadrant). The pain is usually constant and is often present for several days prior to presentation. Nausea and vomiting are often present due to a bowel obstruction or an ileus due to peritoneal irritation. Changes in bowel habits can be observed.

Diverticulosis can be complicated by haemorrhage or diverticulitis. Acute diverticulitis is inflammation of diverticulae usually accompanied by polymicrobial infection. Acute diverticulitis is defined as complicated when there is bowel obstruction, abscess, fistula, or perforation.

GENERAL MEASURES
Increase dietary fibre intake.

MEDICINE TREATMENT
Total duration of antibiotic therapy is 10 days, depending on clinical response. *LoE:III*

Uncomplicated diverticulitis:
- Amoxicillin/clavulanic acid, oral, 875/125 mg 12 hourly.

If unable to tolerate oral therapy:
- Amoxicillin/clavulanic acid, IV, 1.2 g 8 hourly.

LoE:III[iv]

REFERRAL
» Acute diverticulitis with clinical deterioration or failure to improve on medical therapy.
» Peritonitis.
» Complicated diverticulitis (to a centre which can perform colonic surgery).
» Massive haemorrhage.

1.1.3 GASTRO-OESOPHAGEAL REFLUX DISEASE (GORD)
K21.0/K21.9/K22.7

DESCRIPTION
A disorder which develops as a consequence of the reflux of gastric and duodenal contents into the oesophagus. It is usually characterised by heartburn and regurgitation.

Intermittent indigestion, heartburn or dyspepsia may be associated with:
» use of NSAIDs e.g. aspirin, ibuprofen, pain powders
» spicy food, alcohol, carbonated drinks
» smoking

Complications that may develop in severe disease are strictures, ulceration, Barrett's oesophagus and adenocarcinoma of the oesophagus. Two thirds of patients have a normal endoscopy which is termed non-erosive reflux disease (NERD).

GENERAL MEASURES
» Stop smoking.
» Limit alcohol intake.
» Eat small frequent meals.
» Avoid late night meals.
» Check haemoglobin.
» Stop the use of potential ulcerogenic medicines e.g. NSAIDs.

All patients with alarm symptoms, i.e. weight loss, haematemesis or melaena, dysphagia, or anaemia, chest pain or older than 45 years of age should have an endoscopy.

MEDICINE TREATMENT

Proton pump inhibitors (PPIs)

A trial with a PPI confirms acid-related disease. Only if no alarm symptoms:

- PPI, e.g.:
- Lansoprazole, oral, 30 mg daily for 4 weeks. *LoE:I[v]*
  - Ensure adherence to promote healing. *LoE:I[vi]*

Recurrence of symptoms

After endoscopic confirmation of disease:

- PPI, e.g.:
- Lansoprazole, oral, 30 mg daily.
  - Decrease dose of PPI after 4 weeks, e.g: omeprazole, oral, 10 mg daily.

Barrett's oesophagus K22.7

Restart PPI:

- PPI, e.g.:
- Lansoprazole, oral, 30 mg daily.

Note:

» These patients usually need maintenance PPI therapy.
» There is no convincing evidence that long-term treatment of Barrett's oesophagus with PPIs reduces dysplasia or progression to malignancy.

REFERRAL

Discuss with a specialist:

» young patients who are PPI dependent and will require life-long therapy;
» patients unable to take PPIs;
» patients requiring high doses of PPIs;
» patients with large hiatus hernias and "volume reflux";
» a rolling hiatus hernia with obstructive symptoms requires surgery;
» Alarm features that may be suggestive of gastrointestinal malignancy:
  — New onset dyspepsia in patient >60 years,
  — Evidence of gastrointestinal bleeding,
  — Iron deficiency anaemia,
  — Anorexia,
  — Unexplained weight loss,
  — Dysphagia,
  — Odynophagia (painful swallowing),
  — Persistent vomiting,
  — Gastrointestinal cancer in a first-degree relative.

1.1.4 HIATUS HERNIA

K44.0/K44.1/K44.9

Manage GORD. See section 1.1.3: Gastro-Oesophageal Reflux Disease (GORD).

1.1.5 INFLAMMATORY BOWEL DISEASE

K50.0-1/K50.8-9/K51.0-5/K51.8-9/K52.0-3/K52.8-9

DESCRIPTION

Inflammatory bowel disease is a chronic inflammatory disorder of the gastrointestinal tract that includes both Crohn's disease (CD) and ulcerative colitis. Abdominal pain, rectal bleeding, diarrhoea and weight loss characterise both CD and ulcerative colitis.

REFERRAL

All patients with a potential diagnosis of Crohn's disease or ulcerative colitis, should be discussed with a specialist.

1.1.6 PANCREATITIS, ACUTE

K85.0-3/K85.8-9

DESCRIPTION

Acute inflammatory condition of the pancreas.

Acute pancreatitis is based on the fulfilment of '2 out of 3' of the following criteria:

» clinical (upper abdominal pain),
» laboratory (serum amylase or lipase >3x upper limit of normal), and/or
» imaging (CT, MRI, ultrasonography) criteria.

Intense local inflammation results in pain and local as well as systemic complications. DIC, metabolic derangements and shock may occur.

Renal function, electrolytes and calcium, can be used to determine severity.

GENERAL MEASURES

Nasogastric suction when persistent vomiting or ileus occurs.

Parenteral fluid replacement to correct metabolic and electrolyte disturbances.

Parenteral nutrition is associated with adverse outcomes and should only be considered in patients that cannot receive or tolerate nasogastric or enteral nutrition.

Drainage of abscess, pseudocyst, if required.

MEDICINE TREATMENT

<u>For pain:</u>

- Morphine, IV, to a total maximum dose of 10 mg (See Appendix II, for individual dosing and monitoring for response and toxicity).

Acute symptomatic hypocalcaemia E83.5

- Calcium gluconate 10%, IV infusion, 10 mL as a bolus over 10 minutes.
  - Follow with 60–120 mL diluted in 1 L sodium chloride 0.9%, administered over 12–24 hours.
  - Monitor serum calcium at least 12 hourly.

LoE:III

If serum magnesium <0.5 mmol/L:

ADD

- Magnesium sulfate, IV infusion, 25–50 mmol in 12–24 hours.
  - 1 mL magnesium sulfate 50% = 2 mmol magnesium.

Antimicrobial therapy

The administration of prophylactic antibiotics are not necessary.

For abscess of the pancreas:

Broad spectrum IV antibiotics:

- Amoxicillin/clavulanic acid, IV, 1.2 g 8 hourly for 10 days, depending on clinical response.

LoE:III[vii]

REFERRAL

Severe complications, e.g. necrosis, haemorrhagic or systemic complications, infective pancreatitis.

1.1.7 PANCREATITIS, CHRONIC

K86.1

DESCRIPTION

Chronic inflammatory condition of the pancreas with severe abdominal pain, which results in functional and structural damage. In most patients, this is a chronic progressive disease leading to exocrine and/or endocrine insufficiency.

GENERAL MEASURES

Abstinence from alcohol reduces abdominal pain in the early stages of the disease.

Stop smoking.

Small frequent meals, and restricted fat intake reduces pancreatic secretion and pain.

Elemental diets (i.e. parenteral or enteral nutrition) in chronically debilitated patients.

When weight loss is not responding to exogenous enzymes and diet, consider supplementation with medium chain triglycerides.

There is a risk of developing cancer of the pancreas. This should be considered in patients who develop worsening pain, new onset diabetes or deterioration in exocrine function.

Dietary advice by dietician.

MEDICINE TREATMENT

Treatment is aimed at:
» pain,
» malabsorption, and
» endocrine function. See section 8.5.2: Type 1 Diabetes mellitus.

Analgesia

See Section 26.1: Pain, chronic.
Note: Pancreatic enzymes may reduce pain by negative feedback on pancreatic secretion.

Malabsorption

Start treatment when >7 g (or 21 mmol) fat in faeces/24 hours while on a 100 g fat/day diet.
Reduce dietary fat to <25 g/meal.
Supplementation of fat-soluble vitamins may be indicated.

- Lipase, oral, equivalent to lipase 30 000 units per day, in divided doses with meals.

Aim for symptom control and/or 5% of normal faecal fat output.

REFFERAL

Surgical intervention, pseudocyst.
Autoimmune chronic pancreatitis.

1.1.8 PEPTIC ULCER

K25.0-7/K25.9/K26.0-7/K26.9/K27.0-7/K27.9

DESCRIPTION

Ulcer in the stomach mucosa (gastric ulcer: GU) or first few centimetres of the duodenum (duodenal ulcer: DU), which penetrates into or through the muscularis mucosa.
Diagnosis is made after endoscopy, as all GUs require biopsy to exclude malignancy.
Patients with GUs and complicated DUs, those that have bled, perforated or are recurrent, must be rescoped at appropriate intervals until the ulcer has healed.
H. pylori can be assessed at scope by rapid urease testing (RUT) or biopsy.

GENERAL MEASURES

Advise patient to avoid ulcerogenic medications, e.g. NSAIDs.
Advise patient to stop smoking and drinking alcohol.
Dietary advice by dietician.

MEDICINE TREATMENT

H. pylori +ve

The vast majority of GUs and DUs are associated with *H. pylori* infection and eradication therapy is indicated if infection is present. This will greatly reduce

the rate of recurrent ulceration. Empiric eradication of *H. pylori* is not recommended.

Proton pump inhibitors (PPIs)

- PPI, e.g.:
- Lansoprazole, oral, 30 mg 12 hourly.
  - Duodenal ulcer: for 7 days.
  - Gastric ulcer: for 28 days.

LoE:I[viii]

AND

<u>*H. PYLORI* ERADICATION:</u> K25.0-7/K25.9/K26.0-7/K26.9/K27.0-7/K27.9 + (B96.8)

- Amoxicillin, oral, 1 g 12 hourly for 7 days.

OR

<u>For severe penicillin allergy:</u> (Z88.0)

- Azithromycin, oral, 500 mg daily for 3 days.

LoE:II[ix]

AND

- Metronidazole, oral, 400 mg 12 hourly for 7 days.

Failure of *H. pylori* eradication: Discuss with specialist.

***H. pylori* –ve**

These are usually a consequence of NSAID use.
Stop NSAID until ulcer has healed.
If patient is unable to stop NSAID, refer to specialist.

- PPI, e.g.:
- Lansoprazole, oral, 60 mg daily.
  - Duodenal ulcer: for 14 days.
  - Gastric ulcer: for 28 days.

LoE:II[x]

Resistant disease

Ulcer not healing.
High-risk patients, i.e. poor surgical risk and the elderly or concomitant disease.
Maintenance therapy:

- PPIs, e.g.:
- Lansoprazole, oral, 30 mg daily. Specialist initiated.

LoE:III[xi]

1.2 HEPATIC DISORDERS

Hepatitis (inflammation of the liver) may be infectious (caused by viral, bacterial, fungal, and parasitic organisms) or non-infectious (triggered by alcohol, drugs, autoimmune diseases, and metabolic diseases).

Causes of hepatitis includes idiosyncratic drug reactions, viral hepatitis (A, B, C, D, E), alcoholic hepatitis, autoimmune hepatitis, Wilson's disease, ischaemic hepatopathy, Budd-Chiari syndrome, veno-occlusive disease,

acute fatty liver of pregnancy/HELLP syndrome, malignant infiltration, partial hepatectomy, toxin exposure, including mushroom poisoning, sepsis, heat stroke or haemophagocytic lymphohistiocytosis.
For management of hepatitis C, consult a specialist.

1.2.1 HEPATITIS, NON-VIRAL

K70.1/K71.0-9/K75.4
* Notifiable medical condition if caused by agricultural chemicals or insecticides.

DESCRIPTION

Any form of hepatitis not caused by the common hepatotropic viruses.

Liver biopsy is indicated if hepatitis persists or diagnosis is unclear.

GENERAL MEASURES

Diet: If no hepatic encephalopathy, then normal protein intake appropriate. With hepatic encephalopathy, maintain 1 to 1.5mg/kg daily protein intake.
Avoid alcohol and other hepatotoxic agents.
Monitor blood glucose regularly given potential risk of hypoglycaemia.

MEDICINE TREATMENT

If the patient is bleeding, check INR and correct coagulopathy with:

- Lyophilised plasma **or** FFP — *LoE:II*[xii]

Parenteral Vitamin K should be provided and the INR reassessed.

Hepatitis due to infections

Antibiotic therapy based on culture, serology or suspected aetiology e.g. leptospirosis.

Alcohol-induced hepatitis

- Thiamine, oral, 300 mg daily. — *LoE:III*[xiii]

Other vitamins if indicated.

Drug-induced hepatitis

Stop all potentially hepatotoxic medication immediately, in consultation with a specialist.

Auto-immune hepatitis K75.4

Patients with persistent hepatitis, negative viral markers and no hepatotoxins. Biopsy and/or various parameters are required to make the diagnosis.

<u>If autoimmune hepatitis:</u>

- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 0.5 mg/kg daily.
  - Taper dose to a suitable maintenance dose. (Refer to Appendix II for an example of a dose reduction regimen).

AND (in consultation with gastroenterologist or hepatologist)

- Azathioprine, oral, 0.5 mg/kg daily, titrated up to 1 mg/kg daily depending on response and WCC.

REFERRAL

» Where patients cannot be managed locally or biopsy cannot be done, i.e. diagnosis is unclear.
» Non-resolving hepatitis.

Note: Refer timeously before extensive liver damage occurs.

1.2.2 LIVER FAILURE, ACUTE

K72.0/K72.9

DESCRIPTION

Acute liver failure refers to the development of severe acute liver injury with encephalopathy and impaired synthetic function (INR of ≥1.5) in a patient without cirrhosis or pre-existing liver disease. There are many causes, but the commonest are viral hepatitis, alcohol, drug-induced liver injury, toxins or ischemic hepatitis.

GENERAL MEASURES

Patient education.
Avoid hepatotoxic drugs and alcohol.
Rest and reduce physical activity.
Protein restriction indicated for encephalopathy. Severe protein restriction may accentuate catabolism. Use increments of 20 g protein per day as tolerated.
Monitor blood glucose regularly because hypoglycaemia is common.
Correct electrolyte disturbances.
Exclude GI bleed as precipitant.
Avoid any measure, e.g. medications that may worsen or precipitate functional deterioration.
Avoid vigorous paracentesis.
Exclude infection as precipitant.
If the patient is bleeding, check INR and correct coagulopathy with FFP or lyophilised plasma. Routine administration of parenteral vitamin K_1 is of unproven value.

MEDICINE TREATMENT

- Lactulose, oral, 10–30 mL 8 hourly, titrated to attain 2–3 soft stools per day.

Do not give antibiotics unless there is evidence of bacterial sepsis.

REFERRAL

All cases of severe acute liver failure should be discussed with a specialist.

1.2.3 PORTAL HYPERTENSION AND CIRRHOSIS

R18/K72.9/K74.6+ + (I98.2*/I98.3*)

DESCRIPTION

The complications of portal hypertension include:

» variceal bleeds
» ascites
» hepatic encephalopathy (HE)
» splenomegaly with hypersplenism
» hepatorenal syndrome
» hepato-pulmonary syndrome or porto-pulmonary hypertension

GENERAL MEASURES

Ascites: sodium restriction, i.e. ≤ 2 g/day or ≤ 88 mmol/day.
Monitor weight regularly.
Encephalopathy: with acute HE, protein restrict otherwise 1–1.5 mg/kg protein per day.
Exclude infection, high protein load, occult bleed, sedatives and electrolyte disturbances.
Variceal bleeding: endoscopic variceal ligation and/or immediate referral for advanced management.

MEDICINE TREATMENT

Ascites R18

- Single morning dose of oral spironolactone, oral 100 mg and furosemide, oral, 40 mg.
  - Increase the dose by 100 mg and 40 mg, respectively, every 3–5 days, to a maximum dose of 400 mg spironolactone and 160 mg of furosemide.
  - Rapid fluid shifts may precipitate acute liver and/or renal failure.
  - Spironolactone may cause hyperkalaemia.

Monitoring of sodium, potassium and renal function is essential in patients taking spironolactone. Avoid spironolactone if eGFR <30 mL/minute.

LoE:III[xiv]

Measure response to diuretics by weighing patient daily. Aim for maximal weight loss of:

500 g/day	patients without oedema
1 000 g/day	patients with oedema

Tense ascites R18

Albumin replacement should be considered if ≥5 L of fluid is removed or pre-existing renal dysfunction:

- Albumin, IV, 40 g (20%), as an infusion. *LoE:II*[xv]
  - o Refer to specialist unit to consider transjugular intrahepatic portosystemic (TIP) shunt or potential transplant.
- Introduce diuretics and titrate doses as necessary to prevent recurrence of ascites (see above).

Note:

» Avoid NSAIDS and ACE-inhibitors.

» Exclude spontaneous bacterial peritonitis in patients with new onset ascites.

Refractory ascites R18

» No response to optimal diuretic therapy, despite sufficient sodium restriction (≤2 g/day or ≤88 mmol/day) with avoidance of NSAIDs.

» Ascites recurs rapidly following therapeutic paracentesis.

Perform serial large volume paracentesis, as an outpatient, usually not more frequently than every 2 weeks.
Haemodynamic collapse is more likely in patients who are intravascularly volume depleted. Check renal function before paracentesis.

Albumin replacement should be considered if >5 L of fluid is removed:

- Albumin, IV, 40 g (20%), as an infusion. *LoE:II*[xvi]

Encephalopathy

- Lactulose, oral, 10–30 mL 8 hourly, depending on stool number and consistency (aim for 2 soft stools/day).

Look for precipitating factors: Sepsis, protein load, GIT bleed, over diuresis, sedation.

Oesophageal varices

To reduce the risk of bleeding:

- Beta-blocker, e.g.:
- Propranolol, oral, 20–40 mg 12 hourly. Titrate to resting pulse rate of 55-60 beats per minute (bpm). Monitor pulse and BP.

LoE:III[xvii]

REFERRAL

Refer to specialist unit to consider TIP shunt or potential transplant.

1.2.4 HEPATITIS, VIRAL

*Notifiable medical condition.

DESCRIPTION

Hepatitis caused by one of the hepatotropic viruses, hepatitis A, B, C and E.

1.2.4.1 HEPATITIS B, ACUTE

B16.0-2/B16.9

GENERAL MEASURES

Bed-rest until acute phase is over.
Avoid alcohol during the illness and for ≥ 6 months after clinical recovery.
Screen sexual contacts of patients with acute hepatitis B. If they are non-immune (negative for hepatitis B antibodies) then they should receive hepatitis B active immunisation.

MEDICINE TREATMENT

For nausea and vomiting: (R11)

- Metoclopramide, IV/oral, 10 mg 8 hourly as required.

Hepatitis B virus: prophylaxis following exposure e.g. needle stick injury

S61.0 + (W46.22+Z20.5+Z29.8)

Persons at risk can be protected by passive immunisation with hyper immune serum globulin prepared from blood containing anti-HBs.
It is essential that all categories of healthcare workers (HCW) who are at risk of exposure, including cleaning staff, be fully vaccinated against hepatitis B.
All exposure incidents must be adequately documented for possible subsequent compensation.
Recommended post-exposure management for HCW exposed to infectious material from patients with infectious hepatitis B (either surface antigen or e antigen positive).

Vaccination status and antibody response status of HCW	**Source patient status & treatment**		
	HBsAg positive	**HBsAg negative**	**HBsAg unknown**
Unvaccinated **OR** vaccination incomplete	• HBIG, IM, 500 units* • Hep B vaccine (3 doses at monthly intervals)	• Initiate Hep B vaccination (month 0, 1 and 6)	• HBIG, IM, 500 units* • Hep B vaccine (3 doses at monthly intervals)
Vaccinated AND HBsAb >10 units/mL#	No treatment	No treatment	No treatment
Vaccinated **AND** HBsAb <10 units/mL	• HBIG, IM, 500 units * • Repeat Hep B vaccine (3 doses at monthly intervals)	• Initiate Hep B vaccination (month 0, 1 and 6)	• HBIG, IM, 500 units* • Repeat Hep B vaccine (3 doses at monthly intervals)

* HBIG and first dose of vaccine to be given simultaneously, but at different sites.
# If the delay in obtaining HBsAb results is more than 24 hours initiate treatment as for vaccinated AND HBsAb <10 units/mL.

1.2.4.2 HEPATITIS B, CHRONIC (NON-HIV COINFECTION)

B18.0-2/B18.8-9

Consult the most recent Hepatitis Guidelines from the National Department of Health for comprehensive monitoring recommendations.

DESCRIPTION

HBV is most commonly transmitted horizontally, in children <5 years of age. Vertical mother to child transmission and adult transmission, sexually or through a parenteral route, can also occur.

Acute infection may be asymptomatic or present as acute hepatitis.

A proportion of patients develop chronic hepatitis (defined as abnormalities listed in the table below persisting for >6 months), which can result in cirrhosis and hepatocellular carcinoma.

It is essential to know the HIV status of all patients with chronic hepatitis B before considering therapy.

Antiviral therapy is not indicated for acute hepatitis B infection.

There are 5 potential phases of chronic hepatitis B infection which determine the need for treatment:

Phase	Serology	Viral load (HBV DNA) IU/mL	ALT	Management *LoE:III*[xviii]
1. HBeAg-positive chronic HBV infection (Immune Tolerant)	» HBsAg positive » HBeAg positive	>20000 (usually >200000)	Normal	» Treatment not routinely needed, but should be followed up. » Treat only if on immunosuppressive therapy to prevent hepatitis B flares.
2. HBeAg-positive chronic hepatitis B (Immune Clearance)	» HBsAg positive » HBeAg positive	>20000	Elevated	» Treatment required.
3. HBeAg-negative chronic HBV infection (Immune Control)	» HBsAg positive » HBeAg negative	<2000	Normal	» Treatment not routinely needed, but should be followed up. » Treat only if on immunosuppressive therapy to prevent hepatitis B flares.
4. HBeAg-negative chronic hepatitis B (Immune Escape)	» HBsAg positive » HBeAg negative	>2000	Elevated	» Treatment required.
5. Occult hepatitis B	» HBsAg negative » HBsAb negative » HB IgG core Ab positive	<200	-	» No follow-up required. » Treat only if on immunosuppressive therapy to prevent hepatitis B flares.

HBsAg: hepatitis B surface antigen; *HBsAb:* hepatitis B surface antibody; *HBIG:* hepatitis B immunoglobulin

Treat all patients with cirrhosis regardless of ALT level, HBeAg status and DNA level, to prevent hepatitis B flares that will lead to decompensation.

MEDICINE TREATMENT

- Tenofovir, oral, 300 mg daily, if estimated CrCl >50 mL/minute.

LoE:III[xix]

AIMS OF TREATMENT

HBeAg-positive disease

» Sustained HBsAg loss off therapy, with/without the development of anti-HBs, **and**
» Suppression of HBV DNA to undetectable or low (<2000 IU/mL) levels, **and**
» Normalisation of ALT, **and**
» Sustained HBeAg loss and seroconversion to anti-HBe.

HBeAg-negative disease

» Sustained HBsAg loss off therapy, with/without the development of anti-HBs, **and**
» Suppression of HBV DNA to undetectable or low (<2000 IU/mL), **and**
» Normalisation of ALT.

MONITORING WHILST ON TENOFOVIR

Baseline	FBC+diff, ALT, INR, urine protein, serum phosphate and serum creatinine
Week 4 and every 12 weeks	FBC+diff, ALT
Week 4	INR
Week 4, then at 3, 6 and 12 months after initiation and every 12 months thereafter if on TDF	Serum creatinine
Every 6 months	HBeAg-positive patients: HbsAg after anti-HBe seroconversion HBeAg-negative patients: HBsAg with persistently undetectable HBV DNA
Every 12 months	HBeAg-positive patients: HBeAg, anti HBe
HBeAg-positive patients: 12 months after HBeAg seroconversion	HBV DNA levels

Adapted from: National Department of Health, National guidelines for the management of viral hepatitis, 2018. Available at www.health.gov.za

DISCONTINUE TREATMENT WITH TENOFOVIR WHEN:

» **HBeAg-positive patients:** 12 months after HBeAg seroconversion and in association with persistently normal ALT levels and undetectable HBV DNA levels.
» **HBeAg-negative patients:** Long-term therapy unless HBsAg seroconversion is achieved.

» **Cirrhotic patients:** Lifelong treatment.

REFERRAL
Failure of or contraindications to tenofovir.

1.2.4.3 HEPATITIS B, CHRONIC (HIV CO-INFECTION)
See chapter 10: HIV and AIDS.

1.2.5 LIVER ABSCESS, PYOGENIC
K75.0

DESCRIPTION
Focal bacterial infection, usually polymicrobial, of the liver with pus. Multiple abscesses are not uncommon.

GENERAL MEASURES
Drainage is essential in all cases. This should preferably be done percutaneously by inserting a catheter under ultrasound guidance.

MEDICINE TREATMENT
Empiric antibiotic therapy
- Amoxicillin/clavulanic acid, oral, 875/125 mg 12 hourly.

If unable to tolerate oral therapy:
- Amoxicillin/clavulanic acid, IV, 1.2 g 8 hourly.

Duration of antibiotic therapy is ill defined, but may need to be for as long as 12 weeks in cases of multiple abscesses. Continue until drainage is complete and CRP has returned to normal values. Ultrasound resolution is very slow and is not useful for monitoring response to therapy.

1.2.6 LIVER ABSCESS, AMOEBIC
A06.4

DESCRIPTION
Focal hepatic infection due to *E. histolytica*. Only about a third of cases have concomitant amoebic colitis. Diagnosis can be excluded if the serological test is negative. It is essential to exclude pyogenic infection (a diagnostic aspirate should be taken under ultrasound guidance in all cases where there is doubt).

GENERAL MEASURES
Drainage is recommended for abscesses that are large, i.e. >10 cm diameter, involve the left lobe or are near the surface of the liver. Drainage can be achieved by percutaneous aspiration under ultrasound guidance.

MEDICINE TREATMENT
- Metronidazole, oral, 800 mg 8 hourly for 10 days. *LoE:III*[xx]

1.2.7 CHOLECYSTITIS, ACUTE AND CHOLANGITIS, ACUTE

K81.0/K83.0

GENERAL MEASURES

Surgical drainage/cholecystectomy according to indication and/or patient's condition.

MEDICINE TREATMENT

Acute cholecystitis

Mild and asymptomatic cases without risk factors may not require antibiotic treatment. If signs of infection present and/or risk factors for severe disease are present, such as:

» Elderly patients (>60 years of age)
» Co-morbid conditions
» Immune compromised

Acute cholecystitis and acute cholangitis

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

If unable to tolerate oral therapy:

- Amoxicillin/clavulanic acid, IV, 1.2 g 8 hourly.

REFERRAL

» Clinical deterioration or failure to improve.
» Fistulae or perforation.
» Need for complicated surgery.

1.3 DIARRHOEA

1.3.1 CHOLERA

A00.0-1/A00.9

*Notifiable medical condition.

DESCRIPTION

Diarrhoea due to *Vibrio cholerae*, often in outbreaks.

GENERAL MEASURES

Rehydration is the cornerstone of management. This should be done with oral rehydration solution (ORS) unless the patient is vomiting or profoundly dehydrated.

MEDICINE TREATMENT

- Ciprofloxacin, oral, 500 mg 12 hourly for 3 days.
  - o Adjust antibiotic choice, according to the sensitivity of the isolate responsible for the local epidemic.

LoE:III[xxi]

1.3.2 DYSENTERY (ACUTE INFLAMMATORY DIARRHOEA)

A03.0-3/A03.8-9/A41.0-5/A41.8-9

DESCRIPTION

Diarrhoea with neutrophils, blood and/or mucus.

GENERAL MEASURES

Rehydration is the cornerstone of management. This should be done with oral rehydration solution (ORS) unless the patient is vomiting or profoundly dehydrated.
Stool culture is advised.

MEDICINE TREATMENT

Loperamide is contraindicated as it may result in toxic megacolon.

Antibiotic therapy

Consider in patients with signs of sepsis and severe cases or significant underlying disease:

- Ceftriaxone, IV 1g daily.
  - Switch to oral therapy when clinically appropriate i.e. ciprofloxacin, oral, 500 mg 12 hourly.

For uncomplicated dysentery in patients with no co-morbidity:

- Ciprofloxacin, oral, 500 mg 12 hourly for 3 days.

For uncomplicated dysentery in patients with significant co-morbidity e.g. immunocompromised patients:

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

REFERRAL

Persistent diarrhoea with blood and mucus for longer than 2 weeks.

1.3.3 DIARRHOEA, ACUTE NON-INFLAMMATORY

A04.1

DESCRIPTION

Diarrhoea without macroscopic blood or mucus, or neutrophils on microscopy. Common causes include viruses and enterotoxigenic strains of *E. coli*.
Note: Neutropenic patients may have inflammatory diarrhoea in the absence of neutrophils.

GENERAL MEASURES

Rehydration is the cornerstone of management. This should be done with oral rehydration solution (ORS) unless the patient is vomiting or profoundly dehydrated.

MEDICINE TREATMENT

- Loperamide, oral, 4 mg immediately, followed by 2 mg after each loose stool.
  - Maximum dose: 16 mg daily.

1.3.4 CLOSTRIDUM DIFFICILE DIARRHOEA

A04.7

*Notifiable medical condition.

DESCRIPTION

Diarrhoea caused by altered bowel flora due to antibiotic exposure.

Clostridium difficile infection may result in severe disease and/or the development of pseudomembranous colitis.

Diagnosis is confirmed in the laboratory on a stool sample. Patients with unexplained and new-onset diarrhoea of more than 3 unformed stools in 24 hours should be tested. Repeat testing (within 7 days) is not recommended.

GENERAL MEASURES

» The most important aspect of management is discontinuing antibiotics.
» Rehydration may be necessary. This should be done with oral rehydration solution (ORS) unless the patient is vomiting or profoundly dehydrated.
» Patients with known or suspected *Clostridium difficile* infection should be placed on contact precaution according institutional infection control and prevention measures.
» Contact precautions should be maintained for at least 48 hours after diarrhoea has resolved.
» Healthcare workers and all close contacts should perform regular handwashing with soap and water. Alcohol-based hand sanitizer does not kill spores.

MEDICINE TREATMENT

Loperamide is contraindicated as it may result in toxic megacolon.

Mild to moderate infection

Laboratory results confirm toxigenic *Clostridium difficile* infection, diarrhoea does not settle on antibiotic withdrawal:

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

Severe infection

Laboratory results confirm toxigenic *Clostridium difficile* infection, WCC >15 micromol/L or serum creatinine >132 micromol/L, or other risk predictors of severity (immunodeficiency, intensive care admission, serious comorbidity, age >65 years of age).

- Vancomycin, oral, 125 mg 6 hourly (give parenteral formulation orally) for 10 days.

Fulminant infection

If ileus or toxic megacolon or hypotension/shock:

- Vancomycin, oral, 125 mg 6 hourly (give parenteral formulation orally) for 10 days.

AND

- Metronidazole, IV, 500 mg 8 hourly for 10 days.

Switch to oral metronidazole, if possible, to complete 10 day course.

Recurrence

If metronidazole was used during the first episode:

- Vancomycin, oral, 125 mg 6 hourly (give parenteral formulation orally) for 10 days.

If vancomycin was used during the first episode, consider oral vancomycin as tapered and pulsed regimen:

- Vancomycin, oral, 125 mg 6 hourly (give parenteral formulation orally) for 10 days, then 12 hourly for 7 days, then once per day for 7 days, and then every 2nd or 3rd day for 2 to 8 weeks.

LoE:I[xxii]

REFERRAL

» Surgical consult should be obtained in all patients with complicated *Clostridium difficile* infection (e.g. bowel perforation, hypotension requiring vasopressor therapy, clinical signs of sepsis).
» Failure to improve on medical therapy after 5 days.

1.3.5 AMOEBIC DYSENTERY

A06.0-1/A06.7-9

DESCRIPTION

Diarrhoea with blood and/or mucus due to *E. histolytica*. Organism must be demonstrated on a warm stool specimen for microscopy.

GENERAL MEASURES

Rehydration may be necessary. This should be done with oral rehydration solution (ORS) unless the patient is vomiting or profoundly dehydrated.
Surgery for bowel perforation.

MEDICINE TREATMENT

Loperamide is contraindicated as it may result in toxic megacolon.

- Metronidazole, oral, 800 mg 8 hourly for 10 days. *LoE:III*[xxiii]

1.3.6 GIARDIASIS

A07.1

DESCRIPTION

Infection with the protozoan parasite, *G. lamblia* which colonises the proximal

small intestine. Does not typically presents with acute diarrhoea.

GENERAL MEASURES
Fluid and electrolyte replacement in severe diarrhoea.

MEDICINE TREATMENT
- Metronidazole, oral, 2 g daily for 3 days.

1.3.7 TYPHOID
See section 9.11: Typhoid fever.

1.3.8 BACTERIAL PERITONITIS
K65.0/K65.8-9

DESCRIPTION
Infection of the peritoneum, usually secondary to a surgical cause such as perforated bowel. In this setting polymicrobial infection with anaerobes, Gram-positive cocci, and Enterobacteriaceae are usually found.
Primary or spontaneous bacterial peritonitis is much less common and usually complicates ascites in patients with portal hypertension. This is not usually polymicrobial but due generally to Enterobacteriaceae such as *E. coli*. Spontaneous bacterial peritonitis is often culture-negative but is diagnosed by ascitic neutrophil count >0.25 x 10^9/L (250 cells/mm^3).

GENERAL MEASURES
Secondary peritonitis
Intravenous fluids and nasogastric suction.
Prompt surgical intervention is essential.

MEDICINE TREATMENT
Empiric antibiotic therapy
For surgical causes of peritonitis:
- Amoxicillin/clavulanic acid, IV 1.2 g 8 hourly.

As soon as patient can tolerate oral medication:
- Amoxicillin/clavulanic acid, oral, 875/125 mg 12 hourly.

For spontaneous bacterial peritonitis:
- Ceftriaxone, IV, 1 g daily.
  - Patients not responding to ceftriaxone after 48 hours, consult a specialist.

Switch to oral therapy when clinically appropriate according to culture or treat with:
- Ciprofloxacin, oral, 500 mg 12 hourly.
  - Total duration of therapy: 14 days.

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CHAPTER 2

BLOOD AND BLOOD FORMING ORGANS

2.1 ANAEMIA

Defined as a reduction in the absolute number of circulating red blood cells and most commonly diagnosed when the haemoglobin (Hb) concentration is reduced below the reference range for age and gender. The clinical features depend on the severity of anaemia, the rate at which it developed and the oxygen demands of the patient.

Cause
Can be classified according to the mean corpuscular volume (MCV) of the red blood cell (RBC) into macrocytic anaemia (MCV >100 fL); microcytic anaemia (MCV <80 fL) or normocytic anaemia (MCV 80–100 fL).

2.1.1 ANAEMIA, IRON DEFICIENCY

D50.0-1/D50.8-9

DESCRIPTION

Anaemia due to iron deficiency. Common causes of iron deficiency are chronic blood loss, poor iron absorption or poor nutritional intake.

Investigations

» Low MCV and MCH (mean cell Hb – hypochromia) – note that this often normal in early stages.
» Full blood count (FBC) Smear: Hypochromic microcytic anaemia and pencil cells often reported.
» Confirm with low ferritin.
» Investigate for **cause** of iron deficiency.
» Consider upper and lower endoscopies in high risk patients (all males and postmenopausal female patients) and patients not responding to treatment.

GENERAL MEASURES

Identify and treat the underlying cause.
Dietary adjustment if this is the underlying cause.

MEDICINE TREATMENT

Oral iron supplementation

Treatment
Treat underlying cause.

- Ferrous sulfate compound BPC (dried), oral, 170 mg (± 55 mg elemental iron) 12 hourly.

LoE:III[i]

OR

Ferrous fumarate, oral, 200 mg (± 65 mg elemental iron) 12 hourly.
- o Do not ingest with tea, antacids or calcium supplements/milk.
- o Doses should be taken on an empty stomach, but if gastrointestinal side effects occur doses should be taken with meals.
- o Continue with treatment for 3 months once Hb has normalised to replace iron stores.
- o If daily iron is poorly tolerated (e.g. epigastric pain, nausea, vomiting and constipation), administer oral iron on alternate days with meals.

LoE:III[ii]

Follow the patient after one month of treatment and Hb should rise by at least 2 g/dl in the adherent patient without ongoing blood loss.

Prophylaxis O99.0/D50.0-1/D50.8-9/Z29.2
For example during pregnancy:
- Ferrous sulfate compound BPC (dried), oral, 170 mg (± 55 mg elemental iron) daily.

OR

LoE:III[iii]

Ferrous fumarate, oral, 200 mg once daily (± 65 mg elemental iron).

<u>If daily iron is poorly tolerated (e.g. epigastric pain, nausea, vomiting and constipation), intermittent iron supplementation may be administered:</u>

LoE:I[iv]

- Ferrous sulphate compound BPC (dried), oral, 340 mg per week, (± 110 mg elemental iron), with meals.

OR

Ferrous fumarate, oral, 400 mg per week (± 130 mg elemental iron).

Consider the following if there is failure to respond to iron therapy:
» non-adherence,
» continued blood loss,
» wrong diagnosis,
» malabsorption, or
» mixed deficiency; concurrent folate or vitamin B_{12} deficiency.

Parenteral iron

Parenteral iron is seldom required and may very rarely be associated with anaphylaxis.
Parenteral iron is **only** indicated when oral iron is:
» ineffective, defined as lack of response after three months of oral iron therapy, or
» iron deficiency anaemia from 36 weeks of pregnancy, or
» expected to be ineffective, e.g. malabsorption, patients on haemodialysis and erythropoietin therapy, or
» not tolerated.

In people who require repeated therapy, the intravenous route is preferred.

Minimum required dose is 250 mg of iron per gram of Hb below normal.

Note: Use in consultation with a specialist.

- Iron, IV, e.g.:
- Iron sucrose, IV, 200 mg in 200 mL sodium chloride 0.9%, over 30 minutes, given on alternate days until the total dose has been given**.**
  - **Note:** Test dose is not required.
  - An initial total dose of 600 mg is usually adequate to raise the Hb to acceptable levels.

OR

- Low molecular weight iron dextran, administered as a single dose.
  - Determine total dose of iron required (total dose up to 20 mg/kg body weight).
  - **Note:** Start with test dose - 25 mg in 100 ml sodium chloride 0.9%, infused over 15 minutes and observe the patient for 1 hour.
  - If there is no adverse drug reaction, administer the remaining dose in 500 mL of sodium chloride 0.9%, 0.9% over 4-6 hours. Observe the patient for 1 hour after the infusion.

LoE:III[v]

Resuscitation equipment should be ready to manage anaphylaxis.

Red cell concentrate transfusion

Indicated in patients with:

» anaemia leading to cardiac failure or severe dyspnoea;
» active, ongoing bleeding; or
» where correction of anaemia is required prior to performing an urgent invasive procedure or surgery.

2.1.2 ANAEMIA, MEGALOBLASTIC

D53.1/D58.9/D59.9/D55.0-3/D55.8-9/D56.0-4/D56.8-9/D57.0-3/D57.8/D58.0-2/ D58.89/D47.1/L26

DESCRIPTION

Anaemia caused by a deficiency of folate and/or vitamin B_{12}.

Note that several medicines can cause macrocytic anaemia (e.g. hydroxyurea, stavudine and zidovudine) without deficiencies of folate and/or vitamin B_{12}.

Investigations

» Elevated MCV and MCH.
» Pancytopaenia in severe cases.
» FBC smear: oval macrocytes, hypersegmentation of neutrophils, thrombocytopenia with giant platelets.

» Decreased serum vitamin B_{12} or red blood cell folate.
» Intrinsic factor antibodies, and/ or anti-parietal cell antibodies are found in pernicious anaemia.

GENERAL MEASURES

Dietary modifications to ensure adequate intake of folate and vitamin B_{12} (important in vegetarians and malnourished patients).
Identify and treat the underlying cause, e.g. antibiotics for intestinal overgrowth with bacteria.

Metformin use can lead to vitamin B_{12} deficiency by interfering with absorption.

MEDICINE TREATMENT

After blood samples for RBC folate and vitamin B_{12} levels have been taken, start with folic acid and vitamin B_{12} supplementation.
Monitor serum potassium and replace if necessary.
Adjust management according to results.

Give vitamin B_{12} and folic acid together until the test results are available as giving folic acid alone in patients with a B_{12} deficiency may precipitate a permanent neurological deficit.

Folic acid deficiency

- Folic acid, oral, 5 mg daily until Hb returns to normal.

Prolonged treatment may be required for malabsorption states.

Vitamin B_{12} deficiency

- Vitamin B_{12}, IM.
  - 1 mg daily for 5 days, then weekly for a further 3 doses
  - Follow with 1 mg every second month for life in patients with pernicious anaemia.

Note:

» Response to treatment is associated with an increase in energy and strength and improved sense of well-being.
» Reticulocytosis begins 3–5 days after therapy and peaks at about day 7.
» Anaemia normally corrects within 1–2 months. The white cell count and platelets normalise in 7–10 days. As there is an increase in red blood cell production, iron and folic acid supplementation is also recommended, until Hb has normalised. Check for hypokalaemia in the first few days of therapy.

Hypokalaemia: See section 7.2.2: Hypokalaemia.

Consider the following if there is failure to respond:
» Co-existing folate and/or iron deficiency,
» Other causes of macrocytosis:
  - Myelodysplasia,
  - Hypothyroidism,
  - Chronic alcohol use,
» Drug-induced, e.g. hydroxyurea, stavudine and zidovudine.

Prophylaxis O99.0/Z49.1/Z29.2
Vitamin B_{12} is indicated for patients after total gastrectomy or ileal resection.
- Vitamin B_{12}, IM, 1 mg every second month for life.

Indications for folic acid:
» Chronic inherited or acquired haemolytic anaemias, e.g. sickle cell anaemia, thalassaemia.
» Myeloproliferative disorders.
» Exfoliative skin disorders.
» Increased demands, e.g. pregnancy, chronic haemodialysis.

- Folic acid, oral, 5 mg daily.

2.1.3 ANAEMIA, CHRONIC DISORDER
(D63.0/D63.8)

DESCRIPTION
Anaemia due to chronic inflammation. This is characteristically a normochromic normocytic anaemia. Common causes of anaemia of chronic disorder include:
» malignancy, e.g. haematological or solid tumours
» autoimmune disorders, e.g. rheumatoid arthritis
» chronic infections, e.g. HIV and TB
» chronic kidney disease

TREATMENT
Treat the underlying condition.
Transfusion is seldom necessary.
Do not treat with iron, folic acid or vitamin B_{12} unless there is a documented deficiency (note that diagnosing iron deficiency is difficult in chronic disorders as ferritin increases and serum iron decreases due to the acute phase response). A transferrin saturation level less than 20% usually indicates a combination of iron deficiency anaemia and anaemia of chronic disease.

2.1.4 ANAEMIA, HAEMOLYTIC
D59.0-1

DESCRIPTION
Anaemia due to destruction of red blood cells. Destruction may be due to:
» Extracellular factors such as auto-immunity or mechanical factors, e.g. disseminated intravascular coagulation (DIC), hypersplenism, mechanical heart valves.
» Abnormalities of the cell membrane, e.g. hereditary spherocytosis.
» Enzymes, e.g. G6PD deficiency.
» Haemoglobin abnormalities, e.g. sickle cell anaemia, thalassaemia.
» Thrombotic thrombocytopenic purpura is a life-threatening emergency, if treated early. Immediate referral to specialist unit for plasma infusion or

exchange is necessary (see section 2.12: Thrombotic thrombocytopenic purpura-Haemolytic uraemic syndrome).

Investigations

» Evidence of haemolysis: anaemia, reticulocytosis, decreased haptoglobin, increased lactate dehydrogenase (LDH) and unconjugated hyperbilirubinaemia.
» FBC smear: Spherocytes often reported
» Coombs' test (direct antiglobulin) is usually positive with autoimmune haemolysis.
» HIV status.

GENERAL MEASURES

Treat the underlying cause.
Do not transfuse prior to appropriate investigations, unless anaemia is severe.
In situations of life-threatening anaemia, transfuse the **most compatible** unit of red blood cells and get specialist advice urgently. Coombs-positive haemolytic anaemia may be technically difficult to cross match.
Efficacy of transfusion is limited by the shortened red cell survival due to haemolysis.
In G6PD deficiency, avoid drugs known to cause haemolysis, including aspirin, sulphonamides (including cotrimoxazole), dapsone and primaquine.
In patients with cold agglutinins all transfusions must be given through a blood warmer to avoid cold-induced haemolysis.

MEDICINE TREATMENT

All patients:
Because of high red cell turnover, supplement with:

- Folic acid, oral, 5 mg daily.

Autoimmune haemolytic anaemia

Treat under specialist supervision.

- Prednisone, oral.
  - Initial dose:1 mg/kg daily, until Hb stable and >10 g/dL.
  - Taper slowly and monitor Hb at least once weekly. (Refer to Appendix II for an example of a dose reduction regimen). *LoE:III*[vi]
  - Glucocorticoids should be tapered slowly, when there is normalization of the haemoglobin and LDH. The patient should be monitored for recurrence following cessation of treatment.
  - As these conditions can often be life-threatening, specialist advice should be sought as early as possible after diagnosis.

REFERRAL/CONSULTATION

<u>If inadequate response:</u>

» haemolysis remains severe for 3 weeks at prednisone doses of 1 mg/kg, if remission cannot be maintained on low doses of prednisone, or if the

patient has intolerable adverse effects or contraindications to glucocorticoids.

Refer to specialist for second-line treatment:
» Splenectomy: vaccination: see chapter 11: Surgical prophylaxis.

Immunosuppresive therapy is needed in some cases, initiated by specialists.

LoE:III[vii]

2.1.5 ANAEMIA, APLASTIC

D60.0-1/D60.8-9/D61.0-3/D61.8-9

DESCRIPTION

Pancytopenia due to a hypoplastic bone marrow.

Clinical features:

» pallor
» petechiae
» frequent or severe infections
» purpura
» bleeding

Pancytopenia in HIV positive patients B23.2 + (D61.0/D61.9)

Most common causes include:

Direct effect of HIV, medication, secondary opportunistic infections, malignancies and nutritional deficiencies. Many cases are idiopathic.

Investigations

» FBC smear (FBC indicates different degrees of: anaemia, thrombocytopaenia and leucopaenia).Vitamin B_{12} and red cell folate.
» Appropriate investigation to exclude opportunistic infections.
» Bone marrow trephine and aspiration in selected patients (where no other cause is found, in patients with persistent pancytopaenia) to exclude infiltration with opportunistic infections, malignancies, etc.

MEDICINE TREATMENT

If neutropenic and febrile, see section 2.8: Febrile neutropenia.

REFERRAL

Discuss all cases of suspected aplastic anaemia with a specialist. (Stabilise patient, if necessary, with blood products before transport but after consultation with an expert).

2.1.6 ANAEMIA, SICKLE CELL

D57.0-3/D57.8

DESCRIPTION

Homozygous sickle cell anaemia (HbSS). Individuals with sickle cell trait have <50% HbS and are generally asymptomatic. Milder sickle cell disease occurs in individuals with HbSC.

The disease is characterised by recurrent acute vaso-occlusive episodes ("sickle crises") and chronic haemolytic anaemia.
Adults develop hyposplenism, predisposing them to infection with encapsulated bacteria.

Vaso-occlusive episodes
Vaso-occlusion can involve any part of the body, especially the skeleton. Episodes may be triggered by dehydration, infection, stress or menstruation. The most common presentation is with acute episodes of pain, varying in severity, in the affected areas.

Investigations
The diagnosis is suspected from the history, peripheral blood examination, and/or screening tests for sickling.
Diagnosis is confirmed on haemoglobin electrophoresis.

GENERAL MEASURES (SEVERE VASO-OCCLUSIVE EPISODES)

Keep well hydrated with intravenous fluids.
Transfusion is only indicated for severe episodes with severe anaemia – discuss with a specialist.
Pain must be controlled.

MEDICINE TREATMENT (SEVERE VASO-OCCLUSIVE EPISODES)

- Use of Oxygen to maintain adequate saturation.

<u>To prevent venous thromboembolism:</u>

- Low molecular weight heparin, e.g.:
- Enoxaparin, SC, 40 mg daily.

In morbid obesity dosing of LMWH should be individualised, in discussion with a specialist. *LoE:III*[viii]

In renal failure (eGFR <30 mL/minute), the recommended dose of LMWH is 1 mg/kg daily. *LoE:III*[ix]

OR

- Unfractionated heparin, SC, 5 000 units 12 hourly. *LoE:III*[x]

Analgesia
Refer to chapter 12: Anaesthesiology, pain and intensive care.

MEDICINE TREATMENT (CHRONIC MANAGEMENT)

All patients:

- Folic acid, oral, 5 mg daily.

- Vaccination against infections due to pneumococci and haemophilus (see section 9.2: Adult vaccination).

Hydroxyurea (specialist-initiated) is the mainstay of therapy in severe disease. Typical indications include:

- frequent painful vaso-occlusive episodes,
- severe vaso-occlusive episodes (e.g. acute chest syndrome, stroke), and
- severe symptomatic anemia.

REFERRAL

» All patients, for chronic management in a specialised centre.
» Vaso-occlusive episodes should be managed in consultation with a specialist.

2.2 FEBRILE NEUTROPENIA

D70

DESCRIPTION

Febrile neutropenia is conventionally defined as an absolute neutrophil count of $<0.5 \times 10^9$/L with a temperature of greater than 38°C for >1 hour or a single temperature of 38.3°C, but any neutropaenic patient showing clinical signs of sepsis should be investigated.

Note:

» This is a **medical emergency** as a minor infection may become very serious, these patients can rapidly develop features of severe sepsis (multi-organ failure and/or hypotension). It is crucial to monitor and treat patients for signs and symptoms of infection.
» **Cultures should be obtained for appropriate microbiological testing prior to empirical antimicrobial therapy.** It is critical to recognise neutropenic fever early and to initiate empiric systemic antibacterial therapy promptly in order to avoid progression to a sepsis syndrome and possibly death.

LoE:III[xi]

GENERAL MEASURES

Treat the underlying cause of neutropenia, if applicable.
Withdraw any medication that may cause neutropenia.
Consider removing central IV line. Once culture results are available, adjust treatment to the most appropriate narrow spectrum agent.

MEDICINE TREATMENT

For patients with febrile neutropenia within 48 hours of admission:

- Ceftriaxone, IV, 1 g daily.

AND

- Gentamicin, IV, 6 mg/kg daily (see Appendix II for guidance on prescribing).

If IV line, skin infection is suspected as the cause::

ADD:

- Vancomycin, IV, 30 mg/kg as a loading dose. Follow with 20 mg/kg/dose 12 hourly. (See Appendix II for guidance on prescribing and monitoring).

If fever develops after 48 hours of admission:

(Choice of antibiotic will depend on local susceptibility patterns).

- Carbapenem with activity against Pseudomonas, e.g.:
- Meropenem, IV, 1 g 8 hourly

OR

Imipenem/cilastan, IV, 500/500 mg 6 hourly.

Note: Ertapenem is not recommended because it is not effective for *Pseudomonas* species, which are important pathogens in this setting.

OR

- Piperacillin/tazobactam, IV, 4.5 g 8 hourly

AND

Amikacin, IV, 15 mg/kg daily. (See Appendix II, for individual dosing and monitoring for response and toxicity). *LoE:III*[xii]

OR

- Cefepime, IV, 2 g 12 hourly. *LoE:III*[xiii]

If no response after 5–7 days: (In discussion with a Clinical Haematologist or Infectious Disease specialist).

ADD

- Amphotericin B, IV, 1 mg/kg daily in dextrose 5 % over 4 hours.
  - Ensure adequate hydration to minimise nephrotoxicity. (See Appendix II for preventing, monitoring and management of toxicity).

Duration of therapy:

» If neutrophil count increases to $>0.5 \times 10^9$/L, continue for 2 days after fever has settled.

» If neutrophil count remains $\leq 0.5 \times 10^9$/L, continue for 7 days after fever has settled.

REFERRAL/CONSULTATION

All cases – consult with haematologist/oncologist.

2.3 MYELODYSPLASTIC SYNDROMES

D46.0-2/D46.4-7/D46.9

DESCRIPTION

A group of disorders characterised by refractory cytopaenias due to bone marrow failure. Tthere is a risk of disease progression to acute leukaemia.

Investigations
» Evidence of cytopenia, with normal B_{12} and folate levels, and often substantial morphological dysplasia on the blood smear.
» Bone marrow examination confirms dysplasia of the blood elements and the presence of cytogenetic abnormalities.

TREATMENT
Transfusion should ideally be with leucodepleted red cells to delay immunisation, as these patients require frequent transfusions.
Bone marrow transplantation can be curative in selected patients.
If neutropenic and febrile, see section 2.8: Febrile neutropenia.

REFERRAL
All patients for further investigation and management.

2.4 BLEEDING DISORDERS

GENERAL PRINCIPLES
A bleeding tendency may result from:
» a coagulation defect (congenital/acquired),
» a vessel wall defect, or
» a platelet defect (quantitative/qualitative).

A careful and detailed history, thorough examination and review of relevant laboratory investigations will allow differentiation between these three categories, as the management of each of these groups differs significantly.

Screening tests include: FBC, prothrombin time (PT) and activated partial thromboplastin time (aPTT) (if prolonged, mixing studies are required).

Patients with a chronic bleeding tendency should be advised to wear a medic alert bracelet which clearly mentions the type of disorder he/she suffers from, e.g. severe Haemophilia A, Factor VIII <1%, no inhibitors.

2.4.1 HAEMOPHILIA A AND B, VON WILLEBRAND'S DISEASE
D66/D67/D68.0

DESCRIPTION
Haemophilia A, haemophilia B and von Willebrand's disease are chronic bleeding disorders caused, respectively, by a lack of clotting factor VIII, clotting factor IX and von Willebrand factor (VWF, a carrier protein for factor VIII). Presentation depends on severity of the condition (see classification below).

Complications include haemarthrosis with later chronic arthropathy, intracranial haemorrhage, soft tissue and muscle haematomas. Pain/tingling in a joint suggests bleeding into the joint in a known haemophiliac.

Early consultation with a haematologist or a clinician with expertise in the handling of such patients is advisable. Clinicians should make contact with their local haemophilia centre which may be identified at: http://www.haemophilia.org.za/treatment-centres/

All patients diagnosed with haemophilia should at least annually attend a specialised Haemophilia Treatment Centre with a dedicated multi-disciplinary health care team as guided by the local Haemophilia Treatment Centre.

Subclassification (factor VIII and IX deficiency):

CLASS	CLOTTING FACTOR	% OF NORMAL	SIGNS
Mild	VIII or IX	>5–<40%	Occasional bleeds
Moderate	VIII or IX	1–5%	Less frequent bleeding associated with trauma, surgery or dental work
Severe	VIII or IX	<1%	Traumatic or spontaneous bleeds

Investigations
Prolonged partial thromboplastin time (PTT).
Factor VIII or factor IX concentration and inhibitor screen.

TREATMENT GUIDELINES
Treatment approaches are divided into two main categories: prophylaxis and on demand.

Prophylaxis
Secondary prophylaxis is sometimes needed in patients presenting with a target joint in consultation with a Haemophilia Treatment Centre.
The aim is to reduce the number of bleeds and prevent or delay development of joint arthropathy.

Treatment on Demand
Episodic treatment for bleeding episodes is referred to as on-demand therapy (i.e. the use of factor replacement therapy after bleeding occurs).

GENERAL MEASURES
» Patient and family education.
» Enroll on the Haemophilia registry.
» Alert bracelet.
» Dental care (discuss management of tooth extraction with local haemophilia centre).
» Avoid contact sport.

Acute bleeds into joints
Patients with severe haemophilia should be trained to self-administer their clotting factor concentrate.

Adjunctive management
» Protection (splint but no circumferential casting).
» Rest the affected limb until pain free and no weight bearing.
» Ice packs may be applied immediately (apply ice, 5 minutes on and 10 minutes off).
» Elevation of the affected limb.

MEDICINE TREATMENT

For pain: Refer to chapter 12: Anaesthesiology, pain and intensive care.

Exercise great caution when taking blood specimens.
Taking blood from femoral veins is absolutely contra-indicated.
Do not use central lines for transfusions. Do not do joint aspirations
Avoid IM injections.
Avoid aspirin and NSAIDS.

HAEMOPHILIA WITH NO INHIBITORS

The dose of the factor VIII and IX is individualised as it is dependent on body mass, severity of the condition, and the nature and site of the bleeding.

Factor VIII deficiency (with no inhibitor present)

Minor bleeds:
Bleeds into the muscle or soft tissue, mouth or gums, epistaxis, painless haematuria and early joint bleeds.

Treatment:
- Factor VIII, intravenous, 25 IU/kg IV, immediately as a single dose.
  - If there is evidence of ongoing bleeding after 12 hours, consult with local haemophilia treatment centre.

Major bleeds:
Advanced muscle or joint bleeds, bleeds resulting from severe injury, or bleeds that affect the central nervous system; gastrointestinal system; neck or throat; hip or iliopsoas; or forearm compartment.

Treatment:
- Factor VIII, intravenous, 50 IU/kg, immediately as a single dose.
  - All of these patients need hospitalisation.
  - Discuss all patients promptly with local haemophilia treatment centre.

LoE:III[xiv]

Factor IX deficiency (with no inhibitor present)
Minor bleeds:
Bleeds into the muscle or soft tissue, mouth or gums, epistaxis, painless haematuria and early joint bleeds.

Treatment:

- Factor IX, intravenous, 40 IU/kg immediately as a single dose.
  - If there is evidence of ongoing bleeding after 12 hours, consult with local haemophilia treatment centre.

Major bleeds:

Major muscle or joint bleeds, bleeds resulting from severe injury, or bleeds that affect the central nervous system; gastrointestinal system; neck or throat; hip or iliopsoas; or forearm compartment.

Treatment:

- Factor IX, intravenous, 60 IU/kg immediately as a single dose.
  - All of these patients need hospitalisation.

Discuss all patients promptly with local haemophilia treatment centre to plan ongoing treatment and factor replacement.

LoE:III[xv]

Mucous membrane bleeds in haemophilia A and B:

- Tranexamic acid, oral, 1 g, 6 hourly.

Ideally elective surgery should be perfomed at a tertiary centre with a consultation with a haematologist.
In emergencies, treat as major bleed and consult the local Haemophilia Treatment Centre as soon as feasible.

If serious bleeding with known haemophilia, and no factor VIII available:

- Lyophilised plasma, IV, 15 mL/kg.

OR

FFP, IV, 15 mL/kg.

LoE:II[xvi]

HAEMOPHILIA WITH INHIBITORS

Refer for assessment and planning with a haematologist.

VON WILLEBRAND'S DISEASE

Mild bleeding

Such as epistaxis and menorrhagia.
Antifibrinolytics, e.g.:

- Tranexamic acid, oral, 1 g 6 hourly.

Recurrent menorrhagia can also be treated effectively with oral contraceptives. See section 5.2: Uterine bleeding, abnormal.

More severe mucous membrane bleeding

Consult a local haemophilia treatment centre.
During surgery or after major trauma, patients should receive:

- Von Willebrand factor VIII concentrate, IV, 30 units/kg/dose given every 12 hours.
  - Continue for 48–72 hours to ensure optimal haemostasis.
  - For major surgical procedures, use for 7–10 days.

LoE:III

REFERRAL

» All cases with **suspected** haemophilia (prolonged PTT and normal INR) to a haemophilia treatment centre, for assessment, genetic counselling and planning of management.
» Patients with proven antibodies (inhibitors) against factor VIII or IX.
» For further replacement, complex situations and complications in consultation with a haematologist.

2.5 IMMUNE THROMBOCYTOPENIA (ITP)

D69.3

DESCRIPTION

A common bleeding disorder due to immune-mediated destruction of platelets. Clinically apparent associated conditions, drugs (e.g. penicillins, cephalosporins, quinine, rifampicin and heparin), or other agents that may cause thrombocytopenia are NOT present. Patients with suspected ITP should be tested for SLE and for HIV infection.

Investigations

» Thrombocytopenia with normal white cell count and red cell indices (however, anaemia may be present due to blood loss).
» Peripheral blood smear to exclude RBC fragments. Smear may show large platelets.
» Do INR and aPTT, both of which should be normal in ITP.
» If there is a poor response to treatment do a bone marrow aspirate and biopsy.

GENERAL MEASURES

Avoid:
» medication that affects platelet function, e.g. NSAIDs and aspirin,
» platelet transfusions, unless there are life-threatening bleeds,
» dental procedures in acute phase, and
» IM injections.

Reassure the patient that resolution usually occurs in acute ITP.
Medic alert bracelet.
Platelet transfusions may be given if surgery is required or in life-threatening bleeding, discuss with haematologist.
Goal of treatment: reduce the risk of bleeding, not normalise the platelet count.
Avoid unnecessary treatment of asymptomatic patients with mild to moderate thrombocytopenia (platelet count >30 x 10^9/L).

MEDICINE TREATMENT

Acute ITP

- Prednisone, oral, 1 mg/kg daily, until platelet count has normalised.
  - Taper slowly and monitor platelet count. (Refer to Appendix II for an example of a dose reduction regimen).

- Although prednisone is also indicated for HIV-associated immune thrombocytopenia it is important that all these patients should be fast-tracked for ART.

LoE:III[xvii]

Second line therapy

Patients with persistent thrombocytopenia not responding to treatment with glucocorticoids.

Treatment with specialist supervision

There are other multiple treatments available but are dependent on specialist opinion.

REFERRAL

» All cases not responding to steroids and, in the case of HIV-infected patients, not responding to ART – discuss with haematologist.
» Refer for second line treatment.

Acute active life-threatening bleeding and surgery

- Platelet transfusions.

Platelet transfusions are only indicated in acute active bleeding uncontrolled by other means or before procedures. In an adult, 1 unit of platelets, preferably single donor, leucocyte depleted platelets, is usually sufficient to control the bleeding initially. Platelet transfusions have limited benefit in this condition as platelets are rapidly destroyed by the immune system.

- Methylprednisolone acetate 1 g, IV, daily for 3 days. *LoE:III*[xviii]

If the bleeding cannot be controlled, consult with a specialist.

2.6 THROMBOTIC THROMBOCYTOPENIC PURPURA-HAEMOLYTIC URAEMIC SYNDROME (TTP-HUS)

D59.3 + (M31.1)

DESCRIPTION

This is a medical emergency.

Acute syndromes with abnormalities in multiple organ systems with evidence of micro-angiopathic haemolytic anaemia and thrombocytopenia.

This condition presents with varying combinations of the following (only some of which may be present):

» Microangiopathic haemolytic anaemia thrombocytopenia, often with purpura but not usually severe bleeding,
» acute renal insufficiency,
» neurologic abnormalities, and
» fever.

Note: The presence of fragments and low platelets is enough to consider the diagnosis.

Microangiopathic haemolytic anaemia is defined as nonimmune haemolysis with prominent RBC fragmentation (schistocytes) observed on the peripheral blood smear along with thrombocytopaenia.

TTP-HUS is often associated with HIV infection and all patients should be tested for HIV.

TTP-HUS should be distinguished from disseminated intravascular coagulation (DIC) and severe pre-eclampsia where, in the latter, the coagulation profile (PT/PTT) is also deranged.

TREATMENT

- In HIV-associated thrombotic thrombocytopenia, start combination antiretroviral therapy urgently.
- Lyophilised plasma, IV infusion, 30 mL/kg/day in 3–4 divided doses.

OR

FFP, IV infusion, 30 mL/kg/day in 3–4 divided doses.

LoE:II[xix]

Use of platelet transfusions should be discussed with a specialist.

REFERRAL

All patients – discuss with a haematologist urgently.

2.7 ACQUIRED COAGULATION DEFECTS

2.7.1 DISSEMINATED INTRAVASCULAR COAGULATION (DIC)

D65/D68.2/D68.8

DIC is a complication of an underlying condition and is characterised by widespread activation of clotting cascade leading to consumption of clotting factors and platelets with generalized bleeding. No single diagnostic test, but the combination of a prolonged INR and PTT, thrombocytopenia, decreased fibrinogen and increased D-dimer is highly suggestive of the diagnosis.

MANAGEMENT

Identify and treat the underlying cause.
If the patient is bleeding, replace haemostatic factors with cryoprecipitate or FFP/lyophilised plasma.
If the patient is not actively bleeding and platelet count >20 x 10^9/L, then platelet transfusion is not necessary.

Replacement therapy for thrombocytopenia should consist of 1 apheresis single donor unit or 1 pooled random donor unit. In chronic DIC, or in the

absence of bleeding, platelet transfusions should not be given merely to correct the thrombocytopenia.

For hypofibrinogenaemia:

- Cryoprecipitate, IV, 1 unit/10 kg.

For depletion of other coagulation factors:

- Lyophilised plasma, IV, 15 mL/kg as initial dose.
  - Volume: ±200 mL/unit.

OR

FFP, IV, 15 mL/kg as initial dose.
- Volume: ±280 mL/unit.

LoE:II[xx]

Repeat replacement therapy 8 hourly or less frequently, with adjustment according to the clinical picture and laboratory parameters.

Monitor response with frequent estimation of the platelet count and coagulation screening tests.

2.8 VENOUS THROMBO-EMBOLISM

I80.0-3/I80.8-9/I81/I82.0-3/I8.8-9/I26.0/I26.9

DESCRIPTION

Venous thromboembolism (VTE) should be seen as a spectrum from calf deep venous thrombosis (DVT) to pulmonary thrombo-embolism. All patients should be seen as potentially high risk.

Differential diagnosis includes:

- cellulitis
- superficial thrombophlebitis
- lymphoedema
- chronic venous insufficiency
- ruptured popliteal (Baker's) cyst
- calf muscle pull or tear
- internal derangement of the knee

Diagnosis is primarily clinical and confirmed with imaging studies, e.g. Duplex Doppler.

GENERAL MEASURES

Strategies for prevention include: lifestyle modifications like avoiding obesity and inactivity, avoiding dehydration, avoiding cigarette smoking, maintaining normal blood pressure, and mechanical measures like vascular compression stockings and intermittent pneumatic compression boots.

LoE:III[xxi]

Acute management

Thrombolytic therapy may be indicated in patients with confirmed early pulmonary embolism where haemodynamic stability cannot be achieved. Discuss with a specialist.

MEDICINE TREATMENT

PROPHYLAXIS

Risk Assesement

Risk assessment is essential, and treatment needs to be individualised. Risk factors for VTE can be divided into predisposing factors (i.e. patient characteristics) and exposing factors (i.e. underlying medical conditions, nature of surgical intervention, etc.).

SUBCATEGORIES OF VTE RISK IN SURGICAL AND NON-SURGICAL PATIENTS

	Surgical patients	***Medical patients***
Low VTE risk	» Surgery lasting <30 minutes » Injuries without or with only minor soft-tissue trauma » No or only minor additional predisposing risk factors	» Infection or acute inflammatory diseases without bed rest » Central venous catheters » No or only minor additional predisposing risk factors
Moderate VTE risk	» Surgical procedures of longer duration » Immobilisation of lower limb with plaster cast » Lower limb arthroscopic procedures. » No or only minor additional predisposing risk factors	» Acute cardiac insufficiency (NYHA III/IV) » Acute decompensated COPD without ventilation » Infection or acute inflammatory diseases with bed rest » Malignant disease » No or only minor additional predisposing risk factors
High VTE risk	» Major surgical procedures for malignancy » Multiple trauma or severe trauma of the spine, vertebra or » lower limbs » Major orthopaedic surgery, e.g. hip or knee replacement » Major surgical procedure of cardiothoracic and pelvic region	» Stroke with paralysis » Acute decompensated COPD with ventilation » Sepsis » ICU patients

Source: Jacobson BF, Louw S, Büller H, Mer M, de Jong PR, Rowji P, Schapkaitz E, Adler D, Beeton A, Hsu HC, Wessels P, Haas S; South African Society of Thrombosis and Haemostasis. Venous thromboembolism: prophylactic and therapeutic practice guideline. S Afr Med J. 2013 Feb 15;103(4 Pt 2):261-7. https://www.ncbi.nlm.nih.gov/pubmed/23547704

Some risk assesement models for assessing VTE risk:

Model	Url link to tool
Padua Prediction Score[xxii]	https://www.mdcalc.com/padua-prediction-score-risk-vte
IMPROVE VTE risk score[xxiii]	https://www.outcomes-umassmed.org/IMPROVE/risk_score/vte/index.html
Geneva risk score[xxiv]	https://www.mdcalc.com/geneva-risk-score-venous-thromboembolism-vte-prophylaxis

Prophylactic treatment

Prophylaxis is indicated for medical patients with moderate to high risk of VTE (see table above), with restricted mobility during acute illness/ surgical patients.

- Low molecular weight heparin, e.g.: *LoE:I*[xxv]
- Enoxaparin, SC, 40 mg daily.

In morbid obesity dosing of LMWH should be individualised, in discussion with a specialist. *LoE:III[xxvi]*

In renal failure (eGFR <30 mL/minute), the recommended dose of LMWH is 1 mg/kg daily. *LoE:III[xxvii]*

OR

- Unfractionated heparin, SC, 5 000 units 12 hourly. *LoE:III[xxviii]*

Although the risk of bleeding is small, in the following patients prophylaxis should only be used under exceptional circumstances:

» active bleeding
» intraocular, intracranial or spinal surgery
» lumbar puncture or spinal/epidural anaesthesia within 12 hours after prophylactic dose or 24 hours of full therapeutic dose, [Timing of anticoagulants for patients receiving anaesthesia: See section 12.8: Spinal (intrathecal) anaesthesia]
» renal insufficiency
» coagulopathy
» uncontrolled hypertension

ACUTE TREATMENT

Unfractionated or low molecular weight heparin started simultaneously with warfarin. After 5 days, heparin may be stopped if a therapeutic INR level has been reached and maintained for at least 24 hours.

Note: Heparin and warfarin therapy should overlap for at least 5 days.

For proximal deep venous thrombosis and/or pulmonary embolism: *LoE:I[xxix]*

- Low molecular weight heparin, e.g.:
- Enoxaparin, SC, 1.5 mg/kg daily, *LoE:I[xxx]*
  or
  1 mg/kg 12 hourly.

In morbid obesity dosing of LMWH should be individualised, in discussion with a specialist. *LoE:III[xxxi]*

In renal failure (eGFR <30 mL/minute), the recommended dose of LMWH is 1 mg/kg daily. *LoE:III[xxxii]*

OR

- Unfractionated heparin, SC, 333 units/kg as an initial dose.
  - Follow 12 hours later by 250 units/kg/dose 12 hourly.

Units of unfractionated heparin			Volume of heparin in mL (25 000 units/mL)	
Weight (kg)	Loading dose (units)	12 hourly dose (units)	Loading dose (mL)	12 hourly dose (mL)
35 kg	11 000 units	8 750 units	0.44 mL	0.35 mL
40 kg	13 000 units	10 000 units	0.52 mL	0.4 mL
45 kg	15 000 units	11 250 units	0.6 mL	0.45 mL
50 kg	17 000 units	12 500 units	0.67 mL	0.5 mL
55 kg	18 000 units	13 750 units	0.73 mL	0.55 mL
60 kg	20 000 units	15 000 units	0.8 mL	0.6 mL
65 kg	22 000 units	16 250 units	0.87 mL	0.65 mL
70 kg	23 000 units	17 500 units	0.93 mL	0.7 mL
75 kg	25 000 units	18 750 units	1 mL	0.75 mL
80 kg	27 000 units	20 000 units	1.07 mL	0.8 mL
85 kg	28 000 units	21 250 units	1.13 mL	0.85 mL
90 kg	30 000 units	22 500 units	1.2 mL	0.9 mL

Evidence indicates that PTT monitoring is not necessary with weight-based dosing of unfractionated heparin. However, in patients with morbid obesity and renal failure (eGFR <30 mL/minute) unfractionated heparin should be used with PTT monitoring to maintain the PTT at 1.5 to 2.5 times the control.
PTT should be taken 4 hours after SC dose.

LoE:III

Follow with:

- Warfarin, oral, 5 mg daily.
  - INR should be done after 48 hours, then every 1 to 2 days until within the therapeutic range of 2 to 3 (refer to Initiation dosing tables in the Appendix II).
  - Adjust dose to keep INR within therapeutic range (refer to Maintenance dosing tables in the Appendix II).
  - Continue warfarin for 3 months with regular INR monitoring if there was a precipitating cause that has resolved.
  - In patients with a first unprovoked DVT, discuss duration of therapy with a specialist.
  - Contraindications for warfarin: first trimester and the last month of pregnancy. In these instances, replace with heparin.
  - For all major elective surgery and other elective procedures with a significant bleeding risk, such as neuraxial anaesthesia and lumbar punctures, the INR should be <1.5.

Heparin induced thrombocytopenia

A severe immune-mediated drug reaction occurring in 1–5% of patients receiving heparin (more common with unfractionated heparin, but may also occur with low molecular weight heparin) therapy. It presents with

thrombocytopenia and thrombosis. Diagnosis needs a high index of suspicion and should be considered if a patient has a 50% drop in platelet count within 5–10 days after initiating heparin therapy. Confirmation is done by positive antibody testing.
Stop heparin and discuss all patients with a specialist.

REFERRAL/CONSULTATION

Heparin-induced thrombocytopenia.

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CHAPTER 3
CARDIOVASCULAR SYSTEM

3.1 ISCHAEMIC HEART DISEASE AND ATHEROSCLEROSIS, PREVENTION

I20-I25

Major risk factors for ischaemic cardio- and cerebrovascular disease:

» Diabetes mellitus.
» Hypertension.
» Central obesity (waist circumference): men ≥102 cm, women ≥88 cm.
» Smoking.
» Dyslipidaemia:
  - Total cholesterol >5.0 mmol/L, or
  - LDL >3 mmol/L, or
  - HDL <1 mmol/L in men and <1.2 mmol/L in women.
» Family history of premature cardiovascular disease in first degree male relatives <55 years and in first degree female relatives <65 years.
» Age: men >55 years, women >65 years.
» Psychological stress.

LoE:II[i]

GENERAL MEASURES

Lifestyle modification, especially smoking cessation, is essential and often has greater beneficial impact on prognosis than vascular interventions and medications.

All persons should be encouraged to make the following lifestyle changes as appropriate:

» Smoking cessation.
» Weight reduction in overweight patients, i.e. BMI >25 kg/m^2.
» Maintain ideal weight, i.e. BMI <25 kg/m^2.
» Reduce alcohol intake to no more than 2 standard drinks/day
» Follow a prudent eating plan i.e. low saturated fat, high fibre and unrefined carbohydrates, with adequate fresh fruit and vegetables.
» Moderate aerobic exercise, e.g. 40 minutes brisk walking at least 3 times a week.

Calculation of risk of developing cardiovascular disease over 10 years (in the absence of cardiovascular disease)

To derive the absolute risk as the percentage of patients who will have a myocardial infarction over 10 years, add the points for each risk category (Section A). The risk associated with the total points is then derived from Section B.

SECTION A

Age (years)	**MEN**	**WOMEN**
30–34	0	0
35–39	2	2
40–44	5	4
45–49	6	5
50–54	8	7
55–59	10	8
60–64	11	9
65–69	12	10
70–74	14	11
75–79	15	12

Total cholesterol (mmol/L)	**MEN**	**WOMEN**
<4.1	0	0
4.1–5.1	1	1
5–6.2	2	3
6.2–7.2	3	4
>7.2	4	5

HDL cholesterol (mmol/L)	**MEN**	**WOMEN**
>1.6	–2	–2
1.3–1.5	1	–1
1.2–1.3	0	0
0.9–1.1	1	1
<0.9	2	2

	MEN	**WOMEN**
Smoker	4	3
Diabetic*	3	4

*Type 2 diabetics >40 years, qualify for statin therapy irrespective of risk score.

	MEN		**WOMEN**	
Systolic BP (mmHg)	Untreated	Treated	Untreated	Treated
<120	–2	0	–3	–1
120–129	0	2	0	2
130–139	1	3	1	3
140–149	2	4	2	5
150–159	2	4	4	6
≥160	3	5	5	7

SECTION B

Total points

10-year risk %	MEN	10-year risk %	WOMEN
<1	≤–3	<1	≤–2
1.1	–2	1.0	–1
1.4	–1	1.2	0
1.6	0	1.5	1
1.9	1	1.7	2
2.3	2	2.0	3
2.8	3	2.4	4
3.3	4	2.8	5
3.9	5	3.3	6
4.7	6	3.9	7
5.6	7	4.5	8
6.7	8	5.3	9
7.9	9	6.3	10
9.4	10	7.3	11
11.2	11	8.6	12
13.2	12	10.0	13
15.6	13	11.7	14
18.4	14	13.7	15
21.6	15	15.9	16
25.3	16	18.5	17
29.4	17	21.5	18
>30	≥18	24.8	19
		28.5	20
		>30	21+

MEDICINE TREATMENT

Indications for lipid lowering medicine therapy

Patients with any of the following factors are at a relatively high risk for a cardiovascular event and should receive lipid lowering therapy:

» Established atherosclerotic disease:
  – ischaemic heart disease
  – peripheral vascular disease
  – atherothrombotic stroke
» Type 2 diabetes with age >40 years.
» Diabetes for >10 years.
» Diabetes with chronic kidney disease (eGFR <60 mL/minute).

LoE:I[ii]

Patients with any of the following factors are also potentially at risk for cardiovascular disease (other than the categories above):

» diabetes mellitus
» hypertension
» central obesity: waist circumference ≥94 cm (men) and ≥80 cm (women)
» smoking
» age: men >55 years of age, women >65 years of age

These patients should be managed according to their 10–year risk of a cardiovascular event as calculated using either:

A. BMI–based risk assessment – see PHC STGs and EML, section 4.1: Prevention of ischaemic heart disease and atherosclerosis, or
B. Framingham risk score (cholesterol-based assessment) – see tables above.

Management is based on the patient's 10-year risk of a cardiovascular event:

- <10% risk: lifestyle modification and risk assess patient every 5 years
- 10–20% risk: lifestyle modification and risk assess patient annually
- ≥20% risk: lifestyle modification and start statin treatment

Note:

» Lipid lowering medicines should be given to those with a high risk of CVD even if cholesterol is within the desirable range.

▪ HMGCoA reductase inhibitors (statins), according to table below:

INDICATION	HMGCOA REDUCTASE INHIBITOR (STATIN) DOSE
A: Primary prevention - no existing CVD	
» Type 2 diabetes with age >40 years. » Diabetes for >10 years. » Diabetes with chronic kidney disease. » ≥ 20% 10-year risk of cardiovascular event.	▪ HMGCoA reductase inhibitors (statins), e.g.: • Simvastatin, oral, 10 mg at night.
» Patients on protease inhibitors. (Risks as above, after switching to atazanavir – see section below).	• Atorvastatin, oral, 10 mg at night.
B: Secondary prevention – existing CVD	
» Ischaemic heart disease. » Atherothrombotic stroke. » Peripheral vascular disease.	▪ HMGCoA reductase inhibitors (statins), e.g.: • Simvastatin, oral, 40 mg at night *LoE:I[iii]*
» Patients on protease inhibitors.	• Atorvastatin, oral, 10 mg at night. *LoE:I[iv]*
» Patients on amlodipine (and not on protease inhibitor).	• Simvastatin, oral, 10–20 mg at night. *LoE:III[v]*
» If patient complains of muscle pain.	Reduce dose: ▪ HMGCoA reductase inhibitors (statins), e.g.: • Simvastatin, oral, 10 mg at night. **OR** Consult specialist for further management. *LoE:III[vi]*

Note: Lipid-lowering medicines must always be used in conjunction with ongoing lifestyle modification.

Protease inhibitor-induced dyslipidaemia:

» Certain antiretroviral medication, particularly protease inhibitors, can cause dyslipidaemia. Fasting lipid levels should be done 3 months after starting lopinavir/ritonavir. Lopinavir/ritonavir is associated with a higher risk of dyslipidaemia (specifically hypertriglyceraemia) than atazanavir/ ritonavir.
» Patients at high risk (>20% risk of developing a CVD event in 10 years) should switch to atazanavir/ritonavir and repeat the fasting lipid profile in 3 months.
» Patients with persistent dyslipidaemia despite switching, qualify for lipid lowering therapy. Criteria for initiating lipid lowering therapy are the same as for HIV-uninfected patients. Many statins (including simvastatin) cannot be used with protease inhibitors, as protease inhibitors inhibit the metabolism of the statin resulting in extremely high blood levels.
» Patients who fail to respond to lifestyle modification and have dyslipidaemia treat with:

- Atorvastatin, oral, 10 mg at night.

REFERRAL

» Random cholesterol >7.5 mmol/L.
» Fasting (14 hours) triglycerides >10 mmol/L.

3.2 ACUTE CORONARY SYNDROMES

These conditions should be managed in a high care setting with continuous ECG and frequent BP monitoring.

Reference guide for ECG analysis: “ECG APPtitude” smartphone app can be downloaded from the relevant app stores - available for iOS and Android.

3.2.1 ST ELEVATION MYOCARDIAL INFARCTION (STEMI)

I21.0-I21.4/I21.9/I22.0-1/I22.8-9

DESCRIPTION

Ischaemic chest pain that is prolonged, or associated with nausea, sweating and syncope or associated with persistent ST elevation or new or presumed new left bundle branch block (LBBB). Repeat ECG at 20-30 minute intervals if the initial ECG is not diagnostic.

MEDICINE TREATMENT

LoE:I[vii]

- Oxygen if saturation <94%.

LoE:I[viii]

- Clopidogrel, oral, 75 mg daily for one month.

AND

- Aspirin, oral, 150 mg immediately as a single dose (chewed or dissolved).

- Followed with 150 mg daily (continued indefinitely in absence of contraindications).

LoE:I[ix]

AND

Thrombolytic therapy

- Streptokinase, IV 1.5 million units diluted in 100 mL sodium chloride 0.9%, infused over 30–60 minutes. **Do not use heparin if streptokinase is given**.
  - Hypotension may occur. If it does, reduce the rate of infusion but strive to complete it in <60 minutes.
  - Streptokinase is antigenic and should not be re-administered in the period of 5 days to 2 years after 1st administration.
  - Severe allergic reactions are uncommon but antibodies which may render it ineffective may persist for years.

Indications	Contra-indications
» For acute myocardial infarction with ST elevation or left bundle branch block: - maximal chest pain is ≤6 hours - beyond 6 hours and chest pain, consult a specialist - >6 hours and no chest pain, manage with anticoagulants (see section 3.2.2: NSTEMI) - if on-going ischaemic pain LoE:I[x]	» Absolute: - streptokinase used within the last year, - previous allergy, - CVA within the last 3 months, - history of recent major trauma, - bleeding within the last month, - aneurysms, - brain or spinal surgery or head injury within the preceding month, or recent (<3 weeks) major surgery, - active bleeding or known bleeding disorder, - aortic dissection. » Relative (consult specialist): - refractory hypertension, - warfarin therapy, - recent retinal laser treatment, - subclavian central venous catheter, - pregnancy, - TIA in the preceding 6 months, - traumatic resuscitation.

OR

If streptokinase is unavailable:

- Alteplase, IV infusion:
  - Do not exceed 100 mg. LoE:I[xi]
  - if history of onset is less than 6 hours (beyond 6 hours consult a specialist or treat as NSTEMI (see below):

	Bolus	Next 30 minutes	Next 60 minutes
>67 kg	15 mg	50 mg	35 mg
≤67 kg	15 mg	0.75 mg/kg	0.5 mg/kg

  - Indications and contraindications are similar to those for streptokinase as above (except that prior use of streptokinase is not a contraindication).

Monitor the following, continuously and also during transfer:
» pulse
» BP
» respiration depth and rate (count for a full minute)
» ECG

Note: Defibrillator should be readily available at all times including during transport.

Adjunctive treatment

- Enoxaparin (after alteplase, do not use heparins after streptokinase).
  - *Loading dose:* **IV**, 30 mg as a bolus, followed by **SC**, 1 mg/kg as a single dose (total cumulative dose not to exceed 100 mg).
  - *Maintenance dose*: SC, 1.5 mg/kg daily **or** 1 mg/kg 12 hourly.

LoE:I[xii]

In the elderly (>75 years of age), omit **IV** loading dose and reduce SC dose:

  - *Loading dose*: **SC**, 0.75 mg/kg as a single dose.
  - *Maintenance dose*: SC, 1.5 mg/kg daily **or** 1 mg/kg 12 hourly.

LoE:I[xiii]

Pain not responsive to thrombolytics may suggest ongoing unresolved ischaemia.

- Nitrates, e.g.:
- Isosorbide dinitrate, SL, 5 mg immediately as a single dose.
  - May be repeated at 5-minute intervals for 3 or 4 doses.

LoE:III[xiv]

For ongoing chest pain, to control hypertension or treat pulmonary oedema:

- Glyceryl trinitrate, IV, 5–200 mcg/minute, titrated to response.
  - Start with 5 mcg/minute and increase by 5 mcg/minute every 5 minutes until response or until the rate is 20 mcg/minute.
  - No response after 20 mcg/minute, increase by 20 mcg/minute every 5 minutes until a pain response or medicine is no longer tolerated.
  - Flush the PVC tube before administering the medicine to patient.
  - Monitor BP carefully.

Dilution of Glyceryl trinitrate:

Volume of diluent	**Glyceryl trinitrate 5mg/mL**	**Concentration of dilution**
250 mL	5 mL (25 mg)	100 mcg/mL
	10 mL (50 mg)	200 mcg/mL
	20 mL (100 mg)	400 mcg/mL
500 mL	10 mL (50 mg)	100 mcg/mL
	20 mL (100 mg)	200 mcg/mL
	40 mL (200 mg)	400 mcg/mL

Solution Concentration (mcg/mL)	**100 mcg/mL solution**	**200 mcg/mL solution**	**400 mcg/mL solution**

Dose (mcg/min)	Flow rate (microdrops/min = mL/hour)		
5	3	—	—
10	6	3	—
15	9	—	—
20	12	6	3
30	18	9	—
40	24	12	6
60	36	18	9
80	48	24	12
100	60	30	15
120	72	36	18
160	96	48	24
200	–	60	30

For severe pain unresponsive to nitrates:

- Morphine, IV, to a total maximum dose of 10 mg (See Appendix II, for individual dosing and monitoring for response and toxicity).
  - Ongoing severe pain despite all appropriate treatment above is an indication for urgent referral.

When clinically stable without signs of heart failure, hypotension, bradydysrhythmias or history of asthma:

- Cardio-selective β-blocker, e.g.:
- Atenolol, oral, 50 mg daily.

- HMGCoA reductase inhibitors (statins), e.g.:
- Simvastatin, oral, 40 mg at night.

LoE:I[xv]

Patients on protease inhibitor:

- Atorvastatin, oral, 10 mg at night.

LoE:I[xvi]

Patients on amlodipine (and not on a protease inhibitor):

- Simvastatin, oral, 10 mg at night.

LoE:III[xvii]

If patient complains of muscle pain:

Reduce dose:

- HMGCoA reductase inhibitors (statins), e.g.:
- Simvastatin, oral, 10–20 mg at night.

OR

Consult specialist for further management. *LoE:III*[xviii]

For LV dysfunction following myocardial infarction, heart failure or ejection fraction <40%:

- ACE-inhibitor, e.g.:
- Enalapril, oral, target dose, 10 mg 12 hourly.
  - Institute other therapy for heart failure and LV dysfunction as described below – see section 3.4: Congestive cardiac failure.

If ACE-inhibitor intolerant, i.e. intractable cough:

- Angiotensin receptor blocker (ARB), e.g.:
- Losartan, oral, 50–100 mg daily. Specialist initiated.

» Angioedema is a potentially serious complication of ACE-inhibitor/ angiotensin receptor blocker treatment and if it occurs stop the medication and do not re-challenge.
» Concomitant use of fluoroquinolones with ACE-inhibitor/angiotensin receptor blocker is contraindicated in moderate to severe renal impairment (CrCl ≤30 mL/minute) and in the elderly. Assess renal function before initiating treatment and monitor during treatment.

LoE:III[xix]

REFERRAL

» Refractory cardiogenic shock.
» Refractory pulmonary oedema.
» Haemodynamically compromising ventricular dysrhythmia.
» Patients with the combination of new right bundle and posterior fascicular block post MI should be referred for permanent pacemaker consideration as they are at high risk for progression to complete heart block.
» Myocardial infarction-related mitral regurgitation or ventricular septal defect (VSD).
» Contraindication to thrombolytic therapy provided PCI facility available (confirm with cardiologist).
» Ongoing ischaemic chest pain.
» Failed reperfusion (<50% reduction in ST elevation at 90 minutes in leads showing greatest ST elevation, especially in anterior infarct or inferior infarct with right ventricular involvement).

3.2.2 NON-ST ELEVATION MYOCARDIAL INFARCTION (NSTEMI) AND UNSTABLE ANGINA (UA)

I21.4/I21.9/I20.0

DESCRIPTION

Non-ST elevation MI: Chest pain that is increasing in frequency and/or severity, or occurring at rest. The chest pain is associated with elevated cardiac biomarkers and ST segment depression or T wave inversion on ECG. Biomarker elevation in the absence of diagnostic ECG changes or symptoms compatible with myocardial ischemia should prompt consideration of alternative diagnoses (e.g. heart failure, pulmonary embolism, chronic kidney disease, sepsis, myopericarditis).

Unstable angina pectoris: Chest pain that is increasing in frequency and or severity, or occurring at rest. It also encompasses post-infarct angina. The chest pain may be associated with ST segment depression or T wave inversion on ECG. There is no rise in cardiac biomarkers.

MEDICINE TREATMENT

- Oxygen, if saturation <94%. LoE:I[xx]
- Clopidogrel, oral, 300 mg. LoE:I[xxi]
  Followed by 75 mg daily for 3 months.

AND

- Aspirin, oral, 150 mg immediately as a single dose (chewed or dissolved).
  - Followed with 150 mg daily (continued indefinitely in absence of contraindications). LoE:I[xxii]

AND

Anticoagulation:

For NSTEMI and UA (also for STEMI not given thrombolytic therapy):

- Enoxaparin, SC, 1 mg/kg 12 hourly for minimum of 2 days.

OR

- Unfractionated heparin, IV bolus, 5 000 units.
  - Follow with 1 000–1 200 units hourly monitored by aPTT.
  - Continue infusion for minimum of 2 days.

LoE:I[xxiii]

To relieve possible coronary spasm and pain and to reduce preload:

- Nitrates, e.g.:
- Isosorbide dinitrate SL, 5 mg immediately as a single dose.
  - May be repeated at 5-minute intervals for 3 or 4 doses.

For persistent pain and if oral therapy is insufficient:

- Glyceryl trinitrate, IV, 5–200 mcg/minute, titrated to response.
  - Start with 5 mcg/minute and increase by 5 mcg/minute every 5 minutes until response or until the rate is 20 mcg/minute.
  - If no response after 20 mcg/minute, increase by 20 mcg/minute every 5 minutes until pain response or medicine no longer tolerated.
  - Flush the PVC tube before administering the medicine to patient.
  - Monitor BP carefully.

For dilution of glyceryl trinitrate refer to section 3.2.1: ST elevation myocardial infarction (STEMI).

For severe pain unresponsive to nitrates:

- Morphine, IV, to a total maximum dose of 10 mg (See Appendix II, for individual dosing and monitoring for response and toxicity).
  - Ongoing severe pain despite all appropriate treatment above is an indication for urgent referral

When clinically stable without signs of heart failure, hypotension, bradydysrhythmias or asthma:

- Cardio-selective β-blocker, e.g.:
- Atenolol, oral, 50 mg daily.

- HMGCoA reductase inhibitors (statins), e.g.:
- Simvastatin, oral, 40 mg at night.

Patients on protease inhibitor: LoE:I[xxiv]

- Atorvastatin, oral, 10 mg at night.

Patients on amlodipine (and not on a protease inhibitor): LoE:I[xxv]

- Simvastatin, oral, 10–20 mg at night.

If patient complains of muscle pain: LoE:III[xxvi]

Reduce dose:

- HMGCoA reductase inhibitors (statins), e.g.:
- Simvastatin, oral, 10 mg at night.

OR

Consult specialist for further management. LoE:III[xxvii]

If there is cardiac failure or LV dysfunction (see section 3.4: Congestive cardiac failure):

(I50.0)

- ACE-inhibitor, e.g.:
- Enalapril, oral, target dose 10 mg 12 hourly. LoE:III[xxviii]

If ACE-inhibitor intolerant, i.e. intractable cough:

- Angiotensin receptor blocker (ARB), e.g.:
- Losartan, oral, 50–100 mg daily. Specialist initiated.

3.2.3 CHRONIC MANAGEMENT OF STEMI / NSTEMI / UA

I25.2/I20.0

GENERAL MEASURES

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

MEDICINE TREATMENT

Continue oral therapy as above.

If heart failure develops, replace atenolol with carvedilol. See section 3.4: Congestive cardiac failure.

REFERRAL

» Patients with a diagnosis of acute coronary syndrome should be risk stratified at presentation to estimate their likelihood of developing a major adverse cardiac event (acute MI, heart failure, death or readmission for UA) over the subsequent 4-6 weeks. High risk patients (including those with positive troponins) should be discussed with a cardiology service for consideration for angiography and revascularization therapy. , Two widely used and well validated risk stratification scores are TIMI (http://www.mdcalc.com/timi-risk-score-for-uanstemi/) and Grace Risk

Scores (http://www.mdcalc.com/grace-acs-risk-and-mortality-calculator). The patient's co-morbidities and willingness to undergo revascularisation, which may involve coronary surgery, should be taken into account when advising such referral.

» Other important indications for referral include ongoing chest pain, post-infarct angina, sustained dysrhythmias or refractory heart failure.

3.2.4 ANGINA PECTORIS, STABLE

I20.0-I/I20.8-9

DESCRIPTION

Characteristic chest pain due to myocardial ischaemia usually occurring on exercise and relieved by rest. Discomfort may occasionally be experienced in a site of referral (shoulder, jaw) but the characteristic provocation by exercise and relief by rest is a valuable clue.

GENERAL MEASURES

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

MEDICINE TREATMENT

Long-term prophylaxis for thrombosis:

- Aspirin, oral, 150 mg immediately as a single dose (chewed or dissolved).
  - Followed with 150 mg daily (continued indefinitely in absence of contraindications).

LoE:I[xxix]

AND

Relief of angina:

- Nitrates, short acting e.g.:
- Isosorbide dinitrate, SL, 5 mg.
  - May be repeated if required at 5-minute intervals for 3 or 4 doses.
  - Instruct patients to keep the tablets in the airtight and lightproof container in which they are supplied.
  - Instruct patients that nitrates are not addictive.
  - Instruct patients to use prophylactically, before activities which may provoke angina.

AND

Step 1

- Cardio-selective β-blocker, e.g.:
- Atenolol, oral, 50–100 mg daily.
  - Titrate to resting heart rate of approximately 60 bpm.

If ß-blocker cannot be tolerated or is contraindicated, use a long acting calcium channel blocker.

Step 2

ADD

- Long-acting calcium channel blocker, e.g.:

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

Step 3
ADD
- Organic nitrates, e.g.:
- Isosorbide mononitrate: 10–20 mg twice daily.

OR

Isosorbide dinitrate: 20–30 mg twice daily
- Taken at 8:00 and 14:00 as this provides a nitrate-free period to prevent tolerance.
- Modify for night shift workers.

LoE:III[xxx]

ADD
- HMGCoA reductase inhibitors (statins), e.g.:
- Simvastatin, oral, 40 mg at night.

LoE:I[xxxi]

Patients on protease inhibitor:
- Atorvastatin, oral, 10 mg at night.

LoE:I[xxxii]

Patients on amlodipine (and not on a protease inhibitor):
- Simvastatin, oral, 10–20 mg at night.

LoE:III[xxxiii]

If patient complains of muscle pain:
Reduce dose:
- HMGCoA reductase inhibitors (statins), e.g.:
- Simvastatin, oral, 10 mg at night.

OR

Consult specialist for further management.

LoE:III[xxxiv]

REFERRAL
» When diagnosis is in doubt, despite exercise stress testing.
» Failed medical therapy. A common reason for “failed” therapy is that the patient has an alternative diagnosis. Therefore, this conclusion should be reached after reasonable effort for non-invasive diagnosis including exercise stress test.

3.2.5 ATHEROSCLEROTIC PERIPHERAL ARTERIAL DISEASE

I70.90-1

DESCRIPTION
History and palpation of pulses confirms diagnosis.

GENERAL MEASURES
Smoking cessation is essential and is the single most important intervention to prevent progression.

Exercise within exercise tolerance and other lifestyle modifications.
See section 3.1: Ischaemic heart disease and atherosclerosis, prevention.

MEDICINE TREATMENT

Long-term prophylaxis for thrombosis:

- Aspirin, oral, 150 mg daily.

- HMGCoA reductase inhibitors (statins), e.g.:
- Simvastatin, oral, 40 mg at night.

LoE:I[xxxv]

Patients on protease inhibitor:

- Atorvastatin, oral, 10 mg at night.

LoE:I[xxxvi]

Patients on amlodipine (and not on a protease inhibitor):

- Simvastatin, oral, 10–20 mg at night.

LoE:III[xxxvii]

If patient complains of muscle pain:
Reduce dose:

- HMGCoA reductase inhibitors (statins), e.g.:
- Simvastatin, oral, 10 mg at night.

OR

Consult specialist for further management. *LoE:III[xxxviii]*

Therapy should be initiated together with appropriate lifestyle modification.
See section 3.1: Ischaemic heart disease and atherosclerosis, prevention.

REFERRAL

Ongoing vascular insufficiency, which may be surgically reversible.

3.3 CARDIAC DYSRHYTHMIAS

Exclude underlying structural cardiac disease in all patients with cardiac dysrhythmias.

3.3.1 NARROW QRS COMPLEX (SUPRAVENTRICULAR) TACHYDYSRHYTHMIAS

I47.0-2/I47.9

DESCRIPTION

Sustained (>30 seconds) or non-sustained narrow QRS (≤0.1 seconds) tachycardias.

REFERRAL

» Poor rate control.
» Frequent or severe symptoms for curative radiofrequency catheter ablation.
» All symptomatic Wolf-Parkinson-White (WPW) syndrome patients (sinus rhythm ECG shows delta waves) for radiofrequency catheter ablation.

» Asymptomatic patients in whom the WPW pattern is detected on ECG do not need referral.

3.3.1.1 ATRIAL FIBRILLATION

I48.0-I48.4/I48.9

Acute onset (<48 hours)

Assess clinically, e.g. heart failure, mitral stenosis, thyrotoxicosis, hypertension, age and other medical conditions.

Consider anticoagulation with warfarin (see table below on CHA_2DS_2-VASc Score).

Synchronised direct current (DC) cardioversion is occasionally necessary in haemodynamic instability.

Non-acute/chronic (>48 hours)

As above, but not immediate DC cardioversion, unless there is haemodynamic instability.

MEDICINE TREATMENT

The main aims of therapy for patients with atrial fibrillation should be:

1. Reduction of stroke and systemic embolic risk.
2. Rate control.
3. Relief of symptoms attributed to the atrial fibrillation.

Patients <65 years of age with no heart diseases or other risk factors may be managed with aspirin alone.

A simple scoring system allows calculation of risk of stroke in patients with non-valvar atrial fibrillation.

CHA_2DS_2-VASc Score:

Risk Factor	Score
Congestive heart failure/LV dysfunction	1
Hypertension	1
Age ≥ 75 years of age	2
Diabetes mellitus	1
Stroke/TIA/Thromboembolism	2
Vascular disease	1
Age 65–74 years of age	1
Sex (female gender)	1

Source: Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation.Chest. 2010 Feb;137(2):263-72. http://www.ncbi.nlm.nih.gov/pubmed/19762550

» When the score is ≥2, use warfarin or equivalent. The higher the score the greater the risk of stroke and therefore the more compelling the use of effective anticoagulation.

» **Note:** This score has been developed on patients with non-valvular atrial fibrillation and may not be applicable to patients with atrial fibrillation and rheumatic mitral valve disease. Anticoagulation has not been tested in this population but most authorities favour anticoagulation.

Initial therapy aimed at stroke reduction

Anticoagulate with warfarin:

- Warfarin, oral, 5 mg daily.
  - INR should be done after 48 hours, then every 1 to 2 days until within the therapeutic range of 2 to 3 (refer to initiation dosing tables in Appendix II).
  - Adjust dose to keep INR within therapeutic range (refer to Maintenance dosing tables in Appendix II).

For therapy aimed at rate control

- Atenolol, oral, 50–100 mg daily.
  - Contraindicated in asthmatics, heart failure.

OR

If in CCF: (I50.0)

- Carvedilol, oral. See section 3.4: Congestive cardiac failure.

AND

If control not adequate add:

- Digoxin, oral, 0.125 mg daily, adjust according to rate response and trough plasma level
  - Digoxin trough plasma levels (before the morning dose) should be maintained between 0.6-1 nmol/L.
  - Patients at high risk of digoxin toxicity: the elderly, patients with renal dysfunction, hypokalaemia, and patients with lean body mass.

LoE:II[xxxix]

If β-blockers are contra-indicated, e.g. asthma or severe peripheral vascular disease:

- Verapamil, oral, 40–120 mg 8 hourly.
  - Titrate against ventricular rate (verapamil is negatively inotropic, therefore avoid in heart failure due to LV dysfunction).

LoE:III[xl]

If not controlled on these agents, refer to specialist for consideration of alternative therapy, e.g. amiodarone or atrioventricular node ablation and pacemaker insertion.

DC cardioversion in selected cases, after 4 weeks effective warfarin anticoagulation.

Long-term therapy

Continue warfarin anticoagulation long-term, unless contra-indicated:

- Warfarin, oral, 5 mg daily.
  - Control with INR to therapeutic range:
    - INR between 2–3 and patient stable: monitor every 3 months.
    - INR <1.5 or >3.5: monitor monthly.

Caution
Warfarin use requires regular INR monitoring and dose adjustment according to measured INR.

For rate control:
- Atenolol, oral, 50–100 mg daily.
  - Contraindicated in asthmatics, heart failure.

If in CCF: (I50.0)
- Carvedilol, oral. See section 3.4: Congestive cardiac failure.

AND

If control not adequate add:
- Digoxin, oral, start at 0.125 mg daily and adjust according to rate response and trough plasma level.
  - In patients with impaired renal function (eGFR <60 mL/minute), consider 0.125 mg daily and adjust according to trough level monitoring.
  - In all patients, digoxin trough level monitoring is required at all doses.

LoE:II[xli]

If β-blockers are contra-indicated, e.g. asthma or severe peripheral vascular disease:
- Verapamil, oral, 40–120 mg 8 hourly.
  - Titrate against ventricular rate (verapamil is negatively inotropic, avoid in heart failure due to left ventricular dysfunction). *LoE:III*[xlii]

If not controlled on these agents, refer to specialist for consideration of alternative therapy.

Prevention of recurrent paroxysmal atrial fibrillation:
Note: The risk of thromboembolic complications and stroke is similar to that of patients with persistent or paroxysmal atrial fibrillation and similar recommendations as to anticoagulation apply.

Only in patients with severe symptoms despite the above measures:
- Amiodarone, oral, 200 mg 8 hourly for 1 week. Specialist initiated.
  - Followed by 200 mg 12 hourly for one week.
  - Thereafter, 200 mg daily.

Precautions: *LoE:I*[xliii]
  - If on warfarin, halve the dose of warfarin and monitor INR closely, until INR is stable.
  - Avoid concomitant digoxin.
  - Monitor thyroid function every 6 months as thyroid abnormalities may develop.

- Ophthalmological examination every 6 months.

For management of pregnant women with valvular disease and atrial fibrillation, see section 6.3: Heart disease in pregnancy.

3.3.1.2 ATRIAL FLUTTER

I48.0-4/I48.9

Atrial rate >250 bpm with no flat baseline.
Can be difficult to recognise if 2:1 atrioventricular (AV) block, as the first of the two p waves preceding each QRS complex might be confused with the T-wave of the preceding beat. Vagal stimulation might slow the ventricular rate (usually approximately 150 bpm) and make the dysrhythmia more obvious.
Synchronised direct current (DC) cardioversion is occasionally necessary in haemodynamic instability.

MEDICINE TREATMENT

- Midazolam IV, 1–2.5 mg, administered over 2-3 minutes.
  - Monitor and repeat dose after 2-3 minutes, as necessary.

LoE:III

If flutter has been present longer than 48 hours, defer cardioversion until after 4 weeks' anticoagulation with warfarin, unless severe symptoms or heart failure require urgent cardioversion.

DC cardioversion is the most effective therapy.
Do not use verapamil as it will not convert flutter to sinus rhythm and may cause serious hypotension.

Anticoagulants if sustained. (See section 3.3.1.1 Atrial fibrillation). Most consider that the thromboembolic risks in atrial flutter and atrial fibrillation are similar). *LoE:III*

Long-term therapy
Recurrent atrial flutter is an indication for referral as many may be relatively simply cured by radio-frequency catheter ablation.

3.3.1.3 AV JUNCTIONAL RE-ENTRY TACHYCARDIAS

I47.1

Usually paroxysmal.
Often young patients with normal hearts.
AV nodal re-entry or atrioventricular re-entry (WPW syndrome).
P waves usually not visible (hidden by QRS complexes).

GENERAL MEASURES

Vagal manoeuvres: The modified Valsalva manoeuvre is the most effective – it should be done semi-recumbent with 15 seconds of strain, followed immediately

by supine positioning and passive leg raising.
Carotid sinus massage.
Should be done with the patient supine and as relaxed as possible.

MEDICINE TREATMENT

Initial therapy

If vagal manoeuvres fail:

- Adenosine, rapid IV bolus, 6 mg.
  - Follow by a bolus of 10 mL sodium chloride 0.9% to ensure that it reaches the heart before it is broken down.
  - Half life: ± 10 seconds.
  - Run the ECG for 1 minute after the injection as a recording of method of cessation may be helpful diagnostically.
  - If 6 mg fails, repeat with 12 mg.
  - If this fails, repeat with another 12 mg.

» If the medicine reaches the central circulation before it is broken down the patient will experience flushing, sometimes chest pain, wheezing and anxiety.
» If the tachycardia fails to terminate without the patient experiencing those symptoms, the medicine did not reach the heart.

If none of the above is effective or if the patient is hypotensive, consider synchronised cardioversion.

Note: Adenosine is contraindicated when atrial flutter is the obvious diagnosis, administration of adenosine can precipitate 1:1 conduction at ventricular rates 250–360 bpm and should be avoided.

LoE:III

Long term therapy

Teach the patient to perform vagal manoeuvres. Valsalva is the most effective.

For infrequent, non-incapacitating symptoms:

- Cardio-selective ß–blocker, e.g.:
- Atenolol, oral, 50–100 mg daily.

If asthmatic, without heart failure: *LoE:III*[xliv]

- Verapamil, oral, 40–120 mg 8 hourly.

Verapamil and digoxin are contraindicated in WPW syndrome.

REFERRAL

If the patient continues to experience debilitating symptoms refer for radiofrequency ablation.

3.3.2 WIDE QRS (VENTRICULAR) TACHYARRHYTHMIAS

DESCRIPTION

Sustained (>30 seconds) or non-sustained wide QRS (>0.12 seconds)

tachycardias.

3.3.2.1 REGULAR WIDE QRS TACHYCARDIAS

I47.0-2/I47.9

Regular wide QRS tachycardias are **ventricular** until proved otherwise.
Regular wide QRS supraventricular tachycardias are uncommon.
Refer all cases after resuscitation and stabilisation.
Emergency DC cardioversion is mandatory with a full protocol of Cardio-pulmonary resuscitation (CPR) if there is haemodynamic compromise.

GENERAL MEASURES

CPR if necessary.

If no cardiac arrest:
DC cardioversion, 200 J, after sedation with:

- Midazolam, IV, 1–2.5 mg, administered over 2-3 minutes.
  - Monitor and repeat dose after 2-3 minutes, as necessary.
  - If 200 J fails, use 360 J. *LoE:III*

If cardiac arrest:
Defibrillate (not synchronised).

MEDICINE TREATMENT

Caution *LoE:III[xlv]*

Never give verapamil or adenosine IV to patients with wide QRS tachycardia as this may precipitate ventricular fibrillation.

DC cardioversion **is preferred and safest first line therapy** for regular wide QRS tachycardias. Medicines are needed if ventricular tachycardia (VT) recurs after cardioversion, or spontaneous termination.

LoE:III

If in doubt as to the nature of a tachycardia, and in all patients with haemodynamic compromise, DC cardioversion under IV sedation is the safest option.
DC cardioversion, 200 J, after sedation with:

- Midazolam, IV, 1–2.5 mg, administered over 2-3 minutes.
  - Monitor and repeat dose after 2-3 minutes, as necessary.
  - If 200 J fails, use 360 J. *LoE:III*

- Amiodarone, IV, 5 mg/kg infused over 30 minutes.

Follow with:

- Amiodarone, oral, 200 mg 8 hourly for 7 days.
  - Then, 200 mg 12 hourly for 7 days.
  - Maintenance dose: 200 mg daily for the minimum time required to control the arrhythmia

- Consult specialist before instituting long-term (>1 week) therapy.

LoE:III[xlvi]

Precautions:

- If on warfarin, halve the dose of warfarin and monitor INR closely, until INR is stable.
- Avoid concomitant digoxin.
- Monitor thyroid function every 6 months for thyroid abnormalities.
- Ophthalmological examination every 6 months.

3.3.2.2 SUSTAINED (>30 SECONDS) IRREGULAR WIDE QRS TACHYCARDIAS

I47.0-2/I47.9

These tachycardias are usually due to atrial fibrillation with bundle branch block, or pre-excitation (WPW syndrome).

If the QRS complexes have a pattern of typical right or left bundle branch block, with a rate <170 bpm, treat as for atrial fibrillation. See section 3.3.1: Narrow QRS complex (supraventricular) tachycardias.

If the rate is >170 bpm, and/or the complexes are atypical or variable, the likely diagnosis is WPW syndrome with atrial fibrillation, conducting via the bypass tract. Treat with DC conversion.

Do not treat with medication.
Verapamil and digoxin may precipitate ventricular fibrillation by increasing the ventricular rate.

If in doubt as to the nature of a tachycardia, and in all patients with haemodynamic compromise, DC cardioversion under IV sedation is the safest option.
DC cardioversion, 200 J, after sedation with:

- Midazolam, IV, 1–2.5 mg, administered over 2-3 minutes.
  - Monitor and repeat dose after 2-3 minutes, as necessary.
  - If 200 J fails, use 360 J.

LoE:III

3.3.2.3 NON-SUSTAINED (<30 SECONDS) IRREGULAR WIDE QRS TACHYCARDIAS

I47.0-2/I47.9

These tachycardias are usually ventricular. They are common in acute myocardial infarction. Check serum potassium level and correct if low.

MEDICINE TREATMENT

- Amiodarone, IV, 5 mg/kg infused over 30 minutes.

Follow with:

- Amiodarone, oral, 800 mg daily for 7 days.
  - Then 600 mg daily for 3 days.
  - Follow with a maintenance dose of 200–400 mg daily, depending upon

clinical judgement. Consult specialist before instituting long-term (>1 week) therapy.

Precautions:

- o If on warfarin, halve the dose of warfarin and monitor INR closely, until INR is stable.
- o Avoid concomitant digoxin.
- o Monitor thyroid function every 6months as thyroid abnormalities may develop.
- o Ophthalmological examination every 6 months.

OR

Only in haemodynamically stable patients:

- Lidocaine (lignocaine), IV, 50–100 mg (1–2 mg/kg) initially and at 5 minute intervals if required to a total of 200–300 mg.

Thereafter, for recurrent ventricular tachycardia only:

- Lidocaine (lignocaine), IV infusion, 1–3 mg/minute for 24–30 hours.

» Lidocaine will only terminate ± 30% of sustained ventricular tachycardias, and may cause hypotension, heart block or convulsions.

» For emergency treatment of ventricular tachycardia, DC cardioversion is first line therapy, even if stable.

In the absence of acute ischaemia or infarction, consider torsades de pointes, due to QT prolonging medicines.

3.3.2.4 TORSADES DE POINTES VENTRICULAR TACHYCARDIA (VT)

I47.0-2/I47.9

Torsades de pointes Ventricular Tachycardia (VT) has a twisting pattern to the QRS complexes and a prolonged QT interval in sinus rhythm. It is usually due to a QT-prolonging medication, active myocardial ischaemia and/or hypokalaemia and/or a history of alcohol abuse/malnutrition.

GENERAL MEASURES

Defibrillation, as necessary.
Torsades complicating bradycardia: temporary pacing.

MEDICINE TREATMENT

Stop all QT-prolonging medicines (a list of medicines that cause QT prolongation can be viewed at https://www.sads.org.uk/drugs-to-avoid/?doing_wp_cron=1585301751.3996679782867431640625
Correct serum potassium.

- Magnesium sulphate, IV, 2 g administered over 5–10 minutes.

If recurrent episodes after initial dose of magnesium sulphate:

- Magnesium sulphate, IV, 2 g administered over 24 hours. *LoE:III*

Torsades complicating bradycardia:
- Adrenaline (epinephrine) infusion to raise heart rate to >100 bpm (if temporary pacing unavailable).

REFERRAL
All cases of wide QRS tachycardia, after resuscitation and stabilization.

3.3.3 HEART BLOCK (SECOND OR THIRD DEGREE)
I44.1/I44.2

DESCRIPTION
The majority of cases occur in patients >60 years of age and are idiopathic, with an excellent long-term prognosis, provided a permanent pacemaker is implanted. Acute, reversible AV block commonly complicates inferior myocardial infarction. Heart block may also be induced by metabolic and electrolyte disturbances, as well as by certain medicines.

GENERAL MEASURES
Emergency cardio-pulmonary resuscitation (if necessary).
External pacemaker should be available in all secondary hospitals and must be preceded by appropriate analgesia.

MEDICINE TREATMENT
Analgesia if external pacemaker:
- Morphine, IM, 10–15 mg 3–6 hourly.

Apply relevant precautions as indicated in Appendix II (i.e. monitoring for response and toxicity).

AV nodal block **with narrow QRS complex escape rhythm only:**
- Atropine, IV bolus, 0.6–1.2 mg.
  - May be repeated as needed until a pacemaker is inserted.
  - Use in patients with inferior myocardial infarct and hypotension and second degree AV block, if symptomatic.
  - It is temporary treatment of complete AV block before referral (urgently) for pacemaker.

OR

For resuscitation of asystole in combination with CPR:
I46.0-1/I46.9+(I44.1-2)
- Adrenaline (epinephrine) 1:10 000, slow IV, 5 mL (0.5 mg).
  - Used as temporary treatment of complete heart block when other medicines are not effective.

REFERRAL
» All cases with a heart rate <40 bpm after resuscitation and stabilisation.
» All cases of 2nd or 3rd degree AV block, whether or not myocardial infarct or other reversible cause is suspected, and whether or not the patient is thought to be symptomatic.

A permanent pacemaker is the definitive form of treatment. These are only available in tertiary institutions. Refer all symptomatic patients with significant bradyarrhthmias for evaluation.

3.3.4 SINUS BRADYCARDIA

R00.1

DESCRIPTION

This rhythm does not require treatment, unless it is causing symptoms, i.e. syncope, dizziness, tiredness and poor effort tolerance.

Sinus bradycardia <50 bpm or sinus arrest with slow escape rhythm, accompanied by hypotension, strongly suggest a treatable underlying cause such as:

» acute inferior myocardial infarct,
» hyperkalaemia, especially if wide QRS and/or peaked T waves,
» medicines, especially combination of verapamil and ß-blocker or digoxin,
» hypothermia,
» hypoxia, or
» hypothyroidism.

Treat the cause. Consider atropine if inferior myocardial infarct.

3.3.5 SINUS ARREST

I49.5

Refer all urgently to a cardiologist.

3.4 CONGESTIVE CARDIAC FAILURE (CCF)

I50.0

DESCRIPTION

CCF is a clinical syndrome and has several causes. The cause and immediate precipitating factor(s) of the CCF must be identified and treated to prevent further harm.

Potentially reversible causes include:

» hypertension
» thyroid disease
» valvular heart disease
» constrictive pericarditis
» thiamine deficiency
» ischaemic heart disease
» haemochromatosis
» tachycardia

GENERAL MEASURES

Patient and family education.
Monitor body weight to assess changes in fluid balance.
Limit fluid intake to 1–1.5 L/day if fluid overloaded despite diuretic therapy.
Limit alcohol intake to a maximum 2 drinks per day if at all.
Salt restriction (dietician guided when possible).
Regular exercise within limits of symptoms.

Avoid NSAIDs as these may exacerbate fluid retention.
Counsel that pregnancy may exacerbate heart failure and some medicines used in treatment of heart failure are contraindicated in pregnancy e.g. ACE-inhibitors, angiotensin-receptor blockers, spironolactone. *LoE:III*[xlvii]
Advise on contraception or refer for such advice.

MEDICINE TREATMENT

Where heart failure is due to left ventricular systolic dysfunction, mortality is significantly reduced by the use of ACE-inhibitors, ß-blockers and spironolactone and every effort should be made to ensure eligible patients receive all these agents in appropriate doses.

Note: All the guideline evidence presented here relates to treatment of patients in whom the heart failure syndrome is due to left ventricular systolic dysfunction and cannot necessarily be extrapolated to patients in whom heart failure is due to other causes of the syndrome.

Digoxin has only been shown to improve symptoms and reduce hospitalisation.

LoE:I[xlviii]

Diuretic

Mild volume overload (mild CCF) and normal renal function, thiazide diuretic:

- Hydrochlorothiazide, oral, 25–50 mg daily.
  - Caution in patients with gout.
  - Less effective in impaired renal function.
  - Caution in patients with a history or family history of skin cancer; and counsel all patients on sun avoidance and sun protection.

LoE:III[xlix]

Significant volume overload or abnormal renal or hepatic function, loop diuretic:

- Furosemide, oral, daily.
  - Initial dose: 40 mg/day.
  - Higher dosages may be needed, especially if comorbid renal failure.
  - Advise patients to weigh themselves daily and adjust the dose if necessary. *LoE:III*

Note:

» Unless patient is clinically fluid overloaded, reduce the dose of diuretics before adding an ACE-inhibitor. After introduction of an ACE-inhibitor, try to reduce diuretic dose and consider a change to hydrochlorothiazide.
» Routine use of potassium supplements with diuretics is not recommended. They should be used short-term only, to correct documented low serum potassium level.

LoE:I[l]

Renin-angiotensin-aldosterone system (RAAS) blockers

- ACE-inhibitor, e.g.:
- Enalapril, oral, 2.5 mg 12 hourly, titrated to 10 mg 12 hourly.
  - In the absence of significant side-effects always try to increase the

dose to the level shown to improve prognosis (i.e.10 mg 12 hourly). LoE:I[li]

If ACE-inhibitor intolerant, i.e. intractable cough:

- Angiotensin receptor blocker (ARB), e.g.:
- Losartan, oral, 50–100 mg daily. Specialist initiated.

Spironolactone

Use with an ACE-inhibitor and furosemide in patients presenting with Class III or IV heart failure.

Do not use if eGFR <30 mL/minute.

Monitoring of potassium levels is essential if spironolactone is used with an ACE-inhibitor or other potassium sparing agent or in the elderly.

- Spironolactone, oral, 25–50 mg once daily.

LoE:III[lii]

ß-blockers

For all stable patients with heart failure who tolerate it:

Note: Patients should not be fluid overloaded or have a low BP before initiation of therapy.

- Carvedilol, oral.
  - Initial dose: 3.125 mg 12 hourly.
  - Increase at 2-weekly intervals by doubling the daily dose until a maximum of 25 mg 12 hourly, if tolerated.
  - If not tolerated, i.e. worsening of cardiac failure symptoms, reduce the dose to the previously tolerated dose.
  - Up-titration should take several weeks or months. LoE:I[liii]

Digoxin

Patients in sinus rhythm remaining symptomatic despite the above-mentioned agents (Specialist consultation):

- Digoxin, oral, 0.125 mg daily, adjust according to response and trough plasma level.
  - Digoxin trough plasma levels (before the morning dose) should be maintained between 0.6-1 nmol/L.
  - Patients at high risk of digoxin toxicity: the elderly, patients with renal dysfunction, hypokalaemia and patients with lean body mass.

LoE:II[liv]

Anticoagulants

Heparin: for DVT prophylaxis for patients admitted to hospital, unless contraindicated: See section 2.14: Venous thrombo-embolism.

Warfarin: See section 3.3.1: Narrow QRS complex (supraventricular) tachydysrhythmias.

Anti-dysrhythmic medicines

Only for potentially life-threatening ventricular dysrhythmias. See section 3.3: Cardiac Dysrhythmias.

Always exclude electrolyte abnormalities and medicine toxicity first.

Thiamine

Consider as a trial of therapy in all unexplained heart failure:

- Thiamine, oral/IM, 100 mg daily for 4 weeks.

Prophylaxis (Z29.2)

- Annual influenza vaccine. See section 9.2: Adult vaccination.

REFERRAL

» Where specialised treatment and diagnostic work-up is needed and to identify treatable and reversible causes.

» All patients with audible cardiac murmurs should undergo specialist evaluation, as should all patients with potentially reversible causes of the heart failure syndrome and those with persistent and severe symptoms and signs of fluid overload despite adequate doses of diuretic.

» Patients who have LBBB on the ECG are potential candidates for cardiac resynchronization therapy. An ECG should be recorded at baseline and repeated at 6-monthly intervals.

» Patients with LBBB should be referred for consideration for resynchronsation therapy, discussed with a specialist.

3.5 ENDOCARDITIS, INFECTIVE

I33.0

GENERAL MEASURES

Bed rest.

Early surgical intervention in acute fulminant and prosthetic valve endocarditis is often indicated. Consider surgery if there is heart failure, embolism, large vegetations on echocardiography, heart block, evidence of persistent infection despite antibiotics or renal impairment. Refer these patients promptly.

LoE:III

MEDICINE TREATMENT

Treat accompanying complications, e.g. cardiac failure. Such treatment should not delay referral.

Antibiotic therapy

It is essential to do at least 3 blood cultures, taken by separate venipunctures, before starting antibiotics.

In patients with subacute presentation and no haemodynamic compromise, wait for the results of blood culture before starting antibiotics.

Empiric treatment is indicated in patients with a rapidly fulminant course or with severe disease only.

Aminoglycoside therapy should be monitored with trough levels for safety.

Duration of therapy given is the minimum and may be extended based on the response (clinical and laboratory).

Severe penicillin-allergic patients, or methicillin resistant staphylococcal infections: (Z88.0)

- Vancomycin, IV, 20 mg/kg 12 hourly, is the antibiotic of choice. It is essential to monitor trough concentrations of vancomycin regularly and adjust doses accordingly, starting after the third dose.

LoE:III[iv]

Empiric therapy

Native valve	• Benzylpenicillin (penicillin G), IV, 5 MU 6 hourly for 4 weeks **AND** • Gentamicin, IV, 1.5 mg/kg 12 hourly for 2 weeks. (See Appendix II, for guidance on prescribing). If staphylococcal infection is suspected (acute onset): **ADD** • Cefazolin, IV, 2 g, 8 hourly.
Prosthetic valve*	• Vancomycin, IV, 20 mg/kg 12 hourly for 6 weeks. **AND** • Rifampicin, oral, 7.5 mg/kg 12 hourly for 6 weeks. **AND** • Gentamicin, IV, 1.5 mg/kg 12 hourly for 2 weeks. (See Appendix II for guidance on prescribing).

* All cases of prosthetic valve endocarditis should be referred.

Directed therapy (native valve)

Streptococcal	
Fully susceptible to penicillin MIC: <0.2 mg/L	• Benzylpenicillin (penicillin G), IV, 5 MU 6 hourly for 4 weeks.
Moderately susceptible MIC: 0.12–0.5 mg/L	• Benzylpenicillin (penicillin G), IV, 5 MU 6 hourly for 4 weeks. **AND** • Gentamicin, IV, 1.5 mg/kg 12 hourly for 2 weeks (see Appendix II for guidance on prescribing).
Moderately resistant MIC: 0.5–4 mg/L Enterococci and Abiotrophia spp. (nutritionally variant streptococci)	• Benzylpenicillin (penicillin G), IV, 5 MU 6 hourly for 4 weeks. **AND** • Gentamicin, IV, 1.5 mg/kg 12 hourly for 4 weeks. o 6 weeks of therapy may be required in cases with a history of >3 months, or mitral or prosthetic valve involvement (see Appendix II for guidance on prescribing).
Fully resistant MIC: >4 mg/L	• Vancomycin, IV, 20 mg/kg 12 hourly for 6 weeks. **AND** • Gentamicin, IV, 1.5 mg/kg 12 hourly for 6 weeks (see Appendix II for guidance on prescribing).
Enterococcal	
Fully susceptible to penicillin MIC: <4 mg/L	• Benzylpenicillin (penicillin G), IV, 5 MU 6 hourly for 4 weeks.
Moderately resistant MIC: 0.5–4 mg/L Enterococci and Abiotrophia spp. (nutritionally variant streptococci)	• Benzylpenicillin (penicillin G), IV, 5 MU 6 hourly for 4 weeks. **AND** • Gentamicin, IV, 1 mg/kg 8 hourly for 2 weeks. o 6 weeks of therapy may be required in cases with a history of >3 months, or mitral or prosthetic valve involvement (see Appendix II for guidance on prescribing). *LoE:III[lvi]*
Penicillin-resistant MIC ≥ 4 mg/L **or** significant β-lactam allergy **and** Sensitive to vancomycin MIC: ≤4 mg/L	Refer.

Staphylococcal (cloxacillin/methicillin sensitive)	
S. aureus	• Cefazolin, IV, 2g 8 hourly for 4 weeks. *If necessary, add:* • Gentamicin, IV, 6 mg/kg daily for the first 3–5 days (see Appendix II for guidance on prescribing). » The benefit of adding an aminoglycoside has not been established.
Coagulase-negative staphylococci	Consult expert opinion on correct diagnosis in this setting.
Staphylococcal (cloxacillin/methicillin resistant) or methicillin sensitive with significant beta-lactam allergy	
S. aureus	• Vancomycin, IV, 20 mg/kg 12 hourly for 4 weeks.
Coagulase-negative staphylococci	Consult expert on correct on antibiotic choice.

Directed therapy for prosthetic valve endocarditis

Duration of therapy is usually a minimum of at least 6 weeks.
Seek expert opinion on antibiotic choice and the need for referral for repeat cardiac surgery early in the course of treatment.

Endocarditis prophylaxis

Cardiac conditions

Patients with the following cardiac conditions are at high risk of developing infective endocarditis:

» Acquired valvular heart disease with stenosis or regurgitation.
» Patients with prosthetic heart valves.
» Structural congenital heart disease, including surgically corrected or palliated structural conditions, but excluding isolated atrial septal defect, fully repaired ventricular septal defect or fully repaired patent ductus arteriosus.
» Patients who have suffered previous endocarditis.

Procedures requiring prophylaxis

Antibiotic prophylaxis is recommended for all dental procedures that involve manipulation of either the gingival tissue or the peri-apical region of the teeth.

Antibiotic prophylaxis is not recommended for patients who undergo a gastro-intestinal or genito-urinary procedure.

Prophylaxis (Z29.2)

Maintain good dental health.
This is the most important aspect of prophylaxis.
Refer all patients to a dental clinic/dental therapist for assessment and on-going dental care.

• Amoxicillin, oral, 2 g one hour before the procedure.

If patient cannot take oral:
- Ampicillin, IV/IM, 2 g one hour before the procedure.

Severe penicillin allergy: (Z88.0)
- Clindamycin, oral, 600 mg one hour before the procedure.

If patient cannot take oral:
- Clindamycin IV, 600 mg one hour before the procedure.

The NICE review noted the lack of a consistent association between interventional procedures and development of infective endocarditis, and that the efficacy of antibiotic prophylaxis is unproven. It further commented that because the antibiotic is not without risk, there is a potential for a greater mortality from severe hypersensitivity than from withholding antibiotics.

It is very difficult to extrapolate from these guidelines to a South African situation where good dental hygiene may be lacking and valvular heart disease is common. Practitioners need to weigh the risk of the underlying heart disease (particularly previous successfully treated endocarditis) and the essential need for ongoing antibiotic stewardship.

LoE:III[lvii]

3.6 HYPERTENSION

I10

KEY POINTS

Hypertension control has significant benefit for patients.
Detect and treat co-existent risk factors.
Assess cardiovascular risk.
Lifestyle modification and patient education is essential for all patients.
Medicine treatment is needed for SBP ≥140 mmHg and DBP ≥90 mmHg despite lifestyle modification. See medicine treatment choices below.
Immediate medicine treatment is needed for DBP ≥110 mmHg and/or SBP ≥180 mmHg (defined as severe hypertension - see sections 3.6.1, 3.6.2 and 3.6.3) or for patients with 3 or more risk factors, target organ damage and/or associated clinical conditions.

Patients should be evaluated for cardiovascular risk factors, target organ damage and associated clinical conditions.

Other major risk factors for ischaemic cardio- and cerebrovascular disease (see section 3.1: Ischaemic heart disease and atherosclerosis, prevention).

Target organ damage:
» left ventricular hypertrophy,
» hypertensive retinopathy,
» microalbuminuria, or positive dipsticks for albuminuria or elevated albumin/creatinine ratio, or
» elevated creatinine level (or eGFR <60 mL/minute).

Associated clinical conditions:
» ischaemic heart disease,
» heart failure,
» stroke or transient ischaemic attack,
» chronic kidney disease,
» peripheral arterial disease.

Investigations
If overweight, record body weight and waist circumference at each visit when BP is measured. Central obesity is defined as waist circumference:
» 102 cm in men, and
» 88 cm in women.

Do urine test strip analysis for protein, blood and glucose at presentation.
» If normal, repeat urine test strip every 6 months.
» If abnormal, do spot urine ACR. Repeat yearly.
» If haematuria >1+, investigate further.
» If glycosuria, exclude diabetes mellitus.
» If known diabetic, HbA1c.
» Random total cholesterol.
» Perform a resting ECG to exclude left ventricular hypertrophy or ischaemia.
» Assess renal function (serum creatinine and eGFR).

Goals of treatment
Aim for SBP <140 mmHg and DBP <90 mmHg.

GENERAL MEASURES
Lifestyle modification
All persons with hypertension should be encouraged to make the following lifestyle changes as appropriate.
» Smoking cessation.
» Maintain ideal weight, i.e. BMI <25 kg/m^2. Weight reduction in the overweight patient.
» Salt restriction with increased potassium intake from fresh fruits and vegetables (e.g. remove the salt from the table, gradually reduce added salt in food preparation and avoid processed foods). Dietician's advice recommended.
» Reduce alcohol intake to no more than 2 standard drinks per day for males and 1 for females.
» Follow a prudent eating plan i.e. low fat, high fibre and unrefined carbohydrates, with adequate fresh fruit and vegetables. Dietician's advice recommended.
» Regular moderate aerobic exercise, e.g. 40 minutes brisk walking at least 3 times a week.

MEDICINE TREATMENT
Initial medicine choice in patients qualifying for treatment is dependent on the presence of compelling indications (see table on page 3.31); the severity of

the BP; and the presence of target organ damage, cardiovascular risk factors, and associated clinical conditions**.**

Advise patient to take medication regularly, including on the day of the clinic visit, but a single missed dose does not account for severe elevations in BP.

Note:

» Check adherence to antihypertensive therapy by doing pill counts and questioning family members.

» The use of fixed dose combination medication for control of hypertension provides greater adherence and such agents should be used when they are available. *LoE:III*[viii]

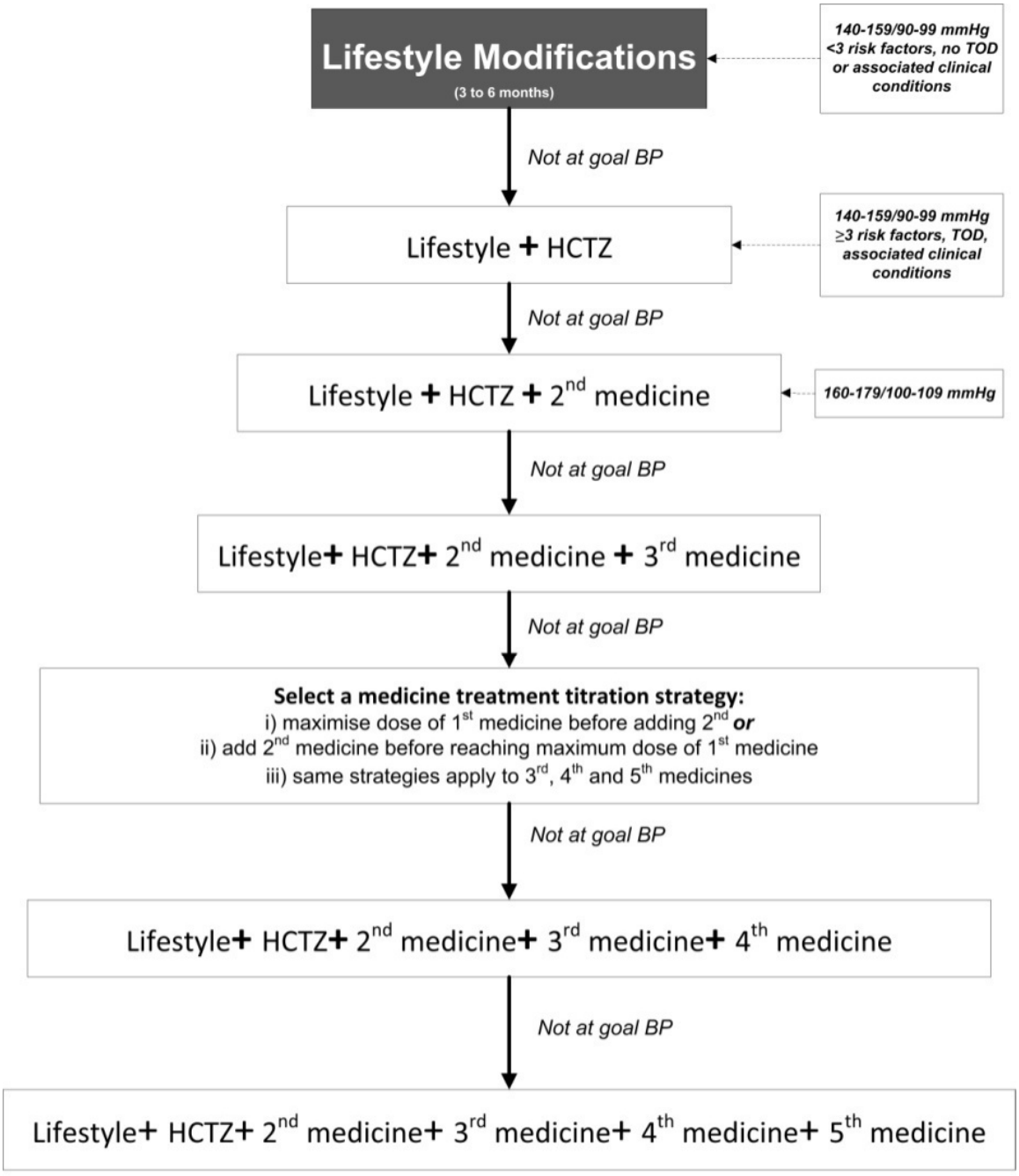
» There is emerging evidence that taking the total daily dose of antihypertensive medication at bedtime rather than on awaking provides both better control of hypertension and a significant reduction in important cardiovascular events. *LoE:III*[ix]

» Monitor patients monthly and adjust therapy if necessary until the BP is controlled.

» After target BP is achieved, patients can be seen at 3–6 monthly intervals.

MEDICINE TREATMENT CHOICES WITHOUT COMPELLING INDICATIONS

Stepped-care approach to BP treatment



Abbreviations:BP=blood pressure; TOD=target organ disease; HCTZ=hydrochlorothiazide

Medicines include: HCTZ; ACE-inhibitors; long-acting calcium channel blockers; spironolactone, atenolol

Note:

» If lifestyle modification failed to achieve BP control: Counsel patient on the risk of major cardiovascular events associated with elevated BP; and initiate monotherapy.

» If BP control is suboptimal: Up titrate treatment (maximise dose of current antihypertensive and/or add additional medicine). Evidence suggests that

treatment inertia contributes to suboptimal BP control with patients remaining on monotherapy and/or suboptimal doses. *LoE:III*[lx]

» Initiate combination medicine therapy in cases of severe hypertension (see section 3.6.1) and hypertension urgency (see section 3.6.2).

BP 140-159/90-99 mmHg:

» < 3 risk factors, no target organ damage or associated clinical conditions:
  - Lifestyle modification for 3–6 months.
  - Start antihypertensive therapy with a single medicine if target BP not achieved.

» ≥ 3 risk factors, target organ damage and/or associated clinical conditions:
  - Start antihypertensive therapy immediately (together with lifestyle modification).

BP 160-179/100-109 mmHg:

» Even in absence of risk factors, or target organ damage or associated clinical conditions:
  - Start antihypertensive therapy (together with lifestyle modifications) with a combination of two medicines.

BP ≥180/100 mmHg: this is severe hypertension: see sections 3.6.1, 3.6.2 and 3.6.3.

Initial antihypertensive medicine:

- Hydrochlorothiazide, oral, 12.5 mg daily.
  - Caution in patients with gout.
  - Less effective in impaired renal function.
  - Caution in patients with a history or family history of skin cancer; and counsel all patients on sun avoidance and sun protection.

LoE:III[lxi]

If target BP is not reached after one month despite adequate adherence (or immediately in patients with BP160-179/100-109 mmHg), add one of the following: ACE-inhibitor or calcium channel blocker.

- Long-acting calcium channel blocker, e.g.:
- Amlodipine, oral, 5 mg at night. *LoE:I*[lxii]

OR

- ACE-inhibitor, e.g.:
- Enalapril, oral, 10 mg at night. *LoE:I*[lxiii]

If ACE-inhibitor intolerant, i.e. intractable cough:

- Angiotensin receptor blocker (ARB), e.g.:
- Losartan, oral, 50 mg daily. Specialist initiated.

If target BP is not reached after one month despite adequate adherence on

two medicines, add one of ACE-inhibitor or calcium channel blocker, whichever has not already been used.

If target BP is still not achieved after one month despite adequate adherence, increase the dose of medication, one medicine every month, to their maximal levels: amlodipine 10 mg daily, enalapril 20 mg daily (losartan 100 mg daily) hydrochlorothiazide 25 mg daily.

<u>If target BP is not reached after one month despite adequate adherence:</u>
ADD

- Spironolactone, oral 25–50 mg daily. *LoE:I*[lxiv]

<u>For refractory hypertension:</u>
ADD

- β-blocker , e.g.: *LoE:I*[lxv]
- Atenolol, oral, 50 mg at night.

Note: In 60–80% of patients a combination of the above antihypertensive therapy is needed. Combination therapy, i.e. hydrochlorothiazide plus a calcium channel blocker or ACE-inhibitor should be considered at the outset in patients with BP >160/100 mmHg.

Medicine treatment choices with compelling indications

Compelling indications	Medicine class
Angina	ß-blocker Calcium channel blocker
Post myocardial infarction	ß-blocker ACE-inhibitor
Heart failure	ACE-inhibitor Carvedilol Spironolactone Hydrochlorothiazide or furosemide
Left ventricular hypertrophy	ACE-inhibitor
Stroke	Hydrochlorothiazide Calcium channel blocker
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: Obstetrics.

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.

Assess for risk of ischaemic disease. See section 3.1: Ischaemic heart disease and atherosclerosis, prevention.

REFERRAL

Referrals or consultation with a specialist are indicated when:

» Patients are adherent to therapy, and BP is refractory, i.e. >140/90 mmHg, while on medicines from 3-4 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, ASYMPTOMATIC SEVERE

I10

DESCRIPTION

These patients have severe hypertension (DBP ≥110 mmHg and/or SBP ≥180 mmHg), 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 medicines together, one of which should be low dose hydrochlorothiazide. The second medicine is either a long-acting calcium channel blocker, e.g. amlodipine, or an ACE-inhibitor, e.g. enalapril.

Follow up carefully and refer as needed.

3.6.2 HYPERTENSIVE URGENCY

I10

DESCRIPTION

Severe hypertension (DBP ≥110 mmHg and/or SBP ≥180 mmHg) which is **symptomatic** and/or with evidence of progressive target organ damage. 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 – see section 14.1.1: Stroke.

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

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.

Note: Avoid if there is severe hyponatraemia, i.e. serum Na <130 mmol/L.

- Spironolactone.
- β-blocker.

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

3.6.3 HYPERTENSIVE CRISIS, HYPERTENSIVE EMERGENCY

I10

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, together with impaired renal function and proteinuria.

The true emergency situation should preferably be treated by a 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 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 the BP to 160/100 mmHg.
This may be achieved by the use of intravenous or oral medicines.

Intravenous therapy

- Labetalol, IV, 2 mg/minute to a total dose of 1–2 mg/kg, while trying to achieve control with other agents.
  - Caution in acute pulmonary oedema.

OR

<u>If myocardial ischaemia and CCF:</u>

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

Refer to dosing table in section 3.2.1: ST elevation myocardial infarction (STEMI).

AND

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

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.

<u>If ACE-inhibitor intolerant, i.e. intractable cough:</u>

- Angiotensin receptor blocker (ARB), e.g.:
- Losartan, oral, 50–100 mg daily. Specialist initiated.

3.7 RHEUMATIC HEART DISEASE

I09.0-2/I09.9/I01.0-2/I01.8-9

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 of rheumatic fever: bed rest and supportive care.

MEDICINE TREATMENT

Acute rheumatic fever

<u>For eradication of streptococci in throat:</u>

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

- For benzathine benzylpenicillin, IM injection, dissolve benzathine benzylpenicillin 1.2 MU in 3.2 mL lidocaine 1% without adrenaline (epinephrine) or 3 mL water for injection. *LoE:III*[lxvi]

OR

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

Severe penicillin allergy: (Z88.0)

- Macrolide, e.g.:
- Azithromycin, oral, 500 mg daily for 3 days. *LoE:I*[lxvii]

For arthritis and fever:

- NSAID, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with meals. *LoE:III*

Prevention of recurrent rheumatic fever

All patients with confirmed rheumatic fever and no persistent rheumatic valvular disease:

» Treat for 10 years or until the age of 21 years, whichever is longer.

All patients with confirmed rheumatic fever and persistent rheumatic valvular disease:

» Treat lifelong. *LoE:III*[lxviii]

- Benzathine benzylpenicillin (depot formulation), IM, 1.2 MU every 3–4 weeks (preferred treatment).
  - For benzathine benzylpenicillin, IM injection, dissolve benzathine benzylpenicillin 1.2 MU in 3.2 mL lidocaine 1% without adrenaline (epinephrine) or 3 mL water for injection.

OR *LoE:III*[lxix]

Phenoxymethylpenicillin, oral, 250 mg 12 hourly.

Severe penicillin allergy: (Z88.0)

- Macrolide, e.g.:
- Azithromycin, oral, 250 mg daily. *LoE:III*

Prophylaxis for infective endocarditis

See section 3.5: Endocarditis, infective.

REFERRAL

» Any patient with rheumatic valvular heart disease who requires a significant dose of diuretic to control fluid overload or who has had an episode of pulmonary oedema should be discussed with a specialist and referred for possible valve surgery.

» Pregnancy poses a particular problem in women with symptomatic rheumatic valvular heart disease and all should be referred for specialist consultation.

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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

L70.0-5/L70.8-9

DESCRIPTION

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

Mild acne:
Predominantly consists of non-inflammatory comedones.

Moderate acne:
Consists of a mixture of non-inflammatory comedones and inflammatory papules and pustules**.**

Severe acne
It is characterised by the presence of widespread nodules and cysts, as well as a preponderance of inflammatory papules and pustules.

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

Primary management: See Primary Health Care Standard Treatment Guidelines and Essential Medicine List, section 5.3: Acne vulgaris.

Women who need oral contraception and have inflammatory acne can be initiated on a cyproterone acetate-containing combined oral contraceptive pill, provided that they have no personal or family history of breast cancer or thrombosis.

- Cyproterone acetate 2 mg plus ethinyl estradiol 35 mcg, oral.

LoE:I[i]

Discuss all severe cases with a dermatologist.

4.2 CELLULITIS AND ERYSIPELAS

L03.0-3/L03.8-9 + (L04.0-3/L04.8-9/B95.0-8) and A46

DESCRIPTION

Skin and subcutaneous infections with pain, swelling, and erythema, usually caused by streptococci and 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. amoxicillin/clavulanic acid) as these infections are often polymicrobial.

GENERAL MEASURES

Elevate the affected limb to reduce swelling and pain.
Hydrate.

MEDICINE TREATMENT

For pain: *LoE:I[ii]*

- NSAID, oral: e.g.
- Ibuprofen, oral, 400 mg 8 hourly with meals.

OR

- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

Antibiotic therapy

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

OR

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

Severe penicillin allergy: (Z88.0)
Macrolide:

- Azithromycin, oral, 500 mg daily for 3 days.

Severe cases may require parenteral antibiotics.

Severe infection

If intravenous antibiotics are given initially, patients should be switched to oral agents as soon as there is clinical improvement.
If there is a rapid progression of erythema, intravenous antibiotics are preferred.
The recommended duration of antimicrobial therapy is 5 days, but treatment should be extended if the infection has not improved within this time period.

LoE:III[iii]

- Cefazolin, IV, 1 g 8 hourly.

When there is clinical improvement, change to: LoE:II[iv]
- Flucloxacillin, oral, 500 mg 6 hourly.

Severe penicillin allergy: (Z88.0)
- Clindamycin, IV, 600 mg 8 hourly.

When there is clinical improvement, change to:
- Clindamycin, oral, 450 mg 8 hourly.

If patient is admitted and bed-bound with lower limb cellulitis, consider deep venous thrombosis prophylaxis. See section 2.14 Venous thrombo-embolism.

If *Taenia pedis* is suspected to be the pre-disposing cause, treat accordingly. See section 4.10: Fungal infections.

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.
» Cellulitis involving wounds in aquatic environment, (salt or brackish water), fresh water or lack of response to treatment, refer for further investigation with an option for a biopsy.

4.3 IMPETIGO
L01.0 + (B95.0-8)

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 staphylococci. 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 lesions in soapy water to soften and remove crusts.

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

Severe penicillin allergy: (Z88.0)
Macrolide:
- Azithromycin, oral, 500 mg daily for 3 days.

4.4 FURUNCLES AND ABSCESSES

L02.0-4/L02.8-9/H00.0/H60.0/N76.4/J34.0 + (B95.6)

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, malnourished, or other immunocompromised patients are more likely to develop complications.Check blood glucose levels and HIV status, if the boils are recurrent.

GENERAL MEASURES

Drainage of the abscess is the treatment of choice. Perform surgical incision only if the lesion is fluctuant.

Note: Needle aspiration is insufficient for adequate abscess drainage.

The treatment of choice for small furuncles is moist warm compress to infected area, several times per day to promote drainage.

Large fluctuant lesions should be treated with incision and drainage.

The following sites should be drained by a surgeon:

» Peri-rectal abscess
» Anterior and lateral neck abscess
» Abscess adjacent to nerves or blood vessels e.g carotid artery, facial nerve, central triangle of face (formed by the corners of the mouth and the nasal bridge).

Systemic antibiotics are used only as indicated below.

MEDICINE TREATMENT

Antibiotic therapy

Systemic antibiotics are seldom necessary, except for facial abscesses, or abscesses associated with tender draining lymph nodes, fever, or extensive surrounding cellulitis.

Antibiotics should usually be given for 5–10 days, depending on clinical response.

- Cefazolin, IV, 1g 8 hourly.

When there is clinical improvement, change to: *LoE:II^{v}*

- Flucloxacillin, oral, 500 mg 6 hourly.

Severe penicillin allergy: (Z88.0)

- Clindamycin, IV, 600 mg 8 hourly.

When there is clinical improvement, change to:

- Clindamycin, oral, 450 mg 8 hourly.

4.5 ATOPIC ECZEMA/ DERMATITIS

L20.0/L20.8-9

DESCRIPTION

Eczema is an pruritic, 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.

Assessing severity

1% of body surface is equal to the size of one hand (including the fingers) of the patient.

Mild

» Less than 5% body surface involved.
» No acute changes.
» No significant impact on quality of life.

Moderate

» 5–30% body surface involved.
» Mild dermatitis with acute changes.
» Mild dermatitis with significant impact on quality of life.

Severe

» More than 30% body surface involved.
» Moderate dermatitis with acute changes.
» Moderate dermatitis with significant impact on quality of life.

GENERAL MEASURES

» Avoid exposure to trigger or precipitating factors, where applicable.
» Avoid irritants such as strong detergents, antiseptics, foam (especially hot) baths, soaps and rough occlusive clothing (silk is better than cotton, which is better than nylon, which is better than wool).
» Good personal hygiene with once daily washing to remove crusts and accretions and avoid secondary infection.
» Keep fingernails short to minimise trauma from 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.
» Avoid smoking.

MEDICINE TREATMENT

<u>To relieve skin dryness:</u>

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

moisturiser. LoE:III[vi]

Moisturising soap, creams and ointments, as described above, should continue permanently as maintenance, even if the dermatitis is controlled.

To control dermatitis:
Creams are preferred to ointments on open or oozing lesions and in intertriginous folds.

Mild eczema
- Hydrocortisone 1%, topical, applied 12 hourly to body and face until control is achieved.
  - Can be used on face and in skin folds.
  - Apply sparingly to the face.
  - Use with caution around the eyes.

Moderate and severe eczema
- Potent topical corticosteroids, e.g.:
- Betamethasone 0.1%, topical, applied daily for 7 days to the affected areas.
  - Apply sparingly to face, neck and flexures.

  Note: There is no clear benefit for more than once daily application.

LoE:I[vii]

If non-responsive:
Refer for dermatologist opinion.
- Prednisone, oral, 0.5 mg/kg daily, for ≤ 2 weeks. Specialist initiated.

Maintenance therapy
Once eczema is controlled, wean to the lowest potency topical corticosteroid that maintains remission, applied twice a week.

Apply moisturiser as needed.
- 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.

Severe penicillin allergy: (Z88.0)
- Clindamycin, oral, 450 mg 8 hourly for 5 days.

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

Eczema herpeticum B00.0
Therapy should be initiated without delay:
- Aciclovir 400 mg, oral, 8 hourly for 7 days.

LoE:III[viii]

If patient is unable to swallow due to odynophagia:

- Aciclovir,IV, 5 mg/kg/dose, 8 hourly for 7 days.
  - Infuse over 1 hour.

LoE:III[ix]

REFERRAL

Severe, non-responsive, or complicated cases or cases with uncertain diagnosis (e.g. severe infection including disseminated herpes simplex).

4.6 ERYTHEMA MULTIFORME, STEVENS JOHNSON SYNDROME, TOXIC EPIDERMAL NECROLYSIS

L51.0-2/L51.8-9

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 (SJS) and Toxic Epidermal Necrolysis (TEN)

Life-threatening acute hypersensitivity reactions with systemic upset, epidermal necrosis, and mucous membrane involvement. TEN and SJS are different ends of the same spectrum: in TEN epidermal necrosis involves >30% of body surface area, while in SJS the involvement is <10%. 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 dusky red macular rash, progressing to confluence with epidermal necrosis and large flaccid blisters which rupture, leaving large areas of denuded skin. Mucous membrane erosions are common and multi-organ involvement may be present.

This condition is usually due to medication, e.g. sulfonamides, non-nucleoside reverse transcriptase inhibitors (especially nevirapine), anti-epileptics (phenytoin, phenobarbitone, carbamazepine, lamotrigine), allopurinol, laxatives (phenolphthalein).

Complications include:
» Dehydration,electrolyte disturbances, and shock,
» hypoalbuminaemia,
» hypo- and more commonly hyperthermia,
» high output cardiac failure,
» secondary infection and sepsis, and
» adhesions and scarring.

Stop all medicines, where safely possible, including complementary, alternative, and self medication.

GENERAL MEASURES

Principles of management

Immediate in hospital evaluation

The foundation of management is supportive, good nursing, and the prevention of dehydration and sepsis.
Management is similar to that of burns.
Stop/substitute all medicines.
Patients usually require care in a high or intensive care unit with dedicated nursing.
Attempt to identify causative agent as early withdrawal of agent improves prognosis.

Monitoring

Monitor vital organ function.
Examine daily for infection and swab infected lesions. Do blood cultures if fever persists or suspicion of infection.

Dressings

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

Do not use silver sulfadiazine if SJS/TEN is thought to be due to cotrimoxazole or other sulfonamides.

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 (see section 18.9: Dry eye) 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 to treat significant dehydration.
Encourage oral fluids to prevent pharyngeal adhesions.
Provide soft, lukewarm food. Restrict nasogastric feeds to those patients that are unable to eat, as they may lead to additional trauma with bleeding, secondary infection, and adhesions.

Note: All patients should receive a notification bracelet/necklace on discharge.

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. They should not be administered routinely, nor be given prophylactically. Organisms identified on skin swabs are not a good indicator of systemic infection.

Analgesia

Appropriate and adequate analgesia for the pain associated with dressing changes, given at least half an hour before dressing change (See section 12.4.1: Perioperative analgesics).

REFERRAL/CONSULTATION

Discuss with a specialist, if considering re-initiation of medicine treatment.
Where there is ocular involvement, consult a specialist immediately.

4.7 LEG ULCERS, COMPLICATED

L97

DESCRIPTION

A chronic relapsing disorder of the lower limbs. 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 venous 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 elevation and compression bandages or stockings 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
» 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.

Dressed frequently with:

- Moistened dressing e.g. gauze with sodium chloride 0.9%.

LoE:I[x]

For exudative, infected wounds:

- Povidone-iodine 5% cream, topical apply daily.

4.8 PSORIASIS

L40.0-5/L40.8-9

DESCRIPTION

This is an inflammatory condition of the skin and joints of unknown aetiology. Scaly red, papules and plaques over extensor surfaces and on 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

Note:

» Systemic steroids should be avoided.

» Patient adherence is the greatest barrier to treatment success with topical therapies.

Local plaques

For maintenance:

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

For flares:

- Potent topical corticosteroids, e.g.: *LoE:III*[xi]
- Betamethasone 0.1%, topical, apply 12 hourly.
  - Decrease according to severity, reduce to hydrocortisone 1%, then stop.

Scalp psoriasis

For maintenance:

- Wash with coal tar containing shampoo.

OR

Coal tar 1% ointment, topical, apply at night, under occlusion and wash out the next morning.

For flares:

- Potent topical corticosteroids, e.g.: *LoE:III*[xii]
- Betamethasone 0.1% lotion, topical, apply once daily.

REFERRAL

» Indequate response to topical treatment.
» Severe disease, especially if joint involvement.

4.9 URTICARIA

L50.0-6/L50.8-9

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 bites are often grouped, show a central bite mark, are on exposed areas of the body, and are often associated excoriations, vesicles, pigmentary changes, and secondary infection.

GENERAL MEASURES

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

MEDICINE TREATMENT

Antihistamines

Regular use is recommended until the urticaria is quiescent.

For chronic urticaria less sedating antihistamines are preferable:

- Cetirizine, oral, 10 mg daily.

Avoid oral corticosteroids.

REFERRAL

All patients with urticarial lesions where the individual lesions remain for longer than 48 hours to a specialist to exclude urticarial vasculitis.

4.9.1 PAPULAR URTICARIA

L50.8

DESCRIPTION

Papular urticaria is a hypersensitivity disorder to insect bites, resulting in recurrent and sometimes chronic itchy papules 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, and malnutrition.

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:

- Potent topical corticosteroids, e.g.: *LoE:III*[xiii]
- Betamethasone 0.1%, topical apply daily for 5 days.

For relief of itch and sedation:

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

REFERRAL

Non-responsive and chronic cases.

4.10 FUNGAL INFECTIONS

B35.0-6/B35.8-9/B36.0-3/B36.8-9/B40.3/B45.2/B46.3

DESCRIPTION

The skin may be infected by fungi and the clinical presentation varies with organism, body site infected, and the body's response to the infection.

GENERAL MEASURES

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

MEDICINE TREATMENT

Yeast and dermatophytes (fungal infection of the skin):

- Imidazole, e.g.:
- Clotrimazole 1%, topical, apply 8 hourly until clear of disease (i.e. for at least 2 weeks after the lesions have cleared).

Pityriasis versicolor: B36.0

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

Systemic antifungal therapy

Topical treatment is generally ineffective for dermatophyte hair and nail infections.
Systemic therapy may be indicated for immunocompromised individuals with extensive skin infection
Recurrent infections are not uncommon if repeat exposure is not prevented.

- Fluconazole, oral, 200 mg weekly for 6 weeks.
  - For onychomycosis, 200 mg weekly for 6 months.

LoE:I[xiv]

REFERRAL

» Non-responsive 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

Patients with anogenital warts are at an increased risk of other STIs.
Anogenital warts:
» Pap smear should be done in women.
» Screen for other STIs.

MEDICINE TREATMENT

Cutaneous warts

Treatment seldom indicated.

Anogenital warts

- Podophyllotoxin 0.5% solution.
  - Apply 12 hourly for 3 consecutive days until lesions disappear (patient application).
  - Apply petroleum jelly to surrounding skin and mucous membrane for protection.
  - Treatment may be repeated at weekly intervals if necessary for a total of four 3-day treatment courses.

OR

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

Note: *LoE:II*[xv]

» Podophyllin is a cytotoxic agent.
» Avoid systemic absorption.
» Contraindicated in pregnancy.

REFERRAL

Extensive or recurrent anogenital warts.

4.11.2 SHINGLES (HERPES ZOSTER)

See section 9.11: Zoster (shingles).

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CHAPTER 5
GYNAECOLOGY

5.1 DYSMENORRHOEA

N94.4-6

DESCRIPTION

Lower abdominal pain that starts with the onset of menstruation and subsides after menses have ended. This may be associated with headaches, nausea and vomiting. It may be primary or secondary. Primary dysmenorrhoea is menstrual pain without organic disease. Secondary dysmenorrhoea is associated with identifiable disease, e.g. chronic pelvic infection, fibroids, endometriosis, adenomyosis and use of intrauterine contraceptive device.

GENERAL MEASURES

For secondary dysmenorrhoea, investigate and treat the underlying condition.

MEDICINE TREATMENT

Symptomatic relief:

- NSAID, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with or after a meal.

OR *LoE:III*[i]

- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

LoE:III

For dysmenorrhoea caused by endometriosis:

ADD

- Combined oral contraceptive and review after 3 months.

OR *LoE:I*[ii]

Medroxyprogesterone acetate (long-acting), IM, 150 mg, 12 weekly.

- Review after 3 months. *LoE:II*[iii]

REFERRAL

» If there is uncertainty about the diagnosis.
» Young women with pain not responding to conventional treatment.
» Older (>40 years of age) women with persistent pain.

5.2 UTERINE BLEEDING, ABNORMAL (AUB)

N92.0–1

GENERAL MEASURES

All women >45 years of age with AUB should have a transvaginal ultrasound and endometrial sampling to exclude pathology.

Actively exclude organic causes, e.g. fibroids, for abnormal uterine bleeding. All women should receive a speculum examination to rule out cervical pathology. A cervical cytology smear should be performed if the cervix appears abnormal or if indicated according to the national screening program.

MEDICINE TREATMENT

Dysfunctional uterine bleeding implies that no organic cause is present.

Arrest of acute haemorrhage

Progestin, e.g.:

- Norethisterone, oral, 5 mg 4 hourly until bleeding stops up to a maximum 48 hours. *LoE:III*[iv]

OR

Tranexamic acid, oral, 1g 6 hourly on days 1–4 of the cycle. *LoE:I*[v]

<u>After bleeding has stopped, continue with:</u>

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

For restoring cyclicity N92.6

<u>For women in the reproductive years:</u> (Z30.2)

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

OR

<u>Alternative to combined oral contraceptives:</u>

Progestin only: (Z30.2)

- Medroxyprogesterone acetate, oral, 30 mg daily from day 5 to day 26 of the cycle. *LoE:III*[vi]
  - 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.

OR

- NSAID, oral: e.g.
- Ibuprofen, oral, 400 mg 8 hourly with or after a meal. *LoE:I*[vii]
  - Begin trial of NSAID starting on 1st day of menses until menses cease.

OR

- Tranexamic acid, oral, 1 g 6 hourly on days 1–4 of the cycle. *LoE:I*[viii]

<u>For perimenopausal women, hormone therapy (HT):</u> N92.4

- Conjugated estrogens, 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:

- NSAID, oral: e.g.
- Ibuprofen, oral, 400 mg 8 hourly for 2–3 days with or after a meal, depending on severity of pain.

REFERRAL

Treatment failure - refer for consideration of levonorgestrel intrauterine system or surgical procedures as dictated by the diagnosis.

5.3 PELVIC INFLAMMATORY DISEASE (PID)

N73.0-1/N73.9

DESCRIPTION

PID includes salpingitis with or without oophoritis 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 I, 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.
Admission for parenteral therapy, observation, further investigation and/or possible surgical intervention should also be considered in the following situations:

» a surgical emergency cannot be excluded
» lack of response to oral therapy
» clinically severe disease
» presence of a tubo-ovarian abscess
» intolerance to oral therapy
» pregnancy

Further Investigation
All sexually active patients should be offered:
» a pregnancy test
» screening for sexually transmitted infections including HIV
Perform a pregnancy test, as an ectopic pregnancy forms part of the differential diagnosis.
Note: Remove IUCDs and provide alternative contraception.

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
» there is a large or symptomatic pelvic mass after 6 weeks.

MEDICINE TREATMENT

Stage I

- Azithromycin, oral, 1 g as a single dose

AND *LoE:II[ix]*

- Ceftriaxone, IM, 250 mg as a single dose.
  - Dissolve ceftriaxone, IM, 250 mg in 0.9 mL lidocaine 1% without adrenaline (epinephrine).

AND *LoE:III[x]*

- Metronidazole, oral, 400 mg 12 hourly for 7 days.

LoE:III[xi]

Severe penicillin allergy: (Z88.0)

- Azithromycin, oral, 2 g as a single dose

AND *LoE:I[xii]*

- Metronidazole, oral, 400 mg 12 hourly for 7 days.

Stage II–IV

- Ceftriaxone, IV, 1 g daily

AND

- Metronidazole, IV, 500 mg 8 hourly.

Continue intravenous therapy until there is definite clinical improvement (within 24-48 hours). Thereafter, change to:

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

AND *LoE:III[xiii]*

To treat chlamydia: A56.1+(N74.4*)

- Azithromycin, oral, 1 g, as a single dose.

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

Severe penicillin allergy: (Z88.0)

- Clindamycin, IV, 600 mg 8 hourly.

AND

- Gentamicin, IV, 6 mg/kg daily (see Appendix II for guidance on prescribing).

Continue intravenous therapy until there is definite clinical improvement (within 24-48 hours). Thereafter, change to:

- Clindamycin, oral, 450 mg 8 hourly.

AND

- Ciprofloxacin, oral, 500 mg 12 hourly to complete 10 days therapy.

To treat chlamydia: A56.1+(N74.4*) *LoE:III*[xiv]

- Azithromycin, oral, 1 g, as a single dose.

Note: The addition of metronidazole to clindamycin is unnecessary as clindamycin has adequate anaerobic cover.

REFERRAL

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

5.4 ENDOMETRIOSIS

N80.0-5/N80.6/N80.9

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.

MEDICINE TREATMENT

For pain:

- NSAID, oral: e.g.
- Ibuprofen, oral, 400 mg 8 hourly with or after a meal. *LoE:III*

AND

- 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

N91.0-2

DESCRIPTION

Primary amenorrhoea: no menstruation by 16 years of age in the presence of secondary sexual characteristics.
Secondary amenorrhoea: amenorrhoea for at least 3 months in women with previous regular menses, or for at least 6 months in women with irregular cycles.

Investigations

» Body mass index.
» Urine pregnancy test.
» Pelvic ultrasound.
» Serum for TSH, FSH, LH, prolactin.
  – FSH>15 units/L in a woman <40 years of age 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.

Progestin challenge test:
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/E25.0/E25.9

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.
Refer 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.

Investigations

» Partner semen analysis.
» Anti-mullerian hormone (AMH) levels to evaluate ovarian reserve (**>**1.1 ng/ml suggests good ovarian reserve)
» If AMH is unavailable - Mid-luteal (day 21) progesterone assay: >30 nmol/L suggests adequate ovulation.
» Laparoscopy and/or hysterosalpingography (Specialist supervision).

MEDICINE TREATMENT

Treat the underlying disease.

<u>For induction of ovulation:</u>

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

Note: Women should be counseled on the risk of multiple births with medicines inducing ovulation.

LoE:I[xv]

<u>For hyperprolactinaemia after further investigation:</u>
See section 8.15.1: Prolactinoma.

REFERRAL

Three cycles of clomifene not resulting in a pregnancy.

5.8 MISCARRIAGE

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 DEATH

O02.1

GENERAL MEASURES

Counselling.
Evacuation of the uterus.

MEDICINE TREATMENT

Before MVA, to ripen the cervix:

- Misoprostol, PV, 400 mcg as a single dose.

Medical evacuation: (004.9)

- 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: (004.9)

- Misoprostol, PV, 800 mcg every 3 hours for 2 doses.
  - Repeat after 24 hours if necessary.

OR

- Misoprostol, SL, 600 mcg every 3 hours for 2 doses *LoE:III*[xvi]
  - Repeat after 24 hours if necessary.

5.8.3 MIDTRIMESTER MISCARRIAGE (FROM 13–22 WEEKS GESTATION)

O03.4/O.03.9

GENERAL MEASURES

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

MEDICINE TREATMENT

If no cervical dilatation:

- Misoprostol, PV/SL/buccal, 200 mcg every 4–6 hours until expulsion of the products of conception.

- Duration of treatment must not exceed 5 doses over 24 hours.

LoE:III[xvii]

Previous Caesarean delivery:

- Misoprostol, PV/SL/buccal 100 mcg every 4–6 hours until expulsion of the products of conception.
  - Duration of treatment must not exceed 5 doses over 24 hours.

LoE:II[xviii]

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, to a maximum dose of 10 mg (See Appendix II, for individual dosing and monitoring for response and toxicity).

If Rh-negative: (O36.0)

- Anti-D immunoglobulin, IM, 100 mcg as a single dose.

REFERRAL

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

5.8.4 SEPTIC MISCARRIAGE

O03.0/O08.0 + (A41.9/N71.0/R57.2)

GENERAL MEASURES

Counselling.
Urgent evacuation of uterus (under general anaesthesia and not a MVA) 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

- Amoxicillin/clavulanic acid, IV, 1.2 g, 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.

LoE:III

Severe penicillin allergy: (Z88.0)

- Clindamycin, IV, 600 mg 8 hourly.

AND

- Gentamicin, IV, 6 mg/kg daily (see Appendix II for guidance on prescribing).

Change to oral treatment after improvement:

- Clindamycin, oral, 450 mg 8 hourly for 5 days.

AND

- Ciprofloxacin, oral, 500 mg 12 hourly for 5 days.

Note: The addition of metronidazole to clindamycin is unnecessary as clindamycin has adequate anaerobic cover.

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')

O01.9

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)

Early ultrasound examination is more accurate than last normal menstrual period at determining gestational age, and also of value in identifying ectopic pregnancy, molar pregnancy or twins.

The legal criteria for TOP follow below. The clinical management for pregnancies up to 14 weeks is the same (outpatient procedures). From 14 weeks onwards, TOP should be done in a medical facility. Note that the gestational ages used for clinical management differs from the legal cut-offs, e.g. a patient at 12 weeks and 1 day will meet the legal requirements as described in the act for TOP after 12 weeks, but the clinical management is the same as for a pregnancy from day one up to 14 weeks (see below).

Summary of Choice of Termination of Pregnancy Act
Women eligibility

Up to 12 weeks and 0 days: On request.

From the thirteenth week (12 weeks and 1 day) up to the twentieth week (19 weeks and 6 days): 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 (≥ 20 weeks 1 day): Doctor and second doctor or registered midwives are satisfied that there is danger to the mother's life, a lethal or severe fetal malformation or fetal death.

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

Practitioner
Up to 12 weeks and 0 days: Doctor, midwife or registered nurse with appropriate training.

From the thirteenth week (12 weeks and 1 day) up to the twentieth week (19 weeks and 6 days): Doctor responsible for decision and prescription of medication; registered nurse/midwife may administer medication according to prescription.

» Pre-and post-termination counselling and contraceptive 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.

5.9.1 TOP: MANAGEMENT OF PREGNANCIES ≤14 WEEKS OF GESTATION

O04.9

GENERAL MEASURES

Counselling.
Outpatient procedure by nursing staff with specific training.
Discuss TOP options with patient: Manual vacuum aspiration of the uterus or medical TOP. *LoE:III*[xix]

MEDICINE TREATMENT

Manual vacuum aspiration:

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

Routine analgesia for vacuum aspiration:

- Morphine, IM, 0.1 mg/kg 30 minutes before aspiration procedure, to a maximum of 10 mg. *LoE:III*[xx]

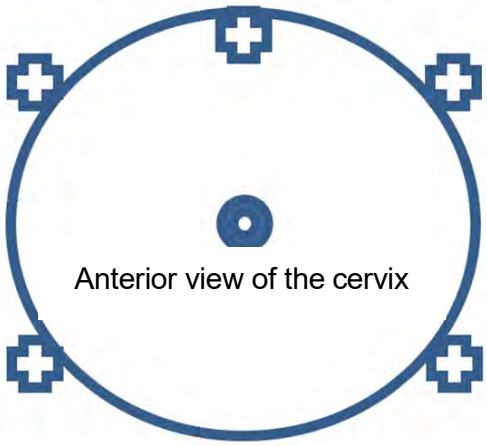
Do not give intravenous benzodiazepines and parenteral opioid analgesics concurrently.

Conscious sedation - see chapter 23: Sedation.

Alternatively, consider a paracervical block:

- Use Lidocaine 1%.
  - Draw up lidocaine 1% in a 20 mL syringe.
  - Attach a 20-gauge spinal needle. Inject 2 mL superficially in the cervix at 12h00 and immediately grab the cervix with a tenaculum at 12h00 to stabilise cervix.
  - Inject remaining 18 mL slowly over 60 seconds into the cervicovaginal junction in four equal doses of 4–5mL at 2, 4, 8, and 10 o'clock (see diagram below).
  - This injection is continuous from superficial to deep (a depth of 3 cm) and again to superficial (injecting with insertion and withdrawal).
  - Manual vacuum aspiration can start after 3 minutes.

Right



Left

LoE:I[xxi]

Oral analgesia as required for 48 hours:

- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

AND

- NSAID, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with or after a meal.

Medical TOP:

Up to 12 weeks and 0 days:

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

LoE:I[xxii]

Followed 1-2 days later by:

- Misoprostol, PV/SL 800 mcg or buccal by self-administration
  - If expulsion has not occurred 4 hours after misoprostol administration, a second dose of misoprostol 400 mcg may be given.

Note: Bleeding may persist for up to 1 week. If there is no bleeding after the second dose of misoprostol, the woman must return to the facility as soon as possible as there is a possibility of an incomplete procedure or ectopic pregnancy.

LoE:III[xxiii]

For pain:

- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

ADD

After expulsion is complete:

- NSAID, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with or after a meal.

5.9.2 TOP: FROM THE THIRTEENTH WEEK (12 WEEKS AND 1 DAY) UP TO THE TWENTIETH WEEK (19 WEEKS AND 6 DAYS)

O04.9

Medical TOP: From 12 weeks onwards, inpatient care in facilities with 24-hour service and facilities for general anaesthesia, as there is a greater risk for bleeding or a need for surgical completion of the procedure.

LoE:III[xxiv]

Manual vacuum aspiration (up to 14 weeks). Misoprostol 400 mcg administered sublingually or vaginally, 2 to 3 hours prior to the procedure for cervical priming.

Surgical TOP (Dilatation and Evacuation procedure after cervical preparation) can be done by specially trained providers as a day theatre procedure after 14 weeks.

GENERAL MEASURES

Manual vacuum aspiration of the uterus, if expulsion of products of conception is not complete after medical termination.

MEDICINE TREATMENT for Medical TOP

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

LoE:I[xxv]

Follow 1-2 days later with:

- Misoprostol, PV/SL/buccal, 400 mcg, every 3 hours until abortion occurs.

LoEII[xxvi]

LoE:III[xxvii]

Analgesia:

- Morphine, IM, 0.1 mg/kg 4 hourly as needed, to a maximum of 10 mg.

If Rh-negative: O36.0

- Anti-D immunoglobulin, IM, 100 mcg as a single dose.

Contraception:

Counsel all women on effective contraception, especially long-acting reversible methods.

All methods can be given at the time of the procedure, with the exception of the IUCD at a medical TOP.

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

5.10 SEXUAL ASSAULT
T74.2 + (Y05.99)

INVESTIGATIONS
Urine pregnancy test.
Blood for:
» Syphilis serology,
» 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: (Z29.8)
- Levonorgestrel 1.5 mg, oral, preferably within 24 hours of event.

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

LoE:I[xxviii]

CAUTION
Emergency contraceptive tablets must be taken as soon as possible, preferably within 72 hours of unprotected intercourse, and not later than 5 days.
Enzyme inducers (including efavirenz, carbamazepine) cause a significant reduction in LNG concentrations. Women on these medicines should preferably have copper IUCD EC inserted or alternatively double the dose of levonorgestrel, because of significant reduction of LNG EC.
Women >80 kg or BMI ≥30 should be given twice the standard dose.

OR

LoE:III[xxix]

- Copper IUCD, e.g.:
- Cu T 380A, within 5 days of unprotected intercourse.

LoE:I[xxx]

An anti-emetic: (Z29.8)
- Metoclopramide oral, 10 mg 8 hourly as needed.

LoE:III

STI prophylaxis (Z29.8)

- Ceftriaxone, IM, 250 mg as a single dose.
  - For ceftriaxone IM injection: Dissolve ceftriaxone 250 mg in 0.9 mL lidocaine1% without adrenaline (epinephrine).

AND

- Azithromycin, oral, 1 g, as a single dose. *LoE:III*[xxxi]

AND

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

HIV post-exposure prophylaxis (PEP) (Z20.6+Z29.8)
See section10.4.2: Non-occupational post exposure prophylaxis, sexual assault and inadvertent exposure.

5.11 URINARY INCONTINENCE

DESCRIPTION

The involuntary leak of urine. Occurs in 10-17% of all women.

Risk factors include: Age (prevalence and severity increase with age), increased parity, obesity, smoking, caffeine intake, diabetes and menopausal vaginal atrophy.

Most common types are stress incontinence, urgency incontinence (overactive bladder) or a mixed incontinence (features of both stress and urgency).

5.11.1 STRESS INCONTINENCE

N39.3

DESCRIPTION

Incontinence that occurs with increased abdominal pressure (e.g. cough, sneeze or laugh) in the absence of a bladder contraction.

GENERAL MEASURES

Exclude urinary tract infection or diabetes.
Pelvic examination to exclude pelvic masses, pelvic organ prolapse or menopausal vaginal atrophy.
Stop smoking.
Manage obesity.
Reduce or avoid caffeine.
Reduce alcohol intake
Manage constipation and avoid excessive fluid intake.
Keep a bladder diary.
Pelvic floor exercises (see section 7.3.6: Overactive bladder).

MEDICINE TREATMENT

There are no pharmacological interventions to manage stress incontinence.

REFERRAL

» If any pelvic pathology, immediate referral to specialist
» If no underlying pathology, refer for bladder stress testing if no improvement with conservative measures after 3-6 months.

5.11.2 URGENCY INCONTINENCE (OVERACTIVE BLADDER)

See section: 7.3.6: Overactive bladder.

5.12 MENOPAUSE AND PERIMENOPAUSAL SYNDROME

N95.9

GENERAL MEASURES

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

MEDICINE TREATMENT

Hormone therapy (HT)

Not indicated in all postmenopausal women. Women with significant menopausal symptoms and those with osteoporosis risk factors will benefit most.
The benefits of HT need to be weighed against the potential harm (e.g. breast cancer, venous thrombo-embolism).
Long-term follow up studies from the Women's Health Initiative Randomised Trials have shown that hormone replacement therapy in post-menopausal women was not associated with an increased risk of all-cause, cardiovascular or cancer mortality. However, long-term use of hormone therapy has safety issues and stopping treatment will result in return of menopausal symptoms.

LoE:III[xxxii]

Note: Contraindications to HT:
» Current, past or suspected breast cancer.
» Known or suspected oestrogen-dependent malignant tumours.
» Undiagnosed genital bleeding.
» Untreated endometrial hyperplasia.
» Previous idiopathic or current venous thrombo-embolism.
» Known arterial CHD.
» Active liver disease.
» Porphyria.
» Thrombophilia.

Intact uterus (no hysterectomy)

HT 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.

CONTINUOUS COMBINED THERAPY
• Estradiol/norethisterone acetate, oral, 1 mg/0.5 mg for 28 days.
OR
• Estradiol/norethisterone acetate, oral, 2 mg/1 mg for 28 days.
OR
• Conjugated estrogens, oral, 0.3–0.625 mg for 28 days. **AND** • Medroxyprogesterone acetate, oral, 2.5–5 mg daily for 28 days.

OR

SEQUENTIALLY OPPOSED THERAPY
Estradiol valerate/cyproterone acetate, oral: • Estradiol valerate, oral, 1–2 mg for 11 days. • Estradiol valerate/cyproterone acetate, 1–2 mg/1 mg for 10 days. • Placebo, oral, for 7 days.
OR
• Estradiol valerate, oral, 1–2 mg daily for 21 days. **ADD** • Medroxyprogesterone acetate, oral, 5–10 mg daily from day 12–21. o Followed by no therapy from day 22–28.
OR
• Conjugated oestrogens, oral, 0.3–0.625 mg daily for 21 days. **ADD** • Medroxyprogesterone acetate, oral, 5–10 mg daily from day 12–21. o Followed by no therapy from day 22–28.

Note:

» Start at the lowest possible dose to alleviate symptoms. The need to continue HT should be reviewed annually. Abnormal vaginal bleeding requires specialist consultation/referral.

» Any unexpected vaginal bleeding is an indication for excluding endometrial carcinoma. The use of transvaginal ultrasound to measure endometrial thickness plus the taking of an endometrial biopsy is recommended.

Uterus absent (post hysterectomy): (Z90.7)

HT is given as estrogen only:

- 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.

HT is contra-indicated, poorly tolerated or ineffective:

- Fluoxetine, oral *LoE:III*[xxxiii]
  - o Initiate at 20 mg on alternate days.
  - o If there is no response after 12 weeks, increase the dose to 20 mg daily.

If on tamoxifen: LoE:III[xxxiv]

- Citalopram, oral, 10 mg daily.
  - If there is no response after 12 weeks, increase the dose to 20 mg daily.

Note:
Start at the lowest possible dose to alleviate symptoms. The need to continue therapy should be reviewed annually.

REFERRAL
» Premature menopause, i.e. <40 years of age.
» Severe osteoporosis.
» Post-menopausal bleeding.
» Hormone-dependent cancers, thrombo-embolism, liver disease; and unacceptable side-effects to hormone replacement therapy e.g. exacerbation of depression, enlargement of uterine fibroids, exacerbation of endometrioses (see section 5.4: Endometriosis).

5.13 MEDICAL MANAGEMENT OF ECTOPIC PREGNANCY

O0.0-2/O0.8-9

GENERAL MEASURES

Ruptured or suspected rupture of an ectopic pregnancy should be managed with urgent resuscitation and surgery.
There must be certainty that there is no viable intra-uterine pregnancy.
If the initial β-hCG level is below the discriminatory zone (<1500 IU/L) to diagnose a pregnancy on ultrasound, and transvaginal ultrasound cannot definitively identify an intrauterine or extra-uterine gestation, then serial β-hCG measurements are necessary to document either a growing, potentially viable, or a nonviable pregnancy.
Repeat the β-hCG in 48 hours. If the level has dropped, conservative management may be appropriate.
The minimum rise in β-hCG for a potentially viable pregnancy in women who present with symptoms of pain and/or vaginal bleeding is 53% every 2 days.
If the level has increased by >50% or is now above the discriminatory zone, do a repeat scan to exclude an intra-uterine pregnancy before methotrexate is administered.

LoE:III[xxxv]

MEDICINE TREATMENT

Methotrexate should be the first-line management for women who are able to return for follow-up and who have the following characteristics:
» haemodynamic stability and no significant pain
» an unruptured ectopic pregnancy with a mass <35 mm with no visible heartbeat
» low serum β-hCG, ideally less than 1500 IU/L but can be up to 5000 IU/L
» certainty that there is no intrauterine pregnancy
» willingness to attend for follow-up

There are single dose or multiple dose methotrexate protocols available. The single dose protocol is less expensive, requires less intensive monitoring and does not require folinic acid rescue. The single dose protocol is recommended for the medical management of ectopic pregnancy. *LoE:I*[xxxvi]

Protocol:
Day 1: Do urea, creatinine, AST and FBC to exclude abnormalities.
- Methotrexate, IM, 50 mg/m^2 of body surface area (BSA).
  - o BSA may be calculated based upon height and weight on the day of treatment using the formula BSA = square root ([cm X kg]/3600)

Day 4: Repeat β-hCG.
Day 7: Repeat β-hCG.
If the decrease from day 4 to day 7 is ≥15%:
» Continue with weekly β -hCG until undetectable.

If decrease <15% and patient still fulfil the criteria for medical management:
- Methotrexate, IM, 50 mg/m^2 BSA.

LoE:III[xxxvii]

Day 14: Repeat β-hCG.

REFERRAL
After two doses of methotrexate, if the decline in β-hCG is still <15% on day 14, refer for specialist care.

5.14 FAMILY PLANNING REFERRALS FROM PRIMARY CARE

5.14.1 INTRA-UTERINE CONTRACEPTIVE DEVICE
N92.1/T83.3 + (Z30.4/8/9)

GENERAL MEASURES
Where there is excessive bleeding after insertion:
» Exclude perforation of the uterus.

Abnormal bleeding for >3 months:
» Exclude cervical or pelvic infection, partial expulsion, intrauterine or ectopic pregnancy (rare) or other pathology.

If no pathology is detected:
» Counsel.

MEDICINE TREATMENT

If no pathology is detected:

- NSAID, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with or after a meal for 5 days. *LoE:I[xxxviii]*
  - Follow up and if bleeding is unacceptable, offer alternative contraception and remove IUCD.

5.14.2 IMPLANTS

Z30.4/8/9

Failure to locate an implant (in the arm) by palpation:

» Ultrasound guided removal of deep implants must be done by specially trained providers at regional hospitals.

5.14.3 INJECTABLE CONTRACEPTION

N92.1 + (Z30.4/8/9)

GENERAL MEASURES

Heavy or prolonged bleeding despite adequate treatment with combined oral contraceptives:

» Do thorough gynaecological examination to exclude other pathology.
» Check haemoglobin and prescribe iron if needed. See section 2.2 Anaemia, iron deficiency.

MEDICINE TREATMENT

- Ethinylestradiol, oral, 50 mcg daily for 3 months. *LoE:III*

OR

Combined oral contraceptive, containing 50 mcg ethinylestradiol, oral, for 3 months.

If no response to high dose ethinylestradiol, replace with:

- NSAID, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with or after a meal for 5 days. *LoE:III[xxxix]*

If no response to NSAID, replace with:

- Tranexamic acid, oral, 500 mg 8 hourly for 4 days. *LoE:I[xl]*

If there is no response to above-mentioned treatment:

» Change to another method of contraception. See Primary Health Care Standard Treatment Guidelines - Chapter 7: Family planning.

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CHAPTER 6
OBSTETRICS

Note: For medical complications during 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 + (D50.9/D64.9)

DESCRIPTION

Haemoglobin (Hb) <11 g/dL. Anaemia in pregnancy is most commonly due to iron deficiency. Hb levels in pregnancy should be routinely checked on-site at the first antenatal visit, and again at 30 weeks and 38 weeks. If Hb falls below 10g/dL, commence treatment with iron and do a FBC.

LoE:III[i]

GENERAL MEASURES

A balanced diet to prevent nutritional deficiency.
Advise against eating soil, clay, charcoal, and excessive consumption of tea and coffee.

MEDICINE TREATMENT

Prophylaxis Z34.9 + (Z29.9)

- Ferrous sulfate compound BPC (dried), oral, 170 mg (± 55 mg elemental iron) daily.

OR

LoE:III[ii]

Ferrous fumarate, oral, 200 mg (± 65 mg elemental iron) daily.

(For folic acid supplementation guidance to prevent neural tube defects, see Primary Health Care STGs and EML, section 6.4.1: Antenatal supplements).

Iron deficiency (Hb <10g/dL)

- Ferrous sulfate compound BPC, oral (dried), 170 mg (± 55 mg elemental iron) 12 hourly.

OR

LoE:I[iii]

Ferrous fumarate, oral, 200 mg (± 65 mg elemental iron) 12 hourly.

LoE:III[iv]

- 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.
- When using iron together with calcium supplementation, ensure that iron and calcium are taken at least 4 hours apart from one another.
- If Hb has not increased after 4 weeks of therapy, do a FBC to confirm hypochromic microcytic anaemia.

Parenteral iron - See section: 2.1.1 Anaemia, iron deficiency.
If there is no response to oral iron, and iron deficiency is confirmed, review adherence to oral iron, and consider:

- Iron, IV, e.g.:
- Iron sucrose, IV, 200 mg in 200 mL sodium chloride 0.9%, over 30 minutes, given on alternate days until the total dose has been given.
  - **Note:** Test dose is not required, but only administer where personnel and therapies are readily available to manage anaphylactic-type reactions.
  - An initial total dose of 600 mg is usually adequate to raise the Hb to acceptable levels.
  - For markedly anaemic or very obese women, consult the package insert on the total dose of iron infusion.

LoE:III

REFERRAL/CONSULTATION

No response to management.

6.2 DIABETES MELLITUS IN PREGNANCY

O24.0-4/O24.9
This condition should ideally be managed in consultation with a specialist.

DESCRIPTION

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

Diagnostic criteria for GDM
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.

The following women should be screened for GDM, between 24 and 28 weeks of gestation:

» Women of Indian ethnic origin.
» BMI >35kg/m^2.
» Age >40 years of age.
» GDM in previous pregnancy.
» Family history (first degree relative) of diabetes.
» Previous unexplained third trimester fetal death.
» Previous baby with birthweight >4 kg.
» Polyhydramnios in index pregnancy.
» Glycosuria (≥1+ glucose in urine).
» A fetus that is large for gestational age.

GENERAL MEASURES

» Stop smoking.

» Moderate exercise.
» Dietary advice.

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 mild type 2 diabetes.

Even with careful selection, approximately half of patients will require addition of insulin for adequate glucose control. *LoE:I[v]*

- 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 capillary glucose profiles, i.e. pre-prandial and 1-hour and 2-hour post-prandial for breakfast, lunch and supper.

Aim for:

» preprandial values <5.3 mmol/L
» 1-hour postprandial <7.8 mmol/L
» 2-hour postprandial <6.4 mmol/L

LoE:I[vi]

Abnormal profiles

Diabetic women should be admitted for poor glucose control, despite metformin therapy.

Start insulin.

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

Preferred insulin regimen

- Insulin, short-acting with all 3 meals to maintain the postprandial levels.

AND

- Insulin, intermediate-acting at bedtime (with a bedtime snack) to maintain preprandial levels.

Insulin dosing:

  - Total daily dose: 0.5 units/kg/day.
  - One third of the total dose: intermediate acting insulin at bedtime.
  - The remaining two thirds divided into three equal doses are given before each meal (breakfast, lunch and supper).

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.

- Insulin, biphasic.
  - Daily dose: 0.5 units/kg/day, two thirds, 30 minutes before breakfast and one third 30 minutes before supper.
  - Titrate to achieve target blood glucose as above. *LoE:I*[vii]

Delivery
Consider induction of labour at 38 weeks gestation, provided glucose control is adequate, or earlier with maternal co-morbid conditions, or if glycaemic control is poor. If the estimated fetal weight (EFW) on ultrasound is >4 kg, offer elective Caesarean delivery.

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 >7 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 pre-pregnancy insulin or oral hypoglycaemic regimen once eating a full diet.

The newborn is at risk of:

» hypoglycaemia
» respiratory distress syndrome
» hyperbilirubinaemia
» congenital abnormalities

Postpartum management
Contraception Z30.0 + (O24.3-4/O24.9)
Tubal ligation should be considered.
Consider:

- Low-dose combined contraceptive in well-controlled cases.
- Progestin-only preparation **or** intra-uterine contraceptive device if planning to breastfeed.

See Primary Health Care chapter 7: Family planning.

Need for ongoing anti-diabetic therapy
Offer women diagnosed with GDM during the index pregnancy an oral glucose tolerance test after 6 weeks postpartum to assess whether they have diabetes needing ongoing therapy.

REFERRAL/CONSULTATION

» Obese women.
» Excessive fetal growth despite adequate diabetes control.
» Poor glucose control despite adequate insulin.

6.3 HEART DISEASE IN PREGNANCY

O99.4 + (S151.9)

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

All pregnant women with haemodynamically significant heart disease require multidisciplinary management in consultation with both obstetrician and physician/cardiologist.

Consider thyrotoxicosis, anaemia and infection, which may precipitate cardiac failure.

Spontaneous delivery is usually preferable to Caesarean delivery, unless there are obstetric reasons for surgery.

Women with prosthetic heart valves should be counselled about the risks of pregnancy to themselves and fetus; and offered effective contraception.

During labour:

» Nurse in semi-Fowler's position.
» Avoid unnecessary intravenous fluids.
» Give adequate analgesia.
» Antibiotic prophylaxis for infective endocarditis, guided by the nature of the heart lesion (for cardiac indications and antibiotic recommendations see section 3.5: Endocarditis, Infective). Procedures for which endocarditis prophylaxis <u>is indicated</u> include:
  – Vaginal delivery in the presence of suspected infection.
  – Caesarean delivery.
  – Assisted vaginal delivery.
  – Prelabour rupture of membranes.
» Avoid a prolonged second stage of labour by means of assisted delivery with forceps (preferably) or ventouse.
» Avoid ergometrine after delivery of the newborn.
» Observe in a high care area for 24 hours post-delivery, as the risk of pulmonary oedema is highest in this period.

Contraception, including the option of tubal ligation should be discussed during the antenatal period and after delivery in all women with significant heart disease.

Women who had life-threatening complications during pregnancy should be advised not to become pregnant again.

<u>Anticoagulation during pregnancy:</u>

Indications for full anticoagulation during pregnancy (high risk):

» *Valvular disease with atrial fibrillation*: Women with valvular heart disease should be guided to consider completing their family early and then consider

family planning including tubal ligation, before progressing to requiring mechanical valves.

» *Mechanical prosthetic heart valves:* Women with mechanical prosthetic heart valves should be offered contraception (preferably a LARC not containing estrogen); see PHC STGs and EML, chapter 7: Family planning. If they conceive, offer the option of TOP or refer to tertiary centre for anticoagulation management by a multi-disciplinary team.

MEDICINE TREATMENT

For pregnant women with valvular disease and atrial fibrillation:

First trimester

- Enoxaparin SC, 1 mg/kg 12 hourly.

OR

- 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 PTT 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 until 36 weeks

- Warfarin, oral, 5 mg daily.
  - Adjust dose to keep INR within the therapeutic range of 2–3.

After 36 weeks until delivery

- Enoxaparin SC, 1 mg/kg 12 hourly.

OR

- 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.

Delivery

Stop heparin on the morning of elective Caesarean delivery (6 hours before scheduled surgery) or when in established labour, and re-start 6 hours after vaginal delivery or 12 hours after Caesarean delivery, as long as there is no concern that the patient is bleeding.

Secondary prophylaxis for venous thromboembolism Z29.9

» More than one previous episode of venous thromboembolism.

» One previous episode without a predisposing factor, or evidence of thrombophilia.

- Low molecular weight heparin, e.g.:

- Enoxaparin, SC, 40 mg daily. *LoE:I[viii]*

OR

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

LoE:I[ix]

Cardiac failure O99.4 + (I50.9)

See section 3.4: Congestive Cardiac Failure.

Treatment is as for non-pregnant women, except that **ACE-inhibitors, ARBs and spironolactone are contra-indicated.** *LoE:III[x]*

If a vasodilator is needed:

- Hydralazine, oral, 25 mg 8 hourly.
  - Maximum dose: 200 mg daily.

AND

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

Delivery O99.4 + (I50.0)

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.

REFERRAL

» All pregnant women with mechanical prosthetic heart valves requiring anticoagulation.

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

6.4 HYPERTENSIVE DISORDERS IN PREGNANCY

O10.0/O11/O14.0-2/O14.9

DESCRIPTION

Hypertensive disorders are one of the most common direct causes of maternal mortality and are responsible for significant perinatal and maternal morbidity. These disorders include chronic hypertension, pre-eclampsia, eclampsia and HELLP Syndrome. Early detection and timely intervention is essential to prevent maternal and perinatal complications.

Preeclampsia

Preeclampsia is hypertension with significant proteinuria developing for the

first time after 20 weeks of gestation, and can also be superimposed on chronic hypertension - evidenced by the new onset (after 20 weeks' gestation) of persistent proteinuria in a woman who had an initial diagnosis of chronic hypertension.

Pre-eclampsia without severe features:
A diastolic BP of 90-109 mmHg and/or systolic BP of 140-159 mmHg; but no symptoms or organ dysfunction.

Maternal features of severe disease:
» Acute severe hypertension (diastolic BP of 110 mmHg and/or systolic >160 mmHg).
» Thrombocytopenia (platelet <100 000/µL).
» Impaired liver function (ALT or AST >40 IU/L).
» Severe persistent right upper quadrant or epigastric pain.
» HELLP syndrome (platelets <100 000 and AST >70 µl and LDH >600 µl).
» Serum creatinine ≥120 micromol/L.
» Pulmonary oedema.
» New-onset severe headache unresponsive to medication.
» Visual disturbances.

GENERAL MEASURES

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

Treatment

Antihypertensives
Medicine 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 when BP >160/100 mmHg, before increasing single medication doses to a maximum.

LoE:III[xi]

- Methyldopa, oral, 250 mg 8 hourly as a starting dose.
  - Increase to a maximum of 750 mg 8 hourly, according to response.

AND/OR

LoE:III[xii]

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

Hypertensive emergency O10.0
SBP ≥160 mmHg and/or DBP ≥110 mmHg. Admit to a high-care setting for close monitoring.

- Nifedipine, oral, 10 mg.

- Repeat after 30 minutes if needed, until systolic blood pressure <160 mmHg and diastolic blood pressure <110 mmHg.
- Swallow whole. Do not chew, bite or give sublingually.

LoE:III[xiii]

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.
  - Once hypertensive crisis has been resolved, switch to an oral preparation.

LoE:I[xiv]

Delivery

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

LoE:III[xv]

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

Pre-eclamptic and eclamptic women are often 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.

Prevention of pre-eclampsia O10.0/O24.0-3/O99.1/O99.8 + (D68.6/M32.9)

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

From 6 weeks' gestation onwards, preferably before 16 weeks gestation:

- Aspirin, oral, 150 mg daily.

LoE:I[xvi]

At confirmation of pregnancy

- 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.

LoE:I[xvii]

Prevention of eclampsia

To prevent eclamptic seizures, magnesium sulfate is recommended for patients with severe features. In some cases this allows for delivery to be delayed to improve neonatal outcome. When used for prevention of eclampsia, magnesium sulfate is administered for 24 hours, and then stopped. The same dose regimens are used as for eclampsia. Women with severe features should be managed

under specialist care.

6.5 ECLAMPSIA

O11/O14.0-2/O14.9/O15.0-2/O15.9

DESCRIPTION

Generalised tonic-clonic seizures after 20 weeks of pregnancy and within 7 days after delivery associated with hypertension and proteinuria. 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.
Abort seizures with magnesium sulfate.

MEDICINE TREATMENT

If necessary:

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

Treatment

Where infusion pumps are not available:

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

Follow with:

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

In high-care setting:

- Magnesium sulfate, IV, 4 g in 200 mL sodium chloride 0.9% over 20 minutes (loading dose).

Follow with:

- Magnesium sulfate, IV infusion, 1 g every hour, until 24 hours after delivery, or after the last convulsion (maintenance dose).

STOP MAGNESIUM SULFATE IF KNEE REFLEXES BECOME 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.

Recurrent eclamptic seizure despite magnesium sulfate loading dose administration:

- Magnesium sulfate, IV, 2 g over 10 minutes.

For agitated and restless women with eclampsia:

- 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

Refer all eclampsia cases to a high or intensive care facility.

6.6 CHRONIC HYPERTENSION

O10.0-4/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 <140/90 mmHg.
Screen for end-organ damage.
Fetal surveillance by symphysis-fundus height (SFH) growth.
Ask mother about fetal movements at each antenatal visit.

Consider labour induction if:

» BP persistently ≥160/110 mmHg, or
» pregnancy of ≥38 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 and diuretics to methyldopa and/or amlodipine. Women should be advised that there is an increased risk of congenital abnormalities if ACE-inhibitors were taken during pregnancy.

6.7 HIV IN PREGNANCY

O98.7 + (Z21/B24)

Consult the most recent National Department of Health Guideline for the Prevention of Mother to Child Transmission of Communicable Infections
https://www.knowledgehub.org.za/elibrary/guideline-prevention-mother-child-transmission-communicable-infections

All pregnant women should receive routine counselling and voluntary HIV testing at their very first antenatal visit.

All women who test negative should be offered repeat HIV testing at every routine visit throughout pregnancy (8 visits in all), at labour/delivery, at the 6-week EPI visit and three monthly throughout breastfeeding.

HIV-infected pregnant women upon diagnosis, should be clinically staged, and have a blood sample taken for CD4 cell count and serum creatinine taken on the same day. The result must be obtained within a week.

Postpartum contraceptive use should be discussed in the antenatal period.

All women should be educated during the antenatal period about the benefits of exclusive breastfeeding for the first 6 months and breastfeeding with complimentary feeding from 6 months until at least 2 years after delivery (Only in circumstance where the mother has confirmed 2nd or 3rd line ART regimen failure (VL >1000 copies/mL), advise not to breastfeed and prescribe replacement feeds).

All pregnant women should have a TB symptom screen at each visit, with further TB investigations if any of the answers to the screening questions are positive. A TB geneXpert test must be done for all pregnant women with a new diagnosis of HIV disease, or known HIV positive women with a new pregnancy diagnosis.

Patients should be screened and treated for syphilis and other STIs, in line with basic antenatal care.

Initiate lifelong ART in all pregnant or breastfeeding women on the same day of diagnosis regardless of CD4 count or infant feeding practice.

Provide adequate support and counselling, particularly addressing ART adherence.

Assist women with unwanted pregnancies <20 weeks' gestation with access to TOP services.

MEDICINE TREATMENT

» Patients should receive ART at the first antenatal visit, whether newly diagnosed or known to be living with HIV but not on ART.
» Perform a baseline ALT and serum creatinine at commencement of ART.
» Tenofovir should not be used in pregnant women with a calculated creatinine clearance <60 mL/minute or a serum creatinine ≥85 micromol/L (the latter is a more sensitive measure of renal impairment in pregnancy).

» Pregnant women may be initiated on/switched to dolutegravir-containing regimen after 6 weeks gestational age. Counsel appropriately on the risk of NTDs in subsequent pregnancies and effective postpartum contraception to enable patient to make an informed choice of ART-regimen. Switching between TEE and TLD regimens with a VL <50 copies/mL in the last 6 months. See section 10.1: Antiretroviral therapy.
» Initiate antenatal supplementation (see PHC STGs and EML, section 6.4.1: Antenatal supplements), noting that calcium and DTG should not be taken together on an empty stomach, but can be taken together with food.
» Test partner for HIV and perform routine cervical cancer screening.

1st ANC visit	
Pregnant women >6 weeks gestation - not on ART, with normal renal function, **without** TB, with no desire for more children and who chooses to use DTG after understanding the risk and benefits. (DTG associated with NTDs, ≤6 weeks gestation)	• TDF, oral, 300 mg daily. **AND** • 3TC, oral, 300 mg daily. **AND** • DTG, oral, 50 mg daily. Provided as a fixed dose combination (FDC).
Pregnant women >6 weeks gestation - not on ART, with normal renal function, **with** TB, with no desire for more children and who chooses to use DTG after understanding the risk and benefits. (DTG requires boosting with TB treatment)	• TDF, oral, 300 mg daily. **AND** • 3TC, oral, 300 mg daily. **AND** • DTG, oral, 50 mg daily. Provided as a fixed dose combination (FDC). **WITH** DTG, oral 50 mg 12 hours later.
Pregnant women ≤6 weeks gestation, or planning a pregnancy after this one.	• TDF, oral, 300 mg daily. **AND** • FTC, oral, 200 mg daily. **AND** • EFV, oral, 600 mg at night. Provided as a fixed dose combination (FDC).
Pregnant woman already on TDF+3TC+DTG and understands the risk and benefits of DTG. (Document in the antiretroviral pregnancy register http://www.APRegistry.com/)	Chooses to remain on TDF+3TC+DTG: Enter in antiretroviral pregnancy register http://www.APRegistry.com/
Pregnant woman (>6 weeks gestation) already on TDF + FTC + EFV and understands the risk and benefits of DTG. Obtain consent for DTG use (Document in patient's clinical notes, sign notes and provide patient with medicine information leaflet)[xviii]	Chooses to switch to TDF+3TC+DTG: » Switch only if VL is <50 copies/mL in the last 6 months

Pregnant woman already on ART with a VL between 50-1000 copies/ml	See section 10.1: Antiretroviral Therapy
2nd ANC visit (1 week later)	
Creatinine ≤85 micromol/L	Continue ART as a FDC
Creatinine >85 micromol/L (TDF is contraindicated)	Stop FDC: TDF+FTC/3TC+EFV/DTG Replace TDF with ABC: • ABC, oral, 600 mg daily
Active psychiatric illness (EFV may be contraindicated; consult an HIV specialist and/or psychiatrist, if required) O98.7 + (Z21/B24 + 099.3 +F-ICD10 code)	Replace EFV with DTG <u>If DTG not suitable:</u> Replace EFV with LPV/r, oral, 400/100 mg 12 hourly

LoE:III[xix]

Caesarean Delivery (CD):

Provide antibiotic prophylaxis to all pregnant women, including HIV-infected pregnant women prior to surgery (See chapter 11: Surgical antibiotic prophylaxis).

Women with the following risk factors may be at higher risk of infection post Caesarean delivery:

» Advanced immunosuppression.
» Prolonged rupture of membranes (>18 hours).
» Multiple vaginal examinations during labour (>5 PVs).
» Second stage CD.

Monitor carefully and treat infection appropriately.

<u>HIV-infected pregnant women not on ART undergoing elective Caesarean delivery/or in labour:</u>

- NVP, oral, 200 mg as a single dose.

WITH

- TDF, oral, 300 mg as a single dose.

AND

- 3TC, oral, 300 mg as a single dose.

AND

- DTG, oral 50 mg as a single dose (as a FDC 4 hours before Caesarean delivery).

Followed by lifelong:

- TDF+3TC+DTG (provided as a FDC), provided the mother has been adequately counselled on the risk of NTDs in subsequent pregnancies and effective postpartum contraception.

If the mother chooses not to use effective contraception and is of child-bearing potential or has fertility intentions:

- TDF+ FTC+EFV (provided as a FDC). *LoE:III[xx]*

For management of the HIV-exposed infant, see PHC STG and EML, section 11.5.

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

6.8 SYPHILIS

O98.1

DIAGNOSTIC CRITERIA

Positive syphilis serology (RPR titre ≥1:16).

GENERAL MEASURES

Inform contact(s).

MEDICINE TREATMENT

Mother

- Benzathine benzylpenicillin (depot formulation), IM, 2.4 million units diluted in 6 mL 1% lidocaine without adrenaline (epinephrine), weekly for 3 doses.

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

Severe penicillin allergy (Z88.0)
For penicillin sensitive pregnant women: penicillin desensitisation.
(See page xxxi for detailed information).

Oral penicillin desensitisation regimen.

A: Reconstitute phenoxymethylpenicillin 250mg/ 5mL		
Step	**Medicine mg/mL**	**Amount to administer (mL)**
Strictly every 15 minutes	**B**: To make 0.5 mg/mL solution Dilute 0.5 mL of reconstituted phenoxymethylpenicillin solution in 49.5 mL water.	
1	0.5 mg/mL solution (1000 units/mL)	0.1 mL
2		0.2 mL
3		0.4 mL
4		0.8 mL
5		1.6 mL
6		3.2 mL
7		6.4 mL
	C: To make 0.5 mg/mL solution Dilute 1 mL of reconstituted phenoxymethylpenicillin solution in 9 mL water.	
8	5 mg/mL solution (10000 units/mL)	1.2 mL
9		2.4 mL
10		4.8 mL
	D: Reconstituted phenoxymethylpenicillin 250 mg/5 mL = 50 mg/mL	
11	50 mg/mL (80000 units/mL)	1.0 mL
12		2.0 mL
13		4.0 mL
14		8.0 mL

After step 14, observe for 30 minutes, then 1.0 g IV; Interval between doses: 15 minutes.

Asymptomatic, well baby:
Mother has syphilis and 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 IV use).

OR

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

6.9 HEPATITIS B IN PREGNANCY

O98.0

DESCRIPTION

Hepatitis B virus (HBV) is transmitted sexually or by percutaneous exposure to infectious body fluids, i.e. blood, saliva, vaginal fluid & semen. Diagnosis is confirmed serologically by a positive hepatitis B surface antigen (HBsAg).

Screening in pregnancy for HBsAg should ideally be performed in the first trimester. HBeAg positive pregnant women are more infectious than HBsAg positive women, as they have higher rates of HBV replication and perinatal transmission.

GENERAL MEASURES

Screen sexual contact(s); if they are sero-negative, give hepatitis B vaccination.
All infected patients should be counselled with regard to lifestyle modifications to reduce hepatotoxicity, including alcohol, substance abuse, and co-prescription of herbal and traditional medicines.

MEDICINE TREATMENT

Indications for medical therapy in HIV-uninfected pregnant women are the same as for non-pregnant adults.
» For management of chronic hepatitis B, **without** chronic HIV infection, see section 1.2.4.2 Hepatitis B, chronic (non-HIV coinfection).
» For management of chronic hepatitis B **with** chronic HIV infection, see chapter 10: HIV and AIDS. (ART should include ARV active against hepatitis B).

Note:
» Ensure normal renal function before starting treatment with tenofovir (serum creatinine <85 micromol/L or creatinine clearance >60 mL/minute).
» Monitor ALT and HBV DNA viral load at 6 months after commencing treatment.
» An adequate virological response is an HBV DNA VL<2000 IU/mL.

Prevention of perinatal transmission
» Caesarean delivery is reserved for obstetric indications only.

» Babies born to mothers with acute hepatitis B infection at the time of delivery or to mothers who are HBsAg-positive or HBeAg-positive, see Primary Health Care STGs and EML, section 6.6.5: Hepatitis B exposed infant.

REFERRAL
» Cirrhosis.
» Liver failure.
» Renal dysfunction (eGFR <60 mL/minute).
» Treatment failure.
» Refer all infected babies to a specialist paediatrician for further management.

6.10 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.

6.11 HYPEREMESIS GRAVIDARUM
O21.0/1/9

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.

AND

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

AND

- Vitamin B complex, IV, 10 mL.

In refractory cases:
Administer daily until hyperemesis is controlled:

- Dexamethasone, IM/IV, 4–8 mg daily.

AND

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

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

O60.0/O42.2/O60.0

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.

AND

- 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 <32 weeks and where nifedipine contra-indicated:

- Indomethacin, oral, 50 mg immediately then 25 mg 4 hourly for up to 48 hours. *LoE:I*[xxi]

  Note: Indomethacin may cause oligohydramnios, and its use is associated with a risk of premature closure of the ductus arteriosus. Use only if there is intolerance to nifedipine.

To improve fetal lung maturity at 26–34 weeks: (Z29.2)

- Betamethasone, IM, 12 mg, 2 doses 12–24 hours apart.

If betamethasone is not available: *LoE:I*[xxii]

- Dexamethasone, IM, 8 mg, 3 doses 8 hours apart. *LoE:III*[xxiii]

Note: Corticosteroids are maximally effective about 24 hours after administration of the first dose. Therefore, give as soon as possible following diagnosis of PTL or PPROM.

Antibiotic therapy (Z29.2)
Indicated routinely for PPROM only:

- Amoxicillin, oral, 500 mg 8 hourly for 5 days.

AND

- Metronidazole, oral, 400 mg 8 hourly for 5 days.

LoE:I[xxiv]

Severe penicillin allergy: (Z88.0)

- Azithromycin, oral, 500 mg daily for 3–5 days

AND *LoE:III*[xxv]

- Metronidazole, oral, 400 mg 8 hourly for 5 days.

Prepare for appropriate care of preterm infant.

REFERRAL

» Fetus that may require neonatal intensive care, e.g. estimated weight <1.5 kg or gestation <32 weeks.
» Fetus requiring specialised treatment after birth, e.g. surgery.
» Severely ill mother.

6.13 PREVENTION OF PRETERM LABOUR (SINGLETON PREGNANCIES ONLY)

Z35.2

DESCRIPTION

Women with a previous spontaneous preterm delivery are at higher risk for preterm delivery in the next pregnancy. In certain high-risk cases, pregnancy may be prolonged by the careful consideration of either cervical cerclage or vaginal progesterone therapy.

The following high-risk women should undergo cervical screening and offered a choice of cerclage or progesterone:

» A history of 2nd trimester miscarriage (between 16 and 26 weeks) suggestive of cervical incompetence: (Painless dilatation with a quick labour, and birth of a live baby or fresh stillbirth) after excluding other causes of mid-trimester losses, e.g. intra-uterine death that required induction, abruptio placentae, fetal abnormalities, polyhydramnios, and medical terminations.
» Previous history of spontaneous preterm birth between 27 and 34 weeks (exclude non-spontaneous causes e.g. iatrogenic delivery for pre-eclampsia, or syphilis). No need to refer previous late preterm deliveries (34-37 weeks).

Do not screen low-risk women routinely, as it is not cost-effective.

GENERAL MEASURES

Cervical length must be measured by a skilled operator using transvaginal ultrasound.
Cervical measurement can be done between 16 and 24 weeks.
A cervical length of ≤25 mm indicates a higher risk for recurrent preterm labour.
Discuss the risks and benefits of both options with the patient to make an informed shared decision of the most appropriate treatment.

MEDICINE TREATMENT

Women should be counselled that 20 cerclage procedures will prevent one preterm delivery (NNT 17 to 20) and that progesterone is successful in 1 out of every 8 cases (NNT 6 to 8), to assist them in making an informed decision. *LoE:I*[xxvi]

Consider prophylactic vaginal progesterone ***or*** cervical cerclage (MacDonald suture) for women with:

» history of spontaneous preterm birth (27-34 weeks) or mid-trimester loss (16-24 weeks), ***and***
» cervical length ≤ 25 mm confirmed on ultrasound (16-24 weeks).

- Progesterone, PV, 200 mg daily. *LoE:I*[xxvii]
  - Stop treatment at 34 weeks and refer to antenatal services at primary level of care for further management.

(**Note**: Vaginal progesterone may be considered for high-risk women with a normal cervix length on ultrasound).

Consider prophylactic cervical cerclage (MacDonald suture) ***only*** for women with:

» cervical length ≤ 25 mm confirmed on ultrasound (16-24 weeks),

AND

» history of preterm prelabour rupture of membranes (PPROM), ***or***
» history of cervical trauma.

Rescue cerclage:

» If the cervix is already open and the membranes exposed, but unruptured, consider a rescue cervical cerclage (16-27 weeks).
» Do not insert a rescue cerclage if there are contractions, active vaginal bleeding or signs of infection.

Cerclage should be removed at 36 weeks, and thereafter the patient can be referred to antenatal services at primary level of care. *LoE:I*[xxviii]

REFERRAL

Women with recurrent losses and previous cerclage that torn out (severe cervical trauma), as they may require an abdominal cerclage.

6.14 SUPPRESSION OF LABOUR FOR FETAL DISTRESS

O68.9 + (Z51.2)

DESCRIPTION

Tocolysis is useful to treat fetal distress in labour and to suppress labour in women needing transfer or awaiting Caesarean delivery. 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 make a solution of 50 mcg/mL. Administer 5 mL (250 mcg) of this solution.
    - Monitor pulse. Do not administer if mother has cardiac disease.
    - Place the mother in the left lateral position.
    - If pulse increases >120 bpm, discontinue salbutamol.

LoE:I[xxix]

6.15 LABOUR INDUCTION

Z35.9/Z51.2

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 delivery.

Cervix favourable and confirmed HIV-uninfected mother

Artificial rupture of the membranes.

Cervix unfavourable (Bishop score <7)

Extra-amniotic Foley catheter with/without saline infusion:

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.
Alternatively, attach sodium chloride 0.9% 1 L with giving set to catheter, and infuse sodium chloride 0.9% at 50 mL/hour. Remove after 24 hours.

LoE:III

MEDICINE TREATMENT

Cervix unfavourable (Bishop score <7)

Extra-amniotic Foley catheter (as above) **PLUS** one of the options below:

LoE:I[xxx]

Prostaglandins, e.g.:

- Dinoprostone gel, intravaginally, 1 mg.
  - Repeat after 6 hours.

- Do not exceed 4 mg.

OR

- Dinoprostone tablets, intravaginally, 1 mg.
  - Repeat after 6 hours.
  - Do not exceed 4 mg. *LoE:III*[xxxi]

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.
  - 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 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.

Non-stress test and cardiotocography:

Note: Perform a non-stress test (NST), before starting the induction, and cardiotocography (CTG) within an hour of each dinoprostone insertion, to evaluate the fetal condition during labour induction.

When using oral misoprostol, do a baseline NST before commencing IOL, followed by CTG 4-hourly (prior to every alternate dose).

Repeat CTG once contractions have started, or more frequently only if clinically indicated. *LoE:III*

Cervix favourable (Bishop score ≥7)

Amniotomy followed 2 hours later by:

- Oxytocin, IV, 2 units in 200 mL sodium chloride 0.9%. *LoE:III*[xxxii]
  - Start at an infusion rate of 12 mL/hour (i.e. 2 milliunits/minute). If absent or inadequate contractions, increase infusion rate according to the table below:

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	14	84
210	16	96
240	18	108
270	20	120

Note:

» It is safe to perform amniotomy in pregnant women with HIV on ART who have an undetectable plasma VL at delivery. *LoE:II*[xxxiii]

» Avoid oxytocin in women with previous Caesarean section or parity ≥5.

» Continuous electronic fetal heart rate monitoring is essential.

» Aim for adequate uterine contractions (3–5 contractions in 10 minutes). Once adequate contractions achieved, do **not** increase rate further.

» Most women will experience adequate contractions at a dose of 12 milliunits/minute.

» If tachsystole develops (>5 contractions in 10 minutes), reduce or stop the oxytocin infusion to achieve 3-5 contractions in 10 minutes. If there are fetal heart rate abnormalities which persist despite stopping the oxytocin, administer salbutamol as above.

6.16 LABOUR PAIN, SEVERE

O62.9 +(Z51.2)

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

- Pethidine, IM, 1 mg/kg 4 hourly as needed, to a maximum of 100 mg.

OR

- Morphine, IM, 0.1 mg/kg 4 hourly as needed, to a maximum of 10 mg.

Titrate dose and dose frequency according to pain. *LoE:III*[xxxiv]

Supplement with premixed nitrous oxide 50%/ oxygen 50% in late first stage.

Epidural anaesthesia
Offer this service only at hospitals with anaesthetic expertise, monitoring, capacity and equipment for epidural. (See chapter 12: Anaesthesiology, pain and intensive care).

Perineal analgesia: R10.2
- Lidocaine, 1 or 2%, infiltration, locally or by a pudendal block.

Postpartum and post-episiotomy pain O90.9 + (R10.2 + Z51.2)
- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

OR
- NSAID, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with meals.

OR
- Pethidine, IM, 1 mg/kg 4 hourly as needed, to a maximum of 100 mg.

OR
- Morphine, IM, 0.1 mg/kg 4 hourly as needed, to a maximum of 10 mg.

LoE:III[xxxv]

6.17 DEHYDRATION/KETOSIS IN LABOUR
O99.2 + (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.

6.18 POSTPARTUM FEVER
O85/O86.0-4/O86.8

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.
Consider excessive use of misoprostol for PPH (doses >600 mcg) as a possible non-infectious cause of postpartum fever.

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

- Amoxicillin/clavulanic acid, IV, 1.2 g 8 hourly, until patient apyrexial for 24 hours.

Follow with: *LoE:III*

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

REFERRAL

» No clinical response in 48 hours of antibiotic treatment.
» Septic shock.

6.19 POSTPARTUM HAEMORRHAGE

O72.1-3 + (Z51.2)

DESCRIPTION

Blood loss >500 mL after birth of the baby or any blood loss which results in haemodynamic instability (tachycardia and/or hypotension).

GENERAL MEASURES

Bimanual compression of the uterus.
Ensure delivery of placenta is complete.
Check for local causes of bleeding.
Balloon tamponade of the uterine cavity should be considered if the patient is to be transferred to another facility.

MEDICINE TREATMENT

Prevention Z29.2

Active management of the 3rd stage of labour:

- Oxytocin, IM, 10 units.

Note:

» Delay cord clamping and cutting (after 1 minute)
» Deliver the placenta by controlled cord traction.

Treatment
Resuscitate.
Put up two IV lines of crystalloid, one of which should contain oxytocin 20 IU.
Cross match and hold blood for transfusion.
Monitor BP and pulse, and response to uterotonics every 15 minutes.

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

If uterus remains atonic (palpable above the umbilicus):
ADD
- Ergometrine, IM, 0.5 mg.

OR
- Oxytocin, IM, 5 units.

AND
- Ergometrine, IM, 0.5 mg.
  - Avoid ergometrine in women with hypertension or cardiac disease, except in severe cases where the benefit is considered to outweigh the risk (discuss with a specialist).
  - Repeat ergometrine 0.5 mg IM after 15 minutes if no response

If still no response after 15 minutes:
- Tranexamic acid 1 g, IV, slowly over 10 minutes. *LoE:I*[xxxvi]
  - Repeat after 30 minutes if there is ongoing vaginal bleeding.

In settings where oxytocin had NOT been administered as prophylaxis at birth:
- Misoprostol, sublingual, or rectal, 600 mcg as a single dose.

LoE:I[xxxvii]

6.20 THE RHESUS NEGATIVE WOMAN
O36.0 + (Z29.1)

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 <20 weeks:
- Anti-D immunoglobulin, IM, 50 mcg. *LoE:III*[xxxviii]

After external cephalic version or potentially sensitizing event ≥20 weeks:
- 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 haemorrhage is suspected:

- Anti-D immunoglobulin, IM, 300 mcg for every 30 mL haemorrhage.
  - Maximum dose: 1 200 mcg.

AND
Do a maternal blood Kleihauer test (consult a specialist).

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.

6.21 URINARY TRACT INFECTION (UTI) IN PREGNANCY

6.21.1 CYSTITIS

O23.1

DESCRIPTION

This condition usually presents with lower abdominal pain, frequency of micturition, and/or dysuria. There are no features of sepsis, e.g. fever. Urine dipstick testing usually shows nitrites, with/without leukocytes; and/or blood.

GENERAL MEASURES

Encourage oral fluid intake.
Midstream urine for microscopy, culture and sensitivity.

MEDICINE TREATMENT

Empiric treatment (symptoms present with nitrites positive **AND** leukocytes positive on dipstick):

- Fosfomycin, oral, 3 g as a single dose — *LoE:III*[xxxix]

OR

- Nitrofurantoin, oral, 100 mg, 6 hourly for 5 days. — *LoE:I*[xl]

LoE:I[xli]

REFFERAL/CONSULTATION

No response to treatment, or resistant organism on culture.

6.21.2 PYELONEPHRITIS, ACUTE

O23.0

DESCRIPTION

This condition is more serious and may result in preterm labour.
Features of pyelonephritis include:
temperature ≥ 38ºC
renal angle tenderness (often bilateral)
other features of sepsis, i.e. vomiting, tachypnoea, tachycardia, confusion and hypotension.

GENERAL MEASURES

Admit to hospital.
Ensure adequate hydration with intravenous fluids, up to 3 L of sodium chloride 0.9% over 24 hours.
Midstream urine for microscopy, culture and sensitivity.

MEDICINE TREATMENT

Empiric therapy:

- Ceftriaxone, IV, 1 g, daily for 48 hours, or until fever subsides.

OR

- Gentamicin, IV, 6 mg/kg, daily (ensure normal renal function).

Switch to oral therapy as soon as the patient is able to take oral fluids:

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

Change antibiotics according to culture and sensitivity results.
After treatment, ensure that two urine specimens are negative to confirm eradication.

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CHAPTER 7
NEPHROLOGY/UROLOGICAL DISORDERS

7.1 NEPHROLOGY DISORDERS

CAUTION
Check all medicines for possible dose adjustment based on eGFR/CrCl.

The doses of many medicines need to be adjusted in renal impairment. Recommendations for medicines that require dose adjustment in renal impairment can be found in the SAMF, package insert, and from many online resources e.g.: http://www.globalrph.com/index_renal.htm

7.1.1 CHRONIC KIDNEY DISEASE (CKD)

N18.1-5/N18.9

DESCRIPTION

Structural or functional kidney damage present for >3 months, with or without a decreased estimated glomerular filtration rate (eGFR).
Markers of kidney damage include:

- proteinuria; ACR-urine (albumin creatinine ratio) ≥30 mg/g or ≥3 mg/mmol; PCR-urine (protein creatinine ratio) >0.05 g/mmol
- urine dipstick positive for blood and/or protein (for females with haematuria: exclude current menstrual cycle)
- increased serum creatinine or low eGFR
- abnormal kidneys on ultrasound, e.g. polycystic, small in size, scarring
- abnormalities on renal biopsy
- electrolyte abnormalities due to tubular disorders
- history of kidney transplant

eGFR calculator online access:
https://www.kidney.org/apps/professionals/egfr-calculator

Common causes of CKD include:

Category	Example
Vascular	Hypertension, vasculitis etc.
Glomerular diseases	Diabetes, autoimmune diseases, systemic infections, drugs, neoplasia
Tubulointerstitial diseases	UTI, drug induced interstitial nephritis (e.g. rifampicin, allopurinol, fluoroquinolones, sulphonamides)
Structural	Polycystic kidney/s, renal artery stenosis, small or enlarged kidneys, renal masses, obstruction (stones, strictures)
Others	Congenital

Chronic kidney disease can be entirely asymptomatic until over 75% of kidney function is lost.

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.

Adults with early CKD i.e. stages 0–3 can all be managed at primary care level once the cause and plan for care has been established.

All stage 4 and 5 patients require referral/consultation with a specialist. If the patient is a candidate for long-term dialysis nephrological referral is advised.

Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012

				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				ACR* <30 mg/g <3 mg/mmol	ACR* 30–300 mg/g 3–30 mg/mmol	ACR* >300 mg/g >30 mg/mmol
eGFR categories (ml/min per 1.73m^2) - description and range	G1	Normal or high	≥90			
	G2	Mildly decreased	60 –89			
	G3a	Mildly to moderately decreased	45–59			Refer
	G3b	Moderately to severely decreased	30–44		Refer	Refer
	G4	Severely decreased	15–29	Refer	Refer	Refer
	G5	Kidney failure	<15	Refer	Refer	Refer

ACR: albumin to creatinine ratio in urine specimen.

Green: low risk (if no other markers of kidney disease, no CKD); yellow: moderately increased risk; orange: high risk; red: very high risk; A1, A2, A3 = categories of albuminuria; G1, G2, G3a, G3b, G4, G5 = categories of eGFR

Adapted from: Levin A, Stevens PE. Summary of KDIGO 2012 CKD Guideline: behind the scenes, need for guidance, and a framework for moving forward. Kidney Int. 2014 Jan;85(1):49-61. https://www.ncbi.nlm.nih.gov/pubmed/24284513

GENERAL MEASURES

» Address cardiovascular disease risk factors. See section 3.1 Ischaemic heart disease and atherosclerosis, prevention.

» Limit salt intake unless salt wasting kidney disease.
» Limit dietary protein intake to 0.8 g/kg/day.
» Avoid nephrotoxic medicines like NSAIDs.
» Regular exercise, target BMI according to South African calculations.
» Screen for proteinuria.
  - If urine dipstick 1+ or greater, repeat on a properly collected midstream urine specimen on another occasion.
  - If proteinuria persists, quantify protein with a spot urine protein creatinine ratio. Significant proteinuria = spot urine PCR of >0.1 g/mmol.
  - If urine dipstick < 1+, ACR.

Patients differ in their ability to excrete a salt and water load and therefore fluid balance should be individualised.

MEDICINE TREATMENT

The following interventions may delay progression of renal disease.

Proteinuria reduction

Ideal targets are: PCR <0.03 g/mmol or ACR <3 mg/mmol.
Most benefit is achieved by reducing protein creatinine ratio to <0.1 g/mmol or ACR <100 mg/mmol.

- Start treatment with a low dose of ACE-inhibitor and titrate up to the maximum tolerated dose, e.g.
- Enalapril, oral.
  - Start with 5 mg 12 hourly and titrate to 20 mg 12 hourly, if tolerated. *LoE:III*[i]
  - Monitor creatinine and potassium after 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. *LoE:III*[ii]

<u>ACE-inhibitor not tolerated due to intractable cough (specialist initiated):</u>

- Consider an angiotensin II receptor blocker (ARB), e.g.:
- Losartan, oral, *LoE:III*[iii]
  - Start with 50 mg daily and titrate to 100 mg daily, if tolerated.
  - Replacing ACE-inhibitor with ARB does not preclude the risk of angioedema. *LoE:II*[iv]

CAUTION

ACE-inhibitors and ARBs can cause or exacerbate hyperkalaemia in CKD. Check the serum potassium before starting these medicines, and monitor serum potassium on therapy.

Hypertension
Optimise BP control with additional antihypertensive agents. BP control results in a lowering of proteinuria and slower decline in eGFR.
Target BP for patients with hypertension: <140/90 mmHg.
Target BP for patients with hypertension and confirmed CKD and/or diabetes: <130/80 mmHg.
See section 3.6: Hypertension.

Hyperlipidaemia
If hyperlipidaemia is a co-existent cardiovascular risk factor, manage according to section 3.1 Ischaemic heart disease and atherosclerosis, prevention.

Diabetes mellitus
In diabetics, optimise control according to section 8.5: Diabetes mellitus.
In diabetics with kidney disease there is an increased risk of hypoglycaemia.

Insulin is the safer option to control blood glucose in patients with eGFR<60 mL/minute.

Note:
» Insulin requirements will decrease as renal disease progresses.
» Stop glibenclamide when eGFR <60 mL/minute because of an increased risk of hypoglycaemia.
» Reduce metformin dose when eGFR <60 mL/minute (maximum dose 500 mg 12 hourly).
» Discontinue metformin when eGFR <30 mL/minute because of the risk of lactic acidosis.

LoE:III[v]

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 $mmol^2/L^2$, to prevent calcium deposition in vessels and tissue which aggravates vascular disease.

Restrict dietary phosphate intake. (Dietitian consultation)
https://www.kidney.org/

Patients with CKD stage 3–5, not on dialysis:

Hyperphosphataemia and/or hypocalcaemia:

- Calcium carbonate, oral, equivalent to elemental calcium, approximately 500 mg 8 hourly with meals.
  - Increase to approximately 1 g 8 hourly with meals, if hyperphosphatemia persists.

Hypocalcaemia and low or normal serum phosphate:

- Calcium carbonate, oral, equivalent to elemental calcium, approximately 500 mg 8 hourly between meals, increase to approximately 1 g 8 hourly between meals.

In patients with CKD stage 5 who are not candidates for renal replacement therapy, the benefits of phosphate binding are unclear, and regular PTH (parathyroid hormone) monitoring is not necessary.

Patients considered suitable candidates for renal replacement therapy:
Monitor Ca^{++}, PO_4 and PTH levels, as per table: Staging of kidney disease.

For hyperphosphataemia uncontrolled on calcium carbonate:

- Aluminium hydroxide BP (300 mg/5 mL), 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 times upper limit of normal range: (Specialist initiated)
(N25.8)

- Calciferol, oral, 50 000 IU once weekly. *LoE:III*[vi]

OR

Calcitriol, oral, 0.25–4 mcg daily.

Anaemia associated with CKD in patients on dialysis programmes N18.1-5†/N18.9† + (D63.8*/Z49.1-2)

Patients on chronic haemodialysis or peritoneal dialysis are often anaemic due to iron deficiency and deficiency of erythropoietin (EPO).
Simultaneous administration of iron and EPO is recommend, as **EPO should be administered in a patient with normal iron stores.** Adequate iron stores are required to assist with red blood cell production immediately after EPO administration (see section 2.2: Anaemia, iron deficiency).

LoE:I[vii]

- Iron, elemental, oral. See section 2.2 Anaemia, iron deficiency.
  - If no response, consider parenteral iron.

AND

- Erythropoietin, 40–50 IU/kg/dose, IV/SC 2–3 times weekly and assessed at 4 weekly intervals.
  - Administer IV dose over 1–5 minutes.

- If necessary, dose may be increased by 25 IU/kg.
- **Note**: There is an increased risk of cardiovascular events with haemoglobin levels >12 g/dL.

LoE:III[viii]

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
Specialist consultation for possible renal replacement therapy.

Check all medicines for possible dose adjustments.
http://www.globalrph.com/index_renal.htm

CONSULT WITH A SPECIALIST AT THE LOCAL REFERRAL CENTRE

» Unknown cause of kidney failure.
» Rapid deterioration in renal function.
» Resistant hypertension despite appropriate medication and adherence.
» All patients with persistent proteinuria: on urine dipstick ≥ 1+ or proteinuria >1 g/24 hours (PCR >0.1 g/mmol).

REFERRAL

» All ESRD patients who may qualify for long term dialysis programs. See section 7.1.5: Renal replacement therapy.
» CKD stage 3 and above (see prognosis table).

7.1.2 GLOMERULAR DISEASE AND NEPHRITIC SYNDROME

N04.9/N05.9

DESCRIPTION

Acute glomerulonephritis presents with one or more of the following: haematuria, proteinuria, an acute decrease in eGFR, fluid retention, or hypertension.

GENERAL MEASURES

» Give oxygen, and place patient in semi-Fowler's position if patient has respiratory distress.
» Early consultation with a specialist.
» Regulate fluid and electrolyte balance. Monitor weight closely.
» Dietary modification if severe kidney dysfunction, e.g. restrict salt, protein, potassium and phosphate intake.
» Avoid potential nephrotoxins: e.g. NSAIDs, aminoglycosides.

MEDICINE TREATMENT

Fluid overload

- Furosemide, as a slow IV bolus, 80 mg.
  - o Avoid unnecessary intravenous fluids.

If hypertension present: I12.0/I12.9

Diastolic BP >100 mmHg or systolic BP >150 mmHg:

- Amlodipine, oral, 5 mg as a single dose.

AND

- Hydrochlorothiazide, oral, 25 mg (if eGFR ≥30 mL/minute).

OR

Furosemide, oral, 40–80 mg (if eGFR <30 mL/minute).

Check all medicines for possible dose adjustments.
http://www.globalrph.com/index_renal.htm

CONSULTATION/REFERRAL

The management of glomerular disease is individualised and management of all patients should be discussed with a specialist.

7.1.3 NEPHROTIC SYNDROME

N04.9

DESCRIPTION

Glomerular disease characterised by:

» severe proteinuria, i.e.: PCR >0.25 g/mmol

and

- oedema,
- hypoalbuminaemia, and
- hyperlipidaemia.

The cause cannot be determined accurately without a biopsy.

GENERAL MEASURES

Regulate salt and fluid intake.
Weigh regularly to assess fluid retention.
Check for postural hypotension to identify excessive diuresis.
Evaluate proteinuria with PCR:

» 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 specialist.

CONSULTATION/REFERRAL

All patients.

7.1.4 ACUTE KIDNEY INJURY

N17.9

DESCRIPTION

Kidney injury may be due to a combination of factors.
Acute kidney injury (AKI) is defined as any of the following:

» Increase in serum creatinine by ≥26.5 µmol/L within 48 hours; or
» Increase in serum creatinine to ≥1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or
» Urine volume <0.5 mL/kg/hour for 6 hours.

GENERAL MEASURES

A detailed history and good clinical examination is necessary to identify potentially reversible causes. Ensure volume status, perfusion and oxygenation. Monitor serum creatinine, potassium and urine output.
If radiocontrast diagnostic procedures are required, see section 22.1: Diagnostic contrast agents and related substances.
Avoid any nephrotoxic medicines e.g. NSAIDs, aminoglycosides. Check all medicines for possible dose adjustments.

MEDICINE TREATMENT

Fluid overload

In patients with fluid overload where dialysis is not immediately available, a short trial of high dose furosemide in consultation with a specialist may be appropriate.

LoE:III

Acute dialysis

Discuss all cases with the referral centre.
Common indications for acute dialysis include:

» Pulmonary oedema and anuria.
» Intractable metabolic acidosis **(pH < 7.2)** and severe hyperkalaemia (>7 mmol/L).
» Uraemic complications, e.g. pericarditis, encephalopathy and bleeding.
» Medication overdose if due to dialysable toxin. See section 19: Exposure to poisonous substances.

Note: HIV infection is not a contra-indication for acute dialysis.

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

Peritoneal dialysis fluid is potentially infectious for HIV and viral hepatitis.

Hyperkalaemia

Serum K^+ >6.5 mmol/L.

Emergency measures

- Calcium gluconate 10%, slow IV bolus, 10 mL over 10 minutes.
  - 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 nebulisation, 5 mg.
  - Dilute in 4 mL of sodium chloride 0.9%.

These are short-term measures - patients should be dialysed or if this is not feasible:

- 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.

LoE:III

Glycaemic control

Close glycaemic control can reduce the incidence and severity of AKI.
See section 8.5: Diabetes mellitus.

Some patients do not recover kidney function and should be treated as CKD.

7.1.5 RENAL REPLACEMENT THERAPY

Z99.2

Refer to the current National Department of Health Guidelines for renal dialysis.

PATIENT SELECTION

The final decision for selection of patients for renal replacement therapy should be made by a multidisciplinary team using standardised selection criteria.
The ideal patient for renal replacement therapy has uncomplicated CKD stage 5 (ESRD), and is a suitable candidate for renal transplantation.

Individual renal units have their own criteria for acceptance and these may include:

» presence of systemic illnesses,
» age,
» BMI, and
» psychosocial factors.

Obtain these guidelines from the referral centre.

7.2 MAJOR ELECTROLYTE ABNORMALITIES

Guidance provided on potassium and sodium electrolyte imbalances.

7.2.1 HYPERKALAEMIA

E87.5

See section 7.1.4: Acute kidney injury.

7.2.2 HYPOKALAEMIA

E87.6

DESCRIPTION

A serum potassium level <3.5 mmol/L.

Mild to moderate symptoms: muscle weakness (respiratory, as well as, GIT muscles) and cramps.

Severe symptoms: rhabdomyolysis, paralysis, dysrhythmias, diaphragmatic weakness.

Signs of hypokalaemia: cardiac arrhythmias as well as ECG abnormalities (ST –segment changes).

It is usually due to gastro-intestinal losses (vomiting, diarrhoea) or renal losses (diuretic therapy, hyperaldosteronism).

MEDICINE TREATMENT

For chronic asymptomatic hypokalaemia, look for and manage the cause:

- Potassium chloride, oral, 600 mg, 1–2 tablets 8 hourly.
  - Each 600 mg potassium chloride tablet contains 8 mmol of potassium chloride. *LoE:III*[ix]
  - Titrate according to response to therapy.
  - Maximum daily dose: 6 g (i.e.10 tablets per day in divided doses).
  - Review potassium levels after 4 weeks.

Note: Routine supplementation with potassium chloride in patients who are on diuretics is usually inappropriate. Co-administration of ACE-inhibitors and/or spironolactone counteracts the hypokalaemia from furosemide or thiazides.

For mild to moderate hypokalaemia in a non-vomiting patient (potassium level usually 3–3.4 mmol/L):

- Each 600 mg potassium chloride tablet contains 8 mmol of potassium chloride.
  - Titrate according to response to therapy.
  - Maximum daily dose: 6 g.
  - Continue treatment until the serum potassium concentration is persistently above 3.5 mmol/L and symptoms or signs have resolved. *LoE:III*[x]

For severe symptomatic hypokalaemia:

- Potassium chloride, IV by peripheral line, 40 mmol in 1 L of 0.9% or 0.45% sodium chloride, mixed thoroughly.

- Administer at a maximum rate of 20 mmol per hour over 3 hours. Beware of volume overload (See Appendix II, for individual dosing and monitoring for response and toxicity).
- Repeat as required, monitoring potassium serum levels after each replacement dose.
- Potassium chloride 15% 10 mL ampoule contains 20 mmol potassium.
- Maximum allowed daily dose of K^+ is 3 mmol/kg/day (or 400 mmol/day).

LoE:III[xi]

CAUTION
Potassium chloride ampoules must always be diluted before infusion.

Reduce the rate of intravenous potassium repletion or change to oral therapy once the hypokalaemia is no longer severe. Continue treatment until the serum potassium concentration is persistently above 3.5 mmol/L and symptoms or signs have resolved.

Online calculator for calculating potassium deficit:
http://www.medicinehack.com/2011/07/hypokalemia-potassium-replacement.html

If not responding to therapy, check for hypomagnesaemia as low serum magnesium may potentiate potassium loss.

7.2.3 HYPERNATRAEMIA

E87.0

DESCRIPTION

A serum sodium level >145mmol/L.

- » Mild to moderate symptoms: Lethargy, weakness, irritability
- » Severe symptoms: Convulsions, coma

It is usually due to inadequate water intake (decreased thirst sensation or inability to drink water) or due to gastro-intestinal losses (vomiting, diarrhoea) or renal losses (diabetes insipidus, osmotic diuresis, furosemide).

GENERAL MEASURES

Treat the cause.

Calculate the water deficit:

Water deficit = (total body water)*(1-(140/Na))
Total body water = correction factor * weight.
(The correction factor is 0.6 for men, 0.5 for women and elderly men, and 0.45 for elderly women).
Online calculator: http://www.nephromatic.com/water_deficit.php

MEDICINE TREATMENT

Correction fluid:

- Oral fluids or via NGT.
- Dextrose 5%, IV infusion.
  - Monitor for hyperglycaemia. Rate of correction of hypernatraemia should be slower than 10 mmol/L over 24 hours to prevent cerebral oedema.
  - Ongoing obligatory water loss through skin and stool (estimated at 30 mL/hour) must also be replaced.

LoE:III[xii]

Desired water replacement in the first 24 hours =
Water deficit x 10 mmol/L ÷ (Serum [Na] – 140)

Hourly infusion rate =
Desired water replacement in the first day ÷ 24 hours + 30 mL/hour.

7.2.4 HYPONATRAEMIA

E87.1

DESCRIPTION

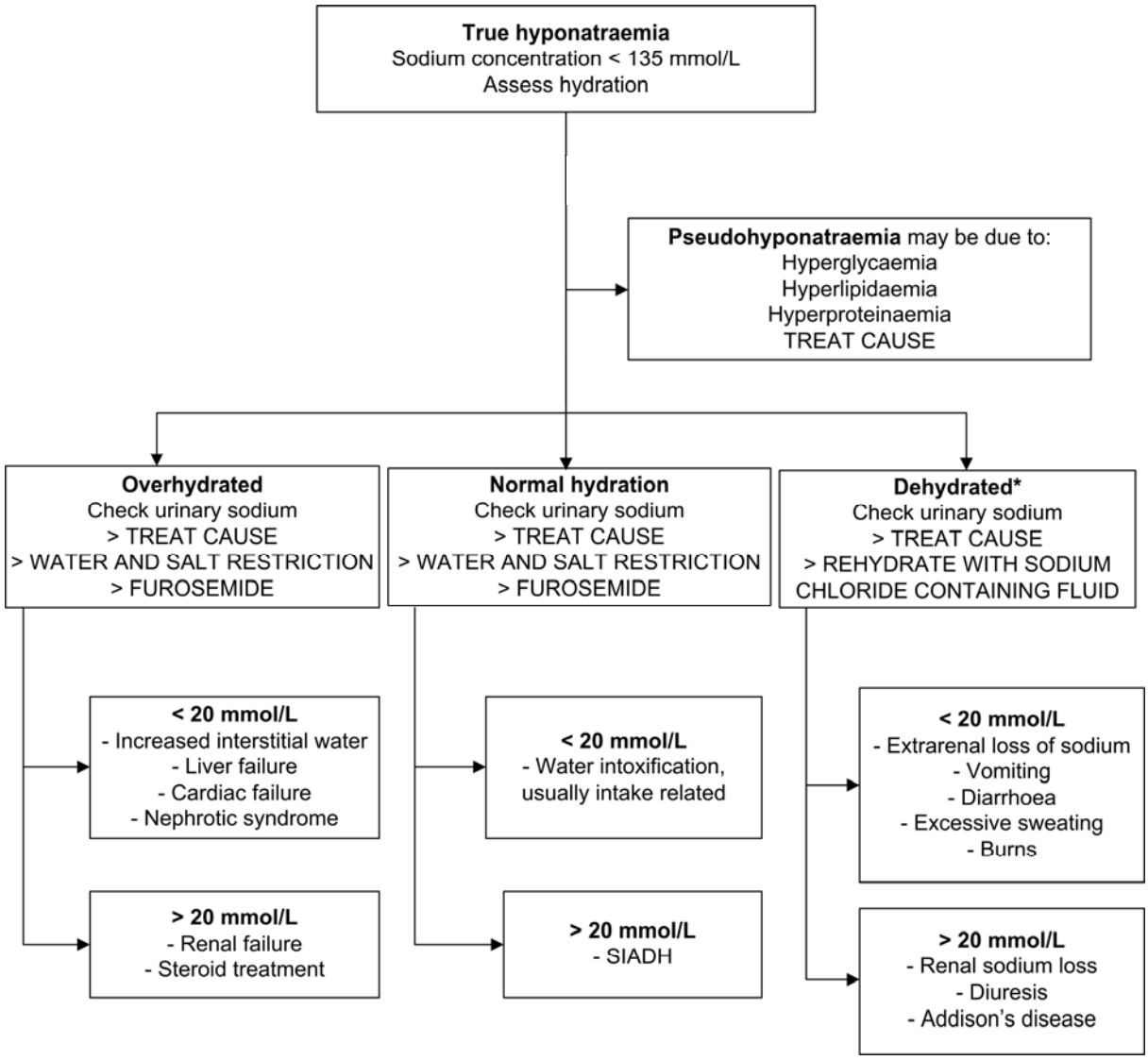
A serum sodium level <135mmol/L.

Mild to moderate symptoms:	Headache, nausea, vomiting, fatigue, gait disturbances, and confusion.
Severe symptoms:	Seizures, obtundation, coma, and respiratory arrest.

Acute hyponatraemia develops within hours due to self-inflicted water-intoxication.

Rapid correction may lead to central pontine myelinolysis, which is often irreversible. Sodium should be frequently monitored and increases should be <9 mmol/L per day.

APPROACH



MEDICINE TREATMENT

In the presence of fluid overload:

- Furosemide, oral, 40 mg 12 hourly.
  - Increase dose to control signs of fluid overload and to improve hyponatraemia.

LoE:III[xiii]

In the absence of fluid overload:

Consult with a specialist before administering sodium chloride, IV infusion.

- Sodium chloride, IV infusion.

CAUTION

Hypertonic sodium chloride should be reserved for severe acute hyponatraemia (sodium level <120 mmol/L with severe symptoms) and exceptional circumstances.

One litre of NaCl infusate	Total Na (mmol/l)	Indication	Fluid	Aim
5% NaCl Expect an increase of 2-3 mmol/L for every 60 mL	855	» Sodium level <120 mmol/L **and** » Severe symptoms (see above) **or** » Acute hyponatraemia due to water intoxication	• Hypertonic sodium chloride, 5%, 60 mL as an IV bolus over 15 min o If symptoms persist/ worsens or sodium is not improving, consult a specialist	» Symptom relief » Correct hypona-traemia: - 4-6 mmol/L immediately **AND** - Maximum 8 mmol/L in 1st 24 hrs
5% NaCl Expect an increase of 2-3 mmol/L for every 60 mL	855	» Sodium level <120 mmol/L with mild to moderate symptoms **or** » Chronic hyponatraemia	• Hypertonic sodium chloride, 5%, 30 mL as an IV bolus over 15 min	» Symptomatic relief. » Correct hypona-traemia: - Maximum 8 mmol/L in 1st 24 hrs
0.9% NaCl	154	» Sodium level >120 mmol/L » Dehydrated. » Asymptomatic or mild symptoms	• Sodium chloride, 0.9%, IV infusion, 1L 8 hourly	» Rehydration

LoE:III[xiv]

To calculate the infusion rate, consult a specialist. https://reference.medscape.com/calculator/hyponatremia-correction-infusate-rate

7.3 UROLOGICAL DISORDERS

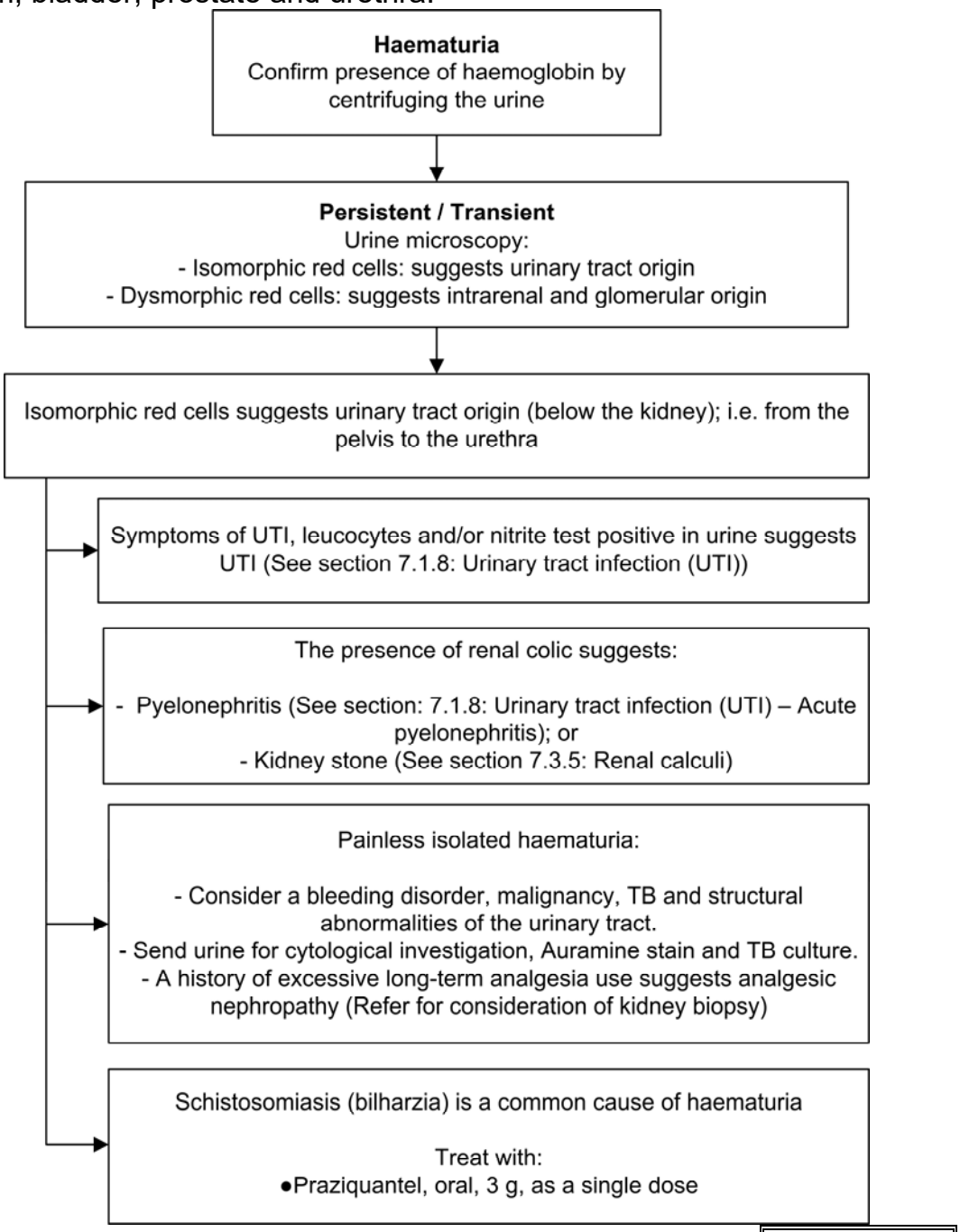
Disorders of the genitourinary system.

7.3.1 HAEMATURIA

R31/ B65.0-3/B65.8-9

DESCRIPTION

Bleeding from the urinary tract, which can be from the kidneys, collecting system, bladder, prostate and urethra.



LoE:III

REFERRAL

Suspected glomerular disease. LoE:III[xv]

7.3.2 URINARY TRACT INFECTION (UTI)

N30.9/O23.4/N10

DESCRIPTION

UTIs include cystitis (infection of the bladder/lower urinary tract) and pyelonephritis (infection of the kidney/upper urinary tract). Pyelonephritis develops when pathogens ascend to the kidneys via the ureters. Uncomplicated UTIs involve either the lower urinary tract (bladder) and/or the upper urinary tract (kidney) in non-pregnant, pre-menopausal woman with no known relevant anatomical and/or functional abnormalities within the urinary tract or any comorbidities. UTIs in other groups of patients are complicated by definition.

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

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

MEDICINE TREATMENT

Women with recurrent UTIs should be advised to:
» void bladder after intercourse and before retiring at night
» not postpone voiding when urge to micturate occurs
» change from use of diaphragm to an alternative type of contraception

Empirical treatment is indicated only if:
» positive leucocytes **and** nitrites on urine test strips on freshly passed urine, or
» leucocytes or nitrites with symptoms of UTI, or
» systemic signs and symptoms indicating an upper UTI and/or urosepsis.

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

Uncomplicated community acquired cystitis N30.9

- Fosfomycin, oral, 3 g as a single dose. LoE:I[xvi]

OR

Gentamicin, IM, 5 mg/kg as a single dose.
- **Note:** Gentamicin should not be used in renal impairment or LoE:I[xvii]

pregnancy (see Appendix II for guidance on prescribing).

OR

Nitrofurantoin, oral, 100 mg 6 hourly for 5 days.

Complicated community acquired cystitis N30.9

- Ciprofloxacin, oral, 500 mg 12 hourly for 7–10 days.

LoE:III[xviii]

CAUTION

Concomitant use of fluoroquinolones with ACE-inhibitor/angiotensin receptor blocker is contraindicated in moderate to severe renal impairment (Creatinine Clearance ≤ 30 ml/minute) and in the elderly. Assess renal function before initiating treatment and monitor during treatment. Evidence suggests a risk of developing acute kidney injury with concomitant use of fluoroquinolones and renin-angiotensin receptor blockers.

LoE:III[xix]

For pregnant women: O23.4

- Nitrofurantoin, oral, 100 mg 6 hourly for 5 days. *LoE:I*[xx]

OR

Fosfomycin, oral, 3 g as a single dose. *LoE:I*[xxi]

Acute pyelonephritis N10

Admit all patients with vomiting, sepsis, diabetes or impaired/worsened renal function (eGFR <60 mL/minute).

Ensure adequate hydration with intravenous fluids.

If there is a poor response, perform an ultrasound on all hospitalised patients urgently as in-patients.

Adjust antibiotic according to sensitivity.

Duration of antibiotic therapy in uncomplicated pyelonephritis:

» fluoroquinolones 7 days

» other antibiotics 14 days.

Longer courses of therapy, 2–3 weeks, should be given for complicated pyelonephritis.

Patients who have features of severe sepsis or who are vomiting, initiate IV therapy and switch to oral therapy as soon as clinical condition improves:

If normal renal function:

- Gentamicin, IV, 6 mg/kg daily (see Appendix II for guidance on prescribing).

Switch to oral therapy as soon as the patient is able to take oral fluids, according to microscopy culture and sensitivity results:

- Ciprofloxacin, oral, 500 mg 12 hourly for 7–10 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, according to microscopy culture and sensitivity results:
- Ciprofloxacin, oral, 500 mg 12 hourly for 7 days.
  - CrCl: <10 mL/minute: 50% of normal dose.

REFFERAL/CONSULTATION
Urgent
» Acute pyelonephritis in pregnant women.
» Acute pyelonephritis with:
- vomiting
- sepsis
- diabetes mellitus
- urinary tract obstruction on ultrasound

Non-urgent
» Failure to improve within 72 hours.
» Women beyond reproductive age.
» >3 uncomplicated UTIs within a one-year period.
» >1 complicated UTI within a one-year period.

7.3.3 RECURRENT UTI
N39.0

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

MEDICINE TREATMENT
Prophylaxis (Z29.9)
To reduce risk of recurrence in patients with >3 infections/year requires continuous prophylaxis for 6 months:
- Cotrimoxazole 80/400 mg, oral, 1 tablet at night.

Treatment
Treat according to microscopy, culture and sensitivity.

REFERRAL/CONSULTATION
» Failure to respond to prophylactic treatment.
» Uncertain diagnosis.

» Recurrent infections where no facilities exist for adequate culture of urine.
» All complicated recurrent UTIs.
» STI pathogens.

7.3.4 PROSTATITIS

N41.1/N41.9 + (N34.2)

DESCRIPTION

Clinical features include:
» pyrexia,
» acute pain in the pelvis and perineum,
» dysuria and frequency,
» 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

If there are features of associated urethritis (STI regimen):

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

LoE:III[xxii]

AND

- Azithromycin, oral, 1 g as a single dose.

LoE:I[xxiii]

If there are **no** features of associated urethritis:

- Ciprofloxacin, oral, 500 mg 12 hourly for 14 days.

LoE:III

Chronic/relapse/persistent infection: N41.1

- Ciprofloxacin, oral, 500 mg 12 hourly for 28 days.

LoE:III

REFERRAL

To urologist if:
» No response to treatment.
» Urinary retention present.
» Chronic/relapsing prostatitis.

7.3.5 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.

May be associated with both obstructive (weak, intermittent stream and urinary hesitancy) and irritative (frequency, nocturia and urgency) voiding symptoms.
Digital rectal examination reveals a uniform enlargement of the prostate.
Urinary retention with a distended bladder may be present in the absence of severe symptoms, therefore it is important to palpate for an enlarged bladder during examination.

GENERAL MEASURES

Consult with an urologist.
Annual follow-up.
For patients presenting with urinary retention, insert a urethral catheter.
Stop medication that may aggravate urinary retention e.g. anticholinergics.

MEDICINE TREATMENT

- Alpha blocker, e.g.:
- Tamsulosin, oral, 0.4 mg daily. *LoE:I*[xxiv]

7.3.6 OVERACTIVE BLADDER

N32.8

DESCRIPTION

A clinical syndrome consisting of urinary frequency (both day-and night time) and urgency, with or without urgency incontinence,

GENERAL MEASURES

Urine dipstick to exclude an UTI.
Health education.
Avoid caffeine containing, alcoholic and carbonated beverages.
Pelvic floor muscle training: three sets of 8-12 contractions sustained for 8-10 seconds each, performed three times a day. Patients should continue for at least 15-20 weeks.

MEDICINE TREATMENT

For detrusor hyperactivity:

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

LoE:III[xxv]

REFERRAL

» For confirmation of diagnosis.
» Complications.
» Not responding to medical therapy.

7.3.7 ERECTILE DYSFUNCTION

F52.2/N48.4 + (E29.1)

DESCRIPTION

The inability to attain and maintain an erect penis with sufficient rigidity for sexual intercourse.
Many cases are psychogenic.
Organic causes include neurogenic, vasculogenic or endocrinological disorders; many systemic diseases; pelvic trauma/surgery; and certain medicines.

GENERAL MEASURES

Thorough medical and psychosexual history.
Examination should exclude gynaecomastia, testicular atrophy or penile abnormalities.
Review all medicines and, if possible, withdraw medicines that may be associated with erectile dysfunction.
Identify and treat cardiovascular risk factors e.g. obesity, hypertension, and dyslipidaemia.
Advise on lifestyle modification e.g. cessation of smoking and excessive alcohol use, physical activity, and weight loss.

MEDICINE TREATMENT

Treat the underlying condition.

In patients with proven testosterone deficiency: (E29.1)

- Testosterone. Specialist initiated.

See section 8.3: Androgen deficiency.

REFERRAL

To an urologist or appropriate specialist if surgical intervention is needed, e.g. penile prostheses, vascular surgery and pelvic fractures.

7.3.8 RENAL CALCULI

N20.0

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 a stone-forming salt.

Clinical features of obstructing urinary stones may include:

» sudden onset of acute colic, localized to the flank, causing the patient to move constantly,
» nausea and vomiting,
» referred pain to the scrotum or labium as the stone moves down the ureter.

Urinalysis usually reveals microscopic or macroscopic haematuria.

Stones may be passed spontaneously, or after medical or invasive treatment. If available, 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.

To prevent recurrence:
Avoid dehydration.
If recurrences occur, consult a specialist.

MEDICINE TREATMENT

Analgesia for renal colic:

- NSAID, oral: e.g. *LoE:I*[xxvi]
- Ibuprofen, oral, 400 mg 8 hourly with meals.

Note: Avoid NSAIDs if renal impairment is present or suspected.

If patient is vomiting:

- Diclofenac, IM, 75 mg as a single dose**.** *LoE:III*

AND/OR

- Tramadol, IM, 50–100 mg, 4–6 hourly. *LoE:III*

OR

- Morphine, IV, to a total maximum dose of 10 mg (See Appendix II, for individual dosing and monitoring for response and toxicity).

Currently, there is no convincing evidence to support the use of hyoscine in this setting.

For vomiting:

- Metoclopramide, IM, 10 mg 8 hourly. *LoE:III*

REFERRAL

» In acute setting for suspected or diagnosed obstruction and/or ongoing pain.
» Complicating urinary tract sepsis.
» Recurrent calculi.

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CHAPTER 8

ENDOCRINE DISORDERS

8.1 ACROMEGALY

E22.0

DESCRIPTION

Acromegaly is a disorder caused by growth hormone (GH) hypersecretion usually due to a pituitary adenoma, with associated morbidities, and increased mortality.
This condition should be managed at a tertiary centre.
Transsphenoidal adenomectomy is the accepted form of primary therapy.
Radiotherapy post operatively may be required. In addition, adjunctive medical therapy may be required in specific circumstances.

Investigations

If the diagnosis is suspected, screening should be done in consultation with a specialist.

REFERRAL

All patients with suspected acromegaly to a hospital with endocrine and neurosurgery facilities.

8.2 ADRENAL INSUFFICIENCY (ADDISON DISEASE)

E27.1/E27.2

DESCRIPTION

Primary adrenocortical insufficiency.

Clinical presentation

Acute crisis: (not all symptoms and signs may occur in a particular patient, so a high index of suspicion is needed).

- » hypotension
- » fever
- » GIT disturbances
- » dehydration
- » weakness
- » depressed mentation
- » hypoglycaemia
- » hyponatraemia
- » hyperkalaemia
- » acidosis

Chronic:

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

Always consider this diagnosis in a thin, hypotensive, hypoglycaemic patient, or during stress e.g. sepsis. **The combination of hyponatraemia and hyperkalaemia should suggest possible primary adrenal insufficiency.**
Note: Treatment of suspected acute adrenal failure should never be delayed to obtain results of diagnostic procedures.

Investigations

08h00 serum cortisol level (or at time of presentation in acute crisis):

- >500 nmol/L: virtually excludes the diagnosis
- with newer assays cortisol concentrations >450 nmol/L are acceptable to exclude hypoadrenalism
- 100–450 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.

LoE:III[i]

GENERAL MEASURES

All patients with confirmed hypoadrenalism.
Investigate for other causes such as sepsis and treat accordingly.

MEDICINE TREATMENT

Acute crisis

E27.2

Before administering hydrocortisone, ensure blood samples are taken for serum cortisol and plasma ACTH, if feasible.

- Hydrocortisone, IV, 100 mg 6 hourly.
  - Change to oral maintenance therapy once stable. *LoE:III*[ii]

To maintain adequate intravascular volume guided by blood pressure:

- Sodium chloride 0.9%, IV with regular glucose monitoring, and 50% dextrose boluses if required.
  - Beware of fluid overload if the combination of sodium chloride 0.9%/dextrose 5% is utilised.
  - The fluid deficit is often several litres. *LoE:III*[iii]

Monitor glucose levels closely and treat hypoglycaemia if present.
Note: All suspected cases should be referred for full evaluation, prior to chronic maintenance therapy.

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.
- In patients requiring a midday dose, a suggested regimen is 10 mg in the morning, 5 mg at midday and 5 mg in the early evening.

OR *LoE:III*

- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral.
  - Start with 5 mg daily.
  - Increase to maximum of 7.5 mg daily, if necessary. *LoE:III[iv]*

For patients who have symptoms of mineralocorticoid deficiency:

- Fludrocortisone, oral, 50–100 mcg daily may be required to normalise the potassium and to reduce postural hypotension in primary hypoadrenalism.
  - Titrate dose of fludrocortisone in consultation with a specialist.

LoE:III[v]

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. *LoE:III[vi]*

Minor stressors e.g.: Influenza, diarrhoeal illness, chest infections and dental procedures warrant doubling of the doses of hydrocortisone for the duration of illness and gradual tapering back 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	Below normal	Normal or below normal

Note: If the serum total testosterone concentration is borderline low repeat the test before replacement therapy is initiated. Don't test during serious illness.

» Measure serum 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. Testosterone therapy can induce prostatic hypertrophy, polycythaemia, liver dysfunction, sleep apnoea and hyperlipidaemia. Baseline investigations for these are required prior to initiation of therapy and long-term surveillance is required.
Individualise dosage and review doses based on clinical response.

- Testosterone cypionate, deep IM, 200–300 mg every 2–4 weeks.
  - Monitor patients for prostate cancer during treatment.
  - Monitor haematocrit. If haematocrit ≥ 54%, stop testosterone therapy.

LoE:I[vii]

8.4 CUSHING SYNDROME

E24.0-4/E24.8-9

DESCRIPTION

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

Investigations

Low dose overnight dexamethasone suppression test (or when unavailable, betamethasone 1 mg equivalent to dexamethasone 1 mg).

- Dexamethasone, oral, 1 mg.
  - Administer at 23:00.
  - Measure plasma cortisol at 8:00, the next morning after breakfast.
  - In people with normal pituitary and adrenal function morning cortisol will be suppressed to <50 nmol/L.
  - Refer if cortisol levels >50 nmol/L.

LoE:III[viii]

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 1.
» Type 2.
» Other specific types, including pancreatic diabetes mellitus.
» Gestational diabetes mellitus: See section 6.2: Diabetes mellitus in pregnancy.

GENERAL MEASURES
All patients require lifestyle modification.
Type 2 diabetes mellitus patients: weight loss if weight exceeds ideal weight.
Correct meal/energy distribution.
Moderate or no alcohol intake.
Encourage smoking cessation.
Increase physical activity, aim for 30 minutes per day 5 times a week.
Education about foot care is essential.
Manage comorbid depression. See section 15.3.1: Depressive disorders.

Diagnosis
» In patients with symptoms of hyperglycaemia and any one of the following criteria:
  - Random plasma glucose ≥11.1 mmol/l; or
  - Fasting plasma glucose ≥7.0 mmol/l; or
  - 2-hour plasma glucose in a 75 g oral glucose tolerance test ≥11.1 mmol/l.

» In asymptomatic patients any one of the following criteria, confirmed by a repeat test on a separate day within 2 weeks:
  - Fasting plasma glucose ≥7.0 mmol/l; or
  - 2-hour plasma glucose in a 75 g oral glucose tolerance test ≥11.1 mmol/l.

LoE:III[ix]

Classification:
After diabetes mellitus has been diagnosed, attempts must be made to classify the patient as type 1, type 2 or one of the other specific types (including pancreatic diabetes, genetic syndromes, infection and other causes). For management of gestational diabetes, see section 6.2: Diabetes mellitus in pregnancy.

Monitoring

At every visit: *LoE:III*[x]

» Finger-prick blood glucose.
» Weight and calculation of body mass index.
» Waist circumference.
» Blood pressure.

Baseline:

» Serum creatinine concentration (and calculate estimated glomerular filtration rate (eGFR)).
» Serum potassium concentration, if on ACE-inhibitor or eGFR <30 mL/minute.
» Urine protein by dipstick.
  – If dipstick negative, request ACR, unless already on an ACE-inhibitor - microalbuminuria is defined as 2.5 to 25 mg/mmol in men, and 3.5 to 35 mg/mmol in women (see section 8.7.2: Diabetic kidney disease).
  – If dipstick positive, see section 8.7.2: Diabetic kidney disease.
» Blood lipids (fasting total cholesterol, triglycerides, HDL and LDL cholesterol).
» Foot examination.
» Eye examination to look for retinopathy.
» Waist circumference.

Measure HbA1c:

» 6-monthly in patients who meet treatment goals, and
» 3-monthly in patients whose control is sub-optimal or if therapy has changed, until stable.

Note: Monitoring of HbA1c implies that active clinical management will be implemented if the level is sub-optimal.

Annually:

» Serum creatinine concentration (and calculate eGFR).
» Serum potassium concentration (if on ACE-inhibitor/ eGFR <30 mL/minute).
» Urine protein by dipstick. *LoE:III*[xi]
  – If dipstick negative, request ACR, unless already on an ACE-inhibitor - microalbuminuria is defined as 2.5 to 25 mg/mmol in men, and 3.5 to 35 mg/mmol in women (see section 8.7.2: Diabetic kidney disease).
  – If dipstick positive, see section 8.7.2: Diabetic kidney disease.
» Eye examination to look for retinopathy.
» Foot examination.
» Assessment for peripheral neuropathy.
» Oral and dental examination.
» Assessment for macrovascular disease.
» Resting ECG.

TARGETS FOR CONTROL

Glycaemic targets for control:

Patient type	Target HbA1c	Target FPG*	Target PPG*
• Young, low risk • Newly diagnosed • No CVS disease	<6.5%	4.0–7.0 mmol/L	4.4–7.8 mmol/L
• Majority of patients	<7.0%	4.0–7.0 mmol/L	5.0–10.0 mmol/L
• Elderly • High risk • Hypoglycaemic unawareness • Poor short-term prognosis	<7.5%	4.0–7.0 mmol/L	<12.0 mmol/L

*FPG: fasting plasma glucose; PPG: post prandial plasma glucose.

Non-glycaemic targets:

» BMI ≤25 kg/m^2.
» BP ≤140/90 mmHg and ≥120/70 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.
» Recurrent severe hypoglycaemia.

8.5.1 TYPE 2 DIABETES MELLITUS

E11.0-9/E12.0-9/E13.0-9/E14.0-9

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 the preferred initial medicine and is added to the combination of dietary modifications and physical activity/exercise. If metformin, in maximal dose, with diet and exercise fails to lower HbA1c to target, a second agent should be added. This second agent may be either a sulphonylurea, or basal insulin. The specific indication is dependent on individual circumstances.

If a combination of two agents fails to lower HbA1c to target, a third agent is added. The preferential sequence of agents to use is metformin, followed by the addition of sulphonylurea, followed by the addition of basal insulin.

If the combination of two oral agents and basal insulin fails to lower HbA1c to target, or if other reasons to adjust therapy exist (such as nocturnal hypoglycaemia), then intensified insulin therapy in consultation with a specialist is required (either twice daily pre-mix, or basal-bolus therapy) and sulphonylureas are discontinued.

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

Metformin

- Metformin, oral, 500 mg twice daily with meals.
  - Adjust dose based on fasting blood glucose levels and/or HbA1c to a maximum dose of 850 mg 8 hourly.
  - Monitor renal function. *LoE:I*[xii]
  - Dose-adjust in renal impairment as follows:

eGFR	Metformin dose
» eGFR >60 mL/min:	Normal daily dose (see above).
» eGFR 45–60 mL/min:	Standard dose, measure eGFR 3–6 monthly.
» eGFR 30–45 mL/min:	Maximum dose 1 g per day; measure eGFR 3–6 monthly.
» eGFR <30 mL/min:	Stop metformin.

  - Contra-indicated in: *LoE:III*[xiii]
    - renal impairment i.e. eGFR <30 mL/minute,
    - uncontrolled congestive cardiac failure,
    - severe liver disease,
    - patients with significant respiratory compromise, or
    - peri-operative cases.

Sulphonylurea derivatives: glimepiride or glibenclamide.

- Glimepiride, oral, 1 mg daily.
  - Titrate the dose by 1 mg at weekly intervals up to 6 mg daily (according to blood glucose levels). *LoE:III*[xiv]
  - Usual dose: 4 mg daily.
  - Maximum dose: 8 mg daily.

OR

- Glibenclamide, oral, 2.5 mg daily 30 minutes before breakfast.

- o Titrate dose slowly depending on HbA1c and/or fasting blood glucose levels to 15 mg daily.
- o When ≥7.5 mg per day is needed, divide the total daily dose into 2, with the larger dose in the morning.
- o Avoid in the elderly and patients with renal impairment (i.e. eGFR <60 mL/minute).

LoE:III[xv]

Oral agents should not be used in type 1 diabetes and should be used with caution in liver and renal impairment.
Metformin should be dose adjusted in renal impairment.
Monitor patients on sulphonylurea derivatives and concomitant rifampicin and dose-adjust sulphonylurea as required. When rifampicin is discontinued, monitor for risk of hypoglycaemia and dose adjustment is required, particularly in the elderly.

Monitor serum creatinine and estimated eGFR three monthly in patients with kidney disease.

Insulin therapy in type 2 diabetes

Indications for insulin therapy:

» Inability to control blood glucose pharmacologically, i.e. combination/substitution insulin therapy.
» Temporary use for major stress, e.g. surgery, medical illness.
» Severe kidney or liver disease.
» 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	Max. daily dose
Add on therapy: • Intermediate to long-acting insulin	10 units, (or 0.3 units/kg/day), in the evening before bedtime, but not after 22h00.	If the starting dose is not effective increase by 2-4 units per dose every 3 to 7 days until fasting glucose is in the target range.	Refer if recurrent hypoglycaemia occurs and targets for control are not met.
Substitution therapy: • Biphasic insulin (30/70 mix)	Total daily dose: 0.3 units/kg/day divided as follows: • 2/3 of total daily dose 30 minutes before breakfast. • 1/3 of total daily dose 30 minutes	4 units weekly. First increment is added to dose before breakfast.	Refer if recurrent hypoglycaemia occurs and targets for control are not met.

Insulin type	Starting dose	Increment	Max. daily dose
	before supper. *LoE:III*[xvi]	Second increment is added to dose before supper.	
Basal bolus insulin therapy	Start with 0.4 to 0.6 units/kg and divide this total daily dose into 50% basal and 50% bolus, using equal pre-meal doses	Basal insulin is adjusted according to fasting glucose levels and bolus insulin is adjusted according to pre- and post-meal glucose, using the patient's home glucose record as a guide.	Refer if recurrent hypoglycaemia occurs and targets for control are not met.

Also see insulin protocols as in section 8.5.2: Type 1 diabetes mellitus.

LoE:III[xvii]

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
See section 8.8: Dyslipidaemia.

Renal impairment
<u>If urine ACR >2.5 mg/mmoL (men) or >3.5 mg/mmoL (women):</u>
Start treatment with a low dose of ACE-inhibitor and titrate up to the maximum tolerated dose.

ADD *LoE:I*[xviii]

- ACE-inhibitor, e.g.:
- Enalapril, oral.
  - Start with 5 mg 12 hourly and titrate to 20 mg 12 hourly, if tolerated (depending on BP and ACR). *LoE:III*[xix]

See section 7.1.1: Chronic Kidney Disease.

If an ACE-inhibitor is not tolerated due to intractable cough, consider an angiotensin II receptor blocker. See section 7.1.1: Chronic Kidney Disease.

8.5.2 TYPE 1 DIABETES MELLITUS

E10.0-9/ E12.0-9/E13.0-9/E14.0-9

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

Insulin preparations

- 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, not later than 22h00.
  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 regimen

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.

Insulin doses

The initial total daily insulin dose:

o 0.6 units/kg body weight.

The total dose is divided into:

o 40–50% basal insulin
o The rest of the total daily dose (TDD) is given as bolus insulin split equally before each meal.

Adjust dose on an individual basis.

Alternative regimen where blood glucose cannot be measured frequently by the patient or caregiver: Twice daily 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.

Note: Optimal glycaemic control is seldom achieved with this regimen.

LoE:III

Insulin delivery devices

In visually impaired patients prefilled syringes should be used.

Home glucose monitoring

Patients on basal/bolus insulin should measure glucose 3-4 times daily. This may be individualised depending on the clinical need of the patient.

LoE:III

All patients with type 2 diabetes, on insulin, should be given test strips for home glucose monitoring appropriate for their care plan.
It is important to maximise the value of home glucose monitoring by careful review of home glucose records at each visit and appropriate patient education in terms of self-dose adjustment.

LoE:I[xx]

Glucagon

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

Repeat prescriptions of glucagon hypoglycaemia kit should only be given if the kit has expired or been utilised.

LoE:III

8.6 DIABETIC EMERGENCIES

Diabetic emergencies includes hypyoglycaemia, diabetic ketoacidosis (DKA) and hyperglycaemic hyperosmolar syndrome (HHS).

8.6.1 HYPOGLYCAEMIA

E10.0-1/E10.6/E11.0-1/E11.6/E12.0-1/E12.0-1/E12.6/E13.0-1/E13.6/E14.0-1/E14.6

Diagnosis: Clinical

Symptoms:

- » Anxiety
- » Palpitations
- » Headaches
- » Sweating
- » Hunger
- » Behavioural changes

Signs:

- » Sweating
- » Tachycardia
- » Bizarre neurological signs
- » Coma
- » Tremor
- » Confusion
- » Seizures

Biochemical

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

TREATMENT

Start immediately.

- Dextrose 50%, rapid IV injection, 50 mL.

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

LoE:III[xxi]

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 the patient has not regained consciousness after 30 minutes with 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 of recurrent hypoglycaemia consider:

» inappropriate management, e.g. too much insulin or too high dose of sulphonylurea,
» poor meal adherence,
» poor adherence,
» alcohol abuse,
» physical exercise,
» 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 may occur in patients with type 1 diabetes. 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 HYPERGLYCAEMIC STATE (HHS)

E10.0-1/E11.0-1/E12.0-1/E13.0-1/E14.0-1

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

Hyperosmolar hyperglycaemic state (HHS) 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 elderly type 2 diabetic patients and develops over days to weeks.

» Blood glucose usually >40 mmol/L.
» Blood ketones usually negative to moderately elevated.
» Urine ketones may be 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.

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, electrolytes and venous blood gas.
» Look for precipitating causes, e.g. infection or 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.
  - Patients <20 years of age: initial volume of 10–20 mL/kg in the 1st 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 <15 mmol/L, but ketones still present:
- Dextrose 5% **or** dextrose 10% in sodium chloride 0.9%, IV.

LoE:III[xxii]

Note:
» Adjust fluid volumes according to clinical criteria.
» 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.

LoE:III

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 continuous intravenous infusions or hourly intramuscular injections (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 acidosis and ketosis have resolved.

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 1st 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 insulin infusion rate to 1–2 units/hour and adjust subsequently according to hourly bedside capillary glucose level measured with glucose test strips.

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/hour) and titrated against the bedside capillary glucose level.

Progress management
Continue insulin therapy 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**:**
- Low molecular weight heparin, e.g.:
- Enoxaparin, SC, 40 mg daily. *LoE:I*[xxiii]

OR

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

8.7 COMPLICATIONS OF DIABETES

Macrovascular complications
Diabetic patients with a history of myocardial infarction, vascular bypass, stroke or transient ischemic attack, peripheral vascular disease, claudication, or angina need secondary prevention with aspirin and a statin – see section 3.1: Ischaemic heart disease and atherosclerosis, prevention.

Hypertension
See section 3.6: Hypertension.

Dyslipidaemia
See section 8.8: Dyslipidaemia.

8.7.1 DIABETIC NEUROPATHIES

E10.4†/ E11.4† + (G63.2*/G99.0*/G59.0*)

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
See section 26.1.4: Management of neuropathic pain.

Gastroparesis

- Metoclopramide, oral, 10 mg 8 hourly, 30 minutes before meals.

If ineffective, consult a specialist.

8.7.2 DIABETIC KIDNEY DISEASE

E10.0/E11.2/E12.2/E13.2/E14.2 + (N18.1-5/N18.9)

See section 7.1.1: Chronic Kidney Disease.

8.7.3 DIABETIC FOOT ULCERS

L97/L08.8 + (E10.5/E11.5/E12.5/E13.5/E14.5)

GENERAL MEASURES

Metabolic control.
Treat underlying comorbidity (e.g.: corns, alcohol misuse, ingrown toenails).
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.

Superficial ulcer with extensive infection

Debridement with removal of all necrotic tissue.

MEDICINE TREATMENT

Superficial ulcer with extensive infection

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

- Amoxicillin/clavulanic acid, IV, 1.2 g 8 hourly.

Severe penicillin allergy (Z88.0)

- Clindamycin, oral, 150–450 mg 8 hourly.

AND

- Gentamicin, IV, 6 mg/kg daily (see Appendix II for guidance on prescribing).

REFERRAL
Arterial revascularisation procedures.

8.8 DYSLIPIDAEMIA
E78.0-9/E78.8-9

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 medicine therapy
Cardiovascular

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

Patients with any of the following factors are at a relatively high risk for a cardiovascular event and would benefit from lipid lowering therapy:
» established atherosclerotic disease
  - confirmed ischaemic heart disease
  - peripheral vascular disease
  - atherothrombotic stroke
» type 2 diabetics with age >40 years of age

» type 1 diabetes with microalbuminuria
» diabetes with chronic kidney disease (eGFR <60 mL/minute). LoE:I[xxiv]

Patients without established vascular disease, with a risk of MI ≥20% in 10 years: lifestyle modification and start statin treatment - 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 >10 mmol/L). Ideally such patients should be discussed with a lipid specialist.

Fibrates are the medicines of choice for severe hypertriglyceridaemia not due to secondary causes.

Choice of medication

Depends on the type of lipid disturbance:
» predominant hypercholesterolaemia: statin
» mixed hyperlipidaemia: statin or fibrate
» predominant hypertriglyceridaemia: fibrate

- HMGCoA reductase inhibitors (statins), according to table below:

INDICATION	HMGCOA REDUCTASE INHIBITOR (STATIN) DOSE
A: Primary prevention - no existing CVD	
» Type 2 diabetes with age >40 years. » Diabetes for >10 years. » Diabetes with chronic kidney disease. » ≥20% 10-year risk of cardiovascular event.	▪ HMGCoA reductase inhibitors (statins), e.g.: • Simvastatin, oral, 10 mg at night.
» Patients on protease inhibitors. (Risks as above, after switching to atazanavir – see section below).	• Atorvastatin, oral, 10 mg at night.
B: Secondary prevention – existing CVD	
» Ischaemic heart disease. » Atherothrombotic stroke. » Peripheral vascular disease.	▪ HMGCoA reductase inhibitors (statins), e.g.: • Simvastatin, oral, 40 mg at night LoE:I[xxv]
» Patients on protease inhibitors.	• Atorvastatin, oral, 10 mg at night. LoE:I[xxvi]
» Patients on amlodipine (and not on protease inhibitor).	• Simvastatin, oral, 10–20 mg at night. LoE:III[xxvii]

» If patient complains of muscle pain.	Reduce dose: ▪ HMGCoA reductase inhibitors (statins), e.g.: • Simvastatin, oral, 10 mg at night. **OR** Consult specialist for further management. *LoE:III*[xxviii]

Note: Lipid-lowering medicines must always be used in conjunction with ongoing lifestyle modification.

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

▪ Fibrates, e.g.:
• Bezafibrate, slow release, oral, 400 mg daily.

Aspirin therapy:
Use in adult patients with diabetes who have a history of cardiovascular disease i.e.

- ischaemic heart disease
- peripheral vascular disease
- previous thrombotic stroke

• Aspirin, oral, 150 mg daily. *LoE:I*[xxix]

Dyslipidaemia in HIV-infected patients: See section 10.1.2: Management of selected antiretroviral adverse drug reactions.

REFERRAL

» Patients with possible familial hypercholesterolaemia (FH) i.e. random cholesterol >7.5 mmol/L or with tendon xanthomata (See section 3.1: Ischaemic heart disease and atherosclerosis).
» Suspected severe familial dyslipidaemias.

8.9 HYPERCALCAEMIA, INCLUDING PRIMARY HYPERPARATHYROIDISM

E83.5 + (E21.0/D71)

DESCRIPTION

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

Aetiology

» Ambulatory patients: most common cause is hyperparathyroidism (>90% of cases).
» Hospitalised patients: malignancies are the most common cause (65% of cases). Hyperparathyroidism accounts for another 25%.
» Granulomatous disease (e.g. sarcoid).

» Immobilisation in those with high bone turnover.

Investigations
Draw blood for parathyroid hormone (PTH) and simultaneous calcium, phosphate, magnesium, albumin, creatinine and sodium and potassium, and 25 hydroxy-vitamin D concentrations.
A detectable PTH in the presence of hypercalcaemia indicates PTH-dependent hyperparathyroidism.

MEDICINE TREATMENT

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

Avoid thiazide diuretics in the acute setting 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, e.g.:
- Zoledronic acid, IV infusion, 4 mg over 15 minutes (specialist initiated).
  - eGFR 35 to 60 mL/minute, adjust dose in consultation with specialist.
  - **Note**: Do not use if eGFR <35 mL/minute. *LoE:I*[xxx]

In patients with granulomatous disease and haematological malignancies:
- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 40 mg depending on response, daily.

LoE:III[xxxi]

REFERRAL

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

8.10 HYPOCALCAEMIA

E83.5 + (E20.0-1/E20.8-9)

DESCRIPTION

Serum calcium (corrected for albumin) 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.

MEDICINE TREATMENT

Therapy is aimed at treating the underlying cause.

For acute hypocalcaemia with neurological problems and prolonged QT time on ECG:

- Calcium gluconate 10%, infusion, 20 mL in 100 mL dextrose 5% given over 20 minutes, with ECG monitoring.

AND

- Calcium gluconate 10%, infusion, 15 mg/kg (= wt [kg] x 1.7 mL) in 1000 mL sodium chloride 0.9% over 4 hours.

LoE:III[xxxii]

For hypoparathyroidism:

- Alfacalcidol, oral, 1–3 mcg daily.

AND

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

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

E03.0-5/E03.8-9

DESCRIPTION

Causes

Common causes of primary hypothyroidism are:
» chronic autoimmune 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. In primary hypothyroidism TSH is elevated and T_4 is low. If TSH is normal or slightly elevated and T_4 is low this suggests hypopituitarism: take blood for cortisol and ACTH, give hydrocortisone replacement before starting levothyroxine and investigate for causes of hypopituitarism.

MEDICINE TREATMENT

- 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. Because T_4 takes a long time to reach steady state and 1st trimester hypothyroidism is undesirable for the fetus, for patients with borderline control (TSH>1.2mU/L) it is advisable to increase the pre-pregnancy dose by 30%. 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.
Note: TSH and T_4 reference range is trimester-specific.

LoE:II[xxxiii]

8.12 OSTEOPOROSIS

M80.00-59/M80.80-99/M81.00-69/M81.80-99/M82.00-19/M82.80-89

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. This is preferably obtained from a dietary source.
Weight bearing exercises, e.g. brisk 30-minute walk 3 times a week.
Smoking cessation.
Avoid excessive alcohol intake - >2 units daily has a 40% increased risk of sustaining any osteoporotic fracture, compared to people with moderate or no alcohol intake.
Avoid falls.

LoE:III[xxxiv]

MEDICINE TREATMENT

Primary prevention

In institutionalised frail elderly patients, supplementation with calcium and vitamin D may reduce the incidence of hip fractures:

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

AND

- Vitamin D (Calciferol), oral, 800 units daily **or** 50 000 units weekly. *LoE:III*[xxxv]

Note: Routine supplementation with calcium and vitamin D marginally increases the risk of myocardial infarction and stroke and is of unclear benefit in other populations. *LoE:I*[xxxvi]

Secondary prevention

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:

- Bisphosphonates, e.g.:
- Alendronic acid, oral, 70 mg weekly, for a maximum duration of 5 years.
  - Taken with a full glass of water, 30 minutes before breakfast – do not lie down.

LoE:I[xxxvii]

Supplement with:

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

AND

- Vitamin D (Calciferol), 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 of, and monitoring response to, therapy, and 18–24 monthly bone mineral density (BMD).
» Fractures suspected to be due to osteoporosis for consideration for alendronate.
» Patients not tolerating oral bisphosphonate.
» Patients with e-GFR < 30 mL/minute.

8.13 OSTEOMALACIA/RICKETS

M83.00-59/M83.80-99/E55.0

DESCRIPTION

A disorder of mineralisation of newly synthesised bone matrix.

REFERRAL

All patients.

8.14 PAGET'S DISEASE

M88.08/M88.80-99

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. The diagnosis is supported by isolated high alkaline phosphatase and typical CXR radiological changes.

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 arthritic pain:

- NSAID, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with meals.

REFERRAL

All patients.

8.15 PITUITARY DISORDERS

Includes prolactinoma, anterior hypothyroid hypopituitarism and diabetes insipidus.

8.15.1 PROLACTINOMA

D35.2 + (M8271/0)

DESCRIPTION

Prolactinoma is the most common functioning pituitary tumour.

Investigations
Serum prolactin, β-hCG.

Note:
» There are numerous causes of hyperprolactinaemia other than a prolactinoma, so secondary causes must be excluded e.g. pregnancy, medicines, physiological, hypothyroidism, chronic renal failure and tumours.
» In patients with prolactinoma, serum prolactin levels are usually elevated ≥4 times the upper limit of the normal reference range for the laboratory method used. Lesser degree of elevation of serum prolactin may also be found in patients with other pituitary tumours associated with pituitary 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.
» Unexplained hyperprolactinemia.

Urgent
» Any visual disturbances, **especially those** suggesting compression of optic chiasm.
» Pituitary apoplexy.

8.15.2 ANTERIOR HYPOPITUITARISM
E23.0-3/E28.3/E29.1

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 (except for most patients with prolactinomas, who generally

respond well to medical therapy).
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 section 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 HT, see section 5.12: Menopause and perimenopausal syndrome.

Men:
- Testosterone cypionate, 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 large amounts of dilute urine, usually >2.5 litres daily.
Causes include head trauma and neurosurgery but most cases are idiopathic.
Consultation with a specialist is recommended.

GENERAL MEASURES

Rehydration with water or hypotonic fluids.

MEDICINE TREATMENT

Postoperative or acutely ill patients:

- Desmopressin, IV/SC, 2–4 mcg daily, either as a single dose or in 2 divided doses.

OR

- Desmopressin, nasal spray, 10–40 mcg daily, either as a single dose or in 2–3 divided doses.

OR

- Desmopressin, oral, 0.05 mg, 8–12 hourly.
  - Optimal dose: 0.1–0.8 mg daily.
  - Adjust dose according to response to a maximum of 1.2 mg daily in divided doses.

If patient has a normal thirst mechanism, and does not receive IV fluids for other purposes:

» oral, intranasal, or IV/SC dosing can be used; and
» keep urine osmolality at 450–600 mOsm/kg.

If patient requires IV fluids and/or is unable to regulate total fluid intake by thirst mechanism:

» IV dosing is preferred; and
» continually adjust the level of antidiuresis to maintain hydration and plasma sodium within the normal.

Replacement therapy:

- Desmopressin, nasal spray, 10–40 mcg daily, either as a single dose or in 2–3 divided doses.
  - Adjust morning and evening doses separately for appropriate diurnal rhythm of water turnover.

OR

- Desmopressin, oral, 0.05 mg, either as a single dose or in 2–3 divided doses.
  - Optimal dose: 0.1–0.8 mg daily.
  - Adjust dose according to response to a maximum of 1.2 mg daily in divided doses.

LoE:III[xxxviii]

REFERRAL

All patients diagnosed or suspected.

Water deprivation may be 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

C74.0-1/C74.9/C79.7/D09.3/D35.0/D44.1 + (M8700/0/3/6)

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.
Patients may also have orthostatic changes in BP.

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.

Screen:

- » young hypertensive patients;
- » hypertensive patients with paroxysmal symptoms; and
- » patients with:
  - — The classic triad of headache, sweating, and tachycardia, whether or not they have hypertension
  - — a family history of a phaeochromocytoma,
  - — A familial syndrome that predisposes to catecholamine-secreting tumours (e.g., multiple endocrine neoplasia type 2 [MEN2], neurofibromatosis type 1 [NF1], or von Hippel-Lindau [VHL]). or
  - — radiologic evidence of an adrenal mass (adrenal incidentaloma) with or without hypertension.

GENERAL MEASURES

Surgical removal of the tumour.

MEDICINE TREATMENT

Once diagnosis is confirmed, initiate medication with immediate referral.

- Alpha blockers, e.g.:
- Doxazosin, oral, 4 mg daily.
  - o Dose increase above 8 mg daily to control blood pressure may be required.

LoE:III[xxxix]

- Calcium channel blockers may be added, e.g.:

- Amlodipine, oral, 5–10 mg daily.

Note:
» Do not give patients diuretic therapy unless pulmonary oedema is present.
» β-blockers must be used with extreme caution in the management of phaeochromocytoma, and only after adequate alpha blockade.

LoE:III[xl]

REFERRAL
All patients.

8.17 PRIMARY ALDOSTERONISM
E26.0

DESCRIPTION
Increased aldosterone production usually due to an adrenal adenoma (Conn's syndrome) or idiopathic bilateral adrenal hyperplasia (the majority of cases).

Clinical
Suspect in a patient with resistant hypertension or hypertension with hypokalaemia.

Diagnosis
Elevated serum aldosterone with a suppressed renin level **and** elevated aldosterone/renin ratio.
ACE-inhibitors, angiotensin receptor blockers (ARBs), and diuretics can give falsely elevated or lowered results. Stop all these drugs for a minimum of 2 weeks before testing. Stop spironolactone for 6 weeks before testing.

Because of limited specificity, a positive screening test result should be followed by a confirmatory test. A negative random ratio test does not necessarily exclude the diagnosis.

MEDICINE TREATMENT
Adrenal adenoma
A surgical resection/removal of adenoma.

Bilateral hyperplasia
Standard anti-hypertensive therapy, including spironolactone.
- Spironolactone, oral, 100–200 mg daily.

REFERRAL
All patients to an endocrinologist or a hypertension centre for confirmation of the diagnosis and further treatment.

8.18 HYPERTHYROIDISM

E05.0-5/E05.8-9

DESCRIPTION

Most common cause of hyperthyroidism is Graves' disease, which is an autoimmune condition resulting from the presence of thyroid stimulating autoantibodies. Other common causes are toxic single or multinodular goitre and sub-acute thyroiditis. Thyrotoxicosis in the setting of any other acute life-threatening condition such as cardiac failure etc. should be managed as thyroid crisis – see section 8.18.5: Thyroid crisis.

Investigation

TSH and free T_4.
If TSH suppressed and free T_4 normal, request free T_3.
The usual biochemical abnormalities are: low TSH, elevated free $T_{4/3}$.
TSH receptor antibodies should be measured in all patients.

Once thyrotoxicosis is confirmed, if cause is uncertain request thyroid uptake scan. If uptake is:

» Elevated or diffuse: Grave's disease.
» Markedly decreased: Thyroiditis.
» Patchy uptake with areas of increased uptake: Toxic multinodular goitre.

REFERRAL

» Consultation with a specialist is recommended in all cases.
» For thyroid scan if necessary.
» Thyroid-associated ophthalmopathy.
» When radioactive iodine or surgery is contemplated.
» If patient is pregnant.

8.18.1 GRAVES' HYPERTHYROIDISM

E05.0

MEDICINE TREATMENT

- Carbimazole, oral, 20–40 mg daily.
  - Titrate dose according to thyroid hormone levels (T_4).
  - Duration of therapy: 12–18 months.
  - Durations of therapy longer than 12 months must be in consultation with a specialist.

ß–blockers

» Used to counteract excessive sympathetic symptoms, e.g. palpitations.
» Dose is titrated according to the heart rate.
» Give for 2–6 weeks, together with carbimazole until T4 levels normalise.

- ß–blocker, e.g.:
- Atenolol, oral, 50 mg daily.

- Titrate according to symptom control up to 100 mg daily. *LoE:III*[xli]

Radioactive iodine
In the setting of Graves' disease radioactive iodine may be administered for failed medical therapy and may be indicated for patients with coexistent heart disease. Refer patient if radioactive treatment is contemplated.

Surgery
Seldom indicated, but to consider in the following situations: large thyroid causing obstructive symptoms, failure of anti-thyroid medicine therapy, allergy to anti-thyroid therapy, 2nd trimester of pregnancy, and not responding to or allergic to anti-thyroid medication.

Monitoring
Patients with Graves' disease who are treated with anti-thyroid drugs should be monitored every 6–8 weeks using a serum T_4. TSH may remain suppressed for months. Once in remission, patients may be monitored less frequently to determine signs and symptoms of recrudescence of thyrotoxicosis.

Because there is a risk of neutropenia or agranulocytosis with carbimazole, therapy should be temporarily stopped and a white cell count (with differential) must be done in patients presenting with an infection or sore throat.

Post-radio-active iodine TSH and free T_4 should be checked at 6 weeks, 3, 6, 9 and 12 months and annually thereafter until either hypothyroidism occurs or patient remains euthyroid for ± 3–4 years. Although uncommon, new onset hypothyroidism can occur years later.

8.18.2 TOXIC MULTINODULAR GOITER
E05.2

MEDICINE TREATMENT
Radio-active iodine
Radioactive iodine is the treatment of choice. Medical therapy is indicated initially for patients with underlying heart disease to achieve euthyroidism before radio-active iodine. Surgery is restricted to patients with obstructive symptoms.

8.18.3 SINGLE TOXIC NODULES
E05.1

MEDICINE TREATMENT
Radioactive iodine
Smaller nodules are best managed with radio-active iodine while larger nodules may require surgery.

ß–blockers
» Used to counteract excessive sympathetic symptoms, e.g. palpitations.
» Dose is titrated according to the heart rate.
» Give for 2–4 weeks.

- ß–blocker, e.g.:
- Atenolol, oral, 50 mg daily.
  - Titrate according to symptom control up to 100 mg daily.

8.18.4 THYROIDITIS

E06.0-5/E06.9

Toxic phase lasts up to 3 months.

MEDICINE TREATMENT

ß–blockers

Used to counteract excessive sympathetic symptoms, e.g. palpitations.
Dose is titrated according to the heart rate.
Give for 2–4 weeks.

- ß–blocker, e.g.:
- Atenolol, oral, 50 mg daily
  - Titrate according to symptom control up to 100 mg daily.

For painful subacute thyroiditis (De Quervain's): E06.1

- NSAID, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with meals.

AND

- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 40 mg daily (Specialist consultation). *LoE:III*[xlii]

8.18.5 THYROID CRISIS

E05.5

MEDICINE TREATMENT

IV fluids as indicated.

- Carbimazole, oral, 40–60 mg 6 hourly until crisis is controlled.

30 minutes after the first dose of carbimazole: *LoE:III*[xliii]

- Lugol's iodine, oral, 10 drops in milk, 8 hourly.

AND

- ß–blocker, e.g.:
- Atenolol, oral, 50 mg daily
  - Titrate according to symptom control up to 100 mg daily.

If life-threatening:

ADD

- Hydrocortisone, IV, 100 mg 8 hourly.

Actively manage precipitating illness and infection. ICU admission is desirable.

REFFERRAL

All patients once stabilised.

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CHAPTER 9
SYSTEMIC AND HEALTHCARE-ASSOCIATED INFECTIONS

ANTIMICROBIAL STEWARDSHIP

Antimicrobial stewardship refers to a systematic approach to optimising the appropriate use of an antibiotic to improve patient outcome(s) and limit emergence of resistant pathogens, whilst ensuring patient safety. It is one arm of the national and international response to the increasing public health crisis of antibiotic resistance. A critical component is adequate infection control. Antibiotics should only be used for the treatment and prevention of bacterial infections. The following checklist will help optimize prescribing:

Checklist for optimal antibiotic prescribing	
1.	**Medicine** – which is the narrowest-spectrum antibiotic that I can use to treat this bacterial infection?
2.	**Dose** – many antibiotics require weight-based dosing and their dosing depends on renal and/or hepatic function
3.	**Dose frequency** – dependent on the half-life of the drug and whether the action of the antibiotic depends on the time above the MIC or the area under the concentration/time curve. Guidance for dosing frequency may require therapeutic drug monitoring, e.g. vancomycin and aminoglycosides.
4.	**Duration** – should be dictated by evidence from randomised controlled trials whenever possible. Expert opinion from national and international guidelines should be consulted where evidence is weak.
5.	**Route** – most antibiotics have good oral bioavailability, but some infections will require intravenous therapy either for the whole or part of the course.
6.	**De-escalation** – applies to the spectrum of antibiotic use and route of administration. All attempts to convert early from parenteral to oral use should be made.
	MIC = minimum inhibitory concentration.

9.1 HEALTHCARE-ASSOCIATED AND HOSPITAL ACQUIRED INFECTIONS

DEFINITION AND PRINCIPLES

Patients with healthcare associated and hospital acquired infections are at increased risk of being infected with drug resistant organisms. A hospital acquired infection is a new infection that develops after at least 48 hours of hospitalisation without evidence that the infection was present or incubating at the time of admission. Healthcare-associated infections should also be

considered in persons with extensive healthcare contact such as: residence in a nursing home or other long-term care facility, hospitalisation in an acute care hospital for >2 days during the prior 90 days, or attendance at a hospital or haemodialysis clinic during the prior 30 days.

It is essential to obtain specimens for culture and sensitivity testing in all cases before starting antibiotics.

Empiric therapy suggestions below are only rough guidelines due to heterogenity of resistance patterns between facilities and over time. Close liaison with regional microbiologists and regular review of hospital antibiotic policy based on local resistance patterns are essential.

9.1.1 INTRAVASCULAR CATHETER INFECTIONS

L53.9/T80.2 + (B95.8/Y84.8/B37.8)

PERIPHERAL LINE INFECTION:

Common organisms:

» coagulase negative staphylococci, particularly *S. epidermis*
» *S. aureus*

The intravascular line should always be removed.

Microbiologic specimens: peripheral blood culture, blood culture from central catheter prior to removal, and culture of the catheter tip.

Small localised area of erythema at the catheter insertion site will usually resolve without antibiotic therapy.

In patients with larger areas of erythema and tenderness extending beyond the insertion site who are systemically well:

- Clindamycin, oral, 450 mg 8 hourly for 5 days. *LoE:III*[i]

If patients with peripheral or central venous catheter infections are systemically unwell they should be treated as a venous catheter related systemic blood infection.

MEDICINE TREATMENT

Empiric antibiotic therapy

Duration of antibiotic therapy should generally be for 48–72 hours after resolution of fever **except** for:

» confirmed *S. aureus* infection, and *LoE:III*[ii]
» candidaemia,
where treatment should be continued for 2 weeks after the 1st negative blood culture. *LoE:III*[iii]

Note: For candidaemia and *S. aureus* infection, perform blood cultures every 2-3 days after therapy has been initiated until 2 consecutive cultures are negative, and 2 weeks after the 1st negative blood culture.

***S. aureus* infection** (B95.8/Y84.8)

- Vancomycin, IV, 30 mg/kg, empirically as a loading dose.
  - Follow with 20 mg/kg/dose 12 hourly. (See Appendix II for guidance on prescribing and therapeutic drug monitoring).
  - Tailor therapy to drug-susceptibility results. *LoE:III*[iv]

Candidaemia (B37.8/Y84.8)

Note: Candida isolated from blood culture should **always** be treated, even if the fever has settled after line removal because of a high risk of late complications. Candidaemia with species other than *Candida albicans* is becoming increasingly common – these species are often resistant to azoles.

Treatment duration should be 2 weeks after 1st negative blood culture:

- Amphotericin B, IV, 0.7 mg/kg daily. *LoE:III*[v]
  - Ensure adequate hydration to minimise nephrotoxicity. (See Appendix II for preventing, monitoring and management of toxicity). *LoE:I*[vi]

Follow up susceptibility:

- Once improved, if sensitive complete course with:
- Fluconazole, oral, 800 mg daily. *LoE:III*[vii]

Intolerance to amphotericin B:

- Fluconazole, oral, 800 mg daily, if sensitive.
  - Dose adjust in renal impariment.

Invasive candidiasis (resistant to fluconazole/amphotericin B or renal impairment is present and amphotericin B cannot be used):

- Echinocandins. (Specialist motivation).

REFERRAL/CONSULTATION

S. aureus endocarditis.

9.1.2 SURGICAL WOUND INFECTIONS

T81.4 + (Y83.6/Y83.8-9/B95.6/U82.1)

DESCRIPTION

Common organisms: Gram positive bacteria, especially *S. aureus*, are the commonest cause. Gram negative and anaerobic bacteria are important causes following gynaecological and intestinal surgery.

Microbiologic specimen: deep wound swab or aspirate of pus, and blood culture.

Suture removal plus incision and drainage is essential. Antibiotics are not usually necessary except if there is marked surrounding cellulitis or features of systemic infection.

MEDICINE TREATMENT

Empiric antibiotic therapy: Total duration of therapy should not exceed 7 days.

If surrounding cellulitis or systemic sepsis not involving the gastro-intestinal (GI) or female genital tract:

- Cefazolin, IV, 1 g 8 hourly.

Follow with oral therapy as soon as patient can swallow and the temperature is <37.8°C for 24 hours: *LoE:II*[viii]

- Flucloxacillin, oral, 500 mg 6 hourly. *LoE:III*[ix]

Check Gram stain of exudate. If Gram negative organism:
ADD

- Piperacillin/tazobactam, IV, 4.5 g 8 hourly.

Severe penicillin allergy: (Z88.0) *LoE:III*

- Clindamycin, IV, 600 mg 8 hourly.

Follow with oral therapy as soon as patient can swallow and the temperature is <37.8°C for 24 hours, based on culture results:

- Clindamycin, oral, 450 mg 8 hourly, and *LoE:III*[x]

Check Gram stain of exudate. If Gram negative organism:
ADD

- Ertapenem, IV, 1g daily. *LoE:I*[xi]

Methicillin (cloxacillin) reistant *S. aureus* (MRSA)
T81.4+ (B95.6+U82.1+Y83.9)

- Vancomycin, IV, 30 mg/kg as a loading dose. Follow with 20 mg/kg/dose 12 hourly. (See Appendix II for guidance on prescribing and monitoring).
  - Drain wound and obtain cultures to verify MRSA.

If female uro-genital tract surgery or open GIT surgery:
T81.4 +(Y83.6/Y83.8)

- Ceftriaxone, IV, 2 g daily.

AND

- Metronidazole, IV, 500 mg 8 hourly. *LoE:III*[xii]

9.1.3 HOSPITAL-ACQUIRED PNEUMONIA (HAP)

J12.0-3/J12.8-9/J13/J14/J15.0-9/J16.0/J16.8/J18.0-2/J18.8-9 + (Y95)

DESCRIPTION

HAP is defined as a new lung infiltrate (not present on admission) plus clinical evidence that the infiltrate is an infection (e.g. new onset of fever, purulent sputum, leukocytosis) occurring >48 hours after admission to hospital. HAP has a high morbidity and mortality and early appropriate antibiotic therapy is essential.

Infection may be due to multi-drug resistant organisms, particularly in

patients with prior intravenous antibiotic use within 90 days. LoE:I[xiii]

Ventilator-associated pneumonia (VAP) ocurs >48 hours after intubation. VAP is more often due to multi-drug resistant organisms than HAP.

Microbiologic specimens: blood culture and sputum/tracheal aspirate bacterial culture. Therapy should be adjusted according to culture result. A good quality Gram stain may be useful in guiding the choice of initial therapy.

MEDICINE TREATMENT

Empiric antibiotic therapy

Duration: 10 days.

HAP with no prior intravenous antibiotic use within 90 days:

- Ceftriaxone, IV, 2 g daily.

and

- Amikacin, IV, 15 mg/kg daily.

Severe Penicillin allergy: (Z88.0)

- Moxifloxacin, oral/IV, 400 mg daily.

and

- Amikacin, IV, 15 mg/kg daily. (See Appendix II, for individual dosing and monitoring for response and toxicity).

HAP with prior intravenous antibiotic use within 90 days *and VAP.*

Antibiotic choice will depend on local susceptibility patterns. One or more of the following antibiotics/classes must be available, dependant on local susceptibility patterns:

- Piperacillin/tazobactam, IV, 4.5 g 8 hourly.

and

- Amikacin, IV, 15 mg/kg daily. (See Appendix II, for individual dosing and monitoring for response and toxicity).

LoE:III[xiv]

OR

- Cefepime, IV, 2 g 12 hourly. (See Appendix II for guidance on dosing in renal impairment).

OR LoE:III[xv]

Instead of piperacillin/tazobactam + amikacin **OR** cefepime:

Carbapenem with activity against Pseudomonas:

- Imipenem/cilastan, IV, 1000/1000 mg 8 hourly (except CNS infections or known epileptics).

LoE:III[xvi]

OR

Instead of piperacillin/tazobactam + amikacin **OR** cefepime **OR** imipenem:

- Meropenem, IV, 2 g 8 hourly (CNS infections or known epileptics).

Note: De-escalate as soon as the culture is available.

9.1.4 URINARY TRACT INFECTIONS, CATHETER ASSOCIATED

T83.5 + (Y84.6+N39.0)

DESCRIPTION

Common organisms: resistant aerobic Gram negative bacteria.
Microbiologic specimen: blood culture and MSU/CSU for microscopy and bacterial culture.
In most patients with long-term catheters bacteria cultured on CSU represent colonisation rather than infection – only treat with antibiotics if there are features of sepsis or pyelonephritis.

GENERAL MEASURES

Remove catheter.

MEDICINE TREATMENT

Empiric antibiotic therapy (Duration of therapy 7–14 days):

- Amikacin, IV, 15 mg/kg daily.

OR

<u>If local resistance patterns show low level resistance to ciprofloxacin or culture shows sensitivity:</u>

- Ciprofloxacin, oral, 500 mg 12 hourly. *LoE:III*[xvii]

9.2 ADULT VACCINATION

Vaccine	Indications	Comments
• Influenza vaccine Z25.1	» Pregnant women » Elderly patients >65 years. » HIV-infected patients. » Patients with chronic pulmonary, cardiac, and renal conditions. » Healthcare workers with direct patient contact.**	o Contraindication: severe egg allergy, <6 months of age. o Dose: IM, 0.5 mL. o Repeat annually.
• Pneumococcal vaccine (23 valent polysaccharide) Z23.8	» Asplenic patients. » Chronic cerebrospinal fluid (CSF) leak.	o Contraindication: pregnancy. o Dose: IM, 0.5 mL. Booster: after 5 years and at 65 years of age. *LoE:III*[xviii]
• Hepatitis B vaccine* Z24.6	» High risk groups, e.g. hospital personnel or sexual contacts of infected patients. » Sexual assault.	o Dose: IM, 1 mL immediately then 1 mL after 1 month and 1 mL 6 months after 1st dose. o Administer deep IM in deltoid muscle.

• Tetanus toxoid vaccine Z23.5	Booster when there is a high risk for tetanus e.g. contaminated wound or pregnant women to prevent neonatal tetanus.	o Dose: IM, 40 iu (0.5 mL).

* Not to be given to patients who have already been immunised.
**Healthcare workers are not routinely offered immunisation during the annual campaign. Although it is recommended that healthcare workers are vaccinated against influenza, they will not be provided with publicly funded vaccines unless they fall within any of the designated high risk groups.
NOTE: Prioritisation strategies may vary in a pandemic.

9.2.1 RABIES VACCINATION

Z24.2
*Notifiable medical condition.

See the Primary Health Care STGs and EML - Section 21.3.1.1: Animal bites.

9.3 BRUCELLOSIS

A23.0-3/A23.8-9
*Notifiable medical condition.

DESCRIPTION

Zoonotic infection, usually due to *B. abortus* in South Africa. Infection is usually acquired from unpasteurised milk products or handling raw meat.

MEDICINE TREATMENT

Exclude TB before starting therapy.

- Doxycycline, oral, 100 mg 12 hourly for 6 weeks.

AND

- Gentamicin, IV, 6 mg/kg daily for 3 weeks (see Appendix II for guidance on prescribing). *LoE:III*[xix]
  - Preferred regimen for osteo-articular or cardiac involvement.

OR

- Doxycycline, oral, 100 mg 12 hourly for 6 weeks.

AND

- Rifampicin, oral, 7.5 mg/kg 12 hourly for 6 weeks.

9.4 EMERGING RESPIRATORY PATHOGENS, e.g. COVID-19: CORONAVIRUS DISEASE-19; MIDDLE EAST RESPIRATORY SYNDROME CORONAVIRUS INFECTION: MERS COV

B34.2/U07.1
*Notifiable medical condition.

Note: Consult most recent guidelines from National Department of Health/ NICD.

DESCRIPTION

Middle East Respiratory Syndrome (MERS) is a viral respiratory illness caused by Middle East Respiratory Syndrome Coronavirus (MERS-CoV). Individuals with MERS-CoV present with a wide spectrum of clinical presentation ranging from asymptomatic infection to acute upper respiratory illness, and rapidly progressing lower respiratory illness; respiratory failure, septic shock and multi-organ failure resulting in death.

A typical presentation of MERS includes:

» fever (>38°C), chills or rigors, cough, shortness of breath

Presentation may include:

» hemoptysis, sore throat, myalgias, diarrhoea, vomiting, abdominal pain

Complications:

» severe pneumonia
» ARDS
» acute renal failure
» refractory hypoxaemia

GENERAL MEASURES

All suspected, probable cases and contacts must be discussed and managed in consultation with the regional virologist or infectious diseases specialist at the referral centre.

In addition cases should be discussed with the Centre for Respiratory Diseases of the National Institute for Communicable Diseases (NICD).

Tel: 011 386 6392/ 011 3866390 , Outbreak hotline: 082 883 9920

COVID-19 HOTLINE NUMBERS
Clinicians: 080011131
Public: 080002999
http://www.nicd.ac.za/ ; https://sacoronavirus.co.za/

Transfer of patients will only occur once all relevant arrangements have been made to limit further exposure to a potential contagious and life threatening agent.

Droplet precautions should be added to the standard precautions. Airborne precautions should be applied when performing aerosol-generating procedures.

ISOLATE SUSPECTED SYMPTOMATIC CASES AT ALL TIMES.

If MERS coronavirus is suspected, isolate patient to limit further exposure.

MANAGEMENT

Treatment

Treatment is supportive.
No antiviral agents or vaccines are currently available.
Management of contact: consult with NICD and isolate contact.
Record and follow-up all patient contacts.

Prevention

Handwashing and the careful disposal of materials infected with nasal

secretions. Antiseptic/disinfectant solutions:choroxylenol, benzalkonium chloride, and cetrimide. Chlorhexidine has been shown to be ineffective.

REFERRAL
All cases after consultation with infectious diseases and NICD.

9.5 HAEMORRHAGIC FEVER SYNDROME
A98.0-4/A98.8/A99
* Notifiable medical condition.

Severe bacterial infections can mimic the features of haemorrhagic fever syndrome, and broad spectrum antibiotics, e.g. ceftriaxone, IV, 2 g daily, are indicated in every case until the diagnosis is confirmed.

DESCRIPTION
High fever, together with disseminated intravascular coagulation (DIC) and bleeding tendency. Other symptoms and organ involvement vary according to the causative virus.
Some important causes other than viral haemorrhagic fevers (VHF) are:
» severe bacterial infections, particularly *N. meningitidis,*
» severe tick bite fever,
» severe falciparum malaria,
» fulminant hepatitis,
» leptospirosis, and
» other causes for DIC or bleeding tendency.
Endemic causes of VHF in South Africa are Crimean-Congo fever and Rift Valley Fever, both of which may be transmitted between humans by means of blood and body fluids.

REFERRAL
All suspected VHF cases need to be discussed and managed in consultation with the Regional Virologist or Infectious Diseases Consultant at the referral centre.
Cases may also be discussed with the Special Pathogens Unit of the National Institute for Communicable Diseases (NICD):

Tel: 011 386 6000, Outbreak hotline: 082 883 9920

Transfer of patients will only occur once all relevant arrangements have been made to limit further exposure to a potentially contagious and life threatening virus.

MANAGEMENT
A detailed travel and clinical history is crucial. If VHF is still considered, isolate patient in a single room and take proper precautions to limit further exposure. These include:

» long sleeved disposable gown,
» vinyl or rubber apron if the patient is bleeding,
» two pairs of latex gloves, one below the gown and one over the gown,
» disposable face mask preferably with a visor,
» goggles if a mask without the visor is used, and
» waterproof boots or 2 pairs of overshoes, one over the other.

Exclude alternate diseases by means of appropriate laboratory testing.
Support patients with packed red cells and fresh frozen plasma, as required.
Testing for VHF may be required, both to confirm or exclude the possibility of VHF - this must be arranged with the NICD (see above), before sending the specimens, as specific precautions apply.
Record and follow up all patient contacts.

9.6 HYDATID DISEASE

B67.0-9

DESCRIPTION

Cysts of *E. granulosus*, acquired from ingestion of helminth ova passed out in dog faeces, particularly in sheep-farming areas. Cysts may occur in any organ, but are most commonly found in the liver and lungs.
Note: Definitive treatment with surgery or PAIR (**p**ercutaneous **a**spiration **i**njection of helminthicidal agent and **r**e-aspiration) is preferred for all accessible lesions.
With medical therapy as below, cure is achieved in about half, improvement in about a quarter and no response in about a quarter of cases.

MEDICINE TREATMENT

- Albendazole, oral, 15 mg/kg/day up to maximum of 400 mg 12 hourly with a fatty meal (e.g. a glass of full cream milk). *LoE:III*[xx]
  - Duration is 3–6 months according to response on imaging for inoperable cysts **or** 14–28 days before and 28 days after PAIR or surgery. *LoE:I*[xxi]
  - Monitor liver function tests and FBCs monthly.

REFERRAL

All cases to a centre with experience in surgery and PAIR.

9.7 MALARIA

See the Primary Health Care STGs and EML - Section 10.7: Malaria.

9.7.1 MALARIA, UNCOMPLICATED

B54/B51.9/B52.9/B53.0
*Notifiable medical condition.

See the Primary Health Care STGs and EML - Section 10.7.1: Malaria, non-

severe/uncomplicated.

9.7.2 MALARIA, SEVERE

B50.0/B50.8
*Notifiable medical condition.

See the Primary Health Care STGs and EML - Section 10.7.2: Malaria, severe/complicated.

DESCRIPTION

P. falciparum malaria with one or more of the following features:

- severe general body weakness (prostration)
- impaired consciousness
- renal dysfunction
- repeated vomiting
- severe diarrhoea
- severe anaemia (Hb <6 g/dL)
- haemoglobinuria
- acidosis (plasma bicarb <15 mmol/L)
- abnormal bleeding (e.g epistaxis)
- convulsions
- heavy parasitaemia (≥5%)
- ARDS
- shock
- hypoglycaemia
- clinical jaundice

GENERAL MEASURES

Maintain hydration but avoid excessive fluid administration as this could contribute to the development of ARDS (especially in pregnancy).
Transfuse if haemoglobin <6 g/dL.
There is no convincing evidence of benefit for the use of exchange transfusion.

MEDICINE TREATMENT

Intravenous therapy:

The preferred agent is parenteral artesunate:

- Artesunate IV, 2.4 mg/kg at 0, 12 and 24 hours; then daily until patient is able to tolerate oral therapy.
  - Administer at least 3 IV doses before switching to oral artemether/lumefantrine.

LoE:I[xxii]

If parenteral artesunate is not available:

- Quinine, IV (1 mL = 300 mg quinine salt).
  - Loading dose: 20 mg/kg in dextrose 5% administered over 4 hours.
  - Maintenance dose: 8 hours after start of the loading dose, give 10 mg/kg in dextrose 5% over 4 hours repeated every 8 hours until there is clinical improvement and the patient can take oral therapy.
  - Monitor for hypoglycaemia and dysrhythmias at least 4 hourly.
  - If there is significant renal failure increase dose interval to 12 hourly after 48 hours.

Follow intravenous therapy with oral therapy:

- Artemether/lumefantrine 20/120 mg, oral, 4 tablets/dose with fat-containing food or full cream milk to ensure adequate absorption.

- Give the first dose immediately.
- Give the second dose 8 hours later.
- Then 12 hourly for another 2 days. (Total number of doses in 3 days = 6; i.e. 24 tablets).

Monitor treatment response with regular blood smears.
An increase in parasitaemia may occur within 24 hours due to release of sequestrated parasites, but a reduction should be seen after 48 hours.
Note: Gametocytes may appear after this stage – this does NOT mean failure of therapy as gametocytes may persist for up to 2 weeks after successful therapy.
Only the reappearance of or failure to clear trophozoites means failure.

Consider concomitant bacteraemia in patients with severe malaria, especially if they have neutrophilia.

REFERRAL
Patient in need of ventilation or dialysis if these are unavailable on site.

9.8 SCHISTOMIASIS
B65.0-3/B65.8-9
*Notifiable medical condition.

DESCRIPTION
A parasitic infestation with:
» *Schistosoma haematobium*: primarily involves the bladder and renal tract, or
» *Schistosoma mansoni*: primarily involves the intestinal tract.

DIAGNOSIS
Acute schistosomiasis syndrome
» Typically occurs in travellers to endemic areas with freshwater exposure 3-7 weeks before onset.
» Clinical features include fever, rigors/chills, urticaria,angioedema, myalgias, arthralgias, dry cough, diarrhea, abdominal pain, and headache. Symptoms are usually relatively mild and resolve spontaneously over a period of a few days to a few weeks.
» The eosinophil count is almost invariably markedly elevated.
» Diagnosis is confirmed serologically – eggs are seldom seen in stool or urine.
» Differential diagnosis includess urinary tract infection, glomerulonephritis, HIV, gastroenteritis (Salmonella), hepatitis A, B and C, malaria.

Chronic schistosomiasis

» Most individuals with schistosomiasis infection are asymptomatic.
» *S. haematobium* may present with macroscopic haematuria and urinary symptoms. Chronic bladder involvement and urinary tract involvement may cause urinary incontinence and obstructive uropathy.
» *S. mansoni* may present with chronic or intermittent dysentery. Periportal fibrosis and portal hypertension may occur.
» Pulmonary hypertension and central nervous system involvement (particularly myelopathy) are uncommon complications.
» Definitive diagnosis is by finding eggs in urine (*S. haematobium*), stool (*S. mansoni*), or on biopsy. Serology is usually positive.

MEDICINE TREATMENT

Acute schistosomiasis syndrome

- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 40 mg daily for 5 days.

LoE:III[xxiii]

4-6 weeks later, after symptoms have resolved:

- Praziquantel, oral, 40 mg/kg as a single dose.

AND *LoE:III*[xxiv]

- Corticosteroids (intermediate-acting)e.g.:
- Prednisone, oral, 40 mg daily for 5 days.

Optimum time for administration of praziquantel is uncertain but sufficient time is required for the worms to mature.

If in 4-6 weeks, eosinoplilia present and high antibody titres, repeat praziquantel treatment:

- Praziquantel, oral, 40 mg/kg as a single dose.

LoE:III[xxv]

Chronic schistosomiasis

Manage as recommended in PHC STGs and EML, section 10.12: Schistosomiasis (bilharzia).

9.9 TETANUS

A35
*Notifiable medical condition.

DESCRIPTION

Painful muscle spasms and rigidity following inoculation by trauma of *Clostridium tetani* spores, which germinate and produce toxins. The wound may be trivial and healing may have occurred before presentation. Incubation period is 3-21 days. Tetanus may be localised, with muscle spasms near the site of inoculation, or generalised, with spasm of the jaw muscles being a common presenting sign.

GENERAL MEASURES

These patients need to be managed in a high care setting where ventilation is available.
Maintain and protect airway.
Monitor ECG and blood pressure.
Maintain and replace IV fluids.
Wound management is essential with debridement and removal of any foreign bodies.
Alleviate fever with mechanical cooling methods.

MEDICINE TREATMENT

For rigidity, spasms: (R25.2)

- Diazepam, IV, 10 mg 4 hourly, for 24 hours, then consider oral route as high doses of parentral diazepam can cause an acidosis.
  - Titrate to effect. *LoE:I*[xxvi]
  - Doses as high as 50–100 mg 2 hourly are sometimes required.
  - Higher doses require monitoring for respiratory depression.

Use muscle relaxants sparingly as these may exacerbate autonomic instability.

Antibiotic treatment:

- Metronidazole, IV, 500 mg 8 hourly for 10 days. *LoE:III*[xxvii]

For passive immunisation: (Z23.5)

- Tetanus immunoglobulin, IM, 3 000 units as a single dose.

For active immunisation of all patients:(as clinical tetanus does not always confer immunity) (Z23.5)

- Tetanus toxoid vaccine, IM, 0.5 mL, total of 3 doses:
  - on admission,
  - at 4 weeks, and
  - at 6 months.
  - Administer at a different site to that used for administering tetanus immunoglobulin.

For pain:

- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours. *LoE:I*[xxviii]
- Morphine, IV, to a total maximum dose of 10 mg (See Appendix II, for individual dosing and monitoring for response and toxicity).

For shock, dehydration, maintenance of hydration: R57.9+ (A35)

- IV fluids.

For prophylaxis for deep vein thrombosis: (Z29.2)
See section 2.14: Venous thrombo-embolism.

REFERRAL
All cases to a facility with resources for artificial mechanical ventilation.

9.10 TICK BITE FEVER
A93.8

DESCRIPTION
Tick-borne infection due to *R. conorii*, acquired from dogs, or *R. africae*, acquired from cattle and game. The hallmark of tick bite fever is the eschar, a round black lesion ± 5 mm in diameter with an inflammatory halo, occurs in about two thirds of patients with *R. conorii* and in most cases of *R. africae* infection, where multiple eschars are common. A rash develops on about the third day of illness in about two thirds of patients with *R. conorii* and in fewer cases of *R. africae* infection. In *R. conorii* infection the rash is maculopapular and involves the palms and soles. In *R. africae* infection the rash is sparse and may be vesicular. Headache is a prominent symptom.

MEDICINE TREATMENT
- Doxycycline, oral, 100 mg 12 hourly, for at least 3 days after the fever subsides with clinical improvement.
  - Total duration of treatment is 7 days.

LoE:III[xxix]

In pregnancy: O98.5+(A93.8)
- Azithromycin, oral, 500 mg 12 hourly for 3 days.
  - In severe cases, initiate therapy with 1–2 days of doxycycline.

LoE:III[xxx]

For the rare patient unable to take oral therapy:
Total duration of therapy: 7 days.
- Ciprofloxacin, IV, 400 mg 8 hourly.

LoE:III[xxxi]

Note:This is inferior to doxycycline and oral doxycyclineshould be commenced as soon as possible.

REFERRAL
Tick bite fever responds rapidly to treatment and fever persisting for >48 hours after initiation of treatment should prompt consideration of an alternative or additional diagnosis*.*

LoE:III[xxxii]

9.11 TYPHOID FEVER (ENTERIC FEVER)
A01.0-4
*Notifiable medical condition (Typhoid fever).

DESCRIPTION
Systemic infection due to *S. enteritica* serotype Typhi or related organisms (e.g. *S. paratyphi*, *S. choleraesuis*). Initial symptoms are abdominal pain, headache, cough and fever, with diarrhoea developing after a few days.

Bacteraemia is common in the first week of illness, subsequently stool culture has the highest yield.

GENERAL MEASURES

Transfusion is indicated for severe haemorrhage.
Replace fluid and electrolytes.
Contact isolation during acute phase of illness.

MEDICINE TREATMENT

Antibiotic therapy

There is increasing resistance to ciprofloxacin in South Africa and it is important to send specimens for culture and sensitivity prior to commencing antibiotic therapy.

Total duration of antibiotic therapy: 10 days.

- Ceftriaxone, IV, 2 g 12 hourly. *LoE:II*[xxxiii]

Follow with oral therapy as soon as patient can swallow and the temperature is <37.8°C for 24 hours, based on culture sensitivity results:

- Ciprofloxacin, oral, 500 mg 12 hourly. *LoE:III*

Stool cultures must be repeated at weekly intervals after convalescence to ensure that a carrier state has not developed. Two consecutive negative stool cultures are required to exclude carrier state. This is of vital importance in food handlers, who must not be permitted to return to work until stools are negative.

Chronic carriers: (Z22.0)

- Ciprofloxacin, oral, 500 mg 12 hourly for 6 weeks (if sensitive to ciprofloxacin).
  - Advise strict hand washing.
  - Avoid food preparation for others during severe illness.

REFERRAL

Surgical consultation for complications such as intestinal haemorrhage, threatening bowel perforation or localisation with metastatic infection with or without abscess formation, and peritonitis.
Drug resistant organism: consult microbiology/infectious diseases services.

9.12 VARICELLA (CHICKENPOX), COMPLICATED

B01.1† + (G02.0*/G05.1*+J17.1*)/B01.8

GENERAL MEASURES

Cool, wet compresses or tepid water baths.
Body hygiene to prevent secondary infection.
Advise against scratching.

MEDICINE TREATMENT

Antiviral therapy is required in complicated cases, e.g.:

» chickenpox pneumonia,
» pregnancy,
» neurological involvement, and
» chickenpox in immunocompromised patients.

- Aciclovir, IV, 10 mg/kg administrerd over one hour 8 hourly for 7 days.

The course can be completed with:

- Antiviral, (active against varicella zoster), e.g: LoE:I[xxxiv]
- Aciclovir, oral, 800 mg five times daily.

Treat secondary bacterial infection if suspected.

For patients who are severely immunologically compromised and are not immune: (Z29.1)

- Varicella-zoster immunoglobulin (VZIG), IM, 125 units/10 kg.
  - Maximum dose: 625 units.
  - Administer within 96 hours after significant exposure.

9.13 ZOSTER (SHINGLES)

B02.9

DESCRIPTION

Dermatomal eruption of vesicles on an erythematous base due to varicella-zoster virus (lies dormant in nerve ganglia following chickenpox).

GENERAL MEASURES

Isolate from immunocompromised or pregnant non-immune individuals (who may develop severe chickenpox).
Offer HIV test, especially in patients <50 years of age.

MEDICINE TREATMENT

Antiviral therapy, for:

» zoster in immunocompromised patients, provided that active lesions are still being formed, and
» in immunocompetent individuals provided they present within 72 hours of onset of clinical symptoms.

- Antiviral (active against herpes zoster) e.g.:
- Aciclovir, oral, 800 mg five times daily for 7 days (4 hourly missing the middle of the night dose). LoE:I[xxxv]

For zoster with secondary dissemination or neurological/ eye involvement:
B02.7/B02.0-2†+(G02.0*/G05.1*/G53.0*/G63.0*)/ B02.3†+(H03.1*/H13.1*/H22.0*/H19.2*/H19.0*)

- Aciclovir, IV, 10 mg/kg administred over one hour 8 hourly for 7 days.

- The course can be completed with aciclovir, oral, 800 mg five times daily.
- Dose adjustment based on renal clearance (See Appendix IIfor guidance on prescribing and monitoring).

LoE:III[xxxvi]

Secondary infection

B02.8

This is seldom present and is over-diagnosed. The vesicles in shingles often contain purulent material, and erythema is a cardinal feature of shingles. If there is suspected associated bacterial cellulitis:

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

For pain:

Pain is often very severe and requires active control. Combination of different classes of analgesics is often necessary.

Recommended therapy for acute phase of infection, e.g.:

- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

AND/OR

If pain is not adequately controlled:

- Tramadol, oral, 50–100 mg 4–6 hourly.

See chapter 26: Pain.

Post-herpetic neuralgia: B02.2+(G53.0*)

Initiate treatment with adjuvant therapy early.

- Amitriptyline, oral, 25 mg at night.
  - Titrate as necessary to a maximum of 75 mg.

See section 26.1.4: Neuropathic pain.

REFERRAL

Refer to an ophthalmologist if there is ocular involvement with ophthalmic zoster (if the tip of the nose is involved then ocular involvement is much more likely). See section 18.4: Herpes zoster ophthalmicus.

Patients who develop complications e.g. myelitis.

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CHAPTER 10
HIV AND AIDS

Consult the most recent HIV Guidelines from the
National Department of Health.
https://www.knowledgehub.org.za/elibrary/2019-art-clinical-guidelines-management-hiv-adults-pregnancy-adolescents-children-infants

10.1 ANTIRETROVIRAL THERAPY

B24

Antiretroviral therapy (ART) consists of combinations of antiretroviral medicines that are capable of suppressing HIV replication (defined as an undetectable viral load). Continued use of ART with a detectable viral load results in the development of resistance to some or all of the medicines in the regimen. High levels of adherence are essential for long-term success with ART.
The current recommended first-line ART regimen contains two nucleoside reverse transcriptase inhibitors (NRTIs) together with an integrase inhibitor (InSTI) dolutegravir. Previously a non-nucleoside reverse transcriptase inhibitor (NNRTI), efavirenz or nevirapine, together with two NRTIs, were recommended for first-line ART. Dolutegravir is better tolerated than the NNRTIs and has a much higher barrier to the development of resistance.
Dolutegravir, together with two NRTIs, is also recommended in second-line ART after failing an NNRTI-based first-line regimen. Previously a protease inhibitor (PI), together with two NRTIs, was recommended for second-line ART, but dolutegravir is better tolerated than PIs. Switching people, established on ART to the newer dolutegravir-based ART regimens needs to be carefully done to reduce the risk of the emergence of resistance (refer to National Department of Health HIV Guidelines).

ELIGIBILITY FOR ART

Eligibility to start ART:
All adults with confirmed HIV infection, irrespective of CD4 count or WHO clinical stage. Where a patient is willing and ready, ART should be initiated on the same day as HIV diagnosis, except in patients with TB or cryptococcal meningitis (see Timing of ART initiation below).

LoE: I[i]

Immediate initiation:
ART should be initiated immediately in pregnancy and during breastfeeding.

LoE:III[ii]

Fast tracking (within 7 days):
Patients with CD4 <200 cells/mm^3.
OR
Patients with WHO stage 4.

LoE:III[iii]

Timing of ART initiation:

» ART should be started as soon as the patient is ready. However, with some opportunistic diseases early ART initiation can cause harm by increasing the risk of the immune reconstitution inflammatory syndrome (IRIS) - see section 10.1.2: Management of selected antiretroviral adverse drug reactions).

» In TB co-infection, start with TB treatment first, followed by ART initiation according to CD4 count (except TB meningitis – see below):
- CD4 <50 cells/mm^3: initiate ART within 2 weeks of starting TB treatment.
- CD4 ≥50 cells/mm^3: defer ART until 8 weeks after starting TB treatment, which has shown to be safe and reduces the risk of deterioration due to IRIS.

LoE:I[iv]

» In patients with TB meningitis (irrespective of CD4 count), defer ART until 8 weeks after initiating TB treatment.

LoE:I[v]

» In patients with cryptococcal meningitis, defer ART until 4–6 weeks after starting antifungal treatment (earlier initiation has been shown to increase the risk of death).

LoE:I[vi]

PSYCHOSOCIAL INDICATORS OF READINESS FOR ART

It is essential that patients have good insight into the need for long-term therapy and high levels of adherence. Give careful attention to adherence planning. Encourage patients to disclose their HIV status to somebody who should act as a treatment supporter. If this is not possible then the patient should join a support group.

Manage depression.

Active substance abuse/alcoholism is an impediment to adherence and, if possible, should be addressed prior to initiating ART.

Women of childbearing potential (WOCP) should be given all necessary information on the benefits and potential risks of neural tube defects (NTDs) with dolutegravir use periconception.

LoE:III[vii]

ART REGIMENS

1ST LINE ART	
Treatment-naïve patients	» Men ≥35kg and ≥10 years of age » WOCP not actively wishing to conceive » Pregnant women ≥6 weeks gestation, and those who make an informed choice to use DTG TDF + 3TC + DTG <u>Patients with TB:</u> TDF + FTC + EFV

	Pregnant women <6 weeks gestation or actively wanting to conceive: TDF + FTC + EFV *(Also see section 6.7: HIV in pregnancy)* *LoE:I[viii]*
Contraindications and intolerance to EFV	TDF + 3TC + DTG » WOCP actively wanting to conceive and pregnant women <6 weeks gestation require adequate counselling to make an informed choice to use DTG.
Contraindications to EFV and DTG	Start protease inhibitor-based regimen: TDF + 3TC/FTC + LPV/r
Contraindication to TDF » eGFR <50 mL/minute. » Use of additional nephrotoxic drug e.g. aminoglycoside.	Replace TDF + 3TC/FTC with either ABC+ 3TC **or** AZT + 3TC *LoE:I[ix]*
Contraindication to TDF and ABC intolerance » eGFR <50 mL/minute. » Use of additional nephrotoxic agent e.g. aminoglycoside. » Hypersensitivity.	AZT+ 3TC with DTG **or** EFV
Note: In the unlikely scenario where there is intolerance/contraindication to all currently available NRTIs, an alternative dual-therapy regimen may be used, e.g. DTG + 3TC (if no resistance/intolerance to 3TC and VL <500 000 copies/mL) **or** EFV + LPV/r **or** DTG + LPV/r may be used. Consult a specialist. *LoE:I[x]*	
2ND LINE ART	
Management of viraemia on 1st line ART	If plasma VL between 50–999 copies/mL: » Address adherence, tolerability, medicine interactions & psychosocial factors. » Repeat VL test 3 months later. If plasma VL > 1000 copies/mL: » Assess adherence, tolerability, medicine interactions & psychosocial factors. Repeat VL test 3 months later If plasma VL 50-999 copies/mL: » Continue enhanced adherence support.

	» Repeat VL test 6 months later. If plasma VL remains at 50-999 copies/mL i.e. persistent low grade viraemia: » Manage as virological failure below.
Management of virological failure on 1st line ART **Note:** Always check hepatitis B surface antigen (HBsAg) before stopping TDF*:* » If patient has chronic hepatitis B, stopping TDF may lead to a fatal hepatitis flare. » If hepatitis B positive, TDF should be continued in the 2ndline regimen.	If plasma VL confirmed ≥1000 copies/mL (on 2 tests), and adherence issues addressed: » Change regimen to 2nd line therapy.
Failing a NNRTI-based 1st line regimen *(TDF+3TC/FTC+EFV/NVP)*	AZT + 3TC + DTG. If HBsAg positive: TDF + 3TC + DTG If DTG contraindicated/ not tolerated: AZT + 3TC +LPV/r (**PLUS** TDF, if HBsAg positive). If AZT and TDF contraindicated/ not tolerated (e.g. anaemia and renal impairment): ABC + 3TC + LPV/r
Failing a DTG- based 1st line regimen for >2 years *(TDF+3TC+DTG)* » Resistance testing for adults and adolescents failing a DTG-based regimen and who meet the definition of confirmed virological failure may be authorized by an expert on a case-by-case basis.	AZT + 3TC +LPV/r If HBsAg positive: TDF + 3TC/FTC +LPV/r
Dyslipidaemia requiring lipid-lowering therapy or diarrhoea associated with LPV/r	Switch LPV/r to ATV/r
3RD LINE ART	
Failing any 2nd line regimen	Refer to a specialist. Resistance to LPV/r or ATV/r and/or DTG must be shown on genotype antiretroviral resistance test in order to qualify for 3rd line – this test is expensive and should only be done in patients with at least 2 years exposure to a PI and objective evidence of good adherence. Application for 3rd line using the standard motivation form is required (available

	from TLART@health.gov.za) –the regimen will be determined by an Expert Committee based on the pattern of resistant mutations and the prior history of antiretroviral exposure.

ABC= Abacavir, 3TC= Lamivudine, TDF = Tenofovir disoproxyl fumarate, AZT=Zidovudine, FTC = Emtricitabine, LPV/r=Lopinavir/ritonavir, DTG= Dolutegravir, EFV= Efavirenz

Currently available ARV FDC preparations on contract circular:

- ABC 600 mg + 3TC 300 mg
- TDF 300 mg + FTC 200 mg
- AZT 300 mg + 3TC 150 mg
- LPV 800 mg + ritonavir 200 mg
- TDF 300 mg + FTC 200 mg + EFV 600 mg *LoE:III*[xi]
- TDF 300mg + DTG 50 mg + 3TC 300 mg

ART: DOSING AND IMPORTANT ADVERSE EFFECTS				
Generic name	**Class**	**Usual dose**	**Renal adjusted dose**	**Important adverse drug reactions and timing**
Tenofovir (TDF)	NRTI	300 mg daily	Avoid in renal impairment (eGFR <50 mL/min)	» Acute kidney injury (rare - weeks to months). » Decline in eGFR (months to years) *LoE:III*[xii] » Fanconi syndrome (rare – months to years) » Reduced bone mineral density (months to years). » Hyperlactataemia/ steatohepatitis (very low risk - months).
Abacavir (ABC)	NRTI	600 mg daily	Dose adjustment not required	» Hypersensitivity reaction (1 to 6 weeks) fever, rash, constitutional symptoms, gastrointestinal symptoms and respiratory symptoms. » Hyperlactataemia/ steatohepatitis (very low risk - months).
Zidovudine (AZT)	NRTI	300 mg 12 hourly	CrCl <10 mL/min: 300 mg daily	» Anaemia, neutropenia (weeks to months). » Gastro-intestinal upset. » Headache. » Myopathy (rare). » Hyperlactataemia / steatohepatitis (medium risk - months). » Lipoatrophy (months to years).
Lamivudine (3TC)	NRTI	300 mg daily (or 150 mg 12 hourly)	CrCl 10-50 mL/min: 150 mg daily CrCl <10 mL/min: 50 mg daily	» Anaemia due to pure red cell aplasia (rare). » Hyperlactataemia / steatohepatitis (very low risk - months).

Emtricitabine (FTC)	NRTI	200 mg daily	<u>CrCl 30-50 mL/min:</u> 200 mg every 2 days <u>CrCl 15-29 mL/min:</u> 200 mg every 3 days <u>CrCl <15 mL/min:</u> 200 mg every 4 days	» Palmar hyperpigmentation. » Hyperlactataemia / steatohepatitis (very low risk - months). » Anaemia due to pure red cell aplasia (rare). *LoE:III*[xiii]
Nevirapine (NVP)	NNRTI	200 mg daily for 14 days *then* 200 mg 12-hourly	Dose adjustment not required	» Rash and/or Hepatitis (1 week to 3 months). *****Avoid in women with a CD4 count >250 cells/mm^3 and men with a CD4 count >400 cells/mm^3 initiating ART due to increased risk of rash associated hepatitis.
Efavirenz (EFV)	NNRTI	600 mg at night	Dose adjustment not required	» Central nervous system symptoms: vivid dreams, problems with concentration, confusion, mood disturbance, psychosis (days to weeks). » Encephalopathy, often with cerebellar features (uncommon – months to years). *LoE:III*[xiv] » Rash (1 to 6 weeks). » Hepatitis (weeks to months) » Gynaecomastia.
Lopinavir/ ritonavir (LPV/r)	Boosted PI	400/100 mg 12-hourly **OR** 800/200 mg daily (only if PI-naïve)	Dose adjustment not required	» Gastrointestinal upset. » Dyslipidaemia (weeks). » Rash and/or Hepatitis (1 to 6 weeks).
Atazanavir/ ritonavir (ATV/r)	Boosted PI	300 mg with ritonavir 100 mg daily	Dose adjustment not required	» Unconjugated hyperbilirubinaemia (common, but benign)). » Dyslipidaemia (low risk). » Hepatitis (rare - 1 to 6 weeks). » Renal stones (not common).
Dolutegravir (DTG)	InSTIs	50 mg once daily	Dose adjustment not required	» Hypersensitivity (rare, weeks) » Insomnia (common) » Headache (common) » Other neuropsychiatric symptoms » Nausea, diarrhea (common) » Hepatitis (uncommon) » Weight gain » Increase in serum creatinine due to inhibition of creatinine secretion by DTG; this is clinically insignificant as glomerular filtration rate is not reduced but will modestly

				affect eGFR which is determined using serum creatinine.
Raltegravir (RAL)		400mg 12 hourly	Dose adjustment not required	» Decreased appetite; headache; nausea; insomnia; dizziness (common) » Anaemia, mental disorders, liver failure, herpes infection, warts, visual disturbance, anxiety, hepatic steatosis, neutropenia (uncommon).

The time-onset information with respect to adverse drug reactions (ADRs) serves as an estimate. Patients may present with ADRs with the onset deviating from that indicated in the table.

LoE:III[xv]

ART: DRUG-DRUG INTERACTIONS

Information can be accessed from:
https://www.hiv-druginteractionslite.org/checker
http://www.mic.uct.ac.za/ and download the ARV/EML interaction checker.
Package inserts.

ART INTERACTIONS WITH RIFAMPICIN AND RECOMMENDATIONS FOR ADMINISTRATION

Class	ARV	Interaction with rifampicin	Dose of ARV with rifampicin
NRTI	3TC/FTC/ TDF/AZT/ ABC	No clinically significant pharmacokinetic interactions	No dose adjustment required.
NNRTI	EFV	Non-significant change (EFV concentrations may increase in patients who are genetic slow metabolisers of EFV due to inhibition by isoniazid)	No dose adjustment required (600 mg at night).
	NVP	NVP concentrations are modestly reduced.	NVP (200 mg 12 hourly) can be used without lead-in dose.
PI	LPV/r	LPV plasma concentrations significantly decreased	Double the dose of LPV/r to 800/200 mg 12-hourly. **Note:** There is an increased risk of ALT/AST elevations and gastrointestinal disorders. Dose adjustments should be gradually titrated upward over 1-2 weeks.*
	All other PIs	Marked reduction in PI concentrations	Do not prescribe concomitantly – replace rifampicin with rifabutin 150 mg daily (see monitoring instructions below).
InSTI	DTG	Significant reduction in concentration of DTG	Dosing frequency increased to 50 mg 12 hourly.*
	RAL	Significant reduction in RAL concentration	Dosing frequency to be increased to 400 mg 12 hourly.

*Dose adjustments should be continued for 2 weeks after rifampicin is stopped.

LoE:III[xvi]

In patients on atazanavir or darunavir, or if double dose LPV/r is not tolerated, replace rifampicin with:

- Rifabutin, oral, 150 mg daily.
  - Monitor FBC monthly for anaemia, and neutropenia.
  - Monitor clinically for symptoms of uveitis (e.g. pain, photophobia, variable loss of vision, circumcilliary injection, a miotic pupil) – immediately stop rifabutin pending ophthalmology opinion.

LoE:III[xvii]

DRUG INTERACTIONS WITH DOLUTEGRAVIR

Interacting medicine	Effect of co-administration	Recommendation
Preparations containing polyvalent cations (Mg^{2+}, Ca^{2+}, Fe^{2+}, Al^{3+}, Zn^{2+}) Antacids Sucralfate Multivitamins Nutritional supplements	Significant reduction in concentration of DTG	Magnesium- and aluminum-containing preparations should be taken 6 hours before or 2 hours after DTG. Calcium- and iron- containing preparations can be taken with DTG together with food. **Note:** Iron and calcium should be taken at least 4 hours apart from one another.
Anticonvulsants: Carbamazepine Phenobarbital Phenytoin	Significant reduction in concentration of DTG	Avoid co-administration if possible. Consider valproate or lamotrigine. *For carbamazepine:* Double DTG dose to 50 mg 12 hourly.
Metformin	Significant increase in metformin levels	Administer metformin to a maximum of 500 mg 12 hourly.
Rifampicin	Significant reduction in concentration of DTG	Double DTG dose to 50 mg 12 hourly.

LoE:III[xviii]

DRUG INTERACTIONS WITH BOOSTED PIs

Interacting medicine	Effect of co-administration	Recommendation
Substrates of cytochrome P450 3A4 (e.g. most statins, calcium channel blockers, most SSRIs, most benzodiazepines)	Significant increase in levels of CYP3A4 substrates	Avoid co-administration or use lower doses of CYP3A4 substrates (always consult interaction resources)
Anticonvulsants: Carbamazepine Phenobarbital Phenytoin	Significant reduction in concentration of PI	Avoid co-administration. Consider valproate or lamotrigine.
Proton pump inhibitors	Significant reduction in ATV levels	Avoid co-administration. *LoE:III*[xix]
Rifampicin	Significant reduction in levels of PI	Double LPV/r dose. Avoid co-administration of other PIs (replace rifampicin with rifabutin)

MONITORING ON ART	
At HIV Diagnosis	» Confirm HIV positive result with antibody test. » WHO staging. » Check CD4 count. - CD4 <100 cells/mm^3: Check cryptococcal antigen (If symptomatic, perform LP). - CD4 <200 cells/mm^3: Fast track for ART initiation, initiate cotrimoxazole prophylaxis. - CD4 <350 cells/mm^3: Prioritise for ART. » Screen for pregnancy or ask if planning to conceive. » Screen for mental health, STIs and NCDs. » Screen for TB using the WHO screening questionnaire (any one of cough, fever, night sweats, or weight loss) – in pregnancy do sputum XpertMTB/RIF Ultra® in all. » Do urine LAM testing if patients are seriously ill or CD4 ≤100 cells/mm^3 and there are signs and symptoms of tuberculosis. Urine dipstick for proteinuria and haematuria *LoE:III*[xx]
Prior to initiating ART	» Check creatinine (avoid TDF if eGFR <50 mL/minute). » Check FBC (avoid AZT if Hb <8 g/dl). » Check HBsAg (if positive, TDF should form part of the regimen).
On ART	» VL at 6 and 12 months after initiating ART and every 12 months thereafter, if virologically suppressed. » CD4 at 12 months after initiating ART*. » Creatinine at 3, 6 and 12 months after initiation, and every 12 months thereafter if on TDF. » FBC and differential count at 3 and 6 months after initiating AZT, then every 12 months. » ALT if symptoms of hepatitis develop. » Fasting cholesterol and triglycerides at 3 months after initiating LPV/r. *Stop CD4 count monitoring when >200 cells/mm^3 and virologically suppressed. However, if virological or clinical failure occurs, then a CD4 count should be done as cotrimoxazole may need to be commenced/recommenced. Repeat CD4 count every 6 months if VL remains > 1000 copies/mL

LoE:III[xxi]

10.1.1 MANAGEMENT OF SELECTED ANTIRETROVIRAL ADVERSE DRUG REACTIONS

E78.4/K71.9 + (Y41.5 + B24)

Dyslipidaemia E78.4 + (Y41.5 + B24)

Certain antiretroviral medication, particularly the protease inhibitors, can cause dyslipidaemia. Fasting lipid levels should be done 3 months after starting protease inhibitors. LPV/r is associated with a higher risk of dyslipidaemia (especially hypertriglyceridaemia) than ATV/r.

Patients on LPV/r who:
» develop triglycerides >10 mmol/L;or
» have a total cholesterol >6 mmol/L with a high risk (>20% risk of developing a CVD event in 10 years)
» should switch to ATV/r and repeat the fasting lipid profile in three months.

Patients with persistent dyslipidaemia despite switching to ATV/r, qualify for lipid lowering therapy. Criteria for initiating lipid lowering therapy are the same as for HIV seronegative patients. (See section3.1: Ischaemic heart disease and atherosclerosis, prevention).

Many statins (including simvastatin) cannot be used with protease inhibitors, as protease inhibitors inhibit the metabolism of the statin resulting in extremely high blood levels.

Patients, who fail to respond to lifestyle modification and have hypertriglyceridemia, treat with a fibric acid derivative, e.g.:
- Bezafibrate, oral, 400 mg at night.

OR

If LDL cholesterol is raised (See section 3.1: Ischaemic heart disease and atherosclerosis, prevention):
- Atorvastatin, oral, 10 mg daily (do not exceed this dose due to a drug interaction with PIs).

Anaemia and neutropenia

AZT causes macrocytosis and can cause anaemia and neutropenia (but note that it does not cause thrombocytopenia). AZT does not need to be stopped with mild anaemia and/or neutropenia, but must be stopped and replaced with an alternative medication if:
» anaemia is symptomatic,
» anaemia is severe (Hb <8.0 g/dL), or
» the neutrophil count is below 0.75×10^9/L.

Lamivudine and emtricitabine can cause pure red cell aplasia, but this is rare.

Hypersensitivity

Note that pre-existing dermatological conditions (especially papulopruritic eruptions and acne) may worsen after commencing ART due to immune reconstitution inflammatory syndrome (see section 10.1.2: Management of selected antiretroviral adverse drug reactions) – this is not a hypersensitivity reaction and ART should be continued.

Other medicines, notably cotrimoxazole, can also cause hypersensitivity.

Hypersensitivity rashes occur commonly in the 8-week period after starting NVP or EFV. NNRTI-associated rashes can be severe and life-threatening, especially with nevirapine. If a rash develops on NVP an ALT should be requested urgently.

If any of the following features occur, then NVP or EFV must be permanently discontinued:

» Blistering – if more than 30% of the skin surface is involved this is called Toxic Epidermal Necrolysis, and requires admission.
» Lesions affecting mucous membranes (mouth, eyes, or genitals) – this is called Stevens-Johnson Syndrome, and requires admission
» Fever.
» Features of hepatitis (with nevirapine) – either ALT > 5 times the upper limit of normal or symptomatic hepatitis with deranged liver function tests. Note that the hepatitis usually starts a week or two after the onset of the rash.

With mild rashes NVP and EFV can be continued with careful observation and the rash will often subside. If mild rashes occur on NVP during the dose lead-in phase (200 mg daily) do not increase the dose to 200 mg 12 hourly until the rash improves.
If rash worsens or does not improve within a week discontinue EFV or NVP.

If NVP has been stopped due to cutaneous hypersensitivity, then EFV can be substituted provided that the rash has settled, and that the reaction was not life-threatening (either Stevens-Johnson Syndrome or Toxic Epidermal Necrolysis). If the reaction was life-threatening then a protease inhibitor, e.g. LPV/r, should be substituted.

DTG can cause systemic hypersensitivity syndrome with rash, but this is very uncommon. DTG should be permanently discontinued if this occurs.

ABC can cause a rash as part of a systemic hypersensitivity reaction, which is confined to people who are HLA-B*5701 positive. ABC should be permanently discontinued if this occurs.

LoE:III[xxii]

Hyperlactataemia

Symptomatic hyperlactataemia occurs due to mitochondrial toxicity of NRTIs. Check for acidosis in such patients.
The estimated risk of lactate elevation differs among the NRTIs, with zidovudine having moderate risk and the other NRTIs low risk.

Risk factors for hyperlactataemia include:

» females,
» obesity,
» prolonged use of NRTIs (> 3 months), or
» development of NRTI-induced peripheral neuropathy or fatty liver.

Clinical symptoms of hyperlactataemia are non-specific and may include:

» nausea
» abdominal pain
» malaise
» liver dysfunction (due to steatosis)
» vomiting
» weight loss
» tachycardia

A high index of suspicion is necessary. Send blood for lactate levels (check with your local laboratory for specimen requirements for lactate). Alternatively, point of care finger prick lactate monitoring can be done. Check the serum bicarbonate level.

Patients with mild hyperlactataemia (lactate 2.5–5 mmol/L):
Therapy should be altered by selecting NRTIs that are less associated with hyperlactataemia.
Monitor serial lactate measurements until the lactate has returned to within the normal range.
Note: The resolution of hyperlactataemia may take a few months.

Patients with lactate levels > 5 mmol/L:
Stop the NRTIs.
If the patient is on a 1st line regimen, continue the EFV or DTG and add LPV/r.
If the patient is on the 2nd line regimen, consult with an HIV specialist.
If there is acidosis, then admission to a high care unit is recommended.

Lactic acidosis carries a poor prognosis. Treatment is largely supportive. It is essential to exclude other causes of lactic acidosis, especially sepsis. High dose vitamin B, especially riboflavin and thiamine, may have a role in therapy.

Hepatotoxicity K71.9 + (Y41.5 + B24)
All currently available antiretrovirals are potentially hepatotoxic. EFV has the highest risk. NRTIs uncommonly cause acute hepatitis, but may result in steatohepatitis after prolonged use, which manifests with mildly elevated liver enzymes, affecting GGT and alkaline phosphatase more than the transaminases, and ALT more than AST. Patients on atazanavir may develop jaundice due an unconjugated hyperbilirubinaemia, which is not accompanied by liver injury. This is a cosmetic issue and the atazanavir can be substituted if the patient is unable to tolerate the jaundice. However, all protease inhibitors can rarely cause hepatitis, so it is important to exclude this in patients developing jaundice on ATV/r.

Other potentially hepatotoxic medicines prescribed to in HIV-infected patients include anti-tuberculous therapy, fluconazole and cotrimoxazole. Cotrimoxazole, amoxicllin/clavulanate and macrolides tend to cause cholestatic hepatitis that may take months to resolve.

The exclusion of viral hepatitis is important in the work-up of drug-induced liver injury (DILI). Testing for hepatitis A, B and C should be undertaken. Hepatitis B is common, and flares of viral hepatitis may occur after ART initiation. Furthermore, life threatening flares may occur when antiretrovirals that are also active against hepatitis B (TDF, 3TC and FTC) are withdrawn.

Other potential causes include disseminated TB, IRIS, alcohol, alternative remedies, fatty liver, sepsis and HIV cholangiopathy.

Investigations:
» Request an ALT.
» Request viral hepatitis screen, full liver function tests and INR in patients if ALT >5 x upper limit of normal (ULN) and/or jaundice and/or symptoms of hepatitis are present.
» Perform a liver ultrasound if GGT or ALP are significantly elevated or if conjugated bilirubin is elevated, to exclude:
  - Extrahepatic biliary obstruction.
  - Fatty liver due to NRTIs.
  - Disseminated TB.

Management:

Upper Limit of Normal (ULN)	<2.5 x ULN	2.5 – 5 x ULN	> 5 x ULN
ALT	Repeat in 2 weeks	Repeat in 1 week	Stop ART
Isolated Hyperbilirubinaemia	Repeat in 1 week	Stop ART	Stop ART

*Stop the relevant medicines at lower levels if symptoms of hepatitis (right upper quadrant pain, nausea / vomiting) or jaundice are present.

If ART is considered to be the cause substitute ART as follows:
» If the hepatitis occurred on efavirenz, substitute with DTG or a boosted PI.
» If hepatitis occurred on PI, substitute with DTG.
» NRTI fatty liver – discontinue AZT (if relevant) and replace with safer NRTI (TDF or ABC) – if not on AZT and hepatitis is severe switch to NRTI-sparing regimen.

Hepatitis in patients on ART and anti-tuberculosis therapy

Drug-induced liver injury (DILI) is a known adverse effect of anti-tuberculosis therapy and ART and is a common problem in HIV/TB co-infected patients. First-line TB medicines associated with DILI include isoniazid (INH), rifampicin (RIF) and pyrazinamide (PZA). Anti-tuberculosis therapy commonly causes transient, mild, asymptomatic elevations in serum aminotransferase levels not requiring discontinuation of therapy.

If hepatitis develops, as defined above, stop all antiretrovirals, cotrimoxazole and all potentially hepatotoxic TB medicines (isoniazid, rifampicin and pyrazinamide).

TB immune reconstitution inflammatory syndrome (TB-IRIS) should be considered in the differential diagnosis (see section 10.1.2: Management of selected antiretroviral adverse drug reactions). This condition presents shortly after ART initiation in patients with TB. The GGT and ALP are elevated to a greater degree than the transaminases. Mild jaundice with a conjugated hyperbilirubinaemia and tender hepatosplenomegaly may be present.

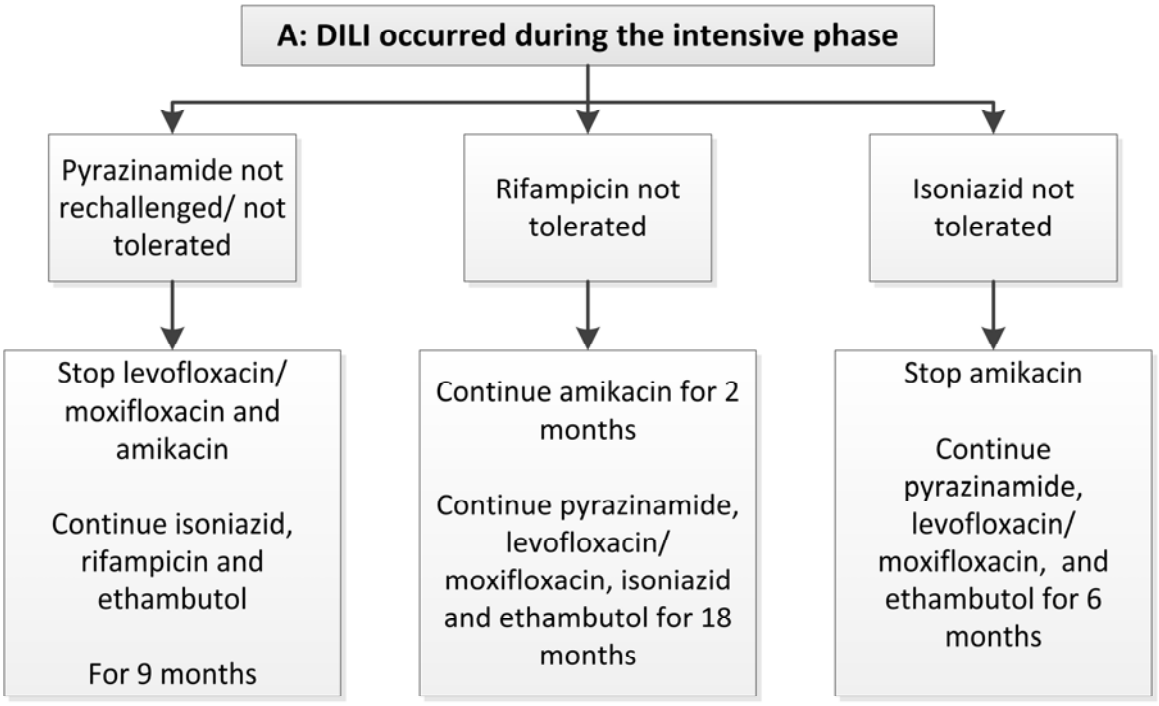
Investigations:
» Request an ALT.

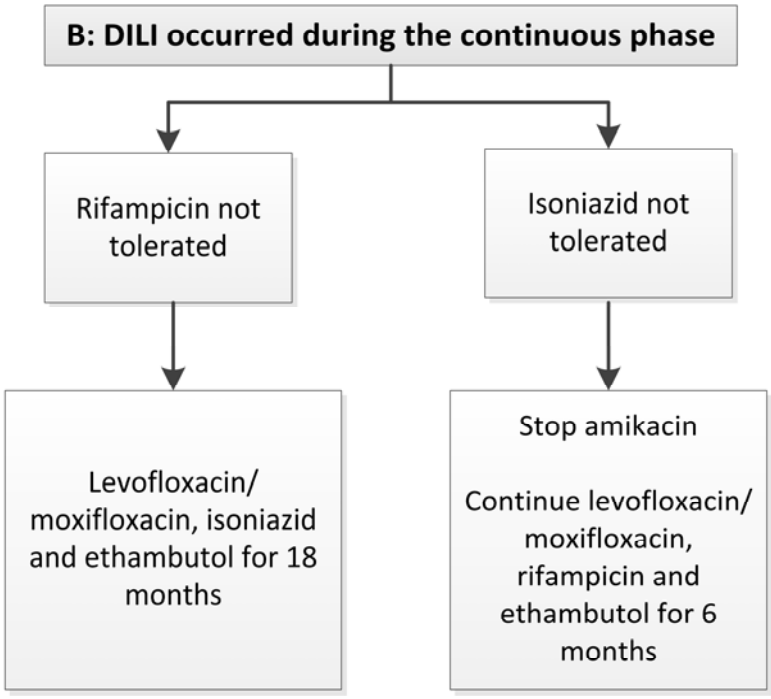
» Request viral hepatitis screen, full liver function tests and INR in patients if ALT >5 x ULN and/or jaundice and/or symptoms of hepatitis are present.
» Perform a liver ultrasound if GGT or ALP are significantly elevated or if conjugated bilirubin is elevated, to exclude extrahepatic biliary obstruction.
» Reassess the grounds for TB diagnosis.
» Check if patient is on intensive or continuation phase of TB treatment.

Management:
» Stop TB therapy and initiate background TB therapy and continue throughout rechallenge:
  - Amikacin, IV, 15 mg/kg daily.
  - Moxifloxacin, oral, 400 mg daily or levofloxacin 750–1000 mg daily.
  - Ethambutol, oral, 800–1200 mg daily.
» Stop cotrimoxazole prophylaxis and do not rechallenge.
» Stop ART as described above.
» Repeat ALT and bilirubin in 2 days (inpatient) or 7 days (outpatient).
» When ALT is <100 IU/L and total bilirubin is less than twice the upper limit of normal, start TB medicine rechallenge as follows:

Day 1:	• Rifampicin, oral 600 mg daily. o If <60 kg: rifampicin, oral 450 mg daily.
Day 3:	» Check ALT.
Day 4–6:	**ADD** • Isoniazid, oral 300 mg daily.
Day 7:	» Check ALT.
Day 8:	» Stop moxifloxacin/levofloxacin and amikacin. Consider a pyrazinamide rechallenge (in cases of TB meningitis or intolerance/resistance to other medicines). • Pyrazinamide, oral 25 mg/kg daily.
Day 10:	» Check ALT. » Thereafter, monitor ALT twice weekly for the first 3 weeks, then every two weeks for a month, then monthly until 3 months. • Restart ART 2 weeks after completing rechallenge of TB therapy. o Monitor ALT every 2 weeks for 2 months after ART rechallenge.

Duration of TB therapy following successful rechallenge





LoE:I[xxiii]

10.1.2 IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME (IRIS)

D89.3 + (Y41.5 + B24)

DESCRIPTION

IRIS occurs when improving immune function unmasks a previously occult opportunistic disease, which has an unusual inflammatory presentation ("unmasking IRIS") or causes paradoxical deterioration of an existing opportunistic disease ("paradoxical IRIS"). IRIS is more common in patients with advanced HIV disease, particularly those with a CD4 count <100 cells/mm^3. IRIS nearly always presents during the first 3 months of ART, with the median time of onset being about two weeks. The diagnosis of paradoxical IRIS is often difficult as new opportunistic diseases or drug resistance of the organism causing the opportunistic infection need to be excluded.

TB is the commonest opportunistic disease involved in IRIS reactions in South Africa. Paradoxical TB IRIS presents as recurrence of TB symptoms/signs, or worsening, or new manifestations. The commonest presentation is with enlarging lymph nodes, often with extensive caseous necrosis. Lung infiltrates or effusions may worsen or develop. It is important to exclude multi-drug resistance in all patients suspected with paradoxical TB IRIS.

Other common IRIS manifestations include:

» Inflammatory reactions to skin diseases, especially acne and Kaposi's sarcoma.
» Worsening cryptococcal meningitis.
» Flares of hepatitis B or C.

GENERAL MEASURES

Counseling is important to ensure that the patient understands that IRIS does not mean failure of ART.
Management of IRIS is mainly symptomatic, e.g. aspiration of TB lymph nodes or effusions.
Continue ART and therapy for the opportunistic infection.

MEDICINE TREATMENT

<u>For pain and fever:</u>

- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

OR

- NSAID, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with meals.

<u>**Treating** severe IRIS manifestations (e.g. compression of major structures by enlarging lymph nodes, expanding CNS tuberculomata, worsening meningitis):</u>

- Corticosteroids (intermediate-acting) e.g.:

- Prednisone, oral, 1.5 mg/kg daily for 2 weeks.
  - Then 0.75 mg/kg daily for 2 weeks.

Preventing severe IRIS in high risk patients (CD4 ≤100 cells/mm^3) and had antituberculosis treatment for <30 days before initiating ART:

- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 40 mg daily for 2 weeks.
  - Then 20 mg daily for 2 weeks.

LoE:I[xxiv]

Note: Do not use steroids in patients with Kaposi sarcoma.

10.2 OPPORTUNISTIC DISEASES

10.2.1 TUBERCULOSIS PREVENTIVE THERAPY (TPT)

Z29.2 + (B24)

Patients with HIV infection are more susceptible to TB infection than HIV-uninfected patients at any CD4 count. TPT is an effective intervention for reducing the incidence of TB in HIV-infected patients

Eligibility

All HIV-infected patients, irrespective of CD4 count and ART status.

Exclusions

» Suspected or confirmed TB
» Liver Disease
» Previous MDR- or XDR-TB
» Painful peripheral neuropathy
» Alcohol abusers

Note:

» TB must be excluded prior to initiating TPT by screening for the following:
  - Cough (any duration)
  - Fever
  - Weight loss
  - Night sweats

» TPT should not be initiated in patients if any of the above is present. These patients require further investigation for active TB.

Start TPT together with ARVs:

- Isoniazid, oral, 300 mg daily for 12 months.

AND

- Pyridoxine, oral, 25 mg once daily for 12 months.
  - Educate patients on the symptoms of hepatotoxicity (nausea, vomiting, yellow eyes, brown urine, and pain in right upper quadrant).
  - Instruct patient to present early if any of these symptoms arise.
  - Patients should be followed up monthly for the first 3 months.

LoE:I[xxv]

In pregnant women, starting ART:

» If CD4 >350 cells/mm^3.	» If CD4 ≤350 cells/mm^3.
• Defer TPT until after delivery.	• Exclude active TB with symptom screen and TB Xpert MTB/RIF Ultra ®, then give TPT. *LoE:II*[xxvi]

10.2.2 OPPURTUNISTIC INFECTION PROPHYLAXIS, WITH COTRIMOXAZOLE

Z29.2 + (B24)

DESCRIPTION

Primary prophylaxis reduces the probability of developing many infections, e.g.:

» Pneumocystis pneumonia
» toxoplasmosis
» bacterial pneumonia
» bacteraemia
» cystoisosporiasis

Indications for primary prophylaxis: *LoE:III*[xxvii]

» WHO Clinical stage II, III or IV.
» CD4 count <200 cells/mm^3.

MEDICINE TREATMENT

Prophylaxis

- Cotrimoxazole, oral, 160/800 daily. *LoE:I*[xxviii]

Note:

Once the CD4 >200 cells/mm^3 (as measured at the routine CD4 count done at 1 year on ART), discontinue prophylaxis. If the CD4 count was >200 cells/mm^3 when cotrimoxazole was commenced (e.g. patients with TB) continue for 6 months**.**

10.2.3 CANDIDIASIS OF OESOPHAGUS/TRACHEA/BRONCHI

B20.4

DESCRIPTION

Mucosal candidiasis involving the oesophagus/trachea/bronchi is AIDS-defining (WHO clinical stage 4). Oesophagitis is by far the commonest manifestation.

Clinical features: symptoms of pain or difficulty on swallowing. Oral thrush is present in most patients.

GENERAL MEASURES

Maintain adequate hydration.

MEDICINE TREATMENT

- Fluconazole, IV/oral, 200 mg daily for 14 days.
  - The usual route is oral but give IV if patient unable to swallow or is vomiting.
  - An early relapse should be treated with a 4-week course of fluconazole as above.

Note: Primary or secondary fluconazole prophylaxis for mucosal candidiasis is not recommended.

10.2.4 CRYPTOCOCCOSIS

10.2.4.1 ASYMPTOMATIC CRYPTOCOCCOSIS, CRAG POSITIVE

B20.5

DESCRIPTION

All ART-naïve patients with CD4 <100 cells/mm^3 should have cryptococcal antigen (CrAg) test done on serum, plasma or whole blood (unless they had a diagnosis of cryptococcal infection). The treatment of patients who are CrAg positive and with no signs or symptoms of meningitis and CSF crag negative is outlined below. Refer to algorithm

LoE:III[xxix]

MEDICINE TREATMENT

Induction phase

- Fluconazole, oral 1200 mg daily for 14 days. *LoE:III*[xxx]

Consolidation phase

Follow with:

- Fluconazole, oral, 800 mg daily for 8 weeks.

Maintenance phase

- Fluconazole, oral, 200 mg daily.
  - Continue for at least 1 year provided that the CD4 count increases to >200 cells/mm^3 on ART. If the CD4 count does not increase continue treatment indefinitely.

LoE:III[xxxi]

- Commence ART after completion of the induction phase i.e. at 2 weeks. See section 10.1: Antiretroviral therapy.

LoE:III[xxxii]

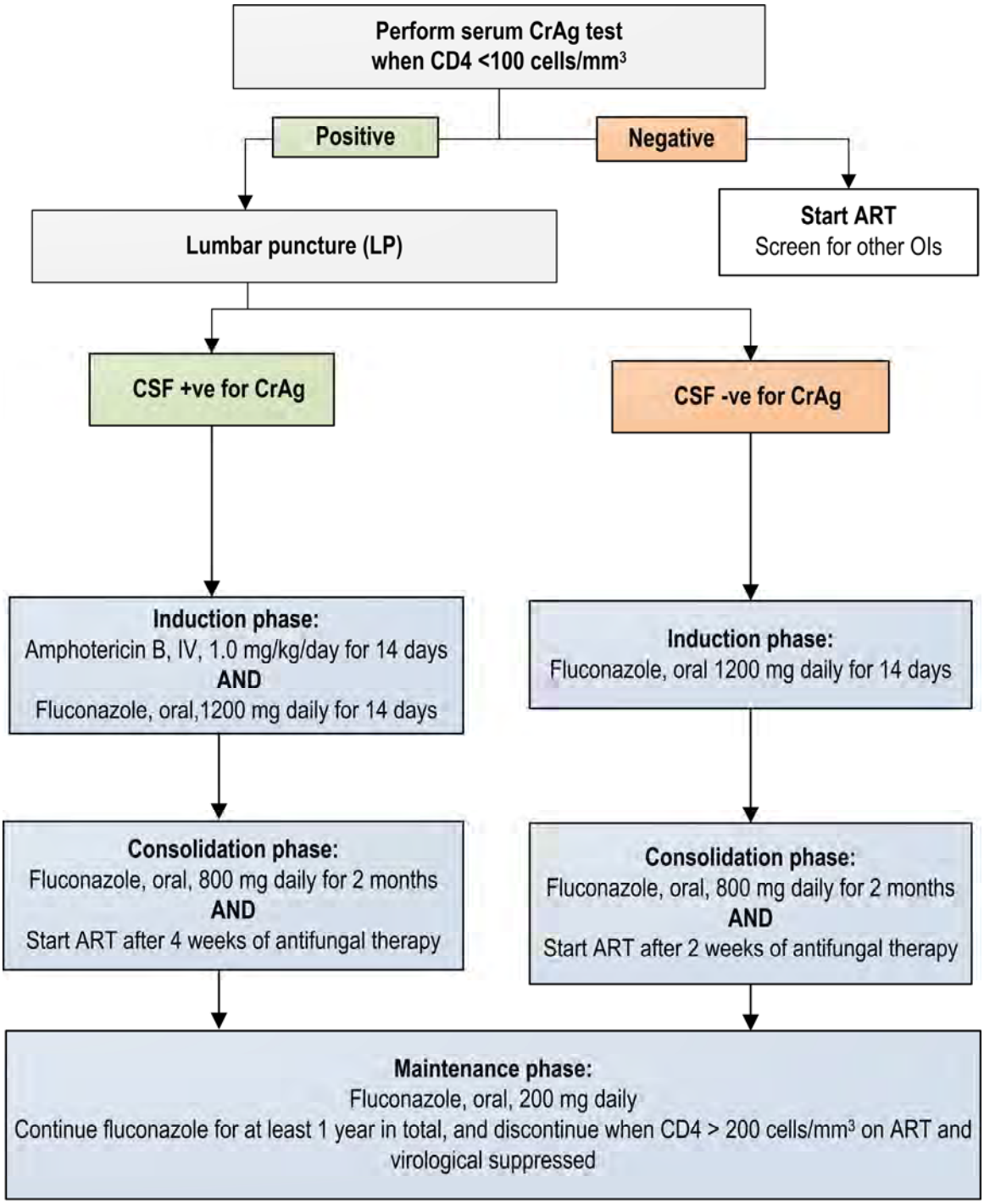
CAUTION

» Fluconazole should be avoided in the 1st trimester, but pregnant women should be counselled that the benefits of fluconazole may outweigh the risks in the management of cryptococcosis.

» All pregnant women <20 weeks gestation exposed to fluconazole should have an ultrasound scan to detect congenital abnormalities. *LoE:III*[xxxiii]

» For management of breastfeeding mothers, consult a specialist; as fluconazole is present at concentrations similar to maternal plasma concentrations in breast milk that will be transmitted to the breastfed infant.

LoE:III[xxxiv]



Note: If there is a delay in performing LP, obtaining LP results or in starting amphotericin B therapy, start fluconazole 1200 mg immediately.

Adapted from: Govender NP, Meintjes G (Chairpersons), Bicanic T, Dawood H, Harrison TS, Jarvis JN, Karstaedt AS, Maartens G, McCarthy KM, Rabie H, Variava E, Venter WDF (Expert panel members), Boulware DR, Chiller T, Meya DB, Scriven J (Reviewers). Guideline for the prevention, diagnosis and management of cryptococcal meningitis among HIV-infected persons: 2013 update. S Afr J HIV Med 2013;14(2):76-86. http://www.sajhivmed.org.za/index.php/hivmed/article/view/82/128

10.2.4.2 SYMPTOMATIC, NON-MENINGEAL CRYPTOCOCCOSIS

B20.5

DESCRIPTION

Cryptococcal infection confirmed on culture or serum CrAg positive with non-meningeal disease. Any anatomical site may be involved, but the lungs are the commonest site.

MEDICINE TREATMENT

Induction phase

- Fluconazole, oral 1200 mg daily for 14 days.

AND

- Amphotericin B, slow IV infusion, 1 mg/kg daily in dextrose 5 % over 4 hours for 14 days.
  - Ensure adequate hydration to minimise nephrotoxicity. (See Appendix II for preventing, monitoring and management of toxicity).

Consolidation phase

Follow with:

- Fluconazole, oral, 800 mg daily for 8 weeks.

Maintenance phase

- Fluconazole, oral, 200 mg daily.
  - Continue for at least 1 year provided that the CD4 count increases to >200 cells/mm^3 on ART. If the CD4 count does not increase continue treatment indefinitely.
- Commence ART 4–6 weeks after starting antifungal therapy. See section 10.1: Antiretroviral therapy.

LoE:III[xxxv]

10.2.4.3. CRYPTOCOCCAL MENINGITIS

B20.5 + (B45.1 + G02.1*)

DESCRIPTION

Cryptococcal meningitis is the commonest manifestation of disseminated cryptococcosis in patients with advanced HIV. Severe headache is common due to raised intracranial pressure.

Diagnosis

Confirmed on lumbar puncture.

GENERAL MEASURES

Therapeutic lumbar puncture is indicated to lower pressure in symptomatic patients and should be done with pressure monitoring. Remove sufficient CSF (maximum 30 mL) to lower pressure to 50% of the opening pressure but not less than 20 cm H_2O.

Therapeutic lumbar puncture should be done daily until there is clinical improvement.

MEDICINE TREATMENT

Induction phase

- Fluconazole, oral 1200 mg daily for 14 days.

AND

- Amphotericin B, slow IV infusion, 1 mg/kg daily in dextrose 5 % over 4 hours for 14 days.
- Ensure adequate hydration to minimise nephrotoxicity. (See Appendix II for preventing, monitoring and management of toxicity).

Consolidation phase

Follow with:

- Fluconazole, oral, 800 mg daily for 8 weeks.

Maintenance phase

- Fluconazole, oral, 200 mg daily.
  - Continue for at least 1 year provided that the CD4 count increases to >200 cells/mm^3 on ART. If the CD4 count does not increase continue treatment indefinitely.

LoE:III[xxxvi]

- Commence ART 4–6 weeks after starting antifungal therapy. See section 10.1: Antiretroviral therapy.

LoE:III[xxxvii]

Note: Adjunctive corticosteroids have been shown to be detrimental.

LoE:I[xxxviii]

REFERRAL

» Focal neurological signs – CT scan required to exclude other pathology e.g. toxoplasmosis.
» Persistent raised intracranial pressure despite daily therapeutic lumbar puncture.

10.2.5 CRYPTOSPORIDIOSIS DIARRHOEA

B20.8 + (A07.2)

DESCRIPTION

Chronic diarrhoea due to *Cryptosporidium parvum*. Disease lasting >4 weeks is AIDS-defining (WHO clinical stage 4).

GENERAL MEASURES

Rehydration with oral rehydration solution (ORS).

MEDICINE TREATMENT

There is no specific antimicrobial therapy for cryptosporidiosis. As with other opportunistic diseases it responds well to ART.

Antimotility agents are partially effective, e.g.:

- Loperamide, oral, 4 mg initially, followed by 2 mg as required up to four times daily.

10.2.6 CYTOMEGALOVIRUS (CMV)

B20.2

DESCRIPTION

CMV disease outside the reticulo-endothelial system is an AIDS-defining illness (WHO clinical stage 4).
CMV disease is seen in patients with CD4 counts <100 cells/mm^3.
The commonest manifestations are:

» retinitis,
» gitulceration,
» pneumonitis, and
» polyradiculitis.

GIT and other organ involvement must be diagnosed on biopsy.
CNS disease must be diagnosed by PCR of CSF.
The diagnosis of CMV retinitis should be confirmed by an ophthalmologist
Note: CMV serology (IgM and IgG), antigenaemia (pp65), or PCR on blood are not helpful in the diagnosis of CMV disease in HIV-infected adults.

MEDICINE TREATMENT

Valganciclovir is the treatment of choice, but this agent is toxic and expensive; and should only be used by a specialist familiar with its use.
To prevent recurrent disease commence patients on ART as soon as possible after initiating valganciclovir (see section 10.1: Antiretroviral therapy).
Maintenance therapy is only applicable to CNS disease and retinitis.
Monitor FBC regularly during therapy. Avoid other medicines associated with bone marrow suppression, particularly zidovudine.

Biopsy-proven GIT disease and pneumonitis

- Valganciclovir, oral, 900 mg 12 hourly for the first 3 weeks, if available. Specialist initiated.

OR

If unable to tolerate oral medication:

- Ganciclovir, IV, 5 mg/kg 12 hourly for 14 days, if available. Specialist initiated.

Maintenance treatment is not indicated unless there has been a relapse.

CNS disease
Initial treatment:
- Valganciclovir, oral, 900 mg 12 hourly for the first 3 weeks, if available. Specialist initiated.

OR
If unable to tolerate oral medication:
- Ganciclovir, IV, 5 mg/kg 12 hourly for 14 days. Specialist initiated.

Maintenance treatment:
Only patients with a good clinical response should be considered for maintenance.
- Valganciclovir, oral, 900 mg daily until CD4 count rises to >100 cells/mm^3 on ART, if available.Specialist initiated.

OR *LoE:III*[xxxix]
If unable to tolerate oral medication:
- Ganciclovir, IV, 5 mg/kg daily until CD4 count rises to >100 cells/mm^3 on ART. Specialist initiated.

REFERRAL/CONSULTATION
Specialist or tertiary
All patients.

10.2.7 CYSTOISOSPORIASIS
A07.3/B20.8

DESCRIPTION
Diarrhoea due to *Cystoisospora belli*. Disease lasting >4 weeks is AIDS-defining (WHO clinical stage 4).

GENERAL MEASURES
Rehydration with oral rehydration solution (ORS).

MEDICINE TREATMENT
- Cotrimoxazole 160/800 mg, oral, 2 tablets 12 hourly for 10 days.

OR
If allergic to cotrimoxazole:
- Ciprofloxacin, oral, 500 mg 12 hourly for 10 days.

Secondary prophylaxis:
Continue for at least 6 months and until CD4 count increases to >200 cells/mm^3 on ART.
- Cotrimoxazole 160/800 mg, oral daily.

10.2.8 MYCOBACTERIOSIS – DISSEMINATED NON-TUBERCULOUS

B20.0

DESCRIPTION

Disseminated infection due to non-tuberculous mycobacteria, usually *Mycobacterium avium* complex.
Diagnosis must be by culture from sterile sources, e.g. blood, tissue or bone marrow. Note that culture from a single sputum specimen is not adequate to make the diagnosis as this often reflects colonisation rather than disease.
Non-tuberculous mycobacteria can cause limited pulmonary disease, which is diagnosed if the sputum culture is positive repeatedly and there is a worsening pulmonary infiltrate.
Disseminated disease is AIDS-defining (WHO clinical stage 4).

MEDICINE TREATMENT

- Azithromycin, oral, 500 mg daily.

AND *LoE:II*[xl]

- Ethambutol, oral, 15–20 mg/kg daily.

Treatment can be stopped when treatment has been continued for at least 12 months **AND** the CD4 count has increased to >100 cells/mm^3 on ART.

10.2.9 PNEUMOCYSTIS PNEUMONIA

B20.6

DESCRIPTION

Interstitial pneumonitis due to *Pneumocystis jirovecii* (formerly *carinii*). AIDS-defining illness (WHO clinical stage 4).

MEDICINE TREATMENT

<u>All patients:</u>

- Cotrimoxazole 80/400 mg, oral, 6 hourly for 21 days.
  - o <60 kg three tablets
  - o ≥60 kg four tablets

Monitor FBC and potassium when on high dose therapy.
OR

<u>If vomiting:</u>

- Cotrimoxazole, IV, 6 hourly for 21 days.
  - o <60 kg 240/1200 mg
  - o ≥60 kg 320/1600 mg

<u>For hypoxic patients:</u>

- Oxygen by face mask or CPAP as necessary.

AND

- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 80 mg daily for 5 days, then taper over 14 days.(Refer to Appendix II for an example of a dose reduction regimen).

Cotrimoxazole intolerance and desensitisation

Attempt desensitisation in patients with a history of cotrimoxazole intolerance, unless this was life-threatening, e.g. Stevens-Johnson syndrome. See section 4.6: Erythema Multiforme, Stevens Johnson Syndrome, Toxic Epidermal Necrolysis. Unless rash is severe or associated with systemic symptoms, continue treatment with careful observation for deterioration.

Desensitisation should be attempted using cotrimoxazole suspension 240 mg/5ml. Dilute the suspension appropriately and consult with your pharmacist if necessary. DO NOT administer antihistamines or steroids.

Time (hours)	Cotrimoxazole dose (mL of 240mg/5mL suspension
0	0.0005
1	0.005
2	0.05
3	0.5
4	5
5	Two single strength tablets (each tablet = 80/400 mg) followed by full dose

Alternatively, in case of intolerance and unsuccessful desensitisation:

- Clindamycin, oral, 600 mg 8 hourly for 21 days.

AND

- Primaquine, oral, 15 mg daily for 21 days.
  - Exclude G6PD deficiency before initiating therapy.

OR

If primaquine is not available, consider:

- Clindamycin, oral, 600 mg 8 hourly for 21 days.

AND

- Dapsone, oral, 100 mg daily for 21 days.

Secondary prophylaxis

Continue for at least 6 months and until CD4 count increases to >200 cells/mm^3 on ART.

- Cotrimoxazole 160/800 mg, oral daily.

Alternatively, in case of intolerance to cotrimoxazole:

- Dapsone, oral, 100 mg daily.

REFERRAL/CONSULTATION

Specialist or tertiary

Intolerance to second line regimen.

10.2.10 CEREBRAL TOXOPLASMOSIS

B20.8

DESCRIPTION

Intracranial space-occupying lesions, with contrast enhancement on imaging, due to *Toxoplasma gondii*. AIDS-defining illness (WHO clinical stage 4).

The diagnosis of toxoplasmosis is very unlikely if either the serum toxoplasma IgG is negative or the CD4 count is > 200 cells/mm^3.

Diagnosis is confirmed by a clinical response to therapy, which occurs in 7–14 days. CT scan improvement usually occurs within 14–21 days. Interpreting the response to therapy may be difficult if steroids have been given concomitantly. Steroid therapy should only be given for life-threatening peri-lesionaloedema.

MEDICINE TREATMENT

- Cotrimoxazole 160/800, oral, 2 tablets 12 hourly for 28 days, followed by 1 tablet 12 hourly for 3 months.

Secondary prophylaxis

Continue for at least 6 months and until CD4 count increases to > 200 cells/mm^3 on ART.

- Cotrimoxazole 160/800 mg, oral, 2 tablets daily.

See cotrimoxazole desensitisation: Page 10.23.

REFERRAL/CONSULTATION

Specialist or tertiary

Intolerance to cotrimoxazole.

Note: Attempt desensitisation first (see section 10.2.9: Pneumocystis pneumonia).

10.3 HIV AND KIDNEY DISEASE

B23.8 + (N28.9)

DESCRIPTION

A number of kidney disorders are associated with HIV infection.

Acute kidney injury due to sepsis, dehydration or nephrotoxicity from medicines occurs commonly.

The commonest chronic kidney disorder is HIV-associated nephropathy (HIVAN).

Typical features of HIVAN are:

» Heavy proteinuria.
» Rapidly progressive chronic kidney disease with preserved kidney size on imaging.
» ART slows progression of chronic kidney disease.

Early detection of kidney disease is important in order to implement interventions that may slow kidney disease progression, and for adjusting the

dose of relevant medicines.
Risk factors for HIV renal disease:
» CD4 count <200 cells/mm^3.
» Use of nephrotoxic medications.
» Comorbidity such as diabetes mellitus, hypertension, or hepatitis C virus co-infection.

Screening for renal disease in HIV
» Tests should include:
  – Urine dipstick for haematuria and proteinuria (request urine protein:creatinine ratio if proteinuria is detected; if this is >0.15 g/mmol discuss with a specialist).
  – Serum creatinine and eGFR.

Dose adjustment of ART in renal impairment: Refer to table: Dosing of ART for renal adjusted doses in section 10.1: Antiretroviral therapy.

10.4 KAPOSI SARCOMA (KS)
B21.0

DESCRIPTION
Kaposi Sarcoma (KS) is a malignancy of lymphatic endothelial origin associated with Human Herpes Virus-8, also known as KS Herpes Virus, infection.
KS may involve the skin, oral cavity, lymph nodes or viscera (especially lung and GIT).
Most patients have multiple lesions.
Lymphoedema is a common complication.
10–20% of cases of visceral KS will have no oral or skin involvement.
KS is an AIDS-defining illness (WHO clinical stage 4).
Although most cases are diagnosed on the typical macroscopic appearance of skin and oral lesions, biopsy confirmation is necessary for atypical lesions and if chemotherapy is considered. One important differential diagnosis is bacillary angiomatosis, which develops more rapidly.

MEDICINE TREATMENT
All patients with KS should be commenced on ART (see section 10.1: Antiretroviral therapy) and cotrimoxazole prophylaxis (see section 10.2.2: Opportunistic infection prophylaxis, with cotrimoxazole) regardless of CD4 count.
Many patients with limited mucocutaneous KS will have complete resolution or substantial regression on ART alone.

REFERRAL
Prior to referral, all patients must be started on ART.
» Radiotherapy/intralesional chemotherapy for symptomatic local lesions.
» Systemic chemotherapy is indicated in patients with poor prognostic factors:
  - more than 25 skin lesions,

- rapidly progressive disease,
- visceral involvement,
- extensive oedema, or
- "B" symptoms, i.e. fever, night sweats, significant constitutional symptoms.

» Failure of KS to respond to ART.

10.5 POST-EXPOSURE PROPHYLAXIS

National HIV Health Care Worker Hotline: 0800 212 506 or 021 406 6782.

10.5.1 POST-EXPOSURE PROPHYLAXIS, OCCUPATIONAL

S61.0 + (W46.22 + Z20.6 + Z29.8)

DESCRIPTION

Antiretroviral therapy may prevent the risk of acquiring HIV following a significant occupational exposure.
It is essential to document occupational exposures adequately for possible subsequent compensation.
Other blood borne infections (hepatitis B and C) should also be tested for in the source patient and appropriate prophylaxis instituted in the case of hepatitis B.

Assessing the risk of occupational exposures

The risk of acquiring HIV following occupational exposure is determined by the nature of the exposure and the infectiousness of the source patient. High-risk exposures involve exposure to a larger quantity of viruses from the source patient, either due to exposure to larger quantity of blood or because the amount of virus in the blood is high.

Any one of the following associated with an increased risk of HIV transmission:

» deep percutaneous sharps injuries
» percutaneous exposure involving a hollow needle that was used in a vein or artery
» visible blood on the sharp instrument involved in a percutaneous injury
» the source patient has terminal AIDS or is known to have a high viral load, i.e. >100 000 copies/mL

In instances when the risk of infection is extremely low or non-existent, post-exposure prophylaxis (PEP) is not indicated, as the risks of PEP will far outweigh the benefits. PEP is **NOT** indicated when:

» The material the healthcare worker was exposed to is not infectious for HIV in the occupational setting, e.g. vomitus, urine, faeces or saliva, unless these are visibly blood stained.
» The exposure was on intact skin.
» The source patient is HIV negative, unless there are clinical features to suggest seroconversion illness, in which case PEP should be commenced until further tests are done – consult with a virologist or infectious diseases

specialist.

» The healthcare worker is HIV infected, as this person should be assessed for ART initiation.

PEP REGIMENS

PEP should be commenced as soon as possible after the injury. Do not delay initiating PEP while awaiting confirmatory test results on the source patient and health care worker. PEP should be considered up to 72 hours after exposure and, in exceptional circumstances involving high-risk exposures, PEP may be considered up to 7 days after exposure.

When PEP is indicated:

- Tenofovir, oral, 300 mg daily for 4 weeks (provided baseline eGFR is >50 mL/minute).

and

- Lamivudine, oral, 200 mg daily for 4 weeks

and

- Dolutegravir, oral 50 mg once daily for 4 weeks. *LoE:III*[xli]

In WOCP, pregnant women <6 weeks gestation, or where DTG is not tolerated:

- Tenofovir, oral, 300 mg daily for 4 weeks (provided baseline eGFR is >50 mL/minute).

and

- Emtricitabine, oral, 200 mg daily for 4 weeks.

and *LoE:III*[xlii]

- Atazanavir/ritonavir 300/100 mg daily for 4 weeks.

Or

- Lopinavir/ritonavir 200/50 mg, oral, 2 tablets 12 hourly for 4 weeks.

If tenofovir is contraindicated or if source patient is known to be failing a tenofovir based regimen, replace tenofovir and emtricitabine with:

- Zidovudine, oral, 300 mg 12 hourly for 4 weeks.

and

- Lamivudine, oral, 150 mg 12 hourly for 4 weeks.

PEP is generally not well tolerated. Adverse effects occur in about half of cases and therapy is discontinued in about a third. Efavirenz is not recommended as it is very poorly tolerated in PEP.

Zidovudine often causes nausea and headache. If zidovudine is not tolerated, switch to tenofovir (check baseline eGFR as above).

Lopinavir/ritonavir often causes diarrhoea. If lopinavir/ritonavir is not tolerated switch to atazanavir/ritonavir. Atazanavir/ritonavir often causes unconjugated jaundice, which is benign but may not be tolerated, in which case switch to lopinavir/ritonavir.

Recommendations for post exposure prophylaxis (PEP) after occupational exposure to infectious material (includes blood, CSF, semen, vaginal secretions and synovial/pleural/ pericardial/ peritoneal/amniotic fluid) from HIV seropositive patients are given in the table, below.

PEP for healthcare worker following occupational HIV exposure:

Exposure	HIV Status of source patient	
	Negative	**Unknown or Positive**
Intact skin	no PEP	no PEP
Mucosal splash or non-intact skin or percutaneous injury	no PEP	3-drug regimen (PI-based)

When the source patient is known to be failing ART, modify the PEP regimen:
» If the patient is on zidovudine , use tenofovir.
» If the patient is on tenofovir then use zidovudine.

Patients failing 2nd line ART usually have no resistance to protease inhibitors, so lopinavir/ritonavir should still be effective, but consultation with a virologist or infectious diseases physician is recommended for advice on which ARVs to use for PEP in this setting.

PEP for healthcare workers following hepatitis B exposure

		Source patient		
		HBsAg positive	**HbsAg negative**	**HBsAg unknown**
Vaccination status and antibody response status of HCW	Unvaccinated or vaccination incomplete	• HBIG, IM, 500 units* • Hep B vaccine (3 doses at monthly intervals)	• Initiate Hep B vaccination (month 0, 1 and 6)	• HBIG, IM, 500 units* • Hep B vaccine (3 doses at monthly intervals)
	Vaccinated **AND** known to have HBsAb >10 units/mL#	No treatment	No treatment	No treatment
	Vaccinated **AND** HBsAb <10 units/mL or level unknown	• HBIG, IM, 500 units * • Repeat Hep B vaccine (3 doses at monthly intervals)	No treatment	• HBIG, IM, 500 units* • Repeat Hep B vaccine (3 doses at monthly intervals)

* HBIG and first dose of vaccine to be given simultaneously, but at different sites.
# If the delay in obtaining HBsAb results is more than 24 hours initiate treatment as for vaccinated AND HBsAb < 10 units/mL.
After vaccination ensure the health care worker has a HBsAb > 10 units/mL 1 – 2 months after the last vaccine dose.

Monitoring in occupational exposures

	Source patient	Exposed health care worker			
	Baseline	**Baseline**	**2 weeks**	**6 weeks**	**4 months**
HIV	Rapid test **PLUS** ELISA	Rapid test **PLUS** ELISA		ELISA	ELISA
Hepatitis B	Surface antigen	Surface antibody*			
Hepatitis C	HCV antibody	HCV antibody*		HCV PCR*	
Syphilis	RPR/ TP antibody	RPR/TP antibody*			RPR/TP antibody*
Creatinine		If TDF part of PEP	If TDF part of PEP		
FBC		If AZT part of PEP	If AZT part of PEP		

*Only if source patient was positive.

10.5.2 NON OCCUPATIONAL POST EXPOSURE PROPHYLAXIS, SEXUAL ASSAULT

Z29.8

PEP should be offered to rape survivors who present within 72 hours (management is the same as for occupational HIV exposure. See section 10.4.1 Post-exposure prophylaxis, occupational).
A patient presenting ≥72 hours since the alleged incident should not be given PEP, but should be counselled about the possible risk of transmission, with HIV testing provided at the time of presentation and 4 months later. Rape survivors who test HIV seropositive should be initiated on ART– see section 10.1: Antiretroviral therapy.
Other important aspects of care for the rape survivor should not be forgotten, i.e. contraception, treatment for sexually transmitted infections, counseling and forensic specimens.

Emergency contraception after pregnancy is excluded
Do a pregnancy test in all women and female adolescents. Children must be tested and given Emergency contraception from Breast Tanner Stage III, if unsure of staging, give Emergency contraception when you detect any breast development (DO NOT REGARD MENARCHE AS AN INDICATION).

- Levonorgestrel 1.5 mg, oral, as a single dose as soon as possible after unprotected intercourse. *LoE:III*[xliii]
  - Repeat the dose, if woman vomits within 2 hours.

CAUTION

Emergency contraceptive tablets must be taken as soon as possible, preferably within 72 hours of unprotected intercourse, and not later than 5 days.
Enzyme inducers (including efavirenz, carbamazepine) cause a significant reduction in levonorgestrel concentrations. Women on these medicines should double the dose of levonorgestrel, because of significant reduction of levonorgestrel. Women > 80 kg or BMI ≥ 30 should also be given twice the standard dose.

LoE:III[xliv]

An anti-emetic:

- Metoclopramide oral, 10 mg 8 hourly as needed.

LoE:III[xlv]

STI prophylaxis

- Ceftriaxone, IM, 250 mg as a single dose.
  - For ceftriaxone IM injection: Dissolve ceftriaxone 250 mg in 0.9 mL lidocaine 1% without epinephrine (adrenaline).

AND

- Azithromycin, oral, 1 g, as a single dose.

AND

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

LoE:III[xlvi]

Inadvertent (non-occupational) exposure to infectious material from HIV sero-positive persons often requires clinical judgement and includes:

» human bites (requires hepatitis B, but not HIV prophylaxis)
» sharing of needles during recreational drug use
» consensual sexual exposure, burst condoms
» contact sports with blood exposure

LoE:III[xlvii]

10.5.3 NON OCCUPATIONAL POST EXPOSURE PROPHYLAXIS, INADVERTENT NON-OCCUPATIONAL

Z29.8

Management of inadvertent (non-occupational) HIV exposure is the same as for occupational HIV exposure. See section 10.4.1 Post-exposure prophylaxis, occupational.

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CHAPTER 11

SURGICAL ANTIBIOTIC PROPHYLAXIS

GENERAL PRINCIPLES

» Prophylactic antibiotic therapy reduces the risk of surgical site infection.

» The need for surgical antibiotic prophylaxis depends on the nature of the expected wound from the procedure.

» Wounds that are expected to be clean (defined as no inflammation encountered; and the respiratory, alimentary, genital, or uninfected urinary tracts were not entered) generally do not require antibiotic prophylaxis, except where the consequences of surgical site infection could be severe (e.g. joint replacement in orthopaedic surgery).

» Antibiotic prophylaxis is indicated for procedures with clean-contaminated wounds (defined as entering the respiratory, alimentary, genital, or urinary tracts under controlled conditions; and without unusual contamination). *LoE:III*[i]

» A course of antibiotic treatment, not antibiotic prophylaxis, is required for procedures with contaminated wounds (defined as fresh open accidental wounds, or operations with major breaks in sterile technique), or dirty or infected wounds (defined as old traumatic wounds with retained devitalized tissue; and those that involve existing clinical infection or perforated viscera). *LoE:III*[ii]
(See chapter 20: Emergencies and injuries for antibiotic treatment).

» The antibiotic of choice should be active against Gram positive organisms, notably *Staphylococcus aureus*, which is the commonest cause of surgical site infections, with additional cover for other common pathogens according to the surgical site (e.g. anaerobic bacteria for GIT surgery).

» Give prophylaxis at induction. *LoE:III*[iii]

» If a tourniquet is used at the site of surgery, administer the entire antibiotic dose before the tourniquet is inflated. *LoE:III*[iv]

» Implement perioperative glycaemic control and use blood glucose target levels less than 11.1 mmol/L in patients with and without diabetes. *LoE:III*[v]

» Maintain perioperative normothermia.

» Antibiotic prophylaxis should be used in conjunction with good pre-, intra-, and post-operative infection prevention strategies. *LoE:III*[vi]

» Advise patient to shower or bathe with soap or antiseptic agent on at least the night before the procedure. *LoE:III*[vii]

» Do not remove hair preoperatively unless the hair at or around the incision site will interfere with the operation. If hair removal is necessary, remove immediately before the operation, with clippers.

LoE:I[viii]

DOSAGE RECOMMENDATIONS:

- Cefazolin, IV.
  - o <60 kg: 1 g
  - o 60–120 kg and BMI ≤35: 2 g
  - o ≥120 kg or BMI >35: 3 g

LoE:III[ix]

Pregnant women:

- o <60 kg: 1 g
- o 60–100 kg: 2 g
- o >100 kg: 3 g

LoE:III[x]

- Metronidazole, IV, 500 mg.
- Azithromycin, IV, 500 mg.
- Gentamicin, IV, 6 mg/kg (See Appendix II, for guidance on prescribing).
- Clindamycin, IV, 600 mg.

In most instances a single antibiotic dose prior to the procedure is sufficient for prophylaxis. Postoperative antimicrobial administration is not recommended for most surgeries as this selects for antimicrobial resistance.

LoE:I[xi]

» Additional intra-operative doses should be administered in circumstances of significant blood loss (>1500 mL) in order to ensure an adequate antimicrobial level until wound closure.

LoE:III[xii]

» With prolonged procedures, antibiotics are required to be re-dosed (i.e. >4 hours for cefazolin; >8 hours for metronidazole; > 6 hours for clindamycin and gentamicin).

LoE:III[xiii]

ANTIBIOTIC PROPHYLAXIS

TYPE OF SURGERY	ANTIBIOTIC RECOMMENDED	
	• *Cefazolin, IV*	• *Cefazolin, IV* ***PLUS***
Orthopaedic surgery	Primary total hip/ total knee replacement; internal fixation of hip; spinal procedures; open reduction and internal fixation of fractures; insertion of prostheses, screws, plates, lower limb amputation, etc.	
Gastrointestinal surgery	Gastric/ duodenal/ oesophageal hernia repair.	Biliary, colorectal, manipulation of viscera, appendicectomy, division of adhesions, exploratory laparotomy: **ADD** • Metronidazole, IV.
Thoracic surgery(specialist)		Pneumonectomy/ lobectomy: **ADD** • Metronidazole, IV.
Cardiac surgery (specialist)	Coronary artery bypass surgery/ routine cardiac valve surgery (continue cefazolin, IV, 8 hourly for 24 hours); cardiac device insertion (pacemaker implantation).	
Vascular surgery (specialist) (Prophylaxis is **not** recommended for other clean procedures).	Vascular reconstruction: abdominal aorta, groin incision (continue 8 hourly for 24 hours); AV fistula formation; and ligation of varicose veins.	Lower limb amputation: **ADD** • Metronidazole, IV.
Urology	Clean procedures	Clean-contaminated procedures: **ADD** • Metronidazole, IV.

Plastic and reconstructive surgery (Prophylaxis is **not** recommended for clean bone or soft tissue surgery).	Craniotomy procedures.	
Otorhinolaryngology/ head and neck surgery (Prophylaxisis **not** recommended for other procedures such as tonsillectomy, sinus procedures, etc.).	No incision through the oropharyngeal mucosa.	With incision through the oropharyngeal mucosa: **ADD** • Metronidazole, IV.
Obstetrics/ gynaecology (Prophylaxis is **not** recommended for early suction termination).		Hysterectomy, laparotomy procedures, vaginal repair: **ADD** • Metronidazole, IV.
		Caesarean delivery: **ADD** • Azithromycin, IV.
Neurosurgery (Prophylaxis is **not** recommended for other minor clean procedures).	Craniotomy; CSF shunt/drain; laminectomy.	
Endoscopic gastrointestinal procedures (Prophylaxis is **not** recommended for all other procedures, with or without biopsy).	Percutaneous endoscopic gastrostomy insertion/revision.	
General Surgery (Prophylaxis is **not** recommended for uncomplicated clean procedures or clean excision procedures i.e. wound revision, excision of scar tissue, etc.).	Clean contaminated procedures (mastectomy, node biopsy, etc.), splenectomy.	

LoE:I[xiv]

Beta lactam allergies: Avoid beta-lactam antimicrobials in patients with a history of anaphylaxis, bronchospasm, urticaria, or angioedema after exposure to one of these agents.

- Clindamycin, IV.

ADD

- Gentamicin, IV **for the procedures listed below:** (See Appendix II, for guidance on prescribing).

» Gastrointestinal surgery, urology procedures (clean-contaminated), and obstetric/gynaecological surgery (hysterectomy, laparotomy procedures, vaginal repair).

Note: Clindamycin has good coverage against Gram positive organisms and anaerobes, so the addition of metronidazole is unnecessary.

LoE:III[xv]

Ophthalmic surgery:

- Chloramphenicol 0.5% ophthalmic drops, instil 1 drop 2–4 hourly for 24 hours prior to surgery.

SPECIAL CONSIDERATIONS

» Elective splenectomy patients should be vaccinated at least 14 days prior to surgery. If splenectomy was urgent, or if vaccination was omitted before elective splenectomy, vaccinate at least 14 days post-splenectomy.

» The following vaccines should be administered: *LoE:II*[xvi]

VACCINE	SCHEDULE
• Polyvalent pneumococcal vaccine, 0.5 mL, SC.	o PCV13, SC, 2 weeks before surgery. o PPS23, SC, 8 weeks later. o Revaccinate with PPS23 after 5 years and then at 65 years. *LoE:II*[xvii]
• Haemophilus influenza type B, 0.5 mL, intramuscular.	–
• Meningococcal polysaccharide vaccine ($ACW_{135}Y$), 0.5 mL, SC	Revaccinate every 5 years.
• Influenza vaccine, 0.5 mL, IM.	Revaccinate annually.

LoE:III[xviii]

PROCESS MEASURES

Measure the percentage of procedures in which antimicrobial prophylaxis was appropriately provided.

These include:

» Correct type of antibiotic.

» Correct dose.

» Administration of the antibiotic(s) within 1 hour before incision.

» Not continuing the antibiotic(s) after surgery (except for 24 hours for cardiac and selected vascular procedures).

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CHAPTER 12
ANAESTHESIOLOGY AND INTENSIVE CARE

Anaesthetic and sedative medication may only be administered by medical practitioners trained and experienced in their use.

Sound theoretical and practical training followed by several years of supervised experience in the administration of anaesthetics is essential to develop the skills of the anaesthetist. Even within the recommended dosage range, anaesthetic agents can cause death when inappropriately used and only as a last resort should they be administered by non-specialised personnel. *LoE:III*[i]

Medicines and equipment for resuscitation should be functional and immediately available whenever general anaesthesia, regional anaesthesia or sedation is administered.

The following is a list of medicines required for anaesthesia that should be available at district and regional hospitals.

The doses of the medicines given are those recommended for healthy adults. Patients who are acutely or chronically sick, and or elderly, may require substantial reductions in the doses given otherwise life-threatening adverse effects may ensue.

12.1 PREMEDICATION

- Lorazepam, 1–2 mg, oral, the night before surgery and 1–2 hours preoperatively
  - Use half the dose in the elderly.
  - Duration of action (10–20 hours).
  - Unsuitable for day case surgery.

LoE:III[ii]

- Midazolam, 5–7.5 mg, oral, one hour preoperatively.
  - **Use only in healthy adults <65 years of age.**
  - Duration of action 1–4 hours.
  - Suitable for day case surgery. *LoE:III*[iii]

12.2 ANAESTHESIA, GENERAL

12.2.1 INTRAVENOUS INDUCTION (AND/OR MAINTENANCE) AGENTS

Inject intravenous induction agents over 30 seconds (>60 seconds in the elderly).
Titrate the dose to effect.

Respiratory depression occurs following induction of anaesthesia and ventilation should be supported as required.
Administer at appropriate doses, after consideration of patient factors, surgical factors and contraindications:

» Propofol is the most widely used IV induction agent but can produce hypotension.
» Etomidate or ketamine is preferred in haemodynamically unstable patients.
» Thiopental has a rapid onset, is contraindicated in porphyria and may be preferred for Caesarean deliveries. *LoE:III*[iv]

- Propofol, IV, 1.5–2.5 mg/kg.
  - 6–12 mg/kg/hour IV infusion for maintenance, if volatile agent use contraindicated.
- Etomidate, IV, 0.3 mg/kg (0.2–0.6 mg/kg)
- Ketamine, IV, 1–2 mg/kg.
- Thiopental, IV, 3–5 mg/kg.

12.2.2 INHALATION AGENTS

12.2.2.1 INDUCTION

In adults, intravenous induction is preferable.
Inhalational induction is reserved for patients with difficult airways or severe needle phobia.
Use only halothane or sevoflurane (isoflurane is too irritant). Halothane can cause hepatitis after repeated exposure within 3 months. Halothane sensitises the heart to catecholamines and may cause cardiac dysrhythmias, particularly if anaesthesia is too light or the patient hypercarbic.
Sevoflurane is not associated with these problems, has a faster onset and emergence time.

- Halothane, titrated to effect.

OR

- Sevoflurane, titrated to effect. *LoE:III*[v]

12.2.2.2 MAINTENANCE

In spontaneously breathing patients, the dose of a volatile agent is titrated to clinical effect. If a neuromuscular blocking agent has been used, the dose of the volatile agents must be adequate to prevent awareness. This is about 1 minimum alveolar concentration (MAC), but must be titrated according to clinical signs of awareness (e.g. tachycardia, hypertension, sweating, lacrimation).

- Isoflurane (MAC = 1.2%).

12.3 MUSCLE RELAXANTS

Used to facilitate intubation and to provide intraoperative muscle relaxation for surgery. It must not be used if difficult intubation anticipated.

12.3.1 DEPOLARISING MUSCLE RELAXANTS

- Suxamethonium, IV, 1–1.5 mg/kg.
  - Onset 30–60 seconds.
  - Duration 5 minutes.
  - Repeated doses associated with bradycardia and prolonged neuromuscular block.
  - Contraindicated in patients at risk for developing suxamethonium-induced hyperkalaemia, e.g. upper or lower motor neuron defect, prolonged chemical denervation (ICU >3 days), direct muscle trauma, tumour or inflammation, burns, disuse atrophy, severe infection, pre-existing hyperkalaemia.

LoE:III[vi]

12.3.2 NON-DEPOLARISING MUSCLE RELAXANTS (NDMR)

Use a nerve stimulator to monitor effect and determine when subsequent doses (about a fifth of the intubating dose) are required.

Higher doses result in shorter onset times but longer duration of action.

- Intermediate-acting neuromuscular blocking agents, e.g.:
- Cisatracurium (shorter-acting) *LoE:III*[vii]
  - Intubation dose 0.1–0.15 mg/kg.
  - Onset 3–5 minutes.
  - Duration of action 45–55 minutes.
  - Eliminated by Hoffman degradation, therefore can be used in renal or liver impairment.
- Vecuronium
  - Intubation dose 0.08–0.1 mg/kg.
  - Intubate after 2 minutes. *LoE:III*[viii]
  - Duration 20–30 minutes.
  - Eliminated by liver and kidney: avoid in renal and liver impairment.

12.3.3 MUSCLE RELAXATION FOR RAPID SEQUENCE INTUBATION

Patients at risk of aspiration (e.g. emergency surgery, incomplete gastric emptying) require a rapid sequence intubation.
An IV induction agent is given through an IV line with fast running fluids, immediately followed by a rapidly acting muscle relaxant.
Cricoid pressure is applied and then intubation proceeds.
The rapid onset of action enables the time to intubation to be short enough to avoid mask ventilation, as this can result in gastric insufflation and aspiration of gastric contents.

- Suxamethonium, 1–1.5 mg/kg, IV. (See section 12.3.1: Depolarising muscle relaxants).
  - Preferred agent as, in the event of a failed intubation, it wears off quickly enabling spontaneous respiration to resume.
  - Contraindications to suxamethonium
    - Congenital and acquired medical conditions associated with severe, potentially lethal suxamethonium-induced hyperkalaemia.
    - Malignant hyperthermia. *LoE:I*[ix]

If suxamethonium is contra-indicated, consider:

- Rocuronium, 0.9 mg/kg, IV.
  - Duration +/- 60 minutes. *LoE:III*[x]

Sub-optimal conditions for intubating and prolonged effect can be problematic in the event of a difficult or failed intubation and if the procedure is short.

12.3.4 MEDICINES TO REVERSE MUSCLE RELAXATION

Only administer when the clinical signs of NDMR are wearing off or at least 2 twitches occur using train-of-four on nerve stimulator.

Neostigmine has profound cholinergic effects and, to counteract resultant profound bradycardia, is administered mixed with an anticholinergic agent, atropine or glycopyrrolate.

Whilst atropine is effective and can be used for this purpose in otherwise healthy patients, the onset of neostigmine and duration of action more closely matches that of glycopyrrolate, so this is the preferred combination agent for patients who poorly tolerate tachycardia or bradycardia.

- Neostigmine, IV, 50 mcg/kg. *LoE:III*[xi]

WITH EITHER:

- Atropine, IV, 20 mcg/kg (maximum 1.2 mg).

OR *LoE:III*[xii]

Glycopyrrolate, IV, 10 mcg/kg.

LoE:III[xiii]

12.4 PERIOPERATIVE ANALGESIA

R52.9

» The perioperative period includes the preoperative, intraoperative and post-operative stages of surgery.
» Perioperative analgesia should be multi-modal, i.e. use analgesics, where possible, from different classes to reduce side effects from high doses of a single agent (e.g. paracetamol, NSAID and a weak/strong opioid) with either a regional block or wound infiltration with local anaesthetic.
» Patients with pain before surgery should be given analgesia preoperatively.
» Paracetamol may be given orally with premedication to prophylactically reduce perioperative pain.
» Intraoperatively, analgesics are given intravenously and/or a central neuraxial or regional local anaesthetic block may be used. The analgesic effect of these may extend into the early postoperative period.
» Postoperatively analgesics are given IV, IM and/or rectally, until the patient is able to take oral medication. Patients with a functioning block may not require analgesia until the block wears off but analgesics should be prescribed in anticipation of this.
» Pain severity should be assessed frequently post-operatively (see Section 12.5.3: Postoperative analgesia ward prescriptions).

12.4.1 PERIOPERATIVE ANALGESICS

12.4.1.1 ORAL ANALGESICS

- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

AND

LoE:I[xiv]

- Tramadol, oral, 50–100 mg 4–6 hourly.
  - Avoid in head injury and epilepsy.
  - Improved effect when given with paracetamol.

AND

LoE:III[xv]

- NSAID, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with meals.

Note: Do not administer NSAIDs to patients at risk of hypovolaemia, renal impairment or gastrointestinal bleeding. Avoid in patients with asthma who experience bronchospasm with NSAIDs.

LoE:III[xvi]

12.4.1.2 INTRAVENOUS ANALGESICS

- Fentanyl, IV, 1–2 mcg/kg
  - Onset ± 3 minutes, duration of action 30–60 minutes. Higher doses last longer. LoE:III[xvii]

- Morphine, IV/IM, 3–5 mg as a single dose then further boluses at intervals of 5–10 minutes and monitor all vitals closely. LoE:III[xviii]
  - Dilute 10 mg up to 10 mL with sodium chloride 0.9%.
  - Total maximum dose: 10 mg.
  - Repeat after 4 hours if necessary.
  - Monitor response to pain and effects on respiration and BP.
  - Onset 5-10 minutes. Duration of action ± 3 hours.
  - Histamine release may cause intraoperative hypotension.

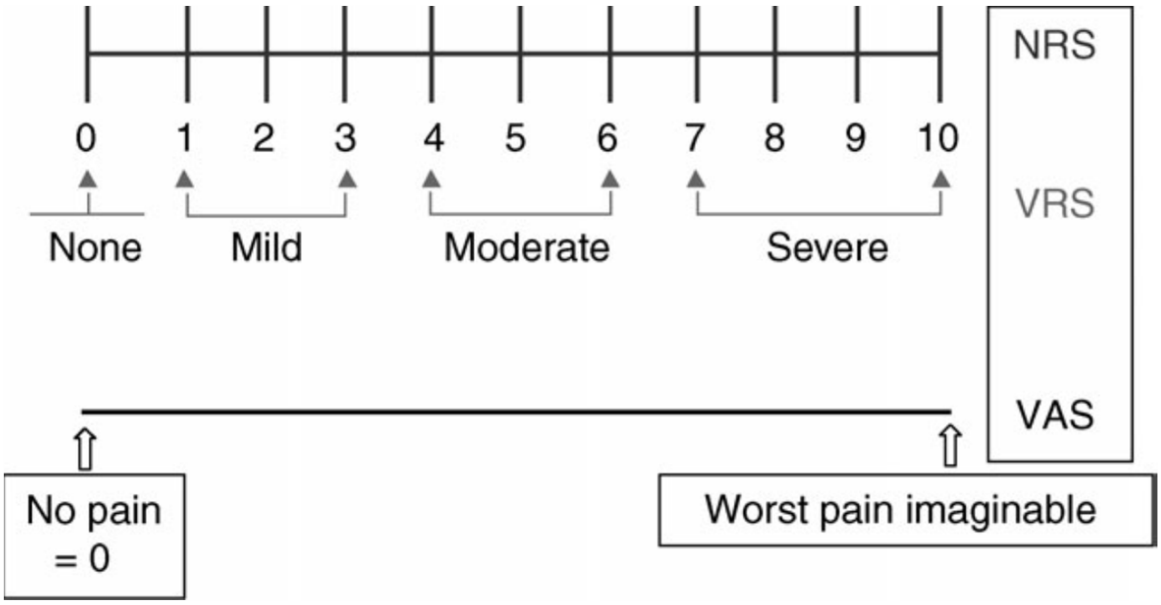
- Ketamine, IV, 0.1–0.3 mg/kg – a subanaesthetic dose given pre-incision may reduce persistent post-surgical pain. LoE:I[xix]

12.4.2 POSTOPERATIVE PAIN IN THE RECOVERY ROOM

R52.0

Pain should be assessed on arrival in the recovery room and at regular intervals postoperatively. Pain Scores should be recorded with other routine postoperative observations.

A Numeric Rating Scale (NRS) can be used to score pain:



Source: Breivik H, Borchgrevink PC, Allen SM, Rosseland LA, Romundstad L, Hals EK, Kvarstein G, Stubhaug A. Assessment of pain. *Br J Anaesth.* 2008 Jul;101(1):17-24.

The patient is asked to indicate on the scale the numeric value that best indicates their pain intensity or verbally if they cannot visualise the scale.

Severe pain (use lower doses if pain less):

- Morphine, IV, to a total maximum dose of 10 mg (See Appendix II, for individual dosing and monitoring for response and toxicity).
  - Monitor conscious level and pulse oximetry continuously. Also monitor respiration, heart rate and BP at 5 minute intervals and for at least 20 minutes after the last IV morphine bolus.

In patients at high risk for respiratory depression, tramadol may be used instead of morphine as it causes less respiratory depression (although respiratory depression may still occur with tramadol).

Tramadol is a weak opioid agonist and increases spinal cord levels of serotonin and noradrenaline.

- Tramadol, IV, 50–100 mg over 3 minutes to reduce side-effects of nausea and vomiting (Specialist prescribed).
  - Ceiling effect i.e. higher doses do not improve pain relief. *LoE:III*[xx]

In addition to morphine or tramadol, diclofenac may also be given to supplement analgesia and reduce opioid requirements:

- Diclofenac, **deep IM**, 75 mg 12 hourly.
  - Administer for a maximum of 2 days.
  - Avoid the same injection site.
  - Counsel patient prior to injection of adverse events (scarring) at inject site, if applicable. *LoE:III*[xxi]

12.4.3 POSTOPERATIVE ANALGESIA WARD PRESCRIPTIONS

Analgesia should be prescribed according to the severity of pain anticipated from the surgery and the anticipated, appropriate, postoperative route of administration.

Pain should be assessed at regular intervals on the ward postoperatively. Pain scores should be recorded with other routine postoperative observations.

Respiratory rate should be monitored for opioid-induced respiratory depression.

12.4.3.1 EXAMPLES OF WARD PRESCRIPTIONS FOR POSTOPERATIVE ANALGESIA ACCORDING TO ANTICIPATED PAIN SEVERITY

R52.9

MILD PAIN:

- Paracetamol, oral, 1 g 4–6 hourly when required.

- Maximum dose: 15 mg/kg/dose.
- Maximum daily dose: 4 g in 24 hours.

AND

- NSAID, oral, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly after meals.

CAUTION

Concomitant use of more than one oral NSAID has no additional clinical benefit and only increases toxicity.

Use of all NSAIDs is associated with increased risks of gastrointestinal bleeding, renal dysfunction, and cardiovascular events (stroke and myocardial infarction).

NSAIDs should be used judiciously at the lowest effective dose for the shortest duration. Explore and manage exacerbating factors for pain. See section 26.1: Chronic pain.

Do not use NSAID in pregnancy or while breastfeeding.

AND

- Tramadol, oral, 50–100 mg 4–6 hourly.
  - Avoid in head injury and epilepsy.
  - Improved effect when given with paracetamol.

MODERATE PAIN:

- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

AND

- NSAID, oral, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with meals.

CAUTION

Concomitant use of more than one oral NSAID has no additional clinical benefit and only increases toxicity.

Use of all NSAIDs is associated with increased risks of gastrointestinal bleeding, renal dysfunction, and cardiovascular events (stroke and myocardial infarction).

NSAIDs should be used judiciously at the lowest effective dose for the shortest duration. Explore and manage exacerbating factors for pain. See section 26.1: Chronic pain.

Do not use NSAID in pregnancy or while breastfeeding.

AND

- Tramadol, oral, 50–100 mg 4–6 hourly.
  - Avoid in head injury and epilepsy.
  - Improved effect when given with paracetamol.

OR

Morphine, IM, 0.1–0.2 mg/kg 4 hourly or IV via a patientcontrolled analgesia device (see below).

SEVERE PAIN:

- Morphine, IM, 0.1–0.2 mg/kg 4 hourly or IV via a PCA device.

AND

- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

AND

- NSAID, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with meals.

LoE:III[xxii]

Note:

Patient controlled analgesia

If a device is available that will administer patient controlled analgesia:

- Morphine, IV, in boluses of 1 mg every 6-10 minutes, with a maximum dose of 0.1–0.2 mg/kg 4 hourly.
  - In the elderly and frail, the dose of morphine should be reduced and the dosage interval increased.

LoE:I[xxiii]

If unable to take oral medication, stop oral ibuprofen and use:

- Diclofenac, **deep IM**, 75 mg 12 hourly, to upper, outer quadrant of buttock.
  - Administer for a maximum of 2 days.
  - Avoid the same injection site.
  - Counsel patient prior to injection of adverse events (scarring) at injection site if applicable.

LoE:III[xxiv]	

12.5 INTRAVENOUS FLUIDS

The following IV fluids should be available for perioperative fluid replacement and maintenance therapy.

12.5.1 CRYSTALLOIDS

Most commonly used crystalloid for perioperative fluid maintenance:

- Sodium chloride 0.9%, IV.

Higher sodium content than indicated if there is a perioperative risk of hyponatraemia e.g. transurethral resection of prostate.
Balanced solutions may be appropriate in some patients (i.e. presentation with hyponatraemia, previous renal placement therapy):

- Balanced solution, e.g.:
- Ringer Lactate, IV.

LoE:I[xxv]

12.6 MEDICINES TO TREAT COMPLICATIONS OF ANAESTHESIA

12.6.1 MALIGNANT HYPERTHERMIA

T88.3

- Dantrolene IV, 2.5 mg/kg as a single dose (preferably through large bore cannula).
  - Reconstitute with 60 mL water for injection. For a 70 kg patient, 175 mg (9 vials) is required.
  - Administer subsequent doses to clinical effect (cardiac and respiratory symptoms stabilise, muscle tone and body temperature reduced).
  - Doses higher than 10 mg/kg is uncommon and the clinician should question the diagnosis.
  - Although, high doses of 10 mg/kg may be required in muscular males.

LoE:III[xxvi]

12.6.2 LOCAL ANAESTHETIC TOXICITY

T41.3

Airway management:

- Ventilate with 100% oxygen.

Seizure suppression:

- Diazepam, IV, 10 mg.

Cardiopulmonary resuscitation may be required:

- Reduce individual adrenaline (epinephrine) doses to <1 mcg/kg.

LoE:III[xxvii]

- Lipid emulsion (20%), IV, 1.5 mL/kg over 1 minute, then continuous infusion 0.25 mL/kg/minute.
  - Repeat bolus 1–2 times for persistent cardiovascular collapse.
  - Double infusion rate to 0.5 mL/kg/minute if BP remains low.
  - Continue infusion for at least 10 minutes after cardiovascular stability attained.
  - Recommended upper limit: approximately 10 mL/kg lipid emulsion over the first 30 minutes.

LoE:III[xxviii]

12.6.3 ANAESTHETIC-RELATED ACUTE HYPOTENSION

I95.81

Treat the cause of hypotension.
Ensure appropriate fluids are given to correct hypovolaemia.
The medicines given below all require significant dilution before administration.

- Adrenergic and dopaminergic agents, e.g.:
- Ephedrine IV, 3–5 mg as a single dose and then further boluses as required to a maximum of 30 mg.
  - Increases heart rate and contractility, and vasoconstrictor.
  - Repeated administration can result in tolerance and tachyphylaxis.
  - Alternative vasopressor infusion (e.g. adrenaline (epinephrine)) may be needed to mitigate unresponsiveness to treatment.

LoE:III[xxix]

OR

Phenylephrine IV, 50–100 mcg as a single dose and then infuse at 60–180 mcg/minute.

- Vasoconstrictor. *LoE:III*[xxx]
- High doses may cause significant reflex. bradycardia: treat this by discontinuing the phenylephrine only.

12.6.4 ANAESTHETIC-RELATED ACUTE HYPERTENSION

I97.3

To obtund the hypertensive response to intubation e.g. pre-eclampsia:

- Alfentanil, IV, 7.5 mcg/kg (with magnesium sulfate, IV 30 mg/kg).

LoE:III

During anaesthesia or post-operatively, establish the cause (e.g. light anaesthesia or inadequate pain relief) and treat as appropriate.

- Labetalol IV, 5–10mg IV over 2 minutes.
  - Repeated at intervals of at least 5 minutes to maximum 200 mg.
  - Duration of action 50 minutes.
  - Vasodilates and slows heart rate. *LoE:III*[xxxi]

12.6.5 POSTOPERATIVE NAUSEA AND VOMITING (PONV)

12.6.5.1 PREVENTION OF PONV

R11.2

Patients identified preoperatively as medium or high risk for PONV should be considered for prophylactic antiemetics.
Prophylactic antiemetics also required if postoperative vomiting is potentially dangerous, e.g. after jaws wired, open eye surgery, oesophageal surgery.

High risk patients should receive anti-emetics from ≥ 1 class.
Adequate IV hydration associated with less PONV.

Risk factors for PONV	Points
Female Gender	1
Non-Smoker	1
History of PONV and/or motion sickness	1
Postoperative opioids	1
Sum	0–4

Points	Risk for PONV (%)	Risk category
0	10	Low
1	20	Low
2	40	Medium
3	60	High
4	80	High

Class	Anti-emetic	Prophylactic Dose and timing	Notes
Corticosteroid (glucorticoids)	e.g.: Dexamethasone	4-8 mg, IV, on induction. *LoE:II*[xxxii]	Increases blood glucose in diabetics. Only used for prophylaxis, not established PONV.
5-HT_3 receptor antagonist	e.g.: Ondansetron	4–8 mg, slow IV/IM, on induction. *LoE:III*[xxxiii]	Prolongs QTc interval
Phenothiazine	Promethazine	6.25–12.5 mg, IV (large bore cannula) diluted to 20 mL over 10-20 minutes, or deep IM, at end of surgery.	Intra-arterial injection causes gangrene. Extravasation or subcutaneous injection associated with skin necrosis. Anticholinergic side effects and sedation.

12.6.5.2 TREATMENT OF PONV

R11.2

Ensure adequate hydration and correct hypotension if present.
Give an emetic from a different class than the prophylactic agent given (except dexamethasone, which is only used for prophylaxis).

- Metoclopramide, IM/IV
  - If <60 kg: 5 mg IM or IV (over 2 minutes).
  - If ≥60 kg: 10 mg IM or IV (over 2 minutes).
  - Repeat 8 hourly if required.

Note: Metoclopramide can cause extrapyramidal side effects.

Treat acute dystonic reactions with:

- Anticholinergic agent, e.g.:
- Biperiden, IM/IV, 2 mg.
  - Repeat as necessary.

If an anticholinergic agent is not available:

- Promethazine, deep IM, 25–50 mg.
  - In the elderly 25 mg.

If an anticholinergic agent or promethazine is not available:

- Diazepam, IV, 5–10 mg for symptom relief. *LoE:III*

12.6.6 ACID ASPIRATION PROPHYLAXIS

O74.0

The use of a non-particulate, non-effervescent antacid reduces the risk of pneumonitis if gastric fluid is aspirated. Give to patients at risk of aspiration, e.g. pregnant women before Caesarean delivery.

- Sodium citrate, 0.3M, oral, 30 mL.
  - Not more than 30 minutes pre-induction of anaesthesia.

LoE:I[xxxiv]

12.7 ANAESTHESIA, SPINAL (INTRATHECAL)

Only preservative free medicines may be used.
Larger doses cause block to spread higher, with risks of respiratory depression, hypotension and loss of consciousness.

- Bupivacaine 0.5% (Spinal use)
  - Give up to 3 mL according to desired level of block.
  - Becomes hypobaric (light) within CSF so block may spread higher than anticipated.

- Bupivacaine 0.5% with dextrose (Spinal use)
  - Give up to 3 mL according to desired level of block.
  - Hyperbaric (heavy) so block spreads according to patient position.

To increase duration of analgesia:

ADD

- Fentanyl, 10–25 mcg (i.e. small amounts).

Caesarean deliveries
Lower doses are required due to physiologic changes of pregnancy:

- Bupivacaine 0,5% with dextrose, 1.8 mL (9 mg).

AND

- Fentanyl, 10 mcg (0.2 mL).

12.7.1 ANTICOAGULANTS AND SPINAL OR EPIDURAL BLOCKS

Patients on anticoagulants are at risk of developing a spinal haematoma with subsequent paralysis after a spinal or epidural block. These anticoagulants should be stopped before the spinal or epidural is performed according to the guidelines given below. In order to encourage safe and quality care of patients, **please consult a specialist prior to attempting blocks on patients on anticoagulants**. There are a range of oral anticoagulation, with each having specific recommendations with regard to neuraxial blocks.

Timing of anticoagulants in patients receiving neuraxial anaesthesia:

Anticoagulant	Before Neuraxial Block	After Neuraxial block
Warfarin, oral	Consult with specialist to stop warfarin.	Restart after neuraxial block performed (do not delay) and epidural catheter removed. Monitor INR daily with indwelling catheter.
Unfractionated Heparin, SC	Neuraxial techniques may be performed if total daily dose is <10 000U. Check PTT if higher doses are used.	
Unfractionated Heparin, IV	Stop heparin 4-6 hours and check PTT<40	Wait 1 hour before next bolus/infusion restarted.
Prophylactic LMWH, SC	12 hours after last dose	4 hours after neuraxial block performed and epidural catheter removed
Therapeutic LMWH, SC	24 hours after last dose	>24 hours *and* consult a specialist (bleeding risk of surgery should be assessed).

LoE:II[xxxv]

Note. After neuraxial block or epidural catheter removal, patients should be observed closely for new or progressive neurological symptoms. A spinal haematoma can result in permanent paralysis unless decompressive surgery is performed within 8 hours of paralysis onset.

Clopidogrel and platelet GPIIb/IIIa inhibitors have variable durations of effects on clotting after stopping these medications. Specialist advice should be

sought before performing neuraxial blocks on patients receiving these medications.

For patients on warfarin the use of bridging anticoagulation (giving heparin after warfarin is stopped in preparation for surgery or invasive procedures) remains unsettled. Practitioners should exercise careful judgment of competing risks in individual patients. Heparin may increase the risk of bleeding. Whatever practice is adopted the most important consideration is to ensure that adequate anticoagulation with warfarin is re-instituted once the risk of bleeding is past.

12.8 ANAESTHESIA, EPIDURAL

Only preservative free medicines may be used.
Local anaesthetics are administered through a catheter inserted into the epidural space at a spinal level appropriate for the surgery.
Aspiration and a test dose (2–3 mL) of local anaesthetic should be given to confirm catheter not intravascular or intrathecal. Subsequent doses should be fractionated (3–5 mL boluses).

- Bupivacaine 0.5%.
  - Onset ±10 minutes.
  - Duration ±4 hours.
  - Motor block is less with lower concentrations.
  - Maximum dose 2 mg/kg.

LoE:III[xxxvi]

12.9 PERIPHERAL NERVE BLOCK OR WOUND INFILTRATION

Only preservative free medicines may be used for nerve blocks.
Lidocaine has a faster onset of action than bupivacaine, but a shorter duration of action.

- Lidocaine 1% or 2%.
  - Higher concentrations cause more pain on injection.
  - Maximum dose: 3 mg/kg.
- Lidocaine 2% plus adrenaline.
  - Not to be used in areas supplied by an end-artery e.g. finger, ear, penis.
  - Maximum dose: 7 mg/kg.
- Bupivacaine 0.5%
  - Not be used in mucosal areas as risk of systemic toxicity.
  - Maximum dose: 2 mg/kg.

LoE:III[xxxvii]

12.10 ANAESTHESIA, TOPICAL

- Lidocaine jelly, topical, 2 g/100mL.
  - For urethral catheterisation: female 5–7 mL, male 10–15 mL.

LoE:III[xxxviii]

- Lidocaine topical spray, 4%.
  - Maximum dose 160 mg.
  - To assist with awake intubation or reduce haemodynamic response to intubation.

LoE:III[xxxix]

For venepuncture analgesia in adults or oncology patients requiring repeated invasive procedures (e.g. lumbar punctures, venepuncture):

- Lidocaine/prilocaine, topical cream, 2.5/2.5%.
  - Apply at least 1 hour before and cover with occlusive dressing.

LoE:III[xl]

12.11 SEDATION

See chapter 23: Sedation.

12.12 PAIN, CHRONIC

See chapter 26: Pain.

12.13 INTENSIVE CARE

12.13.1 NUTRITIONAL SUPPORT

E63.9

Establish a multidisciplinary nutrition support team to assess and address the nutritional requirements of patients. This team should include a dietician.

Nutrition support should be considered in patients at risk, defined as those who have a poor absorptive capacity and/or high nutrient losses and/or increased nutritional needs from causes such as catabolism.

Oral feeding, if feasible, is preferred.
Enteral tube feeding is the next best option.
Total parenteral nutrition (TPN) is indicated in exceptional circumstances.
For short-term care (≤ two weeks), the current standard formulas in multi-chamber bags that have a long shelf-life are considered to provide adequate nutritional support. Clinicians should be aware of the possibility of clinically important hypovitaminosis in individual patients, and replace selected vitamins where appropriate.

Refer to the most current version of the National Department of Health Parenteral Nutrition Practice Guidelines for Adults, available at: www.health.gov.za

In selecting the treatment modality, the team should consider:
» The likely duration of nutrition support.
» Patient activity levels and the underlying clinical condition, e.g. catabolism.
» Gastrointestinal tolerance, potential metabolic instability and risks of re-feeding.

Potential complications harms of nutritional support include:
» Re-feeding syndrome: Hypophosphataemia occurs when patients are re-fed too quickly with high carbohydrate feeds. The syndrome usually begins within 4 days of re-feeding. A multitude of life-threatening complications involving multiple organs may occur, causing: respiratory failure, cardiac failure, cardiac dyshythmias, rhabdomyolysis, seizures, coma, red cell and leukocyte dysfunction. The most effective way to prevent re-feeding syndrome is that feeds should be started slowly with aggressive supplementation of magnesium, phosphate and potassium.
» Diarrhoea.
» Lactose intolerance.

Regularly review the need for ongoing therapeutic nutritional support.

Vitamin and mineral supplementation should be considered on a case-by-case basis.

Enteral tube feeding
Enteral tube feeding should be used in patients who cannot swallow or who are at risk of aspiration.
Patients should be fed via a nasogastric tube unless this is contra-indicated.
Patients with upper gastro-intestinal dysfunction (or an inaccessible upper gastro-intestinal tract) should receive post-pyloric (duodenal or jejunal) feeding.
Percutaneous endoscopic gastrostomy feeding should be used in patients likely to need long-term (≥4 weeks) enteral tube feeding.

Parenteral feeding
The team should consider parenteral nutrition in patients who are malnourished or at risk of malnutrition and fit the following criteria:
» inadequate or unsafe oral and enteral tube nutritional intake, or
» a non-functional, inaccessible or perforated (leaking) gastrointestinal tract.

Note: For short-term care, the current standard formulas in multi-chamber bags that have a long shelf-life are considered to provide adequate nutritional support.

The addition of glutamine does not confer any clear clinical benefits and is thus not recommended.

Parenteral nutrition can be withdrawn once adequate oral or enteral nutrition is tolerated and nutritional status is stable. Withdrawal should be planned and done in a stepwise way with a daily review of the patient's progress.

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CHAPTER 13

MUSCULOSKELETAL CONDITIONS

13.1 ARTHRITIS, RHEUMATOID (RA)

M05.80-89/M05.90-99/M06.00-09/M06.80-09/M06.90-99/M08.30-39/M08.40-49/ M08.80-89/M08.90-99

DESCRIPTION

A chronic, inflammatory, systemic condition with a fluctuating course. It may affect many organs, but the joints are predominantly affected. Characteristic joint manifestations are:

» Swelling or fluid, affecting at least three joint areas simultaneously.
» Pain.
» Limited movement with morning stiffness >1 hour, which improves with activity. This helps distinguish osteoarthritis from rheumatoid arthritis.
» Destruction and deformity of affected joints.
» The small joints of the fingers and hands, with the exception of the distal interphalangeal joints, are usually involved, although any joint can be involved.
» Arthritis is typically symmetrical.

GENERAL MEASURES

Manage by co-ordinated multidisciplinary care.
The primary objective is to improve and maintain functional status.
Early use of non-drug measures, especially nursing, physiotherapy and occupational therapy, is essential.
Acute flare-ups: rest affected joints and consider the use of day and/or night splints.
Obtain a baseline complete blood count, serum creatinine, alanine aminotransferase (ALT), and erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) in all patients.
Obtain X-rays of the hands and wrists, as well as both forefeet to include the metatarsophalangeal joints as a baseline for evaluating change in the joints during treatment.

MEDICINE TREATMENT

All patients with suspected RA should be seen by a specialist. Evaluate all patients with suspected RA for disease-modifying anti-rheumatic drug (DMARD):

- Methotrexate (preferred initial therapy)
- Chloroquine sulphate
- Sulfasalazine

Monitoring response to DMARDs:

» Assess response to DMARD therapy by monitoring the number of swollen and tender joints, restricted to 28 joints (shoulders, elbows, wrists, 5 metacarpophalangeal joints, 5 proximal interphalangeal joints and knees bilaterally) together with ESR or CRP.

» If there is poor response to one DMARD, after 3 months, add another DMARD. *LoE:II*[i]

» Patients on DMARDs must be monitored regularly for toxicity, as outlined below:

- Methotrexate, oral, 7.5 mg once per week. Specialist consultation.
  - o Increase dose gradually to a maximum of 25 mg per week.
  - o Monitor: ALT and FBC before and 12 weekly during treatment.

AND

- Folic acid, oral, 5 mg per week at least 24 hours after the methotrexate dose.

LoE:II[ii]

AND/OR

- Chloroquine sulphate, oral, 150 mg (as base) daily for 5 days of each week.
  - o Do ophthalmic examination at baseline within the first year of treatment and annually thereafter, to monitor for ocular damage.

AND/OR

- Sulfasalazine, oral, 500 mg 12 hourly with meals.
  - o Gradually increase over one month from 500 mg to 1 g 12 hourly.
  - o FBC and ALT monthly for first 3 months then every 3–6 months.

LoE:III[iii]

Oral corticosteroids

Systemic corticosteroids are effective at relieving symptoms in RA and have been shown to modify the course of the disease, but long-term use is discouraged because this is associated with considerable toxicity, notably osteoporosis, which is very common in patients with RA.

Indications:

» As bridging therapy while waiting for DMARDs to take effect.

» Acute disease flares.

» Severe extra-articular manifestations, e.g. scleritis.

- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 40 mg daily for 2 weeks.
  - o Thereafter gradually reduce the dose to ≤7.5 mg daily. (Refer to Appendix II for an example of a dose reduction regimen).
  - o Discontinue at 3–6 months.
  - o If disease flares after stopping corticosteroids DMARD therapy should be optimised. *LoE:II*[iv]

Patients requiring corticosteroids for longer than 3 months should be educated to take in enough calcium in their diet.

For pain:

- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

NSAIDs

NSAIDs are used for symptomatic relief in patients with active inflammation and pain. They have no long-term disease modifying effects.
NSAID dose should be reduced and then stopped once the DMARDs have taken effect.
Reduce NSAID doses in the elderly.
NSAIDs are relatively contra-indicated in patients with significantly impaired renal function, i.e. eGFR <60 mL/minute.

CAUTION

Concomitant use of more than one oral NSAID has no additional clinical benefit and only increases toxicity.
Use of all NSAIDs is associated with increased risks of gastrointestinal bleeding, renal dysfunction, and cardiovascular events (stroke and myocardial infarction).
NSAIDs should be used judiciously at the lowest effective dose for the shortest duration. Explore and manage exacerbating factors for pain. See section 26.1: Chronic pain.
Do not use NSAID in pregnancy or while breastfeeding.

- NSAID, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with meals. *LoE:I*[v]

An extra **night-time** dose of an NSAID may be added in some patients with severe nocturnal pain/morning stiffness.

Note: When an additional night-time dose is added to the patient's regimen, the risk of NSAID toxicity increases. A reduction in the daytime dose of NSAIDs is recommended as the night-time dose will often exceed the recommended total daily NSAID dose.
If a reduction in daytime dose causes increased pain, then the use of the night-time dose must be for the shortest period possible.

In high-risk patients: >65 years of age; history of peptic ulcer disease; on concomitant warfarin, aspirin, or corticosteroids:

ADD *LoE:II*[vi]

- PPI, e.g.:
- Lansoprazole, oral, 30 mg daily while on an NSAID.

Adjunct for pain control:

- Amitriptyline, oral, 10–25 mg at night.

- Titrate dose according to response.
- Initial dose in the elderly: 10 mg at night.
- Maximum dose: 75 mg at night.
- Use with caution in patients with angle closure glaucoma, prostatic hypertrophy and the elderly.

Intra-articular corticosteroids
Consider only in cases where a few joints are very actively inflamed.
To be prescribed by a specialist.
Not more than 2–3 injections per year per joint are recommended.

- Intra-articular corticosteroid, e.g.:
- Methylprednisolone acetate, 20–80 mg depending on joint size.

LoE:III[vii]

REFERRAL

» At initial diagnosis.
» Disease activity cannot be controlled with the measures as mentioned.
» Compression neuropathy.
» For joint replacement.

Urgent

» Rupture of tendons.
» Scleritis.
» Unstable upper cervical spine.
» Vasculitis.
» Cricoarytenoid joint involvement with hoarseness and inspiratory stridor.

13.2 ARTHRITIS, SEPTIC AND OSTEOMYELITIS, ACUTE

M00.90-99/M86.10-19

DESCRIPTION

Septic arthritis is typically an acute infective condition involving one or more joints. The joint is hot, swollen, very painful on movement, and with restricted movements.
Acute osteomyelitis typically involves the long bones or the vertebrae.
Signs of systemic infection are usually present. The infection is usually bloodborne, but may follow trauma. The course may be acute or protracted. The commonest causative organism is *Staphylococcus aureus*. *N. gonorrhoeae* is an important cause of septic arthritis.
Note: Acute gout and haemophiliacs with bleeding into joints may mimic septic arthritis.

GENERAL MEASURES

Baseline X-ray.
Rest and immobilisation.

Septic arthritis: Drainage is important. Discuss with a specialist.

MEDICINE TREATMENT

Empiric antibiotic therapy

Therapy is directed against *S. aureus* unless there is evidence of urethritis or PID, in which case gonococcal infection should be covered.

It is crucial to obtain cultures of blood, joint or aspirate of osteomyelitis focus before administering antibiotics.

- Cefazolin, IV, 2 g 8 hourly for 4 weeks. *LoE:II*[viii]

After 2 weeks of IV therapy, a change to oral therapy may be considered in patients with a good clinical response:

- Flucloxacillin, oral, 1 g 6 hourly to complete the 4 weeks' treatment.

Severe penicillin allergy: (Z88.0)

- Clindamycin, IV, 600 mg 8 hourly.

After 2 weeks of IV therapy, a change to oral therapy may be considered in patients with a good clinical response:

- Clindamycin, oral, 450mg 8 hourly to complete the 4 weeks' treatment.

LoE:III[ix]

For gonococcal arthritis A54.4+ + (M01.30-39*)

- Ceftriaxone, IV, 1 g daily for 1 week.

AND

- Azithromycin, oral, 1 g, as a single dose. *LoE:III*[x]

Severe penicillin allergy: (Z88.0)

Refer.

Analgesia

- NSAID, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with meals. *LoE:I*[xi]

AND/OR

- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

REFERRAL

» Acute osteomyelitis/ septic arthritis for early drainage by specialist surgeon.
» If pyrexia persists despite adequate antibiotic therapy, a sub-periosteal abscess must be sought and drained by a specialist surgeon.
» Chronic osteomyelitis.
» Pathological fractures.

13.3 OSTEOARTHRITIS

M13.00-19/M16.0-9/M17.0-9/M18.0-9/M19.00-09/M19.80-99

DESCRIPTION

A disorder typically affecting weight-bearing joints and the hand (distal and proximal interphalangeals, and first metacarpophalangeal joints).

Signs and symptoms include:
» Pain on effort, relieved by rest.
» Morning stiffness, lasting < 30 minutes.
» Limited movement.
» Joint swelling (effusions and/or osteophytes).

GENERAL MEASURES

Weight reduction.
Exercise: postural and non-weight bearing. Quadriceps strengthening for knee involvement.
Support and alleviate weight bearing of affected joints, i.e. walking stick.
Physiotherapy and/or occupational therapy.

MEDICINE TREATMENT

When only pain relief is required:

- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

If ineffective:

ADD

- NSAID, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with meals. *LoE:I*[xii]

As many of these patients, particularly the elderly, have concomitant medical conditions such as cardiovascular, gastrointestinal disease or renal function impairment, NSAIDs must be used with caution.

Patients on aspirin for cardiovascular risk reduction should take this agent 30 minutes before the 1st dose of NSAID in the morning, as taking aspirin and NSAID at the same time may reduce aspirin's efficacy. *LoE:III*[xiii]

In high-risk patients: >65 years of age; history of peptic ulcer disease; or on concomitant warfarin, aspirin or corticosteroids:

ADD *LoE:II*[xiv]

- PPI, e.g.:
- Lansoprazole, oral, 30 mg daily.

CAUTION

Use of all NSAIDs is associated with increased risks of gastrointestinal bleeding, renal dysfunction, and cardiovascular events (stroke and myocardial infarction).
NSAIDs should be used judiciously at the lowest effective dose for the shortest duration. Explore and manage exacerbating factors for pain. See section 26.1: Chronic pain.
Do not use NSAID in pregnancy or while breastfeeding.

If ineffective:
Adjunct for pain control:
- Amitriptyline, oral, 10–25 mg at night.
  - Titrate dose according to response.
  - Initial dose in the elderly: 10 mg at night.
  - Maximum dose: 75 mg at night.

Intra-articular corticosteroids
Consider in cases where a joint is actively inflamed.
To be prescribed and administered by a specialist only.
Not more than 2–3 injections per year per joint are recommended.
- Intra-articular corticosteroid, e.g.:
- Methylprednisolone acetate, 20–80 mg depending on joint size.

LoE:III[xv]

REFERRAL
» For consideration for joint replacement.
» Intractable pain.
» Neurogenic compression.

13.4 GOUT
M10.90-99

DESCRIPTION
A metabolic disease in which uric acid crystal deposition occurs in joints and other tissues.
Gout is managed in the following three stages:
i) Treating the acute attacks;
ii) Prevention of acute flares;
iii) Lowering excessive uric acid to prevent flares and tissue deposition of urate crystals.

LoE:III[xvi]

Acute gout:
Joint involvement is characterised by recurrent attacks of acute arthritis, which usually affects one joint, and is accompanied by extreme pain and tenderness, swelling, redness, and local heat.
» The inflammation may extend beyond the joint.
» In many patients the first metatarsophalangeal joint is initially involved.
» The instep, ankle, heel, and knee are also commonly involved.
» Bursae (such as the olecranon) may be involved.

Chronic gout:
Gout with one or more of the following:
» uric acid deposits in and around joints, bursae and cartilages of the extremities (tophi)
» initial involvement of the first metatarsophalangeal joint in most patients
» involvement of the instep, ankle, heel and knee

» involvement of bursae (such as the olecranon)
» significant periarticular inflammation
» bone destruction
» prolongation of attacks, often with reduction in pain severity
» incomplete resolution between attacks

GENERAL MEASURES

Acute gout:
Rest and immobilisation.

Chronic gout:
Lifestyle modification, including high fluid intake.
Avoid alcohol intake.
If possible, avoid diuretics, or use the lowest dose possible.

MEDICINE TREATMENT

ACUTE GOUT:

Initiate treatment as early as possible in an acute attack:

- NSAID, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with meals. *LoE:I*[xvii]

In high-risk patients: > 65 years of age; history of peptic ulcer disease; on concomitant warfarin, aspirin, or corticosteroids:

ADD *LoE:II*[xviii]

- PPI, e.g.:
- Lansoprazole, oral, 30 mg daily while on an NSAID.

If NSAIDS are contraindicated, e.g. warfarin therapy and renal dysfunction:

- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 40 mg daily for 5 days.

CHRONIC GOUT:

If possible, avoid known precipitants and medicines that increase uric acid, including:
» low dose aspirin,
» ethambutol,
» pyrazinamide, and
» thiazide and loop diuretics.

If diagnosis uncertain, joint aspiration with microscopy for crystal analysis is recommended.
Investigate for and treat secondary causes (e.g. haematological malignancies) where clinically indicated.
Measure serum creatinine and urate.
Serum urate may be normal during acute attacks.

Urate lowering therapy
Urate lowering therapy is recommended in the following circumstances:

» >2 acute attacks per year
» chronic tophaceous gout
» urate renal stones
» urate nephropathy

When the acute attack has settled, i.e. usually after 2 weeks:

- Allopurinol, oral, 100 mg daily.
  - Increase monthly by 100 mg according to serum urate levels.
  - Titrate dose to reduce serum urate to <0.35 mmol/L.
  - Allopurinol dosage is dependent on severity of disease and serum urate concentration. Doses in excess of 300 mg should be administered in divided doses. *LoE:III*[xix]
  - Maximum dose: 900 mg per day.
  - Elderly: start with 50 mg daily.
  - Renal impairment: Adjust dose according to renal function.
    - eGFR 30–60 mL/minute: start with 50 mg daily.
    - eGFR <10 mL/minute: consult a specialist. *LoE:III*[xx]

Caution in prescribing allopurinol to patients with renal impairment as they have an increased risk of a hypersensitivity reaction. Immediate cessation of allopurinol if rash or fever occurs.

LoE:III[xxi]

Prophylaxis to prevent breakthrough gout attacks:

An increase incidence of gout flares is associated with initiation of urate lowering therapy. Thus, colchicine or NSAIDs is recommended as anti-inflammatory prophylaxis when initiating allopurinol.

Anti-inflammatory prophylaxis should be discontinued at **6 months** provided gout symptoms have resolved**.**

- NSAID, e.g.: *LoE:I*[xxii]
- Ibuprofen, oral, 400 mg 8 hourly with meals.
  - Monitor renal function, as clinically indicated.

OR

Colchicine, oral, 0.5 mg 12 hourly for 6 months. *LoE:III*[xxiii]

- eGFR < 50 mL/minute: consult a specialist

CAUTION

Concomitant use of more than one oral NSAID has no additional clinical benefit and only increases toxicity.

Use of all NSAIDs is associated with increased risks of gastrointestinal bleeding, renal dysfunction, and cardiovascular events (stroke and myocardial infarction).

NSAIDs should be used judiciously at the lowest effective dose for the shortest duration. Explore and manage exacerbating factors for pain. See section 26.1: Chronic pain.

Do not use NSAID in pregnancy or while breastfeeding.

In high-risk patients: i.e. patients > 65 years of age, or with a history of peptic ulcer disease, or on concomitant warfarin, aspirin or corticosteroids:

ADD *LoE:II[xxiv]*

- PPI, e.g.:
- Lansoprazole, oral, 30 mg daily.

Do not stop urate lowering drugs during an acute attack.

REFERRAL

» No response to treatment despite adequate adherence.
» Suspected secondary gout.
» Non-resolving tophaceous gout.

13.5 SERONEGATIVE SPONDYLARTHRITIS

M45.X0-X9/M47.9099

DESCRIPTION

A group of diseases in which the rheumatoid factor is usually negative and the spine is often involved. These disorders have certain similar clinical features and occur predominantly in individuals with HLA-B27 antigen. The rheumatological manifestations in these disorders are variable, typically including asymmetrical lower-limb arthritis, sacro-iliitis, spinal inflammation (spondylitis), and enthesitis (e.g., Achilles tendonitis). The spondyloarthritides include ankylosing spondylitis, reactive arthritis, psoriatic arthropathy, and arthritis associated with inflammatory bowel disease. Extra-articular manifestations occur, especially uveitis, in about one third of patients.

GENERAL MEASURES

Physiotherapy to prevent spine deformity.

MEDICINE TREATMENT

Initiate treatment with NSAIDs.

- NSAID, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with meals. *LoE:I[xxv]*

In high-risk patients: i.e. patients > 65 years of age, or with a history of peptic ulcer disease, or on concomitant warfarin, aspirin or corticosteroids:

ADD *LoE:II[xxvi]*

- PPI, e.g.:
- Lansoprazole, oral, 30 mg daily.

REFERRAL

» Uveitis, to an ophthalmologist.
» Psoriasis, to dermatologist and rheumatologist

» Arthritis refractory to NSAIDs, to a rheumatologist.
» Deformity at diagnosis, to a rheumatologist.

13.5.1 ARTHRITIS, REACTIVE

M02.30-39

DESCRIPTION

A spondylarthritis often preceded by enteric or urogenital infections 1–4 weeks before the arthritis and occurring predominantly in individuals with HLA-B27 antigen.
It is a clinical diagnosis with no laboratory test or radiographic findings.
It occurs more commonly in HIV infection.
It is usually self-limiting.

MEDICINE TREATMENT

- NSAID, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with meals. *LoE:I*[xxvii]

In high-risk patients: i.e. patients > 65 years of age, or with a history of peptic ulcer disease, or on concomitant warfarin, aspirin or corticosteroids:

ADD *LoE:II*[xxviii]

- PPI, e.g.:
- Lansoprazole, oral, 30 mg daily.

If urethritis is present, treatment may prevent further episodes of arthritis:

- Ceftriaxone, IM, 250 mg as a single dose.
  - For ceftriaxone IM injection: Dissolve ceftriaxone 250 mg in 0.9 mL lidocaine 1% without epinephrine (adrenaline).

AND

- Azithromycin, oral, 1 g, as a single dose.

LoE:III[xxix]

13.6 SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

M32.9

These patients need to be managed by a specialist.

GENERAL MEASURES

Education regarding the disease and complications.
Avoid cigarette smoking as it is a trigger for lupus.
Sun protective barrier creams are often indicated.
Regularly monitor urine for blood and protein.
Provide advice regarding family planning as pregnancy may cause a lupus flare.

MEDICINE TREATMENT

MILD DISEASE

For pain:

- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

AND/OR

- NSAID, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with meals. *LoE:I[xxx]*

In high-risk patients: i.e. patients > 65 years of age, or with a history of peptic ulcer disease, or on concomitant warfarin, aspirin or corticosteroids:

ADD *LoE:II[xxxi]*

- PPI, e.g.:
- Lansoprazole, oral, 30 mg daily.

To suppress disease activity

- Chloroquine sulphate, oral, 150 mg (as base) daily for 5 days of each week.
  - Do ophthalmic examination at baseline within the first year of treatment and annually, to monitor for ocular damage.

LoE:I[xxxii]

Corticosteroids

Initiate therapy in patients with life threatening manifestations and organ involvement.

- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 2 mg/kg daily, initial dose.
  - Taper to the lowest maintenance dose after a response has been obtained. Refer to Appendix II for an example of a dose reduction regimen.
  - Usual maintenance dose: 10 mg daily.

Patients requiring corticosteroids for >3 months (long-term) should be managed for secondary prevention of osteoporotic fractures. See section 8.12: Osteoporosis.

Additional immunosuppressive therapy

Is often required for life-threatening disease, particularly kidney and CNS involvement. These medicines should be initiated by a specialist and regular FBC monitoring should be done.

- Azathioprine, oral, 1 mg/kg daily, titrated to a maximum of 3 mg/kg daily.

OR *LoE:III*

Cyclophosphamide, oral, 100 mg daily, titrated to a maximum of 200 mg daily (or 1–3 mg/kg daily).

LoE:III

RAYNAUD'S PHENOMENON I73.0

- Amlodipine, oral, 5 mg daily.

LoE:II[xxxiii]

ANTIPHOSPHOLIPID ANTIBODY SYNDROME

- Aspirin, oral, 150 mg daily.

Patients with previous thrombo-embolic episodes should receive lifelong warfarin (target INR 3 to 4).

LoE:III

Hormonal therapy in women

The use of oral contraceptives is controversial.
Until there is clarity it is advisable to use either progesterone-only, or low dose oestrogens, or non-hormonal methods.

REFERRAL

» All patients to a specialist for initial assessment.
» Lupus flare.
» Nephritis for renal biopsy.
» Persistent haematological derangements i.e. thrombocytopaenia.
» Neurological manifestations of lupus.

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CHAPTER 14

NEUROLOGICAL DISORDERS

14.1 CEREBROVASCULAR DISEASE

14.1.1 STROKE

I63.0-6/I63.8-9/I64

GENERAL MEASURES

Optimise hydration and nutrition; insert nasogastric tube if patient cannot swallow. Take precautions to ensure an open airway if patient is unconscious.

Physiotherapy and good nursing care. Consider rehabilitation for suitable patients, refer if necessary.

Do an ECG to rule out an acute coronary event or atrial fibrillation as precipitants.

Do serology to exclude meningovascular syphilis.

Check lipid profile in ischaemic strokes.

Ischaemic stroke in young adults (<45 years of age) may be due to atherosclerosis, but also consider:

» Embolic: e.g. rheumatic heart disease, atrial fibrillation, cardiomyopathy, previous myocardial infarction, and, very rarely, patent foramen ovale: history, careful clinical cardiac examination, ECG/CXR, and echocardiography.
» Vessel wall disease: e.g. syphilis, HIV infection, collagen-vascular diseases, TB or bacterial meningitis and extracranial arterial dissection. Investigate as dictated by clinical presentation, but at least syphilis and HIV serology, urine dipstix (haematuria and/or proteinuria), and ANF/RF. ANCA, and cerebral angiography or carotid Doppler may be indicated. Note that absence of a carotid bruit does not exclude significant carotid stenosis.
» Hypercoagulable states: e.g. antiphospholipid antibody syndrome, thrombotic thrombocytopenic purpura. Useful screening investigations are FBC and, in women, PTT/Anti-phospholipid Ab. Testing for thrombophilias and their management should only be done in consultation with an expert.

MEDICINE TREATMENT

Hyper-acute management:

Symptom onset ≤ 3 hours:

» Do not give aspirin.
» Refer immediately to hospital that **can provide thrombolytic therapy:**

- Alteplase, IV, 0.9 mg/kg.
  - 10 % of total dose given as a bolus and the remainder continued as an infusion over an hour.

LoE:I[i]

Symptoms >3 hours:

- Aspirin, oral, 300 mg, immediately. LoE:I[ii]

Followed by:

- Aspirin, oral, 150 mg daily.
  If patient is unable to swallow, administer through a naso-gastric tube.

Do not administer aspirin if there are symptoms suggestive of a sub-arachnoid bleed, e.g. headache, stiff neck, etc.

AND

DVT prophylaxis see section: 2.14 Venous thrombo-embolism.
Treat secondary pulmonary and urinary tract infections appropriately.

Secondary prevention:

Measures for secondary prevention may not be appropriate for patients with severe disability.

All patients with a thrombotic stroke, not on anticoagulation and irrespective of the LDL level:

- Aspirin, oral, 150 mg daily. LoE:I[iii]

AND

- HMGCoA reductase inhibitors (statins), e.g.:
- Simvastatin, oral, 40 mg at night.

LoE:I[iv]

Patients on protease inhibitor:

- Atorvastatin, oral, 10 mg at night.

LoE:I[v]

Patients on amlodipine (and not on a protease inhibitor):

- Simvastatin, oral, 10 mg at night.

LoE:III[vi]

If patient complains of muscle pain:

Reduce dose:

- HMGCoA reductase inhibitors (statins), e.g.:
- Simvastatin, oral, 10 mg at night.

OR

Consult specialist for further management. LoE:III[vii]

In patients with cardio embolic strokes (e.g. secondary to atrial fibrillation) with no evidence of haemorrhage on CT scan, the optimal time to start anticoagulation therapy is likely to vary among individual patients; this can be from 7 to 14 days and up to 21 days and is dependent on the infarct size (>1/3 of the hemisphere) and the patient's risk factors for recurrent events.

Bridging anticoagulation with heparin, or earlier initiation of warfarin, is not recommended because, although it reduces ischaemic stroke recurrence, it increases symptomatic intracranial haemorrhage. LoE:III[viii]

LoE:III

Blood pressure management
A transient increase in BP is common after an acute stroke. Do not actively lower a systolic BP <220 mm Hg or diastolic BP <120 mm Hg in the first few days after stroke as this may be associated with an increased risk of death.
In patients presenting with stroke and BP >220/120 mmHg, lower BP to about 180/110 mm Hg in the first 24 hours.

Lowering BP during the acute phase of stroke (within 6 hours of onset) may not improve morbidity. Antihypertensive medicines may be withheld until patients have suitable oral or enteral access. Cautious incremental reintroduction of treatment is advised to achieve long-term standard BP control. See section: 3.6.3 Hypertensive crisis, hypertensive emergency.

LoE:I[ix]

If BP >220/120 mm Hg:
- Long-acting calcium channel blocker, e.g.:
- Amlodipine, oral, 5 mg daily.

OR *LoE:II*[x]

If adequate fluid intake can be ensured:
- Hydrochlorothiazide, oral, 12.5 mg daily. *LoE:III*

Note:
» There is some evidence of harm from BP reduction within 7 days of acute stroke; after 7 days cautious incremental re-introduction of treatment is advised to achieve long term standard BP control.
» Antihypertensive medicines should be stopped in acute stroke unless the BP is >220/120 mm Hg (see above). *LoE:I*[xi]
» The need for re-initiating the patients previous antihypertensive regimen should be reassesed. See section 3.6: Hypertension.

LoE:III[xii]

REFERRAL
To a facility with a CT scan:
» Patients with atypical clinical presentation.
» Selected patients with suspected ischaemic stroke who may benefit from thrombolysis with tissue plasminogen activator if initiated within 3 hours of onset of symptoms.
» Patients with suspected posterior cerebral fossa haemorrhage who may require surgical decompression.
» If there is a history suggestive of subarachnoid haemorrhage or if there is neck stiffness.
» Patients with aspirin intolerance.

14.1.2 TRANSIENT ISCHAEMIC ATTACK (TIA)
G45.9

DESCRIPTION
A transient ischaemic attack is an episode of the brain, spinal cord, or retinal ischaemia causing focal neurological dysfunction usually for less than one

hour. Risk of subsequent stroke is highest in the week after a TIA. Consider hypoglycemia, epilepsy and migraine as alternative causes for the symptoms.

The ABCD^2 scoring system:

Feature	Points
≥60 years of age	1
BP ≥ 140/90 mmHg	1
Clinical features: speech disturbance without weakness OR unilateral weakness	 1 2
Diabetes	1
Duration: 10 to 59 minutes OR ≥1 hour	 1 2

ABCD^2 score of ≥4 is regarded as high risk and warrants urgent investigation and management as the risk of stroke within the next week is ≥4%.

MEDICINE TREATMENT

Cardioembolic disease:

- Warfarin, oral, 5 mg daily.
  - INR should be done after 48 hours, then every 1 to 2 days until within the therapeutic range of 2 to 3 (refer to Initiation dosing tables in the Appendix II).
  - Adjust dose to keep INR within therapeutic range (refer to Maintenance dosing tables in the Appendix II).

LoE:III[xiii]

Other patients:

- Aspirin, oral, 150 mg daily.

LoE:I[xiv]

AND

- HMGCoA reductase inhibitors (statins), e.g.:
- Simvastatin, oral, 40 mg at night.

LoE:I[xv]

Patients on protease inhibitor:

- Atorvastatin, oral, 10 mg at night.

LoE:I[xvi]

Patients on amlodipine (and not on a protease inhibitor):

- Simvastatin, oral, 10 mg at night.

LoE:III[xvii]

If patient complains of muscle pain:

Reduce dose:

- HMGCoA reductase inhibitors (statins), e.g.:
- Simvastatin, oral, 10 mg at night.

OR

Consult specialist for further management.

LoE:III[xviii]

Manage hypertension – see section 3.6: Hypertension.

14.1.3 SPINAL CORD INJURY, ACUTE

T09.3

Substantial evidence is lacking for the use of high dose corticosteroids in this clinical setting.

For symptomatic management of:
» Constipation – see section 24.1.2: Constipation.
» Urinary retention – see section 7.3.6: Overactive bladder.

14.1.4 SUBARACHNOID HAEMORRHAGE

I60.0-9

DESCRIPTION

Bleeding into the subarachnoid space, most commonly due to the rupture of a vascular aneurysm. Patients typically present with an acute onset of severe headache and may have additional neurological symptoms and signs. Diagnosis is confirmed preferably by neurological imaging and, when this is not available, by demonstrating CSF xanthochromia on lumbar puncture.

GENERAL MEASURES

Maintain normal hydration and electrolyte status.
Control blood pressure.

MEDICINE TREATMENT

Analgesia if level of consciousness is not impaired:

- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

If no response:

- Morphine, IV, to a total maximum dose of 10 mg (See Appendix II, for individual dosing and monitoring for response and toxicity).

Avoid NSAIDs.

In all patients presenting with aneurysmal subarachnoid hemorrhage (SAH) while waiting for transfer to neurosurgical facility and in consultation with neurosurgeon:

- Nimodipine, oral, 60 mg 4 hourly for 21 days.

REFERRAL

All patients with minimal impairment of consciousness level for angiography and appropriate neurosurgical management. Patients initially deemed unsuitable for further investigation, may be referred at a later stage, should their condition improve.

14.2 DEMENTIA

E51.2/E52/E63.9 + (F02.8*)

DESCRIPTION

Progressive loss of cognitive function, usually of insidious onset. Initial presentation may be with mild personality or memory changes, before more pronounced defects become evident. Investigate patients for potentially reversible causes:

» Metabolic
  - Hypothyroidism
  - Vitamin B_{12} deficiency
  - Pellagra
  - Thiamine deficiency (Wernicke's syndrome)
» Medications and drugs
  - Alcohol abuse
  - Many medicines with CNS side-effects
» Infections
  - Syphilis
  - HIV
» Surgical
  - Chronic subdural haematoma
  - Normal pressure hydrocephalus
» Severe depression (may mimic dementia)

Conditions which may worsen already existing dementia include:

» electrolyte disturbances and dehydration
» infections
» medicine toxicity

GENERAL MEASURES

Appropriate care and support, according to the level of impairment.
Ambulatory care is preferred to hospitalisation, if feasible.
Family counselling and support.

MEDICINE TREATMENT

Management is mainly symptomatic.

<u>To control restless patients:</u>

- Haloperidol, oral, 0.5–1 mg 8 hourly with a higher dose at night, if required.

Note:

» There is uncertainty of benefit versus harm of long-term use of antipsychotics in dementia, but antipsychotics may be of benefit in severe behavioural and psychological symptoms.
» Inform the family of a possible elevated risk of mortality with prolonged use of antipsychotics.
» If there is no improvement, stop the antipsychotic.

» Initiate treatment at a low dose and titrate to the lowest effective dose for the shortest possible time. Reassess the person at least every 6 weeks, to check whether they still need medication.

LoE:III[xix]

For pellagra:

- Nicotinamide, oral, 100 mg 8 hourly.

Wernicke's syndrome: E51.2 + (F02.8*)

- Thiamine, IV, 500 mg 12 hourly for 3 days, followed by 500 mg daily for 3–5 days.
  - Follow with oral thiamine 100 mg 8 hourly.

Prophylaxis in patients at risk (alcoholism, malnutrition): Z29.2

- Thiamine, IM/oral, 100 mg 8 hourly for 14 days. *LoE:III*[xx]

Treat other commonly associated nutritional deficiencies:

If confirmed Vitamin B_{12} deficiency, manage as section 2.1.2: Anaemia, megaloblastic.

14.3 DELIRIUM

See section 20.8: Delirium with perceptual disturbances.

14.4 EPILEPSY

G40.0-9

GENERAL MEASURES

Take an adequate history to define the type of epilepsy.

Juvenile myoclonic epilepsy and absence seizures should be specifically considered and identified, as some standard medicines may be less efficacious or may even worsen seizure frequency or severity.

Patients with new onset epilepsy should have a CT scan (this is essential in immunocompromised patients) and other investigations as clinically indicated.

A single unprovoked seizure is not always an indication for treatment, although 40% of patients may have a subsequent seizure within 2 years. Such a decision ultimately needs to be made by the patient after discussion of risks and benefits of anti-epileptic medicines. Anticonvulsants should be commenced after a single unprovoked seizure in patients at high risk of subsequent seizures (e.g. abnormal neurological examination, strong family history, abnormal brain imaging).

Record dates and, if possible, times of seizures in a seizure diary. Present seizure diary at each consultation for assessment of therapy.

Disease identification bracelet, necklace or card.

Counselling and advice on:

» the adverse effect of alcohol on seizures,

» sleep hygiene,
» the effect of missing a dose of medication,
» discontinuing the medication without advice of a doctor, and
» family planning is important in women of child-bearing potential as anticonvulsants, are all potentially teratogenic. Note that there are important drug-drug interactions between hormonal contraceptives (except DMPA) and several anticonvulsant medicines (carbamazepine, phenobarbital, phenytoin).
» patients with uncontrolled seizures should avoid driving and operating machinery until they have been seizure free for one year.

MEDICINE TREATMENT

The anticonvulsant treatment strategy should be individualised based on the seizure type, the use of other medicines and co-morbidities.
The choice between therapeutic agents must be made on the acceptability of side effects and how the number of doses influences lifestyle.
The aim is to use monotherapy, i.e. a single anticonvulsant, and to progressively increase the dose until the seizures are controlled or clinically important side effects occur.

Add-on or switching medication:

If the initial medicine fails to achieve satisfactory control with optimal dosages, or causes unacceptable adverse effects, then a second medicine may be started. The first medicine should be continued for 2 weeks and then gradually reduced over 6–8 weeks until stopped, whilst the second medicine is gradually increased over an appropriate period to therapeutic doses. Failure of second-line treatment with the exclusion of alcohol use/misuse and poor adherence, may require combination therapy; this should be done in consultation with a specialist.

Patients with a history of myoclonic seizures or typical absence seizures should preferably be treated with valproate (valproic acid), as those seizures may be aggravated by the use of either phenytoin or carbamazepine (See other epilepsy types, below).

Therapeutic drug monitoring should not be done routinely, but should be done in the following situations:

LoE:III[xxi]

» To confirm toxicity in a symptomatic patient.
» Poor control.
» To confirm poor adherence despite self-reported good adherence.

Acute management

If convulsing:
» Measure blood glucose and treat hypoglycaemia, if present.
» Ensure an open airway and administer oxygen.
» Place in recovery position to prevent aspiration.
» Obtain intravenous access.
» Avoid putting anything in the mouth.

Partial seizures (focal seizures) G40.0-2

- Carbamazepine, oral.
  - Start with 100 mg 12 hourly.
  - Increase by 100–200 mg/day at weekly intervals according to seizure control and adverse events.
  - Usual maximal dose: 600 mg 12 hourly. *LoE:III*[xxii]

OR

Lamotrigine, oral.

- Refer to the lamotrigine dose-titration table, below.

CAUTION

Phenytoin, phenobarbitone and carbamazepine are potent enzyme inducing agents and should be used with caution with other medicines metabolised by the liver, especially warfarin, some ARVs, progestin subdermal implants and oral contraceptives.

Generalised tonic clonic seizures G40.3

- Lamotrigine, oral.
  - Refer to the lamotrigine dose-titration table.

OR

Carbamazepine, oral.

- Start with 100 mg 12 hourly.
- Increase by 100–200 mg/day at weekly intervals according to seizure control and adverse events.
- Usual maximal dose: 600 mg 12 hourly. *LoE:I*[xxiii]

<u>For patients controlled on phenytoin:</u>

- Phenytoin, oral, 4.5–5 mg/kg (lean body mass) daily.
  - Usual starting dose in an adult male: 300 mg once daily.
  - Dose changes above 300 mg should be done only in no more than 50 mg increments at intervals no shorter than 2 weeks.

Note: Caution and frequent monitoring of drug levels are obligatory at doses >300 mg daily as the risk for toxicity is high and could lead to permanent cerebellar damage. *LoE:III*

<u>For patients not controlled on or who do not tolerate the above medications:</u>

- Valproate (valproic acid), oral.
  - Usual starting dose: 200–300 mg 12 hourly.
  - Increase, as required, every 2 weeks to a maximum dose of 1.2 g 12 hourly.

Other epilepsy types G40.4-5/G40.8-9

Manage in consultation with a specialist.

Juvenile myoclonic epilepsy:

Refer all for specialist investigation and initiation of therapy with valproate (valproic acid). *LoE:III*[xxiv]

Absence seizures:

- Valproate (valproic acid), oral (specialist consultation).
  - Usual starting dose: 200–300 mg 12 hourly.
  - Increase, as required, every 2 weeks to a maximum dose of 1200 mg 12 hourly.

OR *LoE:III*[xxv]

- Lamotrigine, oral (specialist consultation).
  - Refer to dose titration table.

Dose-titration of lamotrigine:

NOT ON VALPROATE (VAPROIC ACID)		ON VALPROATE (VALPROIC ACID)	
Weeks	**Dose**	**Weeks**	**Dose**
1,2	25 mg daily	1,2	25 mg alternate days
3,4	25 mg 12 hourly	3,4	25 mg daily
5	25 mg in the morning; 50 mg at night	5	25 mg 12 hourly
6	50 mg 12 hourly	6	25 mg in the morning; 50 mg at night
		7	50 mg 12 hourly

Note: *LoE:III*[xxvi]

- Further increase by 50 mg every 1–2 weeks, according to response.
- Usual maintenance dose: 100–200 mg daily, given in two divided doses with doses up to 500 mg may be required.

Adapted from the Western Cape Department of Health, Lamotrigine dose titration protocol, 2019.

HIV-infected individuals on ARVs (B24)

Phenytoin, phenobarbital and carbamazepine are enzyme inducing anti-epileptic medicines. Due to potential drug interactions with antiretroviral medicines, switch these anticonvulsants to lamotrigine.

- Lamotrigine, oral.
  - Refer to the lamotrigine dose-titration table.

<u>If not on any anti-epileptic medicine:</u>

- Lamotrigine, oral.
  - Refer to the lamotrigine dose-titration table, above.

OR

Valproate (valproic acid), oral.

- Usual starting dose: 200–300 mg 12 hourly.
- Increase, as required, every 2 weeks to a maximum dose of 1200 mg 12 hourly.

<u>Add on therapy to valproate (valproic acid):</u>

- Lamotrigine, oral.
  - Refer to the lamotrigine dose-titration table, above.

CAUTION - LAMOTRIGINE
Lamotrigine may cause Stevens-Johnson Syndrome.

Note:
» Metabolism of lamotrigine is induced by lopinavir/ritonavir and atazanavir/ritonavir. Dose of lamotrigine may need to be increased when patients are switched to a lopinavir/ritonavir or atazanavir/ritonavir.
» In the absence of evidence of benefit, using lamotrigine serum levels for dose titration is discouraged.

LoE:III[xxvii]

Pregnancy
» Optimal control of epilepsy on a single agent is the best management.
» Individualise anti-epileptic treatment.
» Advise women of child-bearing potential (WOCP) to use effective contraception.
» Risk-assess patients who fall pregnant on valproate (valproic acid), in consultation with a specialist to determine if switching is required.
» If alternate treatment cannot be recommended and valproate (valproic acid) required, supplement with:
- Folic acid, oral, 5 mg daily.

LoE:III[xxviii]

CAUTION
Children born to women taking valproate (valproic acid) are at significant risk of birth defects (10%) and persistent developmental disorders (40%). Valproate (valproic acid) is contra-indicated and should be avoided in pregnancy and women of child-bearing potential.

LoE:III[xxix]

Prophylaxis in head trauma Z29.2
Duration of anti-epileptic prophylaxis is dependent on the severity of the head trauma.
Acute management:
- Phenytoin, IV, 20 mg/kg diluted in sodium chloride 0.9% **(not dextrose)** administered not faster than 50 mg/minute preferably with cardiac monitoring.

Patient is awake and able to swallow:
- Phenytoin, oral, 18 mg/kg as a single dose.

LoE:III[xxx]

Maintenance therapy:
- Phenytoin, IV, 5 mg/kg/day (300 mg daily for most adults) diluted in sodium chloride 0.9% **(not dextrose)**, at night for 7 days – monitor clinical response and manage appropriately.
  - If arrhythmias occur, interrupt the infusion temporarily and reintroduce slowly.

LoE:II[xxxi]

Patient is awake and able to swallow:

- Phenytoin, oral, 300 mg at night for 7 days.

REFERRAL

» Epileptics who are poorly controlled on adequate treatment with therapeutic drug concentrations.
» Epilepsy with unexplained neurological symptoms or signs.

14.4.1 STATUS EPILEPTICUS

G41.0-2/G41.8-9

DESCRIPTION

Status epilepticus is defined as either:

1) two or more sequential seizures, lasting more than 5 minutes without full recovery of consciousness between seizures or;
2) continuous seizure activity for longer than 5 minutes.

GENERAL MEASURES

Start treatment immediately. Do not wait for results of special investigations.
Place the patient in a lateral (recovery) position.
Stabilise the patient (i.e. secure airway and check breathing and circulation).
Time seizure from its onset.
Assess oxygenation and give oxygen via nasal cannula/face mask if required.
Check serum glucose, and treat if hypoglycaemic.
Secure intravenous access.
Check electrolytes (e.g. sodium, calcium, urea).
Consider poisoning, e.g. isoniazid, theophylline, tricyclic antidepressants and cocaine poisonings.

MEDICINE TREATMENT

Seizures should be stopped promptly, as prolonged seizures can cause permanent brain damage. Aim for definitive control within 60 minutes of onset.

Initial treatment:

Benzodiazepine:

- Lorazepam, IV, 4 mg, repeat once after 5–10 minutes, if necessary.

LoE:I[xxxii]

OR

Midazolam, IM/IV, 10 mg, repeat once after 5–10 minutes if necessary.

LoE:I[xxxiii]

OR

Midazolam buccal, 10 mg using the parenteral formulation, repeat once after 5–10 minutes if necessary.

LoE:III

OR

Clonazepam, IV, 2 mg, repeat once after 5–10 minutes if necessary.

LoE:III[xxxiv]

If none of the above are available, consider:

- Diazepam, IV, 10 mg, not faster than 2 mg/minute, repeat once after 5–10 minutes if necessary.

LoE:I[xxxv]

AND

- Phenytoin, IV, 20 mg/kg diluted in 200 ml sodium chloride 0.9% **(not dextrose)** administered not faster than 50 mg/minute preferably with cardiac monitoring.
  - Avoid phenytoin if seizures are secondary to poisons with potential cardio-toxic effects.

LoE:II[xxxvi]

  - If arrhythmias occur, interrupt the infusion temporarily and reintroduce slowly.
  - If further/continued seizures, repeat a second phenytoin dose, IV, 10 mg/kg.

LoE:I[xxxvii]

Seizures continuing after 30 minutes:

Intubate and ventilate the patient.

- Thiopental, IV, 2–4 mg/kg, followed by 50 mg bolus every 2–3 minutes to control seizures.
  - Maintenance dose: 1–5 mg/kg/hour, depending on the presence of epileptogenic activity on EEG.
  - Beware of hypotension.
  - Once seizures are controlled for 24 hours, wean off thiopental by decreasing the dose by 1 mg/kg every 12 hours.

OR

LoE:III[xxxviii]

Propofol, IV, 1–2 mg/kg/dose as a bolus, followed by 2–10 mg/kg infusion, titrated to effect

  - Maintenance dose: 3–5 mg/kg/hour.

OR

LoE:I[xxxix]

Midazolam, IV 0.1–0.2 mg/kg bolus, followed by 0.05–0.5 mg/kg/hour infusion, titrated to effect.

LoE:III[xl]

Note:

» Continue anaesthetic for 12−24 hours after the last clinical or electrographic seizure, then taper the dose.

LoE:III[xli]

» Higher initial maintenance doses of phenytoin may be needed in patients who have had previous thiopental exposure.

» After thiopental has been weaned off, use daily therapeutic drug monitoring to guide phenytoin doses, until phenytoin levels have stabilised.

LoE:III[xlii]

Maintenance therapy

Once seizures are controlled:

LoE:III[xliii]

- Phenytoin, IV/oral, 300 mg daily.
  - Adminster the first maintenance dose 12 hours after the loading dose.

Clinical signs that seizures are controlled include autonomic stability and the absence of abnormal movement.

For long-term maintenance therapy, see section 14.4: Epilepsy.

14.5 HEADACHE AND FACIAL PAIN SYNDROMES

14.5.1 MIGRAINE

G43.0-3/G43.8-9

DESCRIPTION

A migraine is an episodic headache, usually located unilaterally and throbbing/ pulsating in nature, which may occur with or without an aura. Migraines are usually accompanied by nausea and/or vomiting, photophobia (sensitivity to light) and phonophobia (sensitivity to noise). There are several variants of migraine.

GENERAL MEASURES

Reassure patient that this is a benign condition.
Attempt to identify any precipitating factors or food triggers from the patient's history.

MEDICINE TREATMENT

Acute treatment

Initiate therapy during the migraine attack or at the onset of the headache.

Analgesia:

- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

OR

- NSAID, e.g.:
- Ibuprofen, oral, 400 mg immediately then 8 hourly with meals, if needed.

For nausea:

- Metoclopramide, oral/IM, 10 mg 8 hourly, as required.

Prophylaxis (Z29.2)

Regular, daily, prophylactic therapy is advised if:

» attacks are frequent, i.e. more than 2–3 per month, or
» severe, causing a significant amount of disability, or
» attacks are long lasting, or
» patient poorly tolerates therapy for acute attacks.

LoE:III[xliv]

- Amitriptyline, oral, 10–25 mg at bedtime.
  - Up-titrate dose to adequate clinical response.

- Doses greater than 25–75 mg are seldom required.

OR LoE:I[xlv]

Poor response or contraindication to amitriptyline:

- β-blocker, e.g.:
- Propranolol, oral, 40 mg 12 hourly.
  - Titrate dose to adequate response
  - Maximum dose 120–240 mg daily. LoE:I[xlvi]

REFERRAL

Inadequate response to treatment.

14.5.2 CLUSTER HEADACHE

G44.0

DESCRIPTION

Repetitive episodes of excruciating headache typically of short duration (up to 2 hours) in clusters for weeks to months at a time. Typically, the headache is of sudden onset, unilateral during the specific cluster, and quickly reaches a climax. Associated redness of the eye with lacrimation and rhinorrhoea occurs.

MEDICINE TREATMENT

- Oxygen inhalation may abort some episodes.

Analgesics are ineffective.

To induce rapid remission in patients with episodic cluster headache:

- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 40 mg daily for 5–10 days.
  - Tapering is not necessary when the above duration is used.

LoE:III[xlvii]

Prophylaxis

- Verapamil, oral, 40–80 mg 12 hourly.

REFERRAL

Inadequate response to treatment.

14.5.3 TRIGEMINAL NEURALGIA

See section 26.1.4 Management of neuropathic pain.

14.5.4 TENSION HEADACHE

G44.2/G93.2

DESCRIPTION

Tension headaches are described as a tight band around the head and is generally worse in the afternoon. Occurs over the back of the head, but may extend over the entire head.

GENERAL MEASURES
Consider use of relaxation techniques.
Exclude medication overuse headache.

MEDICINE TREATMENT
- Amitriptyline, oral, 10–75 mg at night.

REFERRAL
» Atypical pain and/or focal neurological signs and symptoms, suggestive of alternate diagnosis.
» Poor response to therapy.

14.5.5 MEDICATION OVERUSE HEADACHE
G44.4

DESCRIPTION
Medication overuse headache generally occurs for ≥15 days per month for more than 3 months; and develops as a consequence of regular overuse of analgesics for acute pain-relief. The headache develops or markedly worsens during medication overuse, and usually, but not invariably, resolves after the overuse is stopped.

LoE:III[xlviii]

GENERAL MEASURES
Stop all analgesics.
Counsel patient regarding the link between overuse of analgesics and the development of and/or worsening of the headache syndrome.
The headache usually resolves after the overuse is stopped, but may transiently worsen.

MEDICINE TREATMENT
- Amitriptyline, oral, 10 mg at night.
  - Increase to a maximum of 75 mg at night.
  - May be used during withdrawal of acute or symptomatic headache treatment.

LoE:II[xlix]

14.5.6 IDIOPATHIC INTRACRANIAL HYPERTENSION (PSEUDOTUMOUR CEREBRI)
G93.2

DESCRIPTION
Patients present with symptoms (chronic headache, visual disturbance or loss due to papilloedema and tinnitus) and signs (papilloedema) of raised intracranial pressure without structural intracranial abnormality and with normal CSF composition.

Diagnosis
All patients should have neuro-imaging (CT scan).
» If this is normal, i.e. the absence of structural lesions or hydrocephalus, perform a lumbar puncture and measure intracranial pressure.
» Diagnosis is confirmed by the presence of raised CSF pressure >20 cm H_20.

GENERAL MEASURES
Stop medicines associated with benign intracranial hypertension (e.g. doxycycline, corticosteroids, combined oral contraceptives).
Regular monitoring of visual fields is crucial.
Weight loss.
Repeated lumbar punctures with measurement of opening pressure (do lumbar puncture with patient in left lateral position).
Consider surgery if there is progression of visual defects, despite medical therapy, visual loss at onset or severe papilloedema.

MEDICINE TREATMENT
Discuss all cases with a specialist.

For visual involvement, persistent headaches, or severe papilloedema:
- Acetazolamide, oral, 250 mg 12 hourly, maximum dose 2 g daily

OR *LoE:II*

Furosemide, oral, 40 mg daily.

REFERRAL
» For neuro-imaging, if not available locally.
» Visual symptoms or deterioration of visual fields for opthalmology evaluation.
» Patients not responding to therapy or in need of surgical management.

14.6 INFECTIOUS AND PARASITIC CONDITIONS

14.6.1 MENINGITIS
G00.0-3/G00.8-9/G03.0-2/G03.8-9/A32.1
**N. meningitidis*, *H. influenzae* Type B and listeriosis are notifiable medical conditions.

DIAGNOSIS
Computed tomography should be done before lumbar puncture in patients with:
» focal neurological signs,
» new seizures,
» papilloedema, or
» reduced level of consciousness.
In cases where lumbar puncture is delayed or cannot be done (e.g. uncontrolled significant bleeding tendency), commence empiric antibiotic therapy after taking samples for blood cultures. Attempt the lumbar puncture later, if possible.

GENERAL MEASURES

Observe patient closely with regular monitoring of vital signs and neurological state.
Pay close attention to hydration status.
Nurse patients in a quiet, semi-dark surrounding.
Repeated lumbar punctures are of no benefit in uncomplicated bacterial meningitis.
Prompt initiation of antibiotic therapy is associated with improved outcomes in patients with bacterial meningitis.

MEDICINE TREATMENT

All patients require sufficient analgesia:

- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

AND/OR

- NSAID, e.g.:
- Ibuprofen, oral, 400 mg then 8 hourly with meals, if needed.

Severe pain:

- Tramadol, oral, 50–100 mg 4–6 hourly.

Antibiotic therapy

Empiric therapy for bacterial meningitis, until sensitivity results are available:

- Ceftriaxone, IV, 2 g 12 hourly for 10 days. *LoE:III*[li]

Adjunctive corticosteroids are not recommended as trials in low-middle income countries have not demonstrated benefit.

Meningococcal meningitis A39.0 + (G01*)

For confirmed meningococcal disease only:

- Benzylpenicillin (penicillin G), IV, 20–24 MU daily in 4–6 divided doses for one week.

Eradicate nasopharyngeal carriage with a single dose of ciprofloxacin 500 mg after completing course of benzylpenicillin. This is not required if the patient received an initial, pre-referral dose of ceftriaxone.

- Ciprofloxacin, oral, 500 mg immediately as a single dose.

Severe penicillin allergy: (Z88.0)

- Meropenem, IV, 2 g 8 hourly for 7 days. *LoE:III*[lii]

Prophylaxis of contacts:

Only for close household contacts.
Only for healthcare workers who resuscitate patients before they received appropriate treatment.

- Ciprofloxacin, oral, 500 mg immediately as a single dose.

Pneumococcal meningitis G00.1
This organism may be associated with CSF leaks.

If sensitive to penicillin: (Z88.0)
- Benzylpenicillin (penicillin G), IV, 20–24 MU daily in 4–6 divided doses for 10 days.

If resistant to penicillin:
- Ceftriaxone, IV, 2 g 12 hourly for at least 10 days.

Severe penicillin allergy: (Z88.0)
- Meropenem, IV, 2 g 8 hourly for 10 days.

Note: Consult a microbiologist/infectious diseases specialist.

Haemophilus influenzae G00.0
- Ceftriaxone, IV, 2 g 12 hourly for 10 days.

Severe penicillin allergy: (Z88.0)
- Meropenem, IV, 2 g 8 hourly for 10 days.

Note: Consult a microbiologist/infectious diseases specialist.

Listeria monocytogenes **meningitis** A32.1
- Ampicillin, IV, 3 g 6 hourly for 21 days. *LoE:III*[liii]

AND
- Gentamicin, IV, 5 mg/kg daily for 7 days (may be prolonged if response is poor). See Appendix II for guidance on prescribing.

Severe penicillin allergy: (Z88.0)
Consult a specialist.

14.6.1.1 TUBERCULOUS MENINGITIS (TBM)
A17.0 + (G01*)

CSF findings are extremely variable. Generally, lymphocytes predominate, however, polymorphs predominate initially in about a third of patients.
Protein is usually >1 g/L and glucose is usually low.

In cases where the differential diagnosis between bacterial and tuberculous meningitis is in doubt, lumbar puncture should be repeated 2–3 days later while still on ceftriaxone. If the aetiology is bacterial, considerable improvement in CSF findings may be expected, but with untreated tuberculous meningitis the cell counts and protein levels will be the same or higher; and the glucose level will be the same or lower.

Standard combination tuberculosis therapy according to National protocol. See section 16.9: Tuberculosis, Pulmonary.
Duration of therapy: 9 months.

In HIV non-infected individuals:
Corticosteroid use may be of benefit in reducing neurological deficit in

patients with grade II to III disease (focal neurological disease, depressed levels of consciousness Glasgow Coma Scale of 14 or less.

- Dexamethasone, IV,
  - 0.3–0.4 mg/kg/day for 2 weeks.
  - Followed by 0.2 mg/kg daily during week 3.
  - Then 0.1 mg/kg/day during week 4, then 4 mg per day during week 5, and therafter, taper 1 mg off the daily dose each week.
  - Total duration approximately 8 weeks.

LoE:I[iv]

- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 60 mg daily for 2 weeks. *LoE:III[v]*
  - Then taper gradually over the next 6 weeks (See Appendix II for an example of a dose reduction regimen).

LoE:I[vi]

In HIV-infected individuals:
Note: There is uncertainty whether the use of corticosteroids is beneficial in HIV-infected patients with TBM. *LoE:I[vii]*

14.6.1.2 CRYPTOCOCCAL MENINGITIS

HIV-infected patients (see section 10.2.4: Cryptococcosis)

» In HIV infection the aim is to suppress the infection until immune restoration occurs with antiretroviral therapy.

HIV-uninfected patients

» In HIV-uninfected patients the aim is to cure the infection.

14.6.1.2.1 CRYPTOCOCCAL MENINGITIS, HIV-INFECTED

See section 10.2.4: Cryptococcosis.

14.6.1.2.2 CRYPTOCOCCAL MENINGITIS, HIV-UNINFECTED

B45.1 + (G02.1*)

MEDICINE TREATMENT

Initial therapy: *LoE:I[viii]*

- Amphotericin B, IV, 1 mg/kg daily.
  - Ensure adequate hydration to minimise nephrotoxicity. (See Appendix II for preventing, monitoring and management of toxicity).
  - Duration of initial IV therapy:
    - Treat intravenously for 4 weeks, provided that there are no neurological complications and follow up CSF culture at 2 weeks is negative. In patients with neurological complications or persistent positive culture: increase the initial phase of therapy to 6 weeks in consultation with a specialist.

AND LoE:III[lix]

- Fluconazole, oral, 800 mg daily for 2 weeks, followed by 400 mg daily for 2 months.

Maintenance therapy:

- Fluconazole, oral, 200 mg daily for a minimum of 1 year.

Follow all patients closely for relapses.

Therapeutic lumbar puncture: LoE:III[lx]

This should be considered as the intracranial pressure is often elevated with a communicating hydrocephalus. See section 10.2.4: Cryptococcosis.

14.6.2 VIRAL MENINGOENCEPHALITIS

B00.4 + (G05.1*) / A86

DESCRIPTION

Patients present with headache, neck stiffness, and encephalitic symptoms which may include fever, personality or behavioural changes, hallucinations and seizures. Lumbar puncture typically shows mildly elevated protein, normal glucose and mild pleocytosis (< 500), mainly lymphocytes (early on polymorphs may predominate). Treatment for herpes simplex encephalitis should be commenced in all patients until this has been excluded (see below).

MEDICINE TREATMENT

Analgesia:

- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

AND/OR

- NSAID, e.g.:
- Ibuprofen, oral, 400 mg immediately then 8 hourly with meals, if needed.

OR LoE:III[lxi]

- Morphine, IV, to a total maximum dose of 10 mg (See Appendix II, for individual dosing and monitoring for response and toxicity).

Herpes simplex encephalitis

Clinical features are fever, change in behaviour and seizures, which may be either focal or generalised.

Evidence of mucocutaneous involvement is usually not present. Lumbar puncture shows the above features of viral meningoencephalitis. Evidence of encephalitis involving medial temporal lobe region on MRI/CT neuro-imaging or on EEG is strongly supportive of the diagnosis and positive HSV PCR test on CSF is diagnostic.

- Aciclovir, IV, 10 mg/kg 8 hourly for 14 days (21 days in immunocompromised patients).

- Start therapy as early as possible, i.e. before results are available.
- A negative herpes PCR usually excludes the diagnosis unless the specimen was taken within 72 hours of onset of symptoms, when false negatives have been described.

LoE:III[lxii]

Treat seizures appropriately, see section 14.4: Epilepsy.

All suspected cases of herpes encephalitis should be discussed with a specialist.

REFERRAL

» For neuro-imaging: patients not responding or worsening in condition, i.e. decrease in consciousness and cranial nerve palsies, despite appropriate therapy.
» This is especially urgent in patients with tuberculous meningitis, who may develop hydrocephalus and require an urgent shunting procedure.
» Patients with shunts.

14.6.3 MENINGOVASCULAR SYPHILIS (NEUROSYPHILIS)

A52.1 + (G01*)

DIAGNOSIS

Lumbar puncture typically shows lymphocytosis with mildly elevated protein and low/normal glucose.
Serum syphilis serology: a negative TPHA or TPAb excludes the diagnosis; RPR may be negative in some cases.
CSF syphilis serology: a CSF VDRL positive result is highly specific for neurosyphilis, but may be negative in approximately 50%; a negative CSF FTA-ABS excludes the diagnosis of neurosyphilis.

MEDICINE TREATMENT

- Benzylpenicillin (penicillin G), IV, 20 MU daily in 4–6 divided doses for 10 days.

LoE:III

A serum RPR response (4-fold decline in titre) after 6 months is predictive of treatment success for neurosyphilis.

LoE:III[lxiii]

Severe penicillin allergy: (Z88.0)

Refer for consideration of desensitisation and subsequent treatment with benzylpenicillin at a referral centre.

14.6.4 BRAIN ABSCESS

G06.0

DIAGNOSIS

Patient may present with focal neurological signs and signs of infection. Neurological signs may not always be prominent. Neuro-imaging usually confirms diagnosis. Patients may have concomitant infection of ears, paranasal sinuses or lower respiratory tract.

MEDICINE TREATMENT

Empiric antibiotic therapy

- Ceftriaxone, IV, 2 g 12 hourly.

AND

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

Adjust according to antimicrobial sensitivity after surgical drainage.

REFERRAL

All, as patients require urgent neurosurgery opinion and treatment.

14.6.5 ANTIMICROBIAL USE IN PATIENTS WITH HEAD INJURIES

S09.9/S02.10-11/S06.00-01/S06.10-11/S06.20-21/S06.30-31/S06.40-41/S06.50-51/S06.60-61/S06.70-71/S06.80-81/S06.90-91

MEDICINE TREATMENT

Basal skull fractures

Antibiotic prophylaxis is not indicated.

Penetrating brain injuries

Antibiotics are given for therapy.

- Ceftriaxone, IV, 2 g 12 hourly for 7 days. *LoE:III*

14.6.6 NEUROCYSTICERCOSIS

B69.0 + (G99.8*)

DIAGNOSIS

Patients may present with seizures and/or focal neurological deficit. Typical cystic lesions are seen on neuro-imaging. Old calcified lesions are inactive and do not require treatment.

GENERAL MEASURES

Health education.

Surgery for treatable ventricular blockage or spinal or intraocular cysts.

MEDICINE TREATMENT

For active or viable cysts only:

- Albendazole, oral, 12 hourly for 8 days.
  - o ≥ 60 kg: 400 mg.
  - o < 60 kg: 7.5 mg/kg to a maximum of 800 mg daily.
  - o Do not use in pregnancy.

AND *LoE:II*[lxiv]

- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 60 mg daily for 8 days. *LoE:III*[lxv]

Anticonvulsants, if required. See section 14.4: Epilepsy. *LoE:II*[lxvi]

REFERRAL

Uncontrolled seizures despite antiparasitic and anticonvulsant therapy.

14.7 MOVEMENT DISORDERS

DESCRIPTION

Abnormalities of movement/initiation of movement, divided into those with reduction of movement (hypokinesia or bradykinesia), or those with excessive movements (hyperkinesia).

14.7.1 PARKINSONISM, PRIMARY

14.7.1.1 IDIOPATHIC PARKINSON DISEASE

G20/G21.1

DESCRIPTION

Parkinsonism is a syndrome characterised by tremor, rigidity, bradykinesia and postural disturbances. It may be primary, i.e. Parkinson's disease, or secondary, i.e. drug-induced, or due to uncommon disorders that may initially resemble Parkinson's disease.

The objective of treatment is to:

» minimise disabling symptoms
» prevent complications and avoid serious drug-induced side effects

GENERAL MEASURES

General supportive therapy and advice about lifestyle modification, physiotherapy and occupational therapy.

MEDICINE TREATMENT

Note: Set therapeutic targets so that the patient is functioning as well as possible.

Bradykinesia, rigidity and postural disturbance:

- Carbidopa/levodopa, 25/100 mg (1 tablet), oral, 8 hourly, increase gradually according to clinical response.
  - Maximum dose of 200/800 mg daily (8 tablets).
  - Increase dose in consultation with a specialist.

REFERRAL

» Alternative diagnosis suspected (e.g. Parkinson's plus disorders etc.)
» No improvement or poor control with treatment.
» Increasing on/off phenomenon.
» Dyskinesias.

14.7.2 PARKINSONISM, SECONDARY

G21.0-4/G21.8-9

DESCRIPTION

Secondary parkinsonism is caused by certain medicines (typical and atypical antipsychotics, anti-emetics, anticonvulsants (phenytoin, valproate/ valproic acid) and SSRIs), a different nervous system disorder, or another illness.

GENERAL MEASURES

Primary approach in drug-induced parkinsonism should be to stop the offending medicine if possible.
Refer to psychiatric services for review of antipsychotic treatment in patients requiring treatment for parkinsomism (see section 15.5.2: Schizophrenia spectrum disorders).

MEDICINE TREATMENT

Anticholinergics have a limited role in this setting and should be used with caution.

- Anticholinergic agent, e.g.:
- Orphenadrine, oral, 50 mg 8 hourly, increase gradually according to clinical response.
  - Usual dose: 150–250 mg daily. *LoE:III*[lxvii]
  - Maximum dose: 400 mg daily.

Note: Anticholinergic side effects are common and may be exacerbated by antipsychotics.

OR

- Carbidopa/levodopa, 25/100 mg (1 tablet), oral, 8 hourly.

Acute dystonic reaction:

Usually follows administration of dopamine-antagonistic drug, e.g. metoclopramide and phenothiazines.

- Anticholinergic agent, e.g.:
- Biperiden, IM/IV, 2 mg.
  - Repeat as necessary.

OR

Promethazine, deep IM, 25–50 mg.
- In the elderly 25 mg.

LoE:III

14.7.3 ESSENTIAL TREMOR

G25.0

GENERAL MEASURES

Exclude and manage alternate causes, such as drugs, thyrotoxicosis and hyperadrenergic states. Occasionally a patient may present with essential tremor and an additional neurological condition, which may make the diagnosis difficult.

MEDICINE TREATMENT

If tremor is severe and interfering with normal daily activity:

- Propranolol, oral,
  - Start at 20 mg daily and titrate as needed up to 80 mg 8 hourly.
  - Monitor BP.

LoE:III[lxviii]

14.7.4 CHOREA

G25.5

DESCRIPTION

Involuntary random, irregular movements.
Aetiology is classified as:

» primary – Huntington's chorea,; or
» secondary – Sydenham's chorea, hemiballismus secondary to infarction, diabetes (hyperglycemia)

MEDICINE TREATMENT

Treat the underlying cause, if relevant.

- Haloperidol, oral, 0.5–5 mg 8–12 hourly (Specialist consultation).

14.8 NEUROPATHY

See section 26.1.4: Management of neuropathic pain

14.9 MYELOPATHY, ACUTE

G95.9

DESCRIPTION

Patients present with a sudden onset of paraparesis, with associated sensory loss, i.e. a sensory level may be found. Incontinence and autonomic instability may be present.

Note: Do cervical and thoracic spine films, with chest X-Ray to exclude obstructive lesions before performing a lumbar puncture.

REFERRAL
All patients for urgent imaging.

14.10 MULTIPLE SCLEROSIS
G35

DESCRIPTION
A demyelinating disease of the central nervous system, characterised by relapsing and remitting episodes of unifocal or multifocal neurological dysfunction. Diagnosis is confirmed by imaging. The CSF may show oligoclonal bands and raised IgG index.
Recovery between acute flares of illness is common, although a general stepwise deterioration from baseline is usually found.
Consult with neurologist for diagnosis and treatment.

REFERRAL
All patients.

14.11 MYASTHENIA GRAVIS
G70.0

DESCRIPTION
Consider this in patients with new onset weakness and fatiguability. particularly involving the eyes and the swallowing muscles.

MEDICINE TREATMENT
Discuss both diagnosis and treatment with a specialist.
- Pyridostigmine, oral, 60 mg 5 times daily. *LoE:III*[lxix]

Corticosteroids and azathioprine should only be used in consultation with a specialist.

14.12 OEDEMA, CEREBRAL

DESCRIPTION
Swelling of brain parenchymal tissue, due to vasogenic, cytotoxic and osmotic causes. Only the vasogenic causes, such as brain tumours and inflammation, respond to corticosteroids.

14.12.1 BRAIN OEDEMA DUE TO TUMOURS AND INFLAMMATION

G93.6

GENERAL MEASURES

Supportive management. See section 14.1.1: Stroke.

MEDICINE TREATMENT

Treat the underlying cause. This is especially important where brain oedema associated with systemic conditions, such as electrolyte disturbances and organ failure.

Patients with primary brain tumours or brain metastases should be considered for definitive treatment of the tumour, which includes surgery and/or radiotherapy.

- Dexamethasone, IV, 4 mg 6 hourly, initially.

OR

Betamethasone, oral/IV, 4 mg 6 hourly.

- Discontinue if no response has occurred after 48 hours.
- Taper dose according to response and duration of therapy.

14.12.2 BRAIN OEDEMA DUE TO TRAUMATIC INJURY

S06.10-11 + External Cause Code (V,W,X,Y)

GENERAL MEASURES

Refer patient for neurosurgical opinion, if indicated.

Supportive management. See section 14.1.1: Stroke.

Note: DVT prophylaxis with heparin may be contraindicated owing to risk of increased bleeding.

The following measures should be used in patients with raised intracranial pressure:

» head elevation and position,
» airway and ventilation control,
» sedation and analgesia,
» control of fever,
» control of hypertension, and
» prevention of seizures.

Currently, no evidence supports the use of hyperventilation in this setting.

MEDICINE TREATMENT

<u>For raised intracranial pressure, pending a definitive neurosurgical procedure only:</u>

- Mannitol 15–25%, IV, 0.25–1 g/kg administered over 30–60 minutes.
  - Monitor neurological response and urine output.

- Beware of hypovolaemia and electrolyte disturbances, especially hypokalaemia.

Note: Corticosteroids should not be used in this setting as they have a harmful effect.

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CHAPTER 15
MENTAL HEALTH CONDITIONS AND SUBSTANCE MISUSE

MENTAL HEALTH CONDITIONS

Precepts of the Mental Health Care Act No. 17 of 2002 include:

» All patients with mental illness and/or severe to profound intellectual disability receive mental health care as either Voluntary, Assisted or Involuntary Mental Health Care Users.
» All registered medical practitioners, professional nurses, psychologists, occupational therapists (OTs), and social workers whose training includes mental health are designated Mental Health Care Practitioners.
» Mental health care practitioners and heads of health establishments at PHC and Hospital Adults level must be familiar with MHCA Forms 01 – 13A, 14, 17, 22, 25, 26, 27, 48.
» The South African Police Service have an obligation to protect, apprehend, and assist with transfer of people with mental illness to and between health establishments.

15.1 AGGRESSIVE DISRUPTIVE BEHAVIOUR IN ADULTS

R45.1/R45.4-8 + code(s) for underlying/comorbid condition(s)

DESCRIPTION

Agitation may escalate to overt aggression and often manifests with restlessness, pacing, and loud or demanding speech. Aggressive behaviour includes verbally abusive language, specific verbal threats, intimidating physical behaviour, and/or actual physical violence to self, others or property. All agitation and aggression must be considered an emergency and violence prevented wherever possible.

Multiple causes for aggressive, disruptive behaviour include:

» **Physical:** acute medical illness, delirium and its causes, epilepsy (pre-, intra-, and post-ictal), intracerebral lesions, traumatic brain injury.
See section 20.8: Delirium with perceptual disturbances.
» **Psychiatric:** psychosis, mania, agitated depression, neurocognitive disorders (e.g. dementias, old traumatic brain injury), developmental disorders (e.g. intellectual disability and autistic spectrum disorder), severe anxiety.
» **Substance misuse:** alcohol, cannabis, methaqualone (mandrax) intoxication or withdrawal; stimulant (cocaine, methamphetamine (tik), methcaninone (cat)) intoxication; benzodiazepine withdrawal.
» **Psychological factors:** high levels of impulsivity and antagonism, hypersensitivity to rejection or insult, poor frustration tolerance, and

maladaptive coping skills all contribute to aggression and rage.

» **In pregnant women:** labour, obstetric complications, sepsis, organ failure as well as substances and mental disorders (See Primary Health Care STGs and EML, Chapter 6.9: Maternal mental health).

CAUTION

» **Do not assume that the aggression is due to the mental illness.**
» Known psychiatric and intellectually disabled patients often have medical conditions, trauma, and substance misuse.

GENERAL MEASURES

» **Prepare, anticipate and prevent**:
Be aware of high risk patients e.g. those with previous violence, substance misuse, and State Patients on leave of absence. Have:
- A step-wise protocol to ensure safety of all patients and staff.
- Clear roles for all staff members.
- A triage plan for early signs of aggression.
- Available backup – hospital security and SAPS and EMS.
- A designated calming area – suitable for regular monitoring.

» **De-escalate and contain**:
- Be calm, confident, kind, and reassuring.
- Maintain a submissive posture with open hands.
- Do NOT turn your back on the patient; avoid direct eye contact.
- Do NOT attempt to reason with the patient.
- Do NOT argue, confront delusions, or touch the patient.
- Set clear limits regarding behaviour.
- Take patient to quiet, calm area – do NOT leave unobserved.

» **Examine** for delirium, medical and other causes while calming the patient and after sedation.

» **Manual restraint** may be necessary to administer medication – this must be respectful, controlled and kept to a minimum. It should be applied by personnel of the same sex as the patient.

» **Mechanical restraint**:
- Only if absolutely necessary to protect the patient and others for as short a time as possible.
- Document the type, sites and duration of any restraints used.
- 15-minute monitoring: vital signs, the mental state, restraint sites, and reasons for use.
- A MHCA Form 48 (restraint register) must be completed and submitted to the Mental Health Review Board.

» **Pregnant women**
- Never leave unattended.
- Use restraint sparingly, with care, if possible, with mother in a supported semi-seated position (not supine or prone).

Aggressive and Disruptive Behaviour in Adults
District Hospital Casualty & Ward guideline
(For PHC & CHC Casualty – see Chapter 15.1 in PHC STGs and EML)

Patient brought in by SAPS or family/neighbour/other?

SAPS	Family/neighbour/other
Collect Form 22 from SAPS Complete Form 01 Or collect Form 01 if completed by clinic staff	Accompanying person to await results of clinical assessment *and* complete a Form04

Patient is alert, has clear consciousness and is medically stable?

Yes
De-escalate & Contain

No
Manage as Delirium (Chapter 20)
Admit as medical/surgical patient

Contained & co-operative?

No
Proceed with medicine treatment
Complete Form 48 if restraint needed

Yes
Manage main complaint, offer oral sedation
Remains co-operative?

No

Yes – requires admission

Yes – transient disturbance

Complete Forms 04, 2 x 05, and 07 to admit as Involuntary for 72 hour observation or as an Assisted user
Conduct medical / surgical / gynae and pyschiatric evaluation
Contact relatives/ caregivers if not present

Continue sedation in the ward while necessary
Monitor vitals & mental state – every 30 minutes if secluded or restrained
Detox from alcohol / other substances
Institute initial treatment for psychiatric &/or medical condition

Severe behaviour disturbance & uncontainable
Medically stable

Requires further inpatient psychiatric care – complete 2 x Form 06 and Form 08

Psychiatrically and medically stable

Consult specialist psychiatric hospital & transfer with Form11 and investigation results.

Involuntary User

Assisted or Voluntary User

Refer to regional or tertiary hospital psychiatry unit with Form 11 and investigation results

Discharge with Form 03 & investigation results to appropriate outpatient care &/or substance use rehab

MEDICINE TREATMENT– Rapid Tranquillisation

The goal of rapid tranquilisation is to calm the patient so that risk to self or others is minimised and the underlying condition may be managed.

CAUTION

» Rapid tranquillisation may cause cardiovascular collapse, respiratory depression, acute dystonic reactions, and neuroleptic malignant syndrome.
» Pregnant women, elderly, intellectually disabled and those with comorbid medical conditions and/or substance use are at highest risk.
» Late pregnancy: neonatal sedation or extra-pyramidal side effects may occur.
» **Write out single prescriptions and review between each prescription**
» **Allow at least 30 – 60 minutes between prescriptions.**
» **An emergency trolley, airway, bag, oxygen and intravenous line must be available.**

LoE:III[i]

» In pregnancy, the frail and elderly, or where respiratory depression is a concern, use a short-acting benzodiazepine at the lowest dose.
» The safest route of administration of benzodiazepines is oral followed by IM with the IV route having the highest risk of respiratory depression and arrest. Use the safest route possible.
» Monitor vital signs closely during and after administration. Use haloperidol instead of benzodiazepines in patients with respiratory insufficiency.
» Where aggression is clearly caused by psychosis, haloperidol and promethazine may be used as 1st line treatment and not benzodiazepines.

LoE:III[ii]

<u>Offer oral benzodiazepine treatment:</u>

- Benzodiazepines: *LoE:II*[iii]
- Lorazepam, oral, 0.5–2 mg, immediately.

OR *LoE:III*[iv]

Clonazepam, oral, 0.5–2 mg, immediately.

OR *LoE:III*[v]

Diazepam, oral, 5–10 mg, immediately.

OR *LoE:III*[vi]

Midazolam, oral or buccal, 7.5–15 mg, immediately.

LoE:III[vii]

<u>Oral treatment refused, administer parenteral benzodiazepine treatment:</u>

- Lorazepam, IM, 0.5–2 mg, immediately. *LoE:II*[viii]

OR *LoE:I*[ix]

Midazolam, IM, 7.5–15 mg immediately.

OR *LoE:III*[x]

Clonazepam, IM, 0.5–2 mg, immediately.

Note:

» To avoid inappropriate repeat dosing allow at least 30 minutes for the oral/IM medication to take effect. *LoE:III*[xi]

» Repeated IM doses of benzodiazepines may result in toxicity owing to accumulation.

» Lorazepam IM has slower onset of sedation than midazolam IM (32 vs 18 minutes) and longer duration of sedation (217 vs 82 minutes).

» Clonazepam oral or IM may be used if longer duration of sedation is required. Onset of action may be 30-60 minutes, time to maximum concentration is 1-4 hours. Long half-life (18-50 hours) increases risk of accumulation. Allow at least 12 hours between repeat doses.

LoE:III[xii]

Inadequate response to benzodiazepines (after 30-60 minutes):

- Haloperidol, IM, 2.5–5 mg, immediately.

AND

- Promethazine, deep IM, 25–50 mg.

LoE:II[xiii]

Repeat after 30–60 minutes if needed.

Under specialist care in psychiatric wards:

- Zuclopenthixol acetate, IM, 50–150 mg every 2–3 days (specialist/specialist consultation).
  - Maximum dose is 400 mg over a two-week period. *LoE:III*[xiv]

If alcohol use is suspected:

ADD

- Thiamine, oral, 300 mg immediately and daily for 14 days.

LoE:III[xv]

Monitor the patient:

» Nurse in recovery position – prevent aspiration. Nurse pregnant women in supported semi-seated position if possible or left lateral position, and not supine.

» Monitor pulse, respiratory rate, blood pressure, temperature every 5–10 minutes for the first hour, and then every 30 minutes until the patient is ambulatory. Use pulse oximeter if available.

» Pregnant women: monitor fetal heart rate as well as mother's vital signs.

» Continue observation once ambulatory: for falls and further injury (especially elderly and frail), re-emergence of aggression, and to prevent abscondment.

» If patient absconds – request assistance from SAPS with a MHCA Form 25.

Manage acute complications:

» *Respiratory depression:* if respiratory rate drops to .12 breaths/ minute or oxygen saturation <90% - give oxygen; be prepared to ventilate.

» *Circulatory collapse*: See section 20.1: Cardiac arrest in adults.

» *Acute dystonia*: See the PHC STGs and EML, 2018, section 16.2.1: Extra-pyramidal side effects.

» *Neuroleptic Malignant Syndrome:* See the PHC STGs and EML, 2018, section 16.2.2: Neuroleptic malignant syndrome.

15.2 ANXIETY AND OBSESSIVE-COMPULSIVE DISORDERS

F40.0-2/F40.8-9/F41.0-3/F41.8-9/F42.0-9 + (F10.0-F19.9/R45.0-8/Z65.0-5/Z65.8-9/Z81.0-4/ Z81.8)

DESCRIPTION

Anxiety is an emotional response to a perceived or anticipated stress. It is diagnosed as a disorder when it is excessive or persistent and impacts daily functioning. Anxiety disorders often present with medically unexplained symptoms such as non-cardiac chest pain, abdominal discomfort and neck and back muscle tension. However, anxiety symptoms may be caused by various medical conditions. In addition, medical conditions are commonly comorbid with anxiety disorders; they may exacerbate the symptoms and the anxiety disorder may worsen the outcome of treatment of the medical condition.

Tobacco, alcohol and other substance use are commonly associated with anxiety disorders. The substance use may be secondary to the disorder or causative or both. If caused by a substance, then an Anxiety Disorder due to the specific substance (F10 – F19) should be diagnosed.

In pregnancy and postnatally, anxiety may impact negatively on the mother's coping and use of services and is associated with poor psychological and neurodevelopmental outcomes in the child (See Primary Health Care STGs and EML, Chapter 6.9: Maternal mental health).

» **Psychological manifestations** of anxiety include panicky feelings, excessive worry, mood changes, irritability, tearfulness, distress, and difficulty concentrating.
» **Physical symptoms** include muscle tension, headache, abdominal cramps, nausea, palpitations, sweating, a choking feeling, shortness of breath, chest pain, dizziness, numbness, and tingling of the hands and feet.
» **People with intellectual disability** may present with aggression, agitation, and demanding behaviour instead of anxiety.
» **Panic attacks** are abrupt surges of intense anxiety with prominent physical symptoms. They may occur in anxiety, mood, and psychotic disorders, and with alcohol and other substance misuse. They are a marker of increased severity of the primary disorder and may indicate a heightened risk of suicide.
» **Social phobia** (social anxiety disorder) is the fear of social interactions; it usually starts in adolescence. Distorted thoughts are of negative evaluation by others. Self-medication with alcohol or other substances is common and substance intoxication may be the presenting feature.

» **Obsessive thoughts and/or compulsive behaviour** are a core feature of Obsessive Compulsive Disorder but may also occur in other disorders, particularly tic disorders, autistic spectrum, and psychotic disorders. Themes of the distorted thoughts and compulsions include hygiene (cleaning), security, symmetry, sexual and taboo topics, fears of causing harm, perceived physical defects, hair-pulling or hoarding.

GENERAL MEASURES

Most patients can be treated as outpatients, but some may need to be admitted for diagnostic clarification, containment in extreme distress, or at high risk of suicide.

» Maintain patience and an empathic attitude
» Screen for and manage:
  - Causative and comorbid medical illness, e.g. thyroid disease, hyperparathyroidism, phaeochromocytoma, vestibular dysfunctions, epilepsy, and cardiac conditions, hypertension, COPD, asthma, inflammatory bowel disease, GORD.
  - Substance misuse, e.g. caffeine, nicotine, alcohol, analgesics, amphetamines and cocaine
  - Psychosocial stressors, especially in people with intellectual and other disabilities.
» Psycho-educate the patient and family (with patient's permission).
» Refer to local support groups. Provide links to self-help literature, web-sites or groups, e.g. www.sadag.org

MEDICINE TREATMENT

Indicated where symptoms are interfering with normal functions of daily living. Where there is concomitant drug/alcohol dependence or comorbid major depressive episode, an antidepressant may be more appropriate.

» Offer a choice of psychotherapy or medication and monitor response.
» Review every 2–4 weeks for 3 months, then 3–6 monthly.
» Partial response: combine medication with psychotherapy.
» If effective, continue for at least 12 months to prevent relapse.

▪ SSRI, e.g.:
• Fluoxetine, oral.
  o Initiate at 20 mg alternate days for 2 weeks.
  o Increase to 20 mg daily after 2–4 weeks.
  o Delay dosage increase if increased agitation/panicky feelings occur. *LoE:I*[xvi]
  o If partial response, increase to 40 mg daily.

OR

<u>If fluoxetine is poorly tolerated:</u>

▪ Alternative SSRI e.g.:
• Citalopram, oral.
  o Initiate at 10 mg daily for the 1st week.

- Then increase to 20 mg daily. *LoE:I*[xvii]
- If partial response, increase to 40 mg daily (not in cardiac disease or >65 years of age).

CAUTION - SSRIs

SSRIs (e.g. fluoxetine, citalopram) may cause agitation initially. This typically resolves within 2-4 weeks. *LoE:III*[xviii]

Ask about suicidal ideation in all patients, particularly adolescents and young adults (PHC STGs and EML, section 16.7: Suicide risk assessment).

If suicidal ideation present, refer before initiating SSRI.

Once started, monitor closely for clinical worsening, suicidality, or unusual changes in behaviour. Advise families and caregivers of the need for close observation and refer as required**.**

Note: Continue treatment for a minimum of 12 months. Consider slowly tapering and stopping treatment only if patient has had no/minimal symptoms and has been able to carry out routine daily activities.

Prolong treatment if:

» Previous episode/s of anxiety (extend treatment to at least 3 years).

» Any of: onset in adolescence, severe anxiety, suicidal attempt, sudden onset of symptoms, family history of bipolar disorder (extend treatment to at least 3 years).

» If ≥3 episodes of anxiety (advise lifelong treatment). *LoE:III*[xix]

<u>For short term use only in severe acute distress:</u>

- Benzodiazepines, e.g.: *LoE:III*[xx]
- Diazepam, oral, 2.5–5 mg as a single dose.
  - Repeat 8 hourly, if required to a maximum of 30 mg daily (in divided doses).
  - Half the dose in the elderly or debilitated.
  - Duration of therapy: up to 2 weeks, taper off to zero within 6 weeks
  - Commence definitive treatment with psychotherapy/SSRI treatment.

CAUTION - BENZODIAZEPINES

» Associated with cognitive impairment – reversible with short-term use and irreversible with long-term use.

» Elderly are at risk of over-sedation, falls and hip fractures.

» Dependence may occur after only a few weeks of treatment.

» Prescribe for as short a period of time as possible.

» Warn patient not to drive or operate machinery when used short-term.

» Avoid use in people at high risk of addiction: e.g. personality disorders and those with previous or other substance misuse.

LoE:III[xxi]

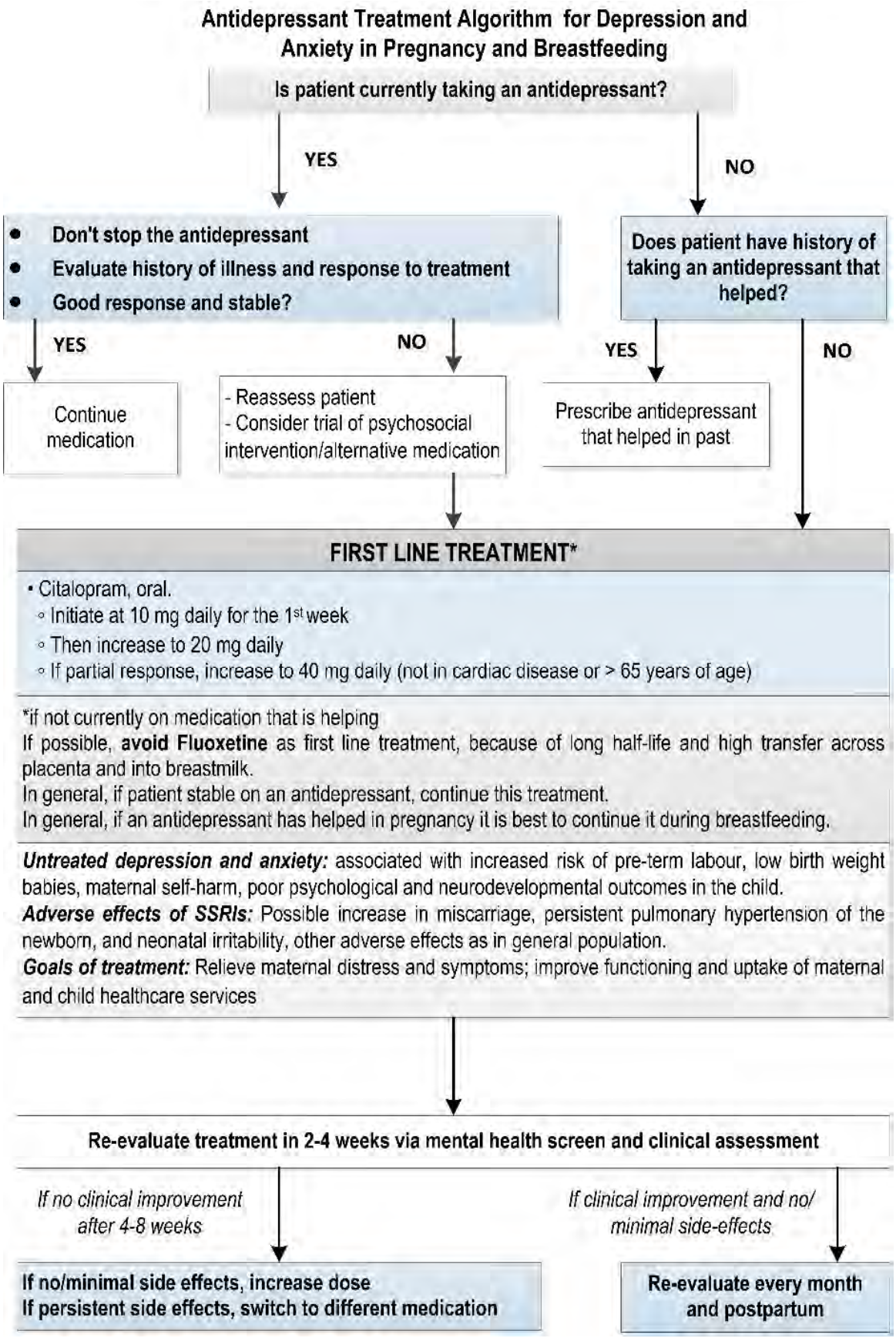
PREGNANCY AND BREASTFEEDING

» SSRI treatment of depression in pregnancy is associated with improved symptoms in the mother and better emotional and psychological development of the child. Benefit is greater with increasing illness severity. Effect of SSRIs on anxiety in pregnancy is less clear.
» Lack of matched case-control studies mean harms of treatment are unclear.
» If stable on an SSRI, do not stop – discuss risk/benefit with mother.
» Index presentations: offer counselling, psychotherapy; discuss risk/benefit of SSRIs.
» Avoid fluoxetine due to long half-life and relatively high concentration in breastmilk. Consider citalopram as alternative
» All antidepressants: possible increased risk of miscarriage, transient neonatal symptoms (jitteriness, irritability), and persistent pulmonary hypertension of the newborn.
» Avoid benzodiazepines – some association with neurodevelopmental delay in the child; neonatal sedation if used late in pregnancy.

LoE:III[xxii]

REFERRAL

» High suicide risk
» Severe symptoms with marked functional impairment
» Co-morbid severe psychiatric or medical conditions
» Poor response to treatment.



Adapted from the MCPAP for Moms Perinatal Depression Toolkit funded by the Massachusetts Department of Mental Health. Original Authors: Byatt N., Biebel K., Mittal L., Lundquist R., Freeman M., & Cohen L., Moore Simas T.

15.3 MOOD DISORDERS

15.3.1 DEPRESSIVE DISORDERS

F32.0-3/F32.8-9/F33.0-4/F33.8-9/F34.1 + (F10.0-F19.9/R45.0-8/Z65.0-5/Z65.8-9/Z81.0-4/ Z81.8)

DESCRIPTION

Depressive disorders may occur as single or recurrent episodes (Major or Minor Depression), or as a chronic, persistent low mood (Dysthymia) or a combination of the two. Depressive episodes may also occur as part of Bipolar Disorder, which requires a different treatment strategy.

Depressive disorders cause significant impairment in social and occupational functioning, and may result in unemployment, poor self-care, neglect of dependent children, and suicide. They may be comorbid with or secondary to other medical illness or substance use. Depression impacts negatively on comorbid conditions, with increased pain, disability and poorer treatment outcomes.

Depression is characterised by a low mood and/or a reduced capacity to enjoy life. However, it is often not recognised by the sufferer or clinicians. It may be regarded as a normal emotional state or it may be unacceptable to the sufferer due to stigma. Thus, associated symptoms may be the presenting complaint rather than the low mood. Symptoms may also be masked in the interview setting. It is important to have a high degree of suspicion and to elicit symptoms, degree of impaired function, and suicide risk with care.

» In general, insomnia and loss of energy are the most common presenting complaints. In African cultures, somatic symptoms (bodily aches and pains) and rumination (‘thinking too much’) may predominate.
» The presence of mood, psychological, and cognitive symptoms help to differentiate between depression and normal sadness following a loss, or the loss of appetite and energy associated with a medical condition.
» Psychotic symptoms (delusions, hallucinations, or thought disorder) are usually mood congruent and indicate marked severity and a high risk to self or others.

In pregnancy and postnatally, depression is associated with preterm delivery, low-birth weight babies, poor maternal self-care, impaired mother-infant engagement, and poor psychological and neurodevelopmental outcomes in the child. Risk of negative impact is increased with increased severity (See Primary Health Care STGs and EML, Chapter 6.9: Maternal mental health).

GENERAL MEASURES

» Maintain an empathic and concerned attitude.
» Discuss uncertainty with a specialist at any point in the care pathway.
» Assess severity of the condition and suicide risk. See PHC STGs and EML, 2018 – section 16.7: Suicide risk assessment.

» Exclude and optimise treatment of underlying and/or comorbid medical conditions (e.g. hypothyroidism, anaemia, HIV/AIDS, TB, cancers, diabetes).
» Screen for and manage underlying or comorbid substance use, e.g. nicotine, alcohol, over the counter analgesics, benzodiazepines.
» Screen for bipolar disorder and comorbid psychiatric disorders – refer for specialist assessment.
» Explore and address psychosocial stressors:
  – Stress management/coping skills – refer for counselling.
  – Relationship and family issues – refer for counselling (www.famsa.org.za). Refer to a social worker if abuse is evident.
» Provide self-help literature, where available, and refer to local support groups (www.sadag.org)

MEDICINE TREATMENT

» Offer choice of psychotherapy (if available) or medication.
» Antidepressants take 4–6 weeks to achieve their maximum effect. There is little evidence to support combination medicine treatment.
» Tricyclic antidepressants (TCA) and selective serotonin reuptake inhibitors (SSRIs) are of equal efficacy.
» Electroconvulsive therapy (ECT) (specialist administered) is indicated under specific circumstances, e.g. severe depression, in pregnancy
» The choice of therapy is guided by comorbid states, risk of overdose, and patient response.

CAUTION - ANTIDEPRESSANTS

» SSRIs (e.g. fluoxetine, citalopram) may cause agitation and an increased suicide risk during the first 2–4 weeks.
» Once started, monitor closely for clinical worsening, suicidality, or unusual changes in behaviour. Advise families and caregivers of the need for close observation and refer as required.
» TCAs can be fatal in overdose. Prescription requires a risk assessment of the patient and others in their household, especially adolescents.
» Avoid TCAs in the elderly and patients with heart disease, urinary retention, glaucoma, and epilepsy.
» Do not prescribe antidepressants to a patient with bipolar disorder without consultation, as they may precipitate a manic episode.
» Be aware of interactions between antidepressants and other agents (e.g. other medicines, St John's Wort or traditional African medicine).

PREGNANCY AND BREASTFEEDING

» SSRI treatment of depression in pregnancy is associated with improved symptoms in the mother and better emotional and psychological development of the child. Benefit is greater with increasing illness severity. Effect of SSRIs in pregnancy on anxiety is less clear.
» Lack of matched case-control studies mean harms of treatment are unclear.
» If stable on an SSRI, do not stop – discuss risk/benefit with mother.
» Index presentations: offer counselling, psychotherapy; discuss risk/benefit of SSRIs.
» Avoid fluoxetine due to long half-life and relatively high concentration in breastmilk. Consider citalopram as alternative.
» All antidepressants: possible increased risk of miscarriage, transient neonatal symptoms (jitteriness, irritability), and persistent pulmonary hypertension of the newborn.
» Avoid benzodiazepines – some association with neurodevelopmental delay in the child; neonatal sedation if used late in pregnancy.

LoE:III[xxiii]

- Selective serotonin reuptake inhibitor (SSRI), e.g.:
- Fluoxetine, oral.
  - Initiate at 20 mg alternate days for 2–4 weeks.
  - Thereafter, increase to 20 mg daily. Delay dosage increase if agitation/panicky feelings occur.
  - Reassess response after 4–6 weeks.
  - If partial response: increase to 40 mg daily and/or augment with psychotherapy.
  - If no response: consult with specialist (re-evaluate diagnosis, repeat general measures, prescribe alternative SSRI, psychotherapy, or ECT).

<u>If fluoxetine is poorly tolerated:</u>

- Alternative SSRI e.g.:
- Citalopram, oral.
  - Initiate at 10 mg daily for the 1st week.
  - Then increase to 20 mg daily.
  - If partial response: increase to 40 mg daily (except in cardiac disease and >65 years) and/or augment with psychotherapy.
  - If no response: consult with specialist (re-evaluate diagnosis, repeat general measures, prescribe alternative SSRI, psychotherapy, or ECT).

LoE:I[xxiv]

<u>If a sedating antidepressant is required:</u>

- Amitriptyline, oral, at bedtime.
  - Initial dose: 25 mg per day.
  - Increase by 25 mg per day at 3–5 day intervals.
  - Maximum dose: 150 mg per day.
  - If no response: discuss with specialist (re-evaluate diagnosis, repeat general measures, prescribe alternative SSRI, psychotherapy, or ECT).

LoE:III[xxv]

Treatment duration
Continue for a minimum of 9 months. Consider stopping only if patient has had no/minimal symptoms and can carry out routine daily activities. Taper medicine slowly to avoid discontinuation symptoms; reinstitute if there is a recurrence.

Prolong treatment if:
» Concomitant generalised anxiety disorder (extend treatment to at least 1 year).
» Previous episode/s of depression (extend treatment to at least 3 years).
» Any of: severe depression, suicidal attempt, sudden onset of symptoms, family history of bipolar disorder (extend treatment to at least 3 years).
» If ≥3 episodes of depression advise lifelong treatment. *LoE:III*[xxvi]

REFERRAL
» Inadequate response to treatment.
» High suicide risk.
» Psychotic features.

15.3.2 BIPOLAR AND RELATED DISORDERS
F30.0-2/F30.8-9/F31.0-9/F34.0/F34.8-9/F38.0/F39/F06.3 + (F10.0-F19.9/R45.0-8/Z65.0-5/Z65.8-9/Z81.0-4/ Z81.8)

DESCRIPTION
Bipolar disorder (BD) is a heterogenous illness, with high overlap in genetic risk with depression and schizophrenia. Usually follows a chronic, relapsing course, commonly starting in youth. The goal of care is euthymia and optimal functioning according to the person's ability.

BD may present with:
» an episode of depression, hypomania, mania or mixed mood symptoms
» psychosis
» treatment resistant depression and/or anxiety
» consequences of disturbed behaviour and/or comorbid substance use
» depression in women; men more likely with disruptive behaviour

Diagnostic requirements include, over the lifetime course:
» Bipolar I disorder (BD I): an episode of mania
» Bipolar II disorder (BD II): an episode of hypomania and of depression.
» Other specified BD (BD OS): symptoms of BD plus clinical distress and/or functional impairment but full DSM criteria are not met.
» BD due to another medical condition: direct physiological cause for the bipolar symptoms from another illness, e.g. right-sided cortical or sub-cortical lesions.

In pregnancy and postnatally, bipolar disorder is associated with pre-eclampsia, preterm delivery, and low-birth weight babies. Risk of relapse is

high, especially postpartum. Psychotic episodes may be dangerous to mother, baby, or others (See Primary Health Care STGs and EML, Chapter 6.9: Maternal mental health).

GENERAL MEASURES

Assess and manage **in consultation with a psychiatrist.**
Risk to self and others is high in BD and unpredictable – repeated risk assessments and a biopsychosocial approach to care is recommended.

Acute management

» Mania, severe depression, and psychosis require urgent hospitalisation in a psychiatric unit, often as an Assisted or Involuntary MHCU.
» Investigate for causative medical conditions, medications, substances.
» Optimise management of comorbid medical illness and substance use.
» Stabilise the immediate mood; electroconvulsive therapy may be required.
» Commence long-term treatment strategy.
» Avoid premature discharge and ensure continuity of care post-discharge.

Long-term management

» Individualise management according to course of illness, cognitive functioning, insight and judgement, and social circumstances.
» Assertive nursing with adherence monitoring is required.
» Screen for and manage comorbid medical illness (thyroid disease, HIV/AIDS, cardiovascular and pulmonary disease, epilepsy, diabetes)
» Screen for and manage substance use.
» Psycho-educate patient, family and carers on the nature of the illness, need for continued treatment, how to self-monitor, early signs of relapse, need for structure and routine.
» Refer to support groups e.g. www.SADAG.org and www.SAFMH.org.za
» Delay important decisions until full recovery from an acute episode; a custodian/ curatorship/ power of attorney may be required.
» Refer to social worker for placement in a residential home, day care or sheltered employment/workshop as needed.

Women in reproductive age-group (See Primary Health Care STGs and EML, Chapter 6.9: Maternal mental health).

» Advise family planning – psycho-educate re need to plan pregnancy and comply with antenatal care.
» Manage pregnancy and postpartum period as high-risk for adverse events.
» Select treatment options which are relatively safe in pregnancy.

MEDICINE TREATMENT

Treatment choice depends on course of illness, gender, comorbid medical, substance use, and psychiatric conditions, and risk of non-adherence. Acute treatment should incorporate a long-term strategy. Combinations of medicines may be required, particularly in depression. See algorithms below.

Lithium is first-line option for long-term treatment:

» Response takes ± 1 week in mania and 6–8 weeks in depression
» Prevents manic episodes by up to 40-50% and depressive episodes by up to 20-30% and reduces aggression, self-harm, and suicide.

- Lithium, oral, usual dose range 200–800 mg at night.
  - Pre-treatment: check eGFR, TFTs, calcium, and ECG in patients with cardiovascular risk factors. Proceed if eGFR, ECG normal and any thyroid or parathyroid disease is treated.
  - Start with 400 mg (200 mg in elderly or high risk for renal disease).
  - Trough (12 hours after night dose) plasma level after 5 days, then 7 days after each dose change, then at 1 month and 3 months.
  - Lithium has a narrow therapeutic window. The therapeutic range is 0.8–1.0 mmol/L in acute mania, 0.6–0.8 mmol/l for prevention of mania and 0.4–0.8 mmol/l for prevention of depressive relapse.
  - Monitor lithium and eGFR 6-monthly (3-monthly in elderly or medical comorbidity); TSH and calcium annually.

CAUTION - LITHIUM

» Abrupt discontinuation may precipitate mania – taper slowly over 4 weeks.
» **Adverse effects** include nephrogenic diabetes insipidus, interstitial nephritis, chronic kidney disease; hypothyroidism; hyperparathyroidism; tremor.
» **Toxicity** occurs with levels >1.2 mmol/l (results in anorexia, nausea, diarrhoea, muscle weakness, drowsiness, ataxia, disorientation, seizures, coma and death. Manage as for lithium poisoning: section 19.9.2.
» Risk of toxicity increased with e.g. change to a low salt diet, dehydration, drug-drug interactions (diuretics, ACE-inhibitors, NSAIDs).
» Therapeutic drug monitoring is essential when using lithium.
» Clinical toxicity may occur even within the therapeutic range.

PREGNANCY AND BREASTFEEDING

Valproate:

» Contraindicated due to high teratogenic risk and adverse neurodevelopmental outcomes with any pregnancy exposure.
» If no alternative, the acknowledgment of risk form must be signed https://www.sahpra.org.za/documents/f150bf3f6.28_Valproate_Annual_Risk_Acknowledgement_Form_Dec18_v1.pdf
» If already on valproate: cross-titrate to an alternative medication if possible (consult specialist if required).
» Not recommended in breastfeeding as associated with adverse neurodevelopmental outcomes. *LoE:III*[xxvii]

Lithium:

» 1st trimester exposure associated with increased risk of congenital anomalies.
» Fetal anomaly ultrasound at 18–22 weeks gestation.
» Adjust dose with physiological changes of pregnancy: monitor levels monthly, then weekly after 36 weeks.
» Neonatal complications: goitre, nephrogenic diabetes insipidus, cardiac arrhythmias, cardiac failure, hypotonia, and lethargy.
» Excreted in breast milk, risk to the infant is unknown but toxicity may occur: breastfeeding is not recommended. *LoE:III*[xxviii]

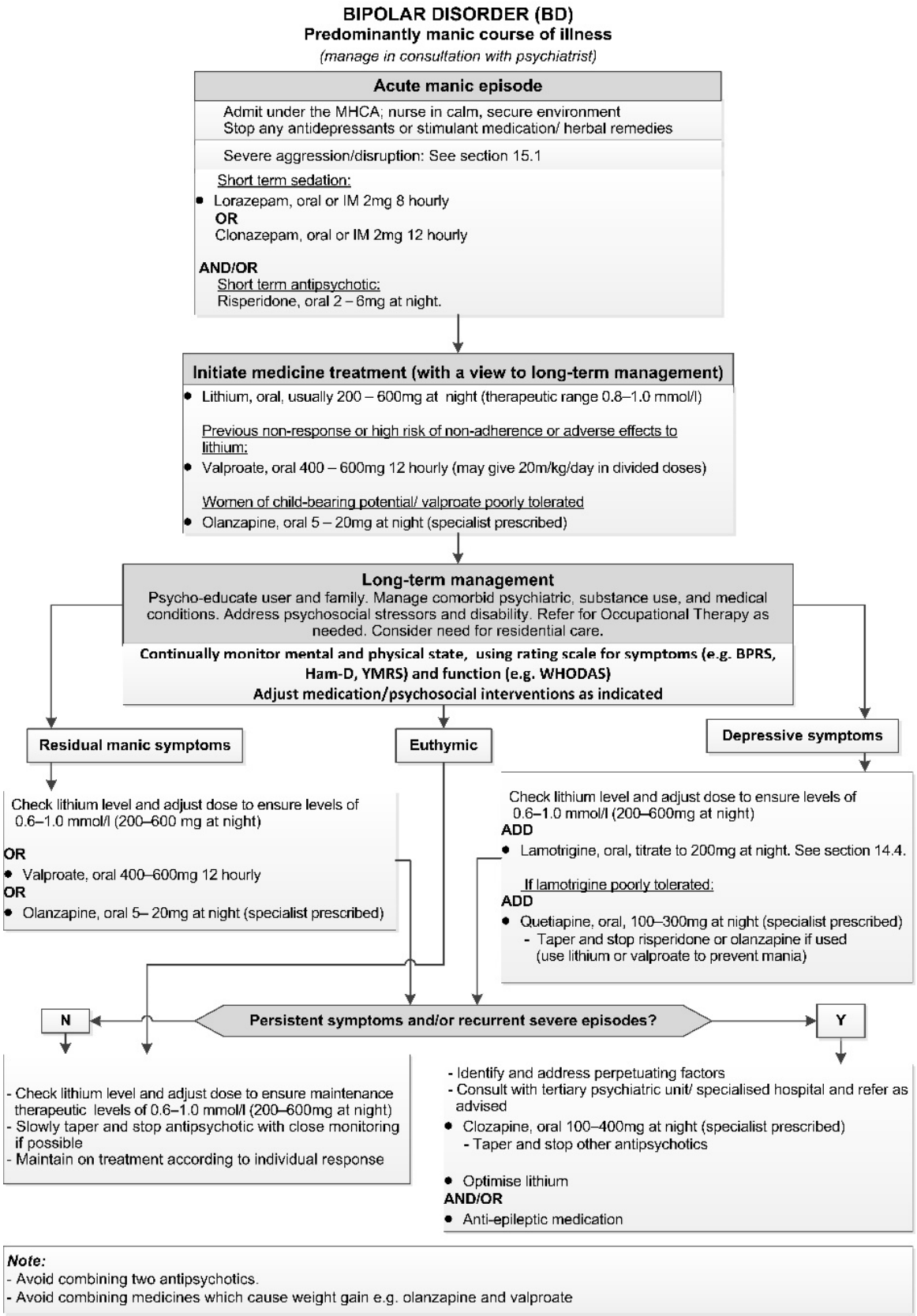
Lamotrigine: Increased hepatic clearance in pregnancy, returns to normal post-partum; adjust dose according to clinical response. May cause a rash in breastfed infant. *LoE:III*[xxix]

Antipsychotics: Considered safest, particularly quetiapine. Increased risk of gestational diabetes and obesity (highest risk with olanzapine, clozapine).
Clozapine is not recommended due to risk of agranulocytosis.

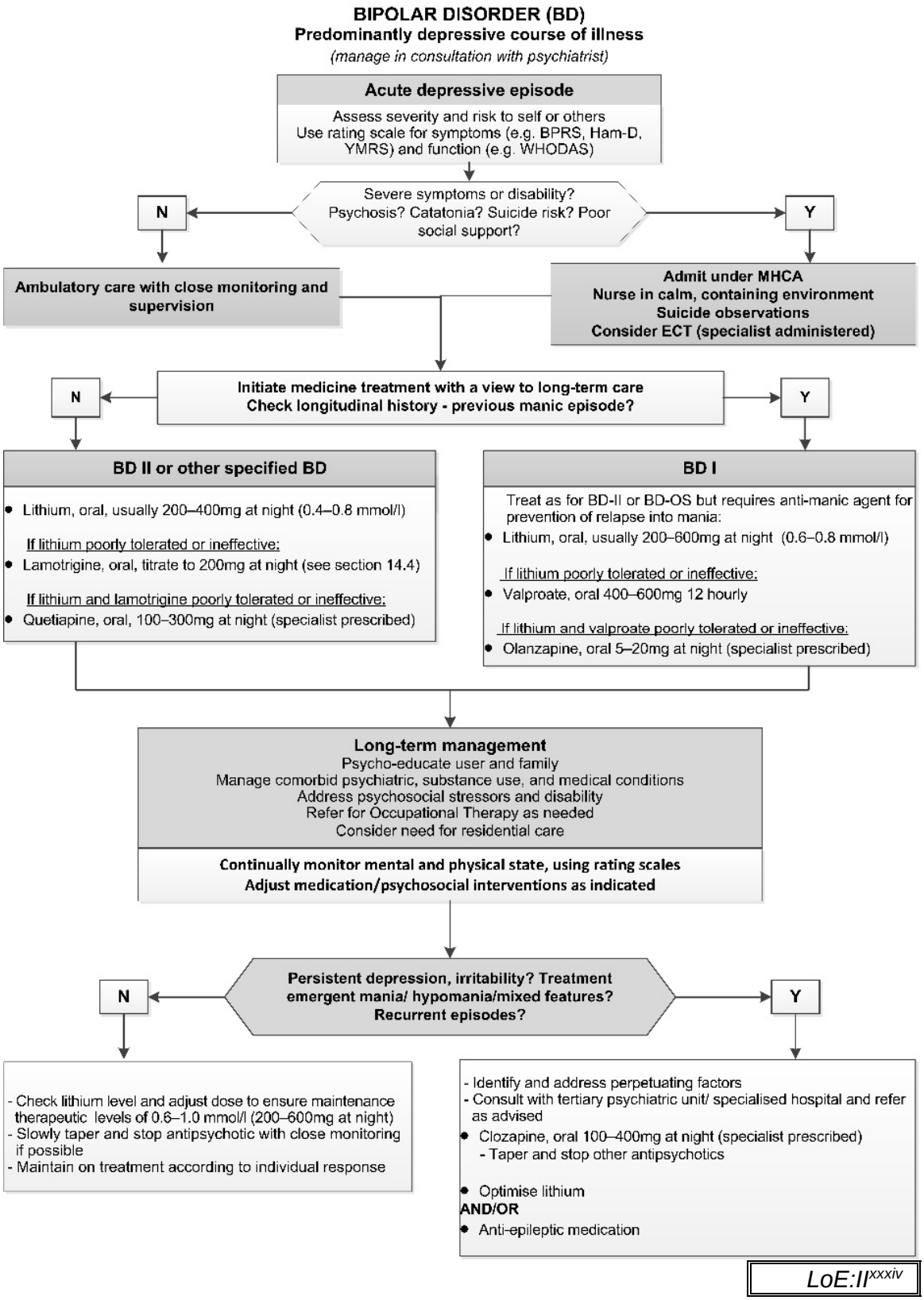
Benzodiazepines: Avoid in pregnancy. *LoE:III*[xxx]
Use only very short-term for severe distress. *LoE:III*[xxxi]

- Quetiapine, oral, usual dose range 100–300 mg at night (specialist prescribed).
  - Titrate to clinical effect, e.g.: Day 1: 50 mg. Day 2: 100 mg. Day 3: 200 mg. Day 4: 400 mg.
  - In the elderly and patients with hepatic impairment: Start with 25 mg and titrate up more slowly according to clinical effect.

LoE:III[xxxii]



LoE:II[xxxiii]



LoE:II[xxxiv]

REFERRAL

All patients to be managed in consultation with a psychiatrist, refer as advised, particularly if:

» High risk to self or others at any time.

» Rapid cycling (repeated episodes despite treatment).
» Poor response to treatment with persistent depressive, manic, or mixed symptoms.

15.4 TRAUMA AND STRESS-RELATED DISORDERS

F43.0/F43.1

DESCRIPTION

Acute stress and post-traumatic stress disorder arise in response to stressful events. The patient should have experienced the event as life threatening or as a physical threat to themselves or others, at which time they felt fear and helplessness.

A range of symptoms are associated with both of these conditions and include:
» Re-experiencing of the event, e.g. flashbacks, dreams.
» Avoidance of situations associated with the event.
» Features of anxiety or increased arousal, e.g. hypervigilance, heightened startle response and insomnia.

The conditions are symptomatically similar but differ with regard to the duration and time of onset of symptoms. The symptoms of acute stress disorder arise within 4 weeks of the event and last up to 4 weeks, whereas the symptoms of post-traumatic stress disorder last longer than 4 weeks, and may arise more than 4 weeks after the traumatic incident.

Child abuse and trauma histories (including traumatic birth experience) and trauma experiences within pregnancy are associated with gestational and postnatal PTSD.

GENERAL MEASURES

Reassurance and support of patient and family.
Psychotherapy, usually of a supportive/cognitive-behavioural nature.
Trauma debriefing is not routinely recommended.

MEDICINE TREATMENT

Acute stress disorder:
Benzodiazepines may be useful in the immediate period following the traumatic event.
Prolonged use >1 week may be detrimental to adaptation, leading to higher rates of post-traumatic stress disorder.

For acute anxiety or agitation:
- Clonazepam, oral 0.5–2 mg in divided doses. *LoE:III*[xxxv]

For sleep disturbance: See section 15.13: Insomnia.

Post-traumatic stress-disorder:

- Selective serotonin reuptake inhibitors, e.g.:
- Citalopram, oral, initial dose 20 mg daily. LoE:III[xxxvi]

OR

Fluoxetine, oral, initial dose 20 mg in the morning.

- A response to SSRI should be expected after 4–6 weeks.
- If there is no or partial response after 4–8 weeks, increase SSRI dose to 40 mg, if well tolerated.
- An adequate trial of treatment is 8–12 weeks, before an alternative treatment should be considered.

REFERRAL

» Persistent symptoms.
» Inadequate response to treatment.
» Comorbid conditions.

15.5 PSYCHOTIC DISORDERS

DESCRIPTION

Psychosis is characterised by a loss of contact with reality. Psychotic disorders may present with:

» Delusions: Fixed beliefs, manifest as disturbed speech content with e.g. persecutory, referential, grandiose, religiose, erotic, bizarre themes.
» Hallucinations: Perceptual disturbances, e.g. auditory hallucinations, which are heard as voices distinct from the patients' thoughts.
» Disorganised thinking: Manifests as disordered flow of speech which impairs communication.
» Grossly disorganised or abnormal motor behavior (including catatonia).
» Negative symptoms: reduced emotional expression, avolition, lack of speech, anhedonia, lack of social interaction.

Psychotic symptoms may occur in other psychiatric conditions (e.g. bipolar mania, major depression), medical conditions (e.g. certain types of epilepsy), or substance use (intoxication or withdrawal).

Psychosis is often accompanied by a lack of insight into the symptoms and poor judgement. The risk to self and others must always be assessed. It may be necessary to treat as an Assisted or Involuntary User under the MHCA.

15.5.1 ACUTE AND TRANSIENT PSYCHOTIC DISORDERS

F23.0-F23.9 + (F10.0-F19.9/R45.0-8/Z65.0-5/Z65.8-9/Z81.0-4/ Z81.8)

DESCRIPTION

Sudden onset of ≥ 1 psychotic symptom (usually delusions, hallucinations or disorganised thinking) which resolve spontaneously, usually within 1 month, with a full return to premorbid social or occupational functioning. Stressful events may precede the psychotic episode. Within 3 years, 40-50% will have a recurrent episode or develop schizophrenia or bipolar disorder.

LoE:III[xxxvii]

GENERAL MEASURES

Assess and manage in consultation with a psychiatrist.

» Assess risk to self and others.
» Exclude and treat medical causes of psychotic symptoms (e.g. delirium, dementia, epilepsy).
» Exclude and manage substance use (e.g. cannabis, alcohol, amphetamines, and cocaine).
» Assess and treat other mental illness, e.g. anxiety disorders (section 15.2) and trauma and stress-related disorders (section 15.4).
» Address psycho-social stressors – refer to social worker, psychologist, counselling services
» Active follow-up is needed: commence treatment for schizophrenia or bipolar disorder if these become evident. (See sections 15.3.2: Bipolar Disorder and 15.6.2: Schizophrenia).

MEDICINE TREATMENT

Manage severe aggressive or disruptive behavior (see section 15.1: Aggressive disruptive behaviour in adults).
Treat according to underlying cause.

15.5.2 SCHIZOPHRENIA SPECTRUM DISORDERS

F20-F20.9; F22.0-22.9; F25.0-25.9 + (F10.0-F19.9/R45.0-8/Z65.0-5/Z65.8-9/Z81.0-4/ Z81.8)

DESCRIPTION

Schizophrenia is characterised by psychotic episodes which are severe, persistent, and accompanied by a marked deterioration in personal, social, and occupational functioning.

Whilst the presentation may be acute, typically the illness has a chronic, relapsing course with progressive cognitive and functional decline. Onset is usually in youth. Prognosis is worsened with delay in initial treatment, repeated episodes, and comorbid substance use. Comorbid metabolic syndrome and cardiovascular disease are common.

GENERAL MEASURES

Manage all patients in consultation with a psychiatrist.
Diagnostic certainty requires careful observation and re-evaluation over time.

Acute psychosis

» Assess risk to self and others.
» Clarify diagnosis.
» Manage within a multi-disciplinary team.
» Use shared decision-making in treatment process.
» Involve family and carers with patient's permission unless risk to self/ others necessitates a breach of confidentiality.
» Provide psychoeducation to patient, family, and carers on the nature of the illness, need for continued treatment, how to self-monitor, early signs of relapse, and need for structure and routine.

Maintenance treatment

» Antipsychotic maintenance treatment is needed to prevent relapse.
» Community-based nursing with adherence support, repeated risk assessment, and shared decision-making is required.
» Monitor psychiatric symptoms (use rating scales, e.g. BPRS or PANSS)
» Monitor extra-pyramidal side effects, weight, BP and glucose 6-monthly
» Adjust treatment according to response, adverse effects, and comorbidity.
» Provide lifestyle and dietary education; encourage exercise
» Treat comorbid mood disorders (section 15.6)
» Treat comorbid hypertension (section 3.6), diabetes mellitus (section 8.5), and other medical conditions as needed
» Manage substance use – refer for rehab (SANCA, Social Development)
» Poor adherence with recurrent episodes:
  - Check reasons – illness, medication, patient factors.
  - Poor previous response/ tolerability – change to alternative antipsychotic (olanzapine or clozapine).
  - Poor insight - try depot antipsychotic – start with test dose (half initial dose in algorithm below).
  - Address psychosocial factors, substance use.
» Refer to social worker for placement in a residential home, day care or sheltered employment/workshop as needed.

Women in reproductive age-group (See Primary Health Care STGs and EML, Chapter 6.9: Maternal mental health).

» Advise family planning – psycho-educate regarding need to plan pregnancy and comply with antenatal care
» If a parent – support childcare; refer to social worker if impaired.
» Risk of psychotic relapse is high in pregnancy and postpartum including the first year post-delivery.
» Continue antipsychotic treatment in pregnancy. All are considered safe except clozapine – only use if benefit outweighs risk.

MEDICINE TREATMENT

Acute psychotic episode

» Treat severe aggression and disturbed behaviour as in Section 15.1: Aggressive disruptive behaviour in adults.
» Initiate treatment with a view to long-term management.
» High risk of tardive dyskinesia (age >50 years, female sex, prominent mood symptoms, cognitive or neurological disturbance e.g. intellectual disability, autistic spectrum, HIV-positive): avoid haloperidol and antiparkinsonian medicines; use chlorpromazine, risperidone or olanzapine at lowest doses possible. *LoE:III*[xxxviii]

Initiate treatment:

- Haloperidol, oral.
  - Initial dose: 0.5–1 mg daily, increasing to 5 mg daily. *LoE:III*[xxxix]

If good response/ tolerability to haloperidol, or patients' preference:

- Depot antipsychotic, e.g:
- Flupenthixol decanoate, IM, 10–40 mg every 4 weeks.

OR *LoE:III*[xl]

Zuclopenthixol decanoate, IM, 200–400 mg every 4 weeks.

LoE:III[xli]

If poor response/ poorly tolerated/ high risk of tardive dyskinesia/ extra-pyramidal side effects:

- Risperidone, oral
  - Initial dose: 2–4 mg at night. *LoE:I*[xlii]
  - Maximum dose: 6 mg daily.
  - Assess efficacy after 4–6 weeks:
    - If a partial response is noted, optimise the dosage.
    - If no response is noted, switch treatment.

OR

- Chlorpromazine, oral, 75–300 mg daily in divided doses. *LoE:III*[xliii]

If poor response/tolerability to haloperidol, risperidone or chlorpromazine:

- Olanzapine, oral (specialist initiated).
  - Initial dose: 5 mg at night, increase to 10 mg at night.
  - Maximum dose: 20 mg at night. *LoE:I*[xliv]

If poor response/ tolerability to olanzapine:

- Clozapine, oral (specialist initiated, preferably as inpatient):
  - Initial dose: 12.5–25 mg at night.
  - Usual dose: 200–450 mg per day in divided doses.
  - Maximum dose: 900 mg/day in divided doses. *LoE:III*[xlv]

CAUTION - CLOZAPINE

» May cause neutropenia (3% of cases) and agranulocytosis (0.8% of cases):
- Pre-treatment: Baseline normal white cell count and absolute neutrophil count.
- Monitor absolute neutrophil count regularly.
- Withdraw clozapine and review medication if neutrophils <1.0 $x10^9$/L (general population).

» Myocarditis: highest risk in first two months of treatment. Monitor pulse, blood pressure, temperature; advise patient to report any palpitations, shortness of breath, chest pain, fever immediately.

» Seizures: risk increased at doses >450 mg/day.
Manage as for epilepsy, section 14.4: Epilepsy. Lamotrigine preferable as it is weight neutral and does not interfere with clozapine metabolism. Avoid carbamazepine because of possible myelosuppression and enzyme induction.

» Constipation: avoid anticholinergics; may require laxatives; prolonged discomfort may indicate intestinal obstruction.

» Weight gain, diabetes, dyslipidaemia: Manage as per PHC STGs and EML, section 16.6: Psychiatric patients general monitoring and care; Prevention of ischaemic heart disease and atherosclerosis (section 3.1), and Type 2 diabetes mellitus (section 8.5.1).

LoE:III[xlvi]

OR

Refer to tertiary and quaternary level care for amisulpiride if excessive weight gain and/or type 2 diabetes, or persistent negative symptoms.

LoE:III[xlvii]

LoE:III[xlviii]

ADVERSE EFFECTS

Extrapyramidal adverse effects

Note: Anticholinergic medicines (e.g. orphenadrine) should not be added prophylactically to antipsychotics to prevent extrapyramidal side effects.

Acute dystonia: See the PHC STGs and EML, section 16.2.1: Extra-pyramidal side effects.

Parkinsonism:

- Anticholinergic agent, e.g.:
- Orphenadrine, oral, 50–150 mg daily according to individual response
  - Usual dose: 50 mg 8 hourly.
  - Maximum dose: 150 mg daily.
  - Use with caution in the elderly as it may cause confusion and urinary retention.
  - Review antipsychotic treatment, and stop orphenadrine if medicine

changed. LoE:III[xlix]

Akathisia (a subjective unpleasant state of inner restlessness where there is a strong desire or compulsion to move):

- Propranolol, oral,
  - Start at 20 mg daily and titrate as needed up to 80 mg 8 hourly. LoE:II[l]
  - Monitor pulse and blood pressure.

Neuroleptic Malignant Syndrome:
See the PHC STGs and EML, section 16.2.2: Neuroleptic malignant syndrome.

REFERRAL

All patients to be managed in consultation with a psychiatrist, refer as advised, particularly if:

» High risk to self or others at any time.
» If diagnosis is uncertain.
» Poor response to treatment.

15.6 INSOMNIA

G47.0/G47.9

DESCRIPTION

Insomnia may be an independent disorder, or associated with comorbid conditions. Insomnia may persist despite successful treatment of the comorbidity, and may necessitate separate treatment.
Patients presenting with insomnia may complain of difficulty falling asleep, frequent waking during the night, early-morning wakening and daytime sleepiness.

GENERAL MEASURES

» Treat the medical condition, psychiatric illness, substance use disorder or sleep disorder that may be precipitating or exacerbating the insomnia, if present.
» All patients should receive basic behavioural counselling about sleep hygiene and stimulus control as first step of treatment.
» Cognitive behavioural therapy is the treatment of choice.

MEDICINE TREATMENT

If medication is needed:

» Use the lowest effective dose.
» Use intermittent dosing if possible (alternate night or less).

Sleep hygiene and stimulus control:

» Maintain a regular sleep cycle (same time wake up in the morning, including week-ends).
» Stimulus control:
  - Keeping the room quiet, dark and at a comfortable temperature.
  - Using the bed and bedroom only for sleeping (and sex).
» Limit intake of caffeine, nicotine, and alcohol, especially before bedtime.
» Eating a light snack before bedtime, but not a large meal late at night.
» Sleep restriction: avoiding daytime naps.
» Increasing daily exercise (not late in the evening).
» Using anxiety management or relaxation techniques.
» Go to bed only when tired. Sleep as much as needed to feel refreshed, not longer.
» If unable to sleep for more than 15–20 minutes, get out of bed and engage in a non-stimulating activity until tired (e.g. listen to soft music, read).

If medication is needed to treat the insomnia:

- Short-acting benzodiazepines, e.g.:
- Oxazepam, oral 15–30 mg at night.

Short-term use of benzodiazepines of 14 days is recommended, as long-term use is often associated with dependence.

LoE:I[Ii]

REFERRAL

Patients with chronic insomnia.

15.7 DISCONTINUATION SYMPTOMS OF SEROTONIN REUPTAKE INHIBITORS

Discontinuation symptoms are experienced due to receptor adaptation or receptor rebound after stopping of antidepressants. It can be avoided or reduced by slowly tapering the drug over at least 4 weeks.
Symptoms include flu-like symptoms, ‘shock-like” sensations, dizziness exacerbated by movement, insomnia, vivid dreaming and irritability, problems with concentration, and memory or movement disorders.

It is managed by reintroduction of the SSRI and slower tapering of the dose.
Note: Fluoxetine seldom causes discontinuation symptoms because of its long half-life.

SUBSTANCE MISUSE

DESCRIPTION

Substance misuse is a general term which encompasses a range of substance use patterns including:

» Hazardous use – a risk of harmful consequences (social, mental, physical) to the user or others;
» Harmful use – the substance use causes harm to the user or others, may be continuous or episodic (e.g. interpersonal violence after an alcohol binge).
» Dependence - characterised by a loss of self-regulation, repeated use despite harm, substance-induced mental illness, and withdrawal syndromes.

People with substance misuse present for related or comorbid health problems e.g. to emergency rooms, infectious disease services (e.g. TB, HIV, Hepatitis, etc.), antenatal clinics, STD services, and mental health services. Early identification and intervention of the substance use is advised to prevent further harm or dependence.

GENERAL MEASURES

» Screen for substance use disorders as a routine part of patient assessment, e.g. with WHO ASSIST[lii]. The outcome of the screen should determine the level of intervention that is recommended– e.g. brief advice, a brief intervention (ASSIST linked brief intervention[liii]) or referral to a local substance treatment programme (through a social worker or a registered NGO).
» Elective detoxification: plan in conjunction with a comprehensive substance treatment plan, co-ordinated by the Department of Social Development.
» Unplanned withdrawal: may occur during treatment for another medical condition or may be the presenting complaint. Provide brief intervention counselling and refer to a substance treatment programme.
» Injection drug use: counsel on harm reduction measures and refer to needle and syringe programmes, e.g. StepUp project[liv] (TB HIV Care), OUT, Anova[lv] and COSUP[lvi].

REFERRAL

» All patients treated for substance withdrawal should be referred to Social Services and/or a rehabilitation service for management of their substance use and aftercare.
» Discuss those with comorbid severe mental disorders services with a psychiatrist; refer to specialist dual diagnosis services where available.

15.8 ALCOHOL

F10.3-4

GENERAL MEASURES

The following patients should be admitted for detoxification:

» past history of convulsions
» past history of psychosis
» suicidal ideation
» significant medical comorbidity such as heart failure and liver disease
» inadequate support at home
» history of withdrawal delirium
» >60 years of age
» pregnancy
» cognitive impairment
» previous failed community detoxification attempts

MEDICINE TREATMENT

Alcohol detoxification may be managed on an outpatient basis in most patients.

- Thiamine, oral, 300 mg daily for 14 days.

AND *LoE:III*[lvii]

- Diazepam, oral, 10 mg immediately.
  - Then 5 mg 6 hourly for 3 days.
  - Then 5 mg 12 hourly for 2 days.
  - Then 5 mg daily for 2 days.
  - Then stop.
  - Higher doses may be needed in individual patients.

15.8.1 ALCOHOL WITHDRAWAL DELIRIUM (DELIRIUM TREMENS)

F10.4

DESCRIPTION

Delirium typically occurs 2–3 days following cessation of prolonged alcohol intake, reaching a peak at around 5 days. However, some withdrawal symptoms, such as tremor, may start within 12 hours.

Typical clinical features include:

» visual hallucinations,
» delusions,
» disorientation, fluctuating level of consciousness,
» agitation,
» tonic-clonic seizures – these do not generally need long term anticonvulsant therapy,
» tachycardia, and
» hypertension.

It is important to consider alternative diagnoses, especially true in cases with an atypical presentation.
Similar symptoms may occur following withdrawal from other sedative-hypnotic agents.

Mortality varies from 1–5%.

GENERAL MEASURES

» See section 20.8: Delirium with perceptual disturbances.
» Cardiac monitoring and oximetry should be used when administering large doses of benzodiazepines.
» Assess for infections and other comorbid conditions.
» Ensure adequate hydration. Overhydration is a common error made in this setting.
» Correct abnormalities of electrolytes.
» Nutritional support.
» Consider referring appropriate patients to a rehabilitation programme after recovery from delirium tremens.

MEDICINE TREATMENT

Administer medicine doses according to severity of symptoms. These patients may require high doses of benzodiazepines because of hepatic enzyme induction.

- Benzodiazepines, e.g.:
- Diazepam, slow IV, 10 mg (**Not IM**).
  - Repeat dose after 5–10 minutes if required.
  - If this dose is not sufficient, use 10 mg every 5–10 minutes for another 1–2 doses.
  - If patient is not yet sedated, continue with doses of 20 mg until this occurs. Usual initial dose is 10–20 mg, but up to 60 mg is occasionally required.

OR

Where intravenous access is not possible:

- Clonazepam, IM, 2 mg as a single dose.
  - If no response, repeat dose after 60 minutes until patient is sedated.
  - Repeat dose regularly to maintain mild sedation.

LoE:III

OR

Lorazepam, IM, 1–4 mg every 30–60 minutes until patient is sedated.
  - Repeat dose regularly to maintain mild sedation. *LoE:III*

Once patient is sedated, i.e. light somnolence, maintain mild sedation with:

- Diazepam, oral, 5–20 mg.
  - Repeat dose regularly to maintain mild sedation. *LoE:III*

CAUTION

Benzodiazepines, especially diazepam IV, can cause respiratory depression. Monitor patients closely as benzodiazepines can exacerbate an abnormal mental state or mask important neurological signs of deterioration.

See the note regarding benzodiazepines in section 15.2: Confusional states/delirium.

Neuroleptic medicines, e.g. haloperidol, are associated with a reduced seizure threshold. **Consider only for severe agitation and restlessness persisting after adequate doses of benzodiazepines.**

- Haloperidol, IV/IM, 0.5–5 mg.
  - Repeat after 4–8 hours as required to a maximum of 20 mg daily.

Once patient has responded and is able to take oral medication:

- Haloperidol, oral, 0.5–5 mg 4–8 hourly.

When administering glucose-containing fluids:

- Thiamine, oral/IM, 300 mg daily.

15.9 OPIATE (E.G. HEROIN, UNGA, WHOONGA, NYAOPE) WITHDRAWAL

F11.2

DESCRIPTION

Opioid withdrawal is generally poorly tolerated, but not dangerous, except in very frail debilitated patients or during pregnancy, with an increased risk of miscarriage in the first trimester and of preterm delivery in the third trimester.

Signs and symptoms of opiate intoxication:

- » Pinpoint pupils
- » Clammy skin
- » Respiratory depression
- » Drowsiness
- » Euphoria
- » Hallucinations

Signs and symptoms of opiate withdrawal:

- » Nausea / vomiting
- » Gooseflesh
- » Abdominal cramps
- » Rhinorrhoea and lacrimation
- » Myalgia
- » Diarrhoea
- » Restlessness / agitation

GENERAL MEASURES:

» The identification and evidence-based management of opioid dependence among patients who are admitted to hospital will increase their likelihood of completing their primary admission-related treatment. Sub-optimal management of opioid withdrawal will increase the likelihood of

absconding from hospital.
» It is extremely important to counsel patients managed for opioid withdrawal upon discharge. Patients' opioid tolerance will be reduced after the down-tapering of methadone (or similar medication) during hospital stay. Upon discharge, patients should be advised to use opioids with caution due to their increased risk of accidental overdose. Opioid related overdose deaths must be prevented.
» Special considerations apply during pregnancy, consult an expert.
» Concomitant withdrawal from opioids and other "downer" drugs, like benzodiazepines or alcohol may complicate withdrawal, consult an expert.

MEDICINE TREATMENT

Monitor for objective signs of withdrawal using a rating scale like the objective opioid withdrawal scale (OOWS)
https://medicine.yale.edu/sbirt/OOWS_251773_284_5_v1.pdf

LoE:III[lviii]

Mild withdrawal (OOWS <4)
May be managed on an outpatient basis.

Symptomatic treatment
- Diazepam, oral, 5–20 mg/day in divided doses.
  - Taper off over 5–7 days.

For stomach cramps:
- Hyoscine butylbromide, oral, 20 mg 8 hourly as required.

For headaches:
- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

LoE:III

For muscle pains:
- NSAID, e.g.:
- Ibuprofen, oral 400 mg 8 hourly, with meals, as required.

LoE:III

For diarrhoea:
- Loperamide, oral, 4 mg immediately.
  - Then 2 mg after each loose stool.
  - Maximum dose: 16 mg in 24 hours.

Moderate to severe withdrawal (OOWS ≥4)
Hospitalise patient.

Opioid assisted withdrawal
» Goal is to safely alleviate withdrawal symptoms without causing intoxication or overdose.
» Symptomatic medication listed above may be used to reduce methadone need.

Day 1:

- Wait for early evidence of withdrawal (OOWS ≥4)
- Methadone, oral, 5–10 mg.
  - If symptoms are still present after 2–-4 hours, give another 5–10 mg.
  - Repeat until objective withdrawal symptoms are adequately managed (OOWS <4).
  - The total 24-hour dose should not be more than 30 mg. Consult a person experienced in opioid withdrawal if >30 mg/day is required.

Day 2:

- Methadone, oral.
  - Repeat total dose of day 1 as a single or 2 divided doses.
  - Monitor for on-going signs and symptoms of withdrawal.
  - If the signs and symptoms of withdrawal are still present on day 2, top-up doses of 5 mg may be given at 2–4 hourly intervals with a total daily dose of up to 30 mg. Consult a person experienced in opioid withdrawal if symptoms not controlled on 30 mg/day.

Day 3 onwards:

- Methadone, oral.
  - Repeat total dose of day 2 if top-ups were needed and begin reductions on day 4.
  - If no top-ups required on day 2 and withdrawal symptoms are adequately controlled, begin dose reduction.
  - Decrease dose by 10–20% per day over a period of 3–10 days.
  - The withdrawal regimen may be shortened, if the patient's withdrawal symptoms allow it.

LoE:III[lix]

<u>If methadone is unavailable:</u>

- Tramadol, oral, 200 mg 12 hourly for 14 days may attenuate withdrawal symptoms.

LoE:II[lx]

Opioid poisoning

See section: 19.5.3. Opioid poisoning.

REFERRAL

» Patients with an opioid use disorder should be offered a referral to access opioid substitution therapy and/or other evidence-based treatment and support.

» Patients identified with current/ recent history of injecting drug use should be provided with sterile injecting equipment (1 ml insulin needles and alcohol swabs) upon discharge from hospital, as well as a referral to a community- based needle and syringe programme.

15.10 STIMULANT WITHDRAWAL, INCLUDING COCAINE AND AMPHETAMINE TYPE STIMULANTS (E.G. METHAMPHETAMINE/ TIK, METHCATHINONE/CAT)

F14.2

GENERAL MEASURES

These patients usually do not require admission.
Beware of depression and assess suicide risk.
Assess and monitor for psychosis.

MEDICINE TREATMENT

No substitute medication available for detoxification.
For severe anxiety, irritability and insomnia:

- Benzodiazepines, short-term, e.g.:
- Diazepam, oral, 5–10 mg 8 hourly for 5–7 days.

15.11 METHAQUALONE (MANDRAX/WHITEPIPE) WITHDRAWAL

F19.4/F19.9

Withdrawal can be dangerous and may lead to seizures or delirium.
If withdrawal is symptomatic:

- Diazepam, oral, 5 mg 8 hourly.
  - Reduce over 3–5 days depending on clinical response.

15.12 CANNABIS WITHDRAWAL

F12.2

Withdrawal is rarely dangerous or poorly tolerated.
Assess for other accompanying psychiatric disorders e.g. mood or psychosis.

15.13 BENZODIAZEPINE WITHDRAWAL

F13.2

DESCRIPTION

Benzodiazepine addiction may occur after only a few weeks of use. Withdrawal symptoms on abrupt dose reduction or cessation includes anxiety, nervousness, irritability, depersonalisation, delirium and seizures, increased sweating, sound sensitivity, nausea, difficulty concentrating, myoclonus, tremor, weakness and fatigue.
Gradual tapering of the benzodiazepine is recommended to facilitate discontinuation.

GENERAL MEASURES

» The therapeutic relationship between client and doctor is extremely important in initiating dose reduction.
» Confirm benzodiazepine dependence – ascertain usage, history of previous withdrawal symptoms; a urine screen may be necessary
» Establish full dosage of all benzodiazepines being taken, including those prescribed by other medical practitioners
» Take time to explain negative impact of ongoing benzodiazepine use, benefits of stopping, and concepts like tolerance and withdrawal
» Encourage the patient not to seek medication from other doctors.
» Evaluate and optimise management of comorbid substance use disorders, mental illness, and general health conditions.
» Avoid abrupt withdrawal of benzodiazepines; be prepared to take time. Negotiate each reduction with the patient. Individualise regular monitoring and motivation.
» Long-term follow-up with repeated motivation may be necessary to prevent relapse.

LoE:I[lxi]

MEDICINE TREATMENT

Replace short-acting benzodiazepine with an equivalent diazepam (long acting benzodiazepine) dose.

Patients may present with medicines that are unavailable in the public sector. Approximate equivalent doses to diazepam 5 mg are: *LoE:III*[lxii]

» chlordiazepoxide 12.5 mg
» clobazam 10 mg
» clonazepam 0.25–1 mg
» lorazepam 0.5 mg
» alprazolam 0.25 mg
» bromazepam 1.5 mg
» flunitrazepam 0.5 mg
» nitrazepam 5 mg
» oxazepam 15 mg
» temazepam 10 mg
» zopiclone 7.5 mg
» zolpidem 10 mg

Note: Medicines have only been included for comparison of estimated equivalent doses.

Higher doses may be required for patients who are dependent on both alcohol and benzodiazepines. Inpatient assessment and initiation of benzodiazepine tapering may be warranted in these patients.

Reduction is done according to clinical response.

- Diazepam, oral.
  - Reduce daily dose every 1–2 weeks by 10 mg/day until a daily dose of 50 mg.

- Then reduce every 1–2 weeks by 5 mg/day until a daily dose of 30 mg.
- Then reduce every 1–2 weeks by 2.5 mg/day until a daily dose of 20 mg.
- Then reduce every 1–2 weeks by 1.25 mg/day until stopped.
- If symptoms reappear, increase the dose a little and reduce dose over longer intervals.
- No more than one week's duration of therapy is generally issued at one time.

LoE:III[lxiii]

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CHAPTER 16

RESPIRATORY DISORDERS

16.1 ASTHMA, ACUTE

J45.0/1/8/9

GENERAL MEASURES

Ensure adequate hydration.

In patients presenting with asthma without an atopic allergic background, the diagnosis of pulmonary oedema due to left ventricular heart failure should be considered.

Patients with severe asthma (characterised by one or more of: unable to complete sentences in one breath, altered mental status, paradoxical chest movement, absence of wheezes, peak expiratory flow (PEF) <50% of predicted/personal best - see PEF charts in Appendix V) should ideally be closely monitored in a High Care or an Intensive Care Unit.

MEDICINE TREATMENT

If hypoxaemic

- Oxygen, if saturation <94%. *LoE:I*[i]

- Salbutamol, nebulisation, 5 mg.
  - Initially nebulise continuously (refill the nebuliser reservoir every 20 minutes) at a flow rate of 6–8 L/minute until PEF >60% of predicted or >60% of personal best (see PEF charts in Appendix V).
  - Once patient reaches 60% of their predicted/personal best PEF, repeat salbutamol 5 mg 4 hourly.

LoE: I[ii]

Severe exacerbations:

ADD

- Ipratropium bromide, nebulisation 0.5 mg. *LoE: II*[iii]
  - Combination salbutamol/ipratropium UDV, 5/0.5 mg preferred.

Mild to moderate exacerbations, if response to nebulised salbutamol is poor:

ADD

- Ipratropium bromide, nebulisation 0.5 mg with the 1st and subsequent refills of the nebuliser reservoir. *LoE: II*[iv]

- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 40 mg daily (start 1 hour of presentation) for 7 days.

OR *LoE:III*[v]

In patients who cannot use oral therapy, or are vomiting or are suspected of having gastric atony from a severe asthma exacerbation:

- Hydrocortisone, IV, 100 mg 6 hourly.

LoE:II[vi]

Once oral medication can be taken, switch to:

- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 40 mg daily for 7 days.

Continue nebulisations until PEF returns to 80% of predicted/ personal best, at which point the patient can be converted to:

- Salbutamol, MDI, 200 mcg, as needed.

AND

LoE:III[vii]

- Inhaled corticosteroid (ICS), e.g.:
- Budesonide, inhalation, 200 mcg whenever salbutamol is taken.

In patients on protease inhibitors, replace ICS with beclomethasone:

- Beclomethasone, inhalation, 200 mcg whenever salbutamol is taken.

LoE:III[viii]

Monitor response with PEF and clinical signs. Patients who fail to respond within 1 hour (symptomatic improvement and PEF >60% of predicted/personal best):

» Exclude upper airway obstruction/stridor, pneumothorax, and anaphylaxis.
» Discuss management with a specialist.
» Intubation and ventilator support may be required.
» If referral to another facility is required, the patient needs to be stabilised prior to transfer and transported by the appropriate level of transport - discuss with the referral centre.

In patients with a poor response:

ADD

- Magnesium sulfate, IV, 2 g in 100mL sodium chloride 0.9%, as a single dose, administered over 20 minutes.

LoE: I[ix]

Intravenous magnesium, single dose, has been shown to reduce the rate of hospitalisation.

There is good evidence to recommend against the use of intravenous aminophylline in acute asthma as its use together with high-dose nebulised $ß_2$-agonists does not result in significant additional bronchodilation and leads to a significant increase in toxicity (vomiting and dysrhythmias).

LoE: I[x]

Intercurrent bacterial respiratory infections

Bacterial infections are seldom present in acute exacerbations of asthma and yellow sputum production is usually related to presence of eosinophils. Antibiotics do not play a role in the management of asthma unless there is air space consolidation on CXR. See section 16.6: Pneumonia, community acquired.

16.2 ASTHMA, CHRONIC PERSISTENT

J45.0/1/8/9

DESCRIPTION

Asthma must be distinguished from chronic obstructive pulmonary disease, which is often mistaken for asthma. The history is a reliable diagnostic guideline and may be of value in assessing treatment response.

Asthma	COPD
» Young age onset, usually <20 years. » History of hay fever, eczema and/or allergies. » Family history of asthma. » Symptoms are intermittent with periods of normal breathing in between. » Symptoms are usually worse at night or in the early hours of the morning, during an upper respiratory tract infection, when the weather changes or when upset. » Increase 20% in PEF 10 minutes after receiving a $ß_2$-agonist. *LoE:II*[xi]	» Older age onset, usually >40 years. » Symptoms slowly worsen over a long period of time. » Long history of daily/frequent cough, before the onset of shortness of breath. » Symptoms are persistent and not only at night or during the early morning. » History of heavy smoking (>20 cigarettes/day for ≥15 years), heavy cannabis use or previous TB. » Little improvement in PEF with $ß_2$-agonist.

GENERAL MEASURES

Patient education: including advice on smoking cessation.
Decrease exposure to triggers, e.g. house dust mite, pollens, grasses, pets, smoke, fumes, etc.

MEDICINE TREATMENT

Concomitant use of preparations of the same therapeutic class is hazardous and must be avoided.
Nocturnal symptoms of cough and wheeze, or the need for bronchodilators > twice a week, or PEF <80% of the patient's best value, indicates poor asthma control.
Patients with poorly controlled asthma need to step up their maintenance therapy as described below.
The Asthma Control Test®, a validated measure of clinical asthma control, can be completed by the patient (after initial instruction) at each visit to the clinic prior to consultation. A value of ≥19 suggests adequate asthma control (see Appendix V).

A patient with poorly controlled asthma should be assessed for the following and identified problems addressed prior to stepping up therapy:

1) Correct inhaler technique should be demonstrated and checked regularly, as many asthmatic patients do not use their inhalers correctly.
2) Adherence to medication, especially the inhaled corticosteroid.
3) Exposure to triggers of bronchospasm.
4) Use of medications that may aggravate asthma e.g. NSAIDS.
5) Other medical conditions such as cardiac disease.
6) Treat allergic rhinitis (see section 17.2: Rhinitis, allergic, persistent) and GORD (see section 1.1.3: Gastro-oesophageal reflux disease (GORD), if present.

Asthma therapy

Inhaled corticosteroids (ICS) are the mainstay of treatment in asthma.

For patients with infrequent asthma symptoms < twice a month:

As reliever/rescue therapy:

- Short acting ß$_2$-agonists, e.g.:
- Salbutamol, MDI, 200 mcg, as needed.

AND *LoE:III*[xii]

- ICS, e.g.:
- Budesonide, inhalation, 200 mcg whenever salbutamol is taken.

In patients on protease inhibitors, replace ICS with beclomethasone:

- Beclomethasone, inhalation, 200 mcg whenever salbutamol taken.

LoE:III[xiii]

For patients with asthma symptoms ≥ twice a month

As controller therapy:

- ICS, low dose, e.g.:
- Budesonide, inhalation, 200 mcg 12 hourly. *LoE: I*[xiv]
  - Well and stable after 6 months: can attempt to reduce budesonide dose to 200 mcg daily.
  - Dose adjustments may be required at change of seasons.

In patients on protease inhibitors, replace ICS with beclomethasone:

- Beclomethasone, inhalation, 200 mcg 12 hourly for 6 months; reduced to 200 mcg daily once well and stable.

LoE:III[xv]

AND

As reliever/rescue therapy:

- Short acting ß$_2$-agonists, e.g.:
- Salbutamol, MDI, 200 mcg, 6 hourly as necessary.

For patients with asthma symptoms almost daily or waking due to asthma at least once a week:

- Long-acting β$_2$-agonist/corticosteroid combination inhaler, e.g.:
- Salmeterol/fluticasone, inhalation, 50/250 mcg 12 hourly.
  - Maximum dose: 50/500 mcg 12 hourly.

- Well and stable for 6 months: step down to budesonide, inhaled, 200 mcg 12 hourly.

LoE: I[xvi]

In patients on protease inhibitors:

- Beclomethasone, inhalation, 400 mcg 12 hourly.

AND *LoE:III*[xvii]

- Formoterol, inhalation, 12 mcg 12 hourly.

Failure of above therapy:
While awaiting appointment with specialist.
ADD

- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 10 mg daily.

  Note: Prednisone should not be used as maintenance therapy but only as a bridging step while awaiting review by specialist.

LoE: III

For short-term exacerbations in patients not responding to the above, while awaiting review with specialist:

- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 40 mg daily for 10 days. *LoE: III*

PATIENT AND CAREGIVER EDUCATION ON INHALER AND SPACER TECHNIQUES:

Spacer devices
Patients who are unable to use inhalers correctly after adequate counselling may benefit from the use of a spacer.

Inhalation therapy without a spacer in adults:

1. Remove the cap from the mouthpiece.
2. Shake the inhaler well.
3. While standing or sitting upright, breathe out as much air as possible.
4. Place the mouth piece of the inhaler between the lips and gently close the lips around it.
5. While beginning to inhale, press down the canister of the metered dose inhaler once to release one puff while breathing in as deeply/slowly as possible.
6. Hold the breath for 5–10 seconds, if possible.
7. Breathe out slowly and rest for a few breaths (30–60 seconds).
8. Repeat steps 2–6 for each puff prescribed.
9. Rinse mouth with water after inhalation of corticosteroids.

Inhalation therapy with a spacer in adults:

1. Remove the caps from the inhaler and the spacer.
2. Shake the inhaler well.
3. Insert the mouthpiece of the metered dose inhaler into the back of the spacer.

4. Insert the mouthpiece of the spacer into the mouth and close the lips around the mouthpiece. Avoid covering any small exhalation holes.
5. Press down the canister of the metered dose inhaler once to release one puff into the spacer.
6. Immediately take 3–4 slow deep breaths.
7. Repeat steps 4–6 for each puff prescribed, waiting at least 30 seconds between puffs.
8. Rinse mouth with water after inhalation of corticosteroids.

16.3 BRONCHIECTASIS

J47

GENERAL MEASURES

Patient education.
Advice on early self-referral for suspected acute infections.
Physiotherapy: Regular chest clearance exercises (20 minutes morning and night) are the mainstay of therapy and must be emphasised and demonstrated to the patients, including cough and chest drainage techniques, and must be emphasised repetitively.

MEDICINE TREATMENT

Antimicrobial therapy

Antibiotic therapy in patients with bronchiectasis should only be used when there is either systemic evidence of sepsis such as pyrexia or increasing sputum purulence or volume. Antibiotic choices should be guided by sputum microscopy, culture and sensitivity. The number and duration of physiotherapy sessions should be increased.

Treatment may need to be prolonged for two weeks, depending on the extent of the bronchiectasis and the organisms suspected.

In patients otherwise stable and before culture results:

- Amoxicillin/clavulanic acid, oral, 875/125 mg 12 hourly for 10 days, or longer depending on the response. *LoE:III*[xviii]

Severe penicillin allergy: (Z88.0)

- Azithromycin, oral, 500 mg daily for 10 days, or longer depending on the response.

More severely ill patients may require hospitalisation and initiation of parenteral antibiotic therapy.

Sputum microscopy, culture and sensitivity determination are indicated in all cases.

- Ceftriaxone 2g, IV, daily, until patient apyrexial for 24 hours.

Follow with: *LoE:III*[xix]

- Amoxicillin/clavulanic acid, oral, 875/125 mg 12 hourly. *LoE:III*[xx]

If Pseudomonas infection is confirmed on culture: (B96.5)
ADD

- Ciprofloxacin, oral, 750 mg 12 hourly for 7 days.

Severe penicillin allergy: (Z88.0)

- Moxifloxacin, oral, 400 mg daily for 7 days.

If penicillin allergic and unable to tolerate oral therapy: (Z88.0)
Management of these patients should be discussed with a specialist for possible referral and alternative parenteral therapy:

- Moxifloxacin, IV, 400 mg daily infused over 60 minutes.

Switch to oral treatment once able to take orally: *LoE:III*[xxi]

- Moxifloxacin, oral, 400mg daily.

Subsequent antibiotic therapy should be based on results of sputum investigations. A sputum smear for Acid Fast Bacilli (AFB), followed by culture if positive, is recommended in patients with a poor response to antibiotics as patients with bronchiectasis are at increased risk for infection with Non-tuberculous Mycobacteria which will not be detected by XpertMTB/RIF® PCR assay.

Inhaled bronchodilators
Bronchodilators may be used as for COPD, if airflow obstruction is present. There is no indication for inhaled corticosteroids.
Any asthmatic component (i.e. reversible obstruction should be treated in the usual way, as for asthma).

Prophylaxis (Z25.1)

- Annual influenza vaccine. See section 9.2: Adult vaccination.

For frequent severe exacerbations, consult a specialist.

REFERRAL

» For exclusion of a possible foreign body.
» For assessment for surgical removal of a bronchiectatic segment.
» Major haemoptysis.

16.4 CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

J43.0/1/2/8/9/J44.0/1/8/9

DESCRIPTION

COPD is characterised by persistent respiratory symptoms (dyspnoea, chronic cough and sputum production), and airflow limitation. Spirometry is required to diagnose COPD, where the post bronchodilator FEV1/FVC ratio is <0.7. COPD is likely to worsen over time, even with optimal care.

Regular follow-up is necessary to monitor lung function, symptoms, exacerbations, co-morbidities, and the need for treatment regimen changes.

COPD can be graded on severity of symptoms and frequency of exacerbations to assist in treatment selection and to monitor treatment success:

LoE:III[xxii]

GOLD grade	mMRC breathlessness score	Exacerbations in past year
A	0–1	<2
B	≥2	<2
C	0–1	≥2
D	≥2	≥2

The mMRC scale:

Grade	Exacerbations in past year
0	Dyspnea with strenuous exercise
1	Dyspnea when hurrying on level ground or walking up a slight hill
2	Walks slower than people of same age group, due to dyspnea
3	Stops for breath after walking 91m, or after a few minutes on level ground
4	Too breathless to leave the house, or dyspnea when dressing/undressing

Url link to the modified Medical Research Council (mMRC) dyspnea scale calculator:
https://www.mdcalc.com/mmrc-modified-medical-research-council-dyspnea-scale

LoE:III[xxiii]

GENERAL MEASURES

Patients with clinical COPD must undergo spirometry to confirm and grade the severity of obstruction.
Patients should be screened for ongoing smoking and advised to stop at each visit. Smoking cessation and avoidance of noxious respiratory particles should form the mainstay of management.

MEDICINE TREATMENT

Note: Correct inhaler technique should be demonstrated and checked regularly.

Management of acute exacerbations

Progression of disease (measured by symptoms and deterioration in lung function) in COPD is variable, but is greater in patients who experience COPD exacerbations which are defined as:

» worsening of dyspnoea,
» increased cough,
» increased sputum production or purulence or,
» greater than usual day to day variability of symptoms.

Severe exacerbations are defined as being sufficiently severe to prompt use of an oral corticosteroid course and/or an antibiotic. COPD exacerbations are not always associated with significant decreases in PEF or FEV_1, and are defined by symptoms and, when severe, measures of respiratory failure. Most are precipitated by viral and/or bacterial infection, and are more common in winter.

Patients should be admitted if there is a marked increase in dyspnoea, symptoms disturb eating or sleeping, change in mental status or poor social circumstances. Causes of worsening symptoms other than an acute exacerbation of COPD such as cardiac failure, pulmonary embolus, or pneumonia must be considered**.**

If available, check blood gases for the presence of hypoxaemia and hypercapnia. In some patients with long-standing lung disease the drive to respiration switches from hypercapnia (increases in $PaCO_2$) to hypoxaemia (level of respiratory failure). In such patients, relief of hypoxaemia with uncontrolled oxygen therapy may result in hypoventilation, with consequent rise in $PaCO_2$ to dangerous levels and associated respiratory acidosis leading to coma and death. For this reason, hypoxaemia should be corrected using controlled use of supplemental oxygen, preferably starting with a nasal cannula 1-2 litres/minute.

If the patient's arterial $PaCO_2$ does not rise, the FiO_2 may be increased until a PaO_2 of 8 kPa is reached (or oxygen saturation of 90%). The FiO_2 must be reduced or removed if worsening hypercapnia occurs; these patients might require non-invasive ventilation or intubation for mechanical ventilation.

Where blood gases are not readily available, the patient's clinical status should be reviewed regularly to check for increasing drowsiness, headache, or confusion, which may precede coma.

Where resources for mechanical ventilation are scarce, oxygen saturation targets for patients with long-standing COPD and limited effort tolerance may be relaxed if the patient is improving clinically.

- Salbutamol, nebulisation, 5 mg.
  - Nebulise continuously (refill the nebuliser reservoir every 20 minutes) at a flow rate of 6–8 L/minute.

<u>If a poor response to nebulised salbutamol:</u>

ADD

- Ipratropium bromide 0.5 mg (UDV) with the first refill of the nebuliser reservoir.
  - Patients who fail to respond within 1 hour must be discussed with a specialist. (Patients with COPD have fixed airway disease and unlike asthmatics, PEF is not a reliable measure of their disease).

<u>Once clinically stabilised, nebulise with:</u>

- Salbutamol, nebulisation 5 mg **OR** fenoterol 1.25–2.5 mg.
  - Repeat 4–6 hourly.

AND

- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 40 mg immediately.

Follow with:

- Prednisone, oral, 40 mg daily for 5 days. *LoE:I*[xxiv]

OR

In patients who cannot use oral therapy:

- Hydrocortisone, IV, 100 mg 6 hourly until patient can take oral medication.

Once oral medication can be taken, follow with:

- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 30 mg daily for 5 days.
  - Monitor response and clinical signs. *LoE:I*[xxv]

Acute infective exacerbation of chronic bronchitis:

- Amoxicillin, oral, 500 mg 8 hourly for 5 days.

Severe penicillin allergy: (Z88.0)

- Doxycycline, oral, 100 mg 12 hourly for 5 days.

Non-responsive to first course of antibiotic therapy or in patients with a moderate to severe exacerbation and who have increased sputum purulence plus ≥ 1 of the following symptoms should receive an antibiotic:

» increased dyspnoea,
» increased sputum volume

- Amoxicillin/clavulanic acid, oral, 875/125 mg 12 hourly for 5 days. *LoE:III*[xxvi]

Severe penicillin allergy: (Z88.0)

- Azithromycin, oral, 500 mg daily for 3 days. *LoE:III*[xxvii]

Chronic therapy
GRADE A

As initial therapy:

- Short acting β_2-agonist (SABA) e.g.:
- Salbutamol, MDI, 200 mcg 6 hourly as needed (educate on correct inhaler use - use a large volume spacer if inhaler technique remains poor).

If no response in symptoms or **GRADE B**:

ADD *LoE:III*[xxviii]

- Long acting β_2-agonist (LABA), e.g.:
- Formoterol, inhalation 12 mcg 12 hourly. *LoE:I*[xxix]

GRADE C and D (frequent exacerbations (≥2 per year)):

- Short acting β_2-agonist (SABA) e.g.:
- Salbutamol, MDI, 200 mcg 6 hourly as needed using a large volume spacer.

AND

- LABA/ICS combination, e.g.:
- Salmeterol/fluticasone, inhalation, 50/250 mcg 12 hourly. *LoE:I*[xxx]

AND

Refer COPD patients for additional assessment and management.

Patients on protease inhibitors:
Replace salmeterol/fluticasone with:
- Beclomethasone, inhalation, 400 mcg 12 hourly.

AND *LoE:III*[xxxi]
- Formoterol, inhalation, 12 mcg 12 hourly.

If inadequate control with above therapy:
- Theophylline, slow release, oral, 200 mg at night. Specialist consultation.
  - Ongoing use of theophylline should be re-evaluated periodically. If there is no benefit after 12 months discontinue theophylline.

LoE:II[xxxii]

Corticosteroids
Oral corticosteroids are not recommended for stable COPD.

For acute exacerbations: J44.1
- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 30 mg daily for 5 days. *LoE:I*[xxxiii]

Pre-operative assessment for surgical procedures:
Patients with chronic lung disease are at an increased risk of post-operative pulmonary complications. Risk is increased with increasing severity of pulmonary disease, and with upper abdominal or thoracic surgery.
Patients undergoing elective surgery must be optimised pre-operatively by following the recommended treatment for their disease. Clinical assessment is sufficient with further investigations such as spirometry, CXR and ABGs reserved for patients with clinically severe disease/ unstable disease or where the diagnosis is uncertain. COPD patients should be wheeze free without dyspnoea on moderate exertion (carrying shopping walking up a flight of stairs) or a history of frequent exacerbations. As COPD is a disease characterised by fixed airway obstruction some patients may have continuous wheezing and will require further pre-operative assessment.

Peri-operative oral corticosteroids may be used to gain optimal control but are not advocated for routine use:
- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 30 mg daily for not longer than 5 days.

AND *LoE:III*
Inhaled therapy must be continued and may be administered via nebulisation peri-operatively:
- SABA, e.g.:
- Salbutamol MDI, 200mcg, 30 minutes pre-intubation. *LoE:III*

Prophylaxis (Z25.1)
- Annual influenza vaccination. See section 9.2: Adult vaccination.

REFERRAL

» Assessment for long-term home-based oxygen therapy, if COPD with PaO_2 <7.3 kPa and non-smoker for at least 3 months,
» Recent onset of respiratory failure or signs of cor pulmonale.
» Symptoms that appear disproportionate to the level of airflow obstruction, as judged by spirometry or clinical evaluation (absence of hyperinflation or unusual pattern of symptoms).
» Onset <40 years of age.
» COPD with a history of little or no smoking.
» Recurrent exacerbations, i.e. ≥2 per year.
» Failure to respond to treatment.

16.5 LUNG ABSCESS

J85.0/J85.1/J85.2/J85.3

GENERAL MEASURES

Physiotherapy and regular emphasis on postural drainage is essential for management.
Instruct patient to do chest clearance exercises (taught by a physiotherapist where possible) for at least 20 minutes, 6 hourly.
Nutritional support.

MEDICINE TREATMENT

- Amoxicillin/clavulanic acid, IV, 1.2 g 8 hourly, until patient apyrexial for 24 hours.

Follow with:

- Amoxicillin/clavulanic acid, oral, 875/125 mg 12 hourly. *LoE:III*

Severe penicillin allergy: (Z88.0)

- Moxifloxacin, IV, 400 mg daily, until patient apyrexial for 24 hours.

Follow with:

- Moxifloxacin, oral, 400 mg daily. *LoE:II*[xxxiv]

Duration of therapy

Usually 4-6 weeks - monitor with repeat CXR every 1-2 weeks, which should show disappearance of air-fluid level and reduction in size of abscess.

REFERRAL

» No response to treatment.
» CXR not resolving or worsening.
» Complications, such as empyema or severe haemoptysis.

16.6 PNEUMONIA, COMMUNITY ACQUIRED

J13/J14/J15.0-9/J16.0/8/J18.0-2/J18.8-9

Pneumonia is an acute infection of the lung parenchyma. Early appropriate antibiotic therapy decreases mortality. The decision to hospitalise a patient and choice of initial antibiotic therapy is guided by age, comorbid diseases (such as HIV infection, diabetes or chronic respiratory disease), and severity. Socio-economic circumstances should form part of the clinical assessment when deciding if a patient is suitable for outpatient treatment.

GENERAL MEASURES

Diagnosis:

Clinical features include cough, fever, tachypnoea, and signs of consolidation on chest examination.

CXR almost invariably shows a focal area of opacification or consolidation. However, empiric antibiotic therapy can be considered for severely ill hospitalised patients with suspected pneumonia and a negative CXR – pneumonia is excluded if repeat CXR after 24-48 hours still shows no opacification. Diffuse bilateral interstitial infiltrates in a patient with HIV infection and hypoxaemia is suggestive of *Pneumocystis jirovecii* pneumonia. *LoE:III*[xxxv]

All patients should be offered HIV testing as HIV infection is associated with a markedly increased risk of bacterial pneumonia.

Even in typical cases of pneumonia, exclude tuberculosis by sending sputum for Xpert MTB/RIF Ultra®.

A follow-up CXR 4–6 weeks after completion of therapy should be done in patients >50 years of age, or if symptoms persist. *LoE:III*[xxxvi]

Follow-up CXRs are indicated earlier only when complications are suspected, e.g. empyema, abscess, or pneumothorax.

MEDICINE TREATMENT

- Oxygen, if saturation <94%. *LoE:I*[xxxvii]

Adequate analgesia for pleuritic chest pain, if present. See section 26.2.1: Medical conditions associated with severe pain.

Antimicrobial therapy

Duration of antibiotic therapy is guided by clinical response, but should be 5–7 days, with a minimum of 7 days for MRSA or Pseudomonas.

Longer duration of antibiotic therapy recommended for:

» pathogen identified that was not susceptible to initial empiric therapy
» extrapulmonary infection (e.g. meningitis or endocarditis)
» empyema, lung abscess or necrotizing pneumonia
» unusual organism present *LoE:I*[xxxviii]

Prolonged fever and clinical signs may be due to unrecognised TB, or of complications (such as empyema), or the incorrect choice of antibiotic (e.g. atypical bacteria), or to an underlying bronchus obstruction (foreign body or carcinoma). These patients should be further investigated.

Community-acquired pneumonia without features of severe pneumonia (see below for definition) and without co-morbidity and in patients <65 years of age J18.0-2/J18.8-9

- Ampicillin, IV, 1 g 6 hourly.

In haemodynamically stable patients with respiratory rate <25 breaths/min and the temperature is <37.8°C switch to:

- Amoxicillin, oral, 1 g 8 hourly. *LoE:I[xxxix]*

Severe penicillin allergy: (Z88.0)

- Moxifloxacin, oral, 400 mg daily for 5 days.

If poor response after 48 hours, exclude TB and consider atypical bacterial pneumonia, which requires treatment with a macrolide.

Community-acquired pneumonia without features of severe pneumonia (see below for definition) in patients >65 years of age or co-morbidity (e.g. COPD, HIV, cardiac failure, diabetes) J13/J14/J15.0-9/J16.0/J16.8/J18.0-2/J18.8-9

- Ceftriaxone, IV, 2 g daily. *LoE:I[xl]*

In haemodynamically stable patients with respiratory rate <25 breaths/min and the temperature is <37.8°C switch to:

- Amoxicillin/clavulanic acid, oral, 875/125 mg 12 hourly for 5 days. *LoE:III[xli]*

Severe penicillin allergy: (Z88.0)

- Moxifloxacin, oral, 400 mg daily for 5 days.

If poor response after 48 hours, exclude TB and consider atypical bacterial pneumonia, which requires treatment with a macrolide.

Severe pneumonia (cyanosis, confusion, hypotension or respiratory rate >30 breaths/min): J13/J14/J15.0-9/J16.0/J16.8/J18.0-2/J18.8-9

» Mechanical ventilation may be required (refer to a centre, if needed).

- Ceftriaxone, IV, 2 g daily:

In haemodynamically stable patients with respiratory rate <25 breaths/min and the temperature is <37.8°C switch to:

- Amoxicillin/clavulanic acid, oral, 875/125 mg 12 hourly for 5 days. *LoE:III[xlii]*

AND

- Azithromycin, 500 mg, slow IV (over not less than 60 minutes) daily for 3 days. *LoE:III[xliii]*

Severe penicillin allergy: (Z88.0)
- Moxifloxacin, IV, 400 mg daily.

In haemodynamically stable patients with respiratory rate <25 breaths/min and the temperature is <37.8°C switch to:
- Moxifloxacin, oral, 400 mg daily for 5 days.

Note: There is no need to add a macrolide, as moxifloxacin has adequate cover for the atypical bacteria.

HIV infected with bilateral diffuse interstitial infiltrates on CXR

Clinically may present with a dry cough of <12 weeks' duration and significant tachypnoea.

Treat as *Pneumocystis jirovecii* pneumonia (exclude TB) - see section 10.2.9: Pneumocystis pneumonia.

16.7 PNEUMONIA, ASPIRATION

J69.0-1/J69.8

DESCRIPTION

Following aspiration, a patient may develop pneumonitis or pneumonia. Aspiration pneumonitis develops within hours of the aspiration event and is more common in previously healthy people who aspirate gastric acid. Antibiotics will not benefit these patients unless there is infection present.

Pneumonia following aspiration of gastric contents and/or commensal organisms from the oropharynx usually occurs in debilitated patients and presents with symptoms and signs of community-acquired pneumonia, but may have a more indolent onset and is more frequently complicated by lung abscess or empyema.

There may be solid (food) particles or other foreign bodies aspirated. The organisms involved are polymicrobial, i.e. Gram-positive and anaerobes. Aspiration pneumonia should be suspected in patients with episodic or prolonged decreased level of consciousness, e.g. in alcoholics, drug overdoses, epileptics, strokes, or those with swallowing problems.

MEDICINE TREATMENT

Antimicrobial therapy

Continue therapy until there are no features of sepsis.
- Amoxicillin/clavulanic acid, IV, 1.2 g 8 hourly, until patient is apyrexial and stable for 24 hours.

Follow with:
- Amoxicillin/clavulanic acid, oral, 875/125 mg 12 hourly.

LoE:III

Severe penicillin allergy: (Z88.0)
- Moxifloxacin, IV, 400 mg daily, until patient is apyrexial for 24 hours.

Follow with:
- Moxifloxacin, oral, 400 mg daily.

LoE:II[xliv]

If **nosocomial infection** present (developed >48 hours post admission), see section 9.1.3 Hospital-acquired pneumonia.

REFERRAL

» Hypoxaemia non-responsive to facemask oxygen.
» Suspected foreign body aspiration.
» Suspected chemical aspiration pneumonia.
» Non-resolving pneumonia.

16.8 EMPYEMA

J86.0/J86.9

DESCRIPTION

Pus in the pleural cavity and/or bacteria present in a pleural effusion.
An empyema is always secondary to another process, e.g. pneumonia (especially aspiration pneumonia), lung abscess, tuberculosis, bacteraemia, or a penetrating chest wall or oesophageal injury.

GENERAL MEASURES

Aspirate and analyse all pleural effusions.
A parapneumonic effusion should be distinguished from an empyema by biochemical analysis, fluid microscopy and culture – tube drainage is indicated if the pH is <7.2, or if bacteria are detected, or if pus is aspirated.
The primary management of empyema is early and complete drainage, by insertion of an intercostal drain, to prevent long-term complications.

MEDICINE TREATMENT

Antimicrobial therapy

If a complication of pneumonia, antimicrobial therapy as in section 16.6: Pneumonia, community acquired (but the duration of therapy should be prolonged until drainage is complete).

<u>If not a complication of pneumonia:</u>

- Amoxicillin/clavulanic acid, IV, 1.2 g 8 hourly, until patient is apyrexial for 24 hours.

Follow with:

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

Treatment duration is until drainage is complete. *LoE:III*

<u>Severe penicillin allergy (and not a complication of pneumonia)</u>: (Z88.0)

- Moxifloxacin, IV, 400 mg daily, until patient is apyrexial for 24 hours.

Follow with:

- Moxifloxacin, oral, 400 mg daily.

Treatment duration is until drainage is complete. *LoE:III*

REFERRAL

» Loculated empyema or inadequate drainage.
» Chronic empyema with pleural thickening and restrictive lung disease, for consideration for surgical decortication.

16.9 TUBERCULOSIS, PULMONARY

A15.0-3/A15.7-8/A16.0-2/A16.3-4/A16.7-9/B20.0
* Notifiable medical condition.

Tuberculosis (TB) treatment guidelines are updated regularly. The most recent National Tuberculosis Control Programme Guidelines should be read in conjunction with recent guidelines.

DESCRIPTION

A chronic, granulomatous infection of the lungs caused by *M. tuberculosis*. Pulmonary tuberculosis is a serious health problem in South Africa, which is exacerbated by HIV and multidrug resistant tuberculosis (MDR-TB).

Note: All patients on TB treatment must be notified.

Diagnosis

Molecular tests are used for the diagnosis of *M.tuberculosis* and the identification of drug resistant organisms. The initial diagnostic test for patients with suspected tuberculosis is the Xpert MTB/RIF Ultra® assay, which also detects rifampicin resistance. GenoType MTBDR*plus*® is a line probe assay (LPA) is used as a confirmatory test for rifampicin resistance detected by Xpert MTB/RIF Ultra® and also detects isoniazid resistance.

The diagnosis of pulmonary TB in adults is made on a positive XpertMTB/RIF Ultra® on sputum. In patients with negative sputum smears, notably HIV-infected patients, XpertMTB/RIF Ultra® is not an adequate 'rule out' test and HIV-infected TB suspects who are XpertMTB/RIF Ultra® negative require further investigation and may need empiric anti-tuberculosis therapy while awaiting TB cultures.

Note: XpertMTB/RIF Ultra® may identify DNA from *M. tuberculosis* in the absence of active disease in patients who have completed TB treatment, especially in the past 2 years; TB should be confirmed on culture in this setting.

All patients who are XpertMTB/RIF Ultra® positive require further sputum to be sent for AFB to allow for monitoring of treatment. XpertMTB/RIF Ultra® should not be used for monitoring.

A sputum sample for "DR-TB Reflex" testing should be sent in all patients with rifampicin resistance detected on XpertMTB/RIF Ultra® .

All TB patients must be screened for HIV. TB HIV co-infected patients are eligible for cotrimoxazole prophylaxis regardless of CD4 count.

Sputum induction with nebulised sodium chloride 5% should be attempted for patients unable to spontaneously produce sputum. A wide needle (e.g. 18G) aspiration for Xpert MTB/RIF Ultra® should be done in patients with suspected TB lymphadenitis. *LoE:III*[xlv]

Urine lipoarabinomannan (LAM) is a good "rule-in" diagnostic test for HIV-infected patients with signs and symptoms of pulmonary and/or extrapulmonary TB and CD4 ≤100 cells/microL and for HIV-infected patients who are seriously ill.

LoE:I[xlvi]

MEDICINE TREATMENT

All patients with active TB who are Xpert MTB/RIF Ultra® positive and rifampicin sensitive, should receive 2 months' intensive phase and 4 months continuation phase (see table below). Patients who are at risk of having resistant TB (e.g. previous episode of TB treatment, prisoners, and health care workers), should have sputum sent for a LPA or culture and sensitivity to exclude INH mono resistance.

National tuberculosis control programme guidelines

Fixed dose drug combinations available:

RH – 150/75 mg	RH – 300/150 mg
RHZE – 150/75/400/275 mg	
R – Rifampicin Z – Pyrazinamide	H – Isoniazid (INH) E – Ethambutol

Treatment for known or presumed drug sensitive TB

Pre-treatment body weight	Two months initial phase	Four months continuation phase	
	RHZE (150/75/400/275)	RH (150/75)	RH (300/150)
30–37 kg	2 tablets	2 tablets	
38–54 kg	3 tablets	3 tablets	
55–70 kg	4 tablets		2 tablets
71 kg and over	5 tablets		2 tablets

The use of INH may result in the development of a peripheral neuropathy due to drug-induced pyridoxine deficiency.

- Pyridoxine 25 mg daily is recommended prophylactically with INH, in patients at high risk of peripheral neuropathy (e.g. HIV, diabetes, alcoholics).

Close contacts (particularly children <5 years of age) of TB patients should be screened and managed as per National TB Guidelines.

16.10 TUBERCULOSIS, PLEURAL (TB PLEURISY)

A16.5

DESCRIPTION

TB pleurisy presents with a few weeks of pleuritic pain; often associated with a dry cough, fever, night sweats, weight loss, and, with large effusions, progressive shortness of breath.

Diagnosis

It is essential to perform a diagnostic tap of pleural effusions confirmed on CXR.

Although a definite diagnosis can only be made by demonstrating the organisms on smear or culture, or on histology of a pleural biopsy, the presence of a lymphocytic exudate on pleural fluid analysis is adequate to start empiric TB therapy in areas with a high TB burden, particularly if the patient has HIV infection.

All patients started on empiric TB therapy for pleural TB must be followed up closely; failure to respond as expected must prompt investigations to exclude other causes. Once TB therapy is started, signs and symptoms should resolve within 2 weeks. Radiographic improvement is usually evident by 6 weeks, but complete resorption can take up to 4 months. However, pleural thickening may persist. A pleural biopsy at initial presentation is strongly recommended for the following patients: >50 years of age, or suspected malignancy, or not presenting with typical TB symptoms.

Treatment is as for pulmonary TB (see section 16.9: Tuberculosis, pulmonary).

Note: Total drainage by aspiration or under-water tube is not needed. For large effusions that cause dyspnoea drain a maximum of 1 litre at a time. However, note that a TB pleural empyema must be drained by intercostal tube.

REFERRAL

» Non-resolving effusions. Suspect an incorrect diagnosis of TB pleurisy if the effusion does not improve on the CXR after 3 months of treatment or if the patient deteriorates.
» Loculated TB empyema, not resolving after intercostal underwater tube drainage and needing assessment for surgical drainage.
» Bronchopleural fistula, not resolving after 6 weeks.

16.11 DRUG-RESISTANT TB

16.11.1 ISONIAZID MONORESISTANT TB

A15.0-3/A15.7-8/A16.0-2/A16.3-4/A16.7-9/B20.0 + (U50.00-01/U50.10-11)

MEDICINE TREATMENT

Confirmed INH monoresistant TB:

- Rifampicin, oral, 10 mg/kg daily.

AND

- Ethambutol, oral, 15 mg/kg daily.

AND

- Pyrazinamide, oral, 25 mg/kg daily.

AND

- Levofloxacin, oral, daily.
  - 30–50 kg: 750 mg
  - >50 kg: 1000 mg

LoE:III[xlvii]

Where single medicines are not available or the pill burden is too high a fixed dose combination of RHZE dosed as per weight may be used, and levofloxacin added to this.

Treatment should be given for at least 6 months.

16.11.2 MULTIDRUG-RESISTANT TB

A15.0-3/A15.7-8/A16.0-2/A16.3-4/A16.7-9/B20.0 + (U50.00-01)

Never treat for MDR TB without laboratory confirmation, either by molecular or phenotypic (culture and sensitivity) results.

All cases should be discussed with a designated specialist centre and MDR TB medicines accessed from the designated centres.

Note: MDR TB guidelines are updated regularly. Consult the most recent National MDR TB Programme Guidelines.

DESCRIPTION

Multidrug resistant tuberculosis (MDR TB) is diagnosed when there is in vitro resistance of *M. tuberculosis* against, at least, rifampicin and isoniazid.
MDR TB is diagnosed exclusively on culture and sensitivity assays or rapid molecular tests. XpertMTB/RIF Ultra® only tests for rifampicin resistance and not isoniazid resistance. However, rifampicin resistance detected by XpertMTB/RIF Ultra® is sufficient to start a patient on MDR treatment pending confirmation of MDR TB by LPA.

GENERAL MEASURES

Screen all close contacts for signs and symptoms of to detect early disease.

MEDICINE TREATMENT

MDR TB prophylaxis

The effectiveness of preventive therapy in adults exposed to MDR TB bacteria is not currently known. Consult a specialist for management.

Treatment

Prolonged treatment, for 9–18 months, is required in patients diagnosed with MDR TB.

Management of MDR TB should be conducted in dedicated MDR TB clinics and hospitals with appropriate infection control measures. Patients diagnosed with MDR TB who are smear positive should be hospitalised for up to eight weeks or until they become smear negative on two consecutive tests.

Smear negative, culture positive patients should be started on MDR TB treatment in the community. MDR TB treatment should not be delayed while waiting for a bed or confirmation of MDR TB by LPA.

XDR TB and Pre-XDR TB

Patients with MDR TB who in addition have resistance to any fluoroquinolone and at least one of the 2nd line injectables (kanamycin, amikacin, or capreomycin). Pre-XDR TB is defined as MDR TB plus resistance to either a fluoroquinolone or an injectable.

Confirmation of XDR TB requires drug susceptibility testing.

Patients with XDR TB need to be referred to a TB hospital. Infection control to prevent airborne transmission is essential to prevent nosocomial transmission.

Individualised regimens based on susceptibility tests and treatment history are recommended to achieve a regimen with a minimum of 4–5 effective medicines.

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CHAPTER 17

EAR, NOSE AND THROAT DISORDERS

17.1 EPIGLOTTITIS

J05.1

DESCRIPTION

Acute epiglottitis can result in severe, sudden or progressive airway obstruction.
Acute epiglottitis can be caused by bacteria (e.g. *H. influenzae*), viruses (e.g. herpes simplex) and non-infectious insults (trauma, chemicals, heat).

GENERAL MEASURES

Airway management may require urgent specialist advice.
Adequate hydration.

MEDICINE TREATMENT

Humidified oxygen.

Antibiotic therapy
Total duration of therapy: 10 days.

- Ceftriaxone, IV, 1 g daily.

Follow with oral therapy as soon as patient can swallow and the temperature is <37.8°C for 24 hours, to complete the 10-day course:

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

Severe penicillin allergy to amoxicillin/clavulanic acid, oral: (Z88.0)

- Macrolide, e.g.:
- Azithromycin, oral, 500mg daily for 3 days.

LoE:III[i]

Acute stage
Imminent airway obstruction:

- Hydrocortisone, IV, 100 mg immediately as a single dose.

AND *LoE:III*[ii]

- Adrenaline (epinephrine) 1:1 000, 1 mL nebulised.
  - Dilute to 5 mL with sodium chloride 0.9% and administer 4–6 hourly.

LoE:III[iii]

17.2 RHINITIS, ALLERGIC, PERSISTENT

J30.1-4

DESCRIPTION

Allergic rhinitis is an allergic inflammation of the nasal airways. Signs and symptoms include rhinorrhoea, itching, sneezing, nasal congestion and obstruction, conjunctival swelling and erythema, puffy eyes, swollen nasal turbinates, and middle ear effusion.

GENERAL MEASURES

Avoid allergens and irritants.
Provide education on the correct technique of administering topical medicines. Incorrect technique is a common cause of treatment failure.

MEDICINE TREATMENT

- Corticosteroid, topical, nasal spray e.g.:
- Fluticasone topical, aqueous nasal spray, 1 spray of 100 mcg in each nostril daily.
  - Aim the nozzle laterally and upwards (aim for the eye) and not to the back of the throat.
  - Do not sniff vigorously.

LoE:I[iv]

Patients on protease inhibitors:

- Beclomethasone, aqueous nasal solution, 1 spray of 100 mcg in each nostril 12 hourly.
  - Aim the nozzle laterally and upwards (aim for the eye) and not to the back of the throat.
  - Do not sniff vigorously.
  - Review 3 monthly.

LoE:III[v]

<u>If symptoms persist despite an adequate trial of topical corticosteroids administered with the correct technique:</u>

ADD

- Non-sedating antihistamine, oral e.g.:
- Cetirizine, oral, 10 mg daily.

LoE:I[vi]

<u>For relief of nasal blockage</u>**:**

- Oxymetazoline 0.05%, intranasal, administered 8 hourly for a maximum of 5 days.

Note: Rebound nasal congestion occurs with prolonged use (>5 days) of topical nasal decongestants.

LoE:III[vii]

<u>Failure of the above:</u>

ADD

- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 30 mg daily for 5 days whilst continuing the topical steroid.

17.3 SINUSITIS, BACTERIAL, COMPLICATED

J01.0-4/J01.8-9

DESCRIPTION

Acute bacterial sinusitis complicated by extension to the orbit or intracranially.
Extension to the orbit causes orbital cellulitis or orbital periosteal abscess, both of which may present with pain on eye movement, partial or complete visual loss

(which can be irreversible), ophthalmoplegia, and proptosis. Eyelid oedema and erythema is usually present, but external signs of inflammation may be absent. Intracranial extension may cause meningitis, subdural empyema, brain abscess, or thrombosis of cavernous sinus/cortical veins.

In immunosuppressed or diabetic patients presenting with features of sinusitis consider fungal infections such as mucormycosis. Features suggesting mucormycosis include necrosis of the nasal or palatal mucosa, and orbital or cerebral involvement.

MEDICINE TREATMENT

- Ceftriaxone, IV, 2 g 12 hourly and **refer**.

Pain:

- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

LoE:III

REFERRAL

Urgent

» Proptosis.
» Ophthalmoplegia.
» Suspected mucormycosis, especially in immunocompromised patients.

Non-urgent

» After initiating antimicrobial therapy, refer for a CT scan, to a centre where an appropriate surgical specialist, i.e. ophthalmologist, ENT specialist or neurosurgeon, is available.
» Suspected fungal sinusitis (other than mucormycosis).

17.4 OTITIS MEDIA, ACUTE

H66.9

DESCRIPTION

Inflammation of the middle ear of rapid onset.

MEDICINE TREATMENT

In previously untreated patients:

- Amoxicillin, oral, 1000 mg 8 hourly for 5 days.

LoE:III[viii]

Patients not responding to amoxicillin:

- Amoxicillin/clavulanic acid, oral, 875/125 mg 12 hourly for 5 days.

LoE:III[ix]

Severe penicillin allergy: (Z88.0)

- Macrolide, e.g.:
- Azithromycin, oral, 500 mg daily for 3 days.

For patients with upper respiratory tract congestion, secondary to allergy: (T78.4)

- Non-sedating antihistamine, oral, e.g.:
- Cetirizine, oral, 10 mg daily for 10 days. *LoE:II*[x]

For management of allergic rhinitis, see section 17.2: Rhinitis, allergic, persistent.

For pain:

- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

If pain is not controlled, see chapter 26: Pain. *LoE:III*[xi]

REFERRAL

» No response to amoxicillin/clavulanic acid.
» No pain relief despite treatment.
» Bulging eardrum, not responding to treatment after 24 hours.
» Swelling and pain on palpation of the mastoid process.
» Recurrent otitis media.

17.5 OTITIS MEDIA, CHRONIC, SUPPURATIVE

H66.1-3

DESCRIPTION

A purulent discharge from the ear for more than 2 weeks.
If the eardrum has been ruptured for 2 weeks or longer, a secondary infection with multiple organisms usually occurs. Multiple organism infection often makes oral antibiotic treatment ineffective and patients may need to be referred.
TB is an important cause of a chronically discharging ear in South Africa.
If pain is present, suspect another condition or complications.
Note:
» A chronically draining ear can only heal if it is dry.
» Drying the ear is time consuming but is the most effective treatment.
» HIV status should be established in chronic otitis media.

GENERAL MEASURES

Dry mopping is the most important part of the treatment. It should be demonstrated to the patient.
» Roll a piece of clean absorbent cloth into a wick.
» Carefully insert the wick into the ear with twisting action.
» Remove the wick and replace with a clean dry wick.
» Repeat this until the wick is dry when removed.

Do not leave anything in the ear.
Avoid getting the inside of the ear wet while swimming and bathing.
Exclude TB as a cause.

MEDICINE TREATMENT

After cleaning and drying the ear:

- Acetic acid 2% in alcohol, topical, 3–4 drops instilled into the ear every 6 hours for 5 days.
- Ciprofloxacin, drops, 3 mg/mL, 3–4 drops instilled into the ear every 8 hours for 7 days after mopping.

LoE:I[xii]

For pain:

- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

If pain is not controlled, see chapter 26: Pain. *LoE:III*[xiii]

REFERRAL

» Focal neurological signs such as facial nerve palsy.
» Vomiting or drowsiness.
» Swelling and pain on palpation of the mastoid process.
» No improvement after 4 weeks.
» Any attic perforation.
» Any perforation not progressively improving after 3 months or closed by 6 months, even if dry.
» Moderate or severe hearing loss.
» Effusion.

17.6 MASTOIDITIS

H70.0/H70.9

DESCRIPTION

Infection of the mastoid air cells, usually complicating otitis media. Most patients have tenderness, erythema, and/or swelling over the mastoid bone. Diagnosis should be confirmed radiographically, preferably by CT scan.

MEDICINE TREATMENT

- Ceftriaxone, IV, 2 g 12 hourly.

REFERRAL

After initiating antimicrobial therapy, refer to a centre for s mastoidectomy.

17.7 OTITIS EXTERNA

17.7.1 OTITIS EXTERNA, NECROTISING

H60.2

DESCRIPTION

Invasive infection of the external auditory canal, which can extend to involve the base of

the skull with cranial nerve palsies and the temporomandibular joint. Presents with severe otalgia and otorrhoea, which is unresponsive to topical therapy for otitis externa. Most common pathogen: *P. aeruginosa*.

Necrotising otitis externa typically occurs in elderly diabetics or other immunocompromised patients.

GENERAL MEASURES

Debridement as indicated.
Insert a dry wick such as a dried sponge, into the canal under direct vision. Remove the wick 2 days later, and replace if necessary.

MEDICINE TREATMENT

- Ciprofloxacin, oral, 750 mg 12 hourly, and refer. *LoE:III*

REFERRAL

» For surgical debridement of necrotic bone in non-responders.
» All cases to a centre where CT scan of the affected area can be done to assess the extent of the disease.
» Cranial nerve palsies.

17.8 ABSCESS, PERITONSILLAR

J36

DESCRIPTION

Peritonsillar abscess or quinsy is a collection of pus lateral to the tonsil, i.e. underneath it pushing it toward the midline. Infections are often polymicrobial. It typically presents with trismus and sore throat. Other features include:

» unilateral throat pain
» dysphagia
» drooling
» muffled voice
» fever

SURGICAL MEASURES

Drainage of pus is the most important intervention.
There are 3 main methods:

» needle aspiration of pus
» incision and drainage
» abscess tonsillectomy, either unilateral or bilateral.

MEDICINE TREATMENT

Antibiotic therapy
Total duration of therapy: 10 days.

- Amoxicillin/clavulanic acid, IV, 1.2 g 8 hourly.

Follow with oral therapy as soon as patient can swallow and the temperature is <37.8ºC for 24 hours:

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

Severe penicillin allergy: (Z88.0)
- Clindamycin, IV, 600 mg 8 hourly.

Follow with oral therapy as soon as patient can swallow and the temperature is <37.8°C for 24 hours:
- Clindamycin, oral, 450 mg 8 hourly.

For pain:
- NSAID, oral: e.g.
- Ibuprofen, oral, 400 mg 8 hourly with or after a meal.

REFERRAL
Refer all for ENT and/or anaesthetic review.

Urgent
» Signs of airway compromise (e.g. stridor)).
» Suspicion of infective spread beyond the peritonsillar space.

17.9 VERTIGO, ACUTE
R42/H81.1

DESCRIPTION
An acute syndrome, consisting of vertigo, nystagmus, nausea, vomiting and postural instability. It is important to differentiate between peripheral and central causes of vestibular dysfunction.

Peripheral causes
Patients frequently present with vertigo, which is most often rotational, with nystagmus. The onset is usually sudden and often intermittent. Associated abnormalities of hearing may be present. Aetiology includes benign paroxysmal positional vertigo (confirm with a positive Dix-Hallpike test, https://www.youtube.com/watch?v=8RYB2QIO1N4), aminoglycoside vestibular toxicity, and vestibular neuritis.

Central causes
It is essential to conduct a thorough neurological examination in patients with vertigo, looking specifically for signs of brainstem or cerebellar dysfunction. Aetiology includes cerebellar stroke and space occupying lesions of the posterior cranial fossa.

GENERAL MEASURES
It is essential to find the cause and treat appropriately. Patients with suspected central causes should be referred for neuro-imaging and possible neurosurgical management.

Benign positional vertigo

H81.1

Good results may be achieved with particle relocation manoeuvres, such as the Epley manoeuvre. https://www.youtube.com/watch?v=jBzID5nVQjk

In a third of patients, symptoms recur after 1 year and repeat manoeuvres may be required.

MEDICINE TREATMENT

This is only for symptomatic relief and is determined by the aetiology.

Discontinue all medication as soon as symptoms subside as the medicine itself may cause vertigo due to involvement of the unaffected side.

- Promethazine, oral, 10 mg 8 hourly.
  - May be increased to 20 mg 8 hourly if necessary.

Note: This is sedating and patients should not drive or operate heavy machinery.

LoE:I[xiv]

REFERRAL

» If there is no peripheral cause, suspect intracranial mass lesions or cerebellar stroke.
» Patients not responding to therapy for exclusion of alternative aetiology.

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CHAPTER 18

EYE DISORDERS

18.1 CONJUNCTIVITIS

H10.9

DESCRIPTION

Inflammation of the conjunctiva, usually due to allergy or infection (viral or bacterial).
Conjunctivitis is usually bilateral. Other causes of a red eye are often unilateral.
The condition is self-limiting and usually resolves within 14 days.

GENERAL MEASURES

If it is due to an infection, counsel on the importance of:
» frequent hand washing,
» using separate linen, towels and washcloths, and
» avoiding direct contact with infected material or individuals.

Contact lenses should not be worn if conjunctivitis is present or during a course of topical therapy. Soft lenses should not be worn within 24 hours of instilling eye drops containing the preservative benzalkonium chloride.

18.1.1 CONJUNCTIVITIS, ADENOVIRAL

B30.1+ (H13.1*)

DESCRIPTION

Adenovirus is a common cause of infective conjunctivitis. It may be unilateral but is usually bilateral.

Clinical features:
» Viral conjunctivitis may be associated with an upper respiratory tract infection.
» A burning, sandy, or gritty feeling in the eyes.
» Morning crusting followed by watery discharge.
» Preauricular lymphadenopathy may be present.

The condition is self-limiting but eye irritation and discharge may get worse for 3-5 days before getting better and symptoms can persist for 2-3 weeks.

MEDICINE TREATMENT

- Sodium chloride 0.9%, eye washes or irrigation.

If sodium chloride 0.9% is not available, use cooled boiled water/sterile water.

- Oxymetazoline 0.025%, ophthalmic drops, instil 1 drop 6 hourly for 7 days.

18.1.2 CONJUNCTIVITIS, ALLERGIC

See Primary Health Care Standard Treatment Guidelines and Essential Medicine List, 2018; section 18.1.1 Conjunctivitis, allergic.

18.1.3 CONJUNCTIVITIS, BACTERIAL

H10.0

DESCRIPTION

Clinical features:

» It may be either unilateral or bilateral.
» There is matting of lashes in the morning with the eyelids stuck shut.
» There is a mucopurulent discharge throughout the day.
» The eyelids may be swollen.

MEDICINE TREATMENT

During the day:

- Chloramphenicol 1%, ophthalmic ointment 6 hourly for 7 days.

LoE: III[i]

OR

- Fluoroquinolone ophthalmic drops as second-line treatment, e.g.:
- Ciprofloxacin 0.3%, ophthalmic drops, instil 1 drop 2 hourly for 2 days.
  - Then reduce frequency to 1 drop 4 hourly during waking hours, for 5 days.

LoE: II[ii]

REFERRAL

No response to treatment.

18.2 ENDOPHTHALMITIS, BACTERIAL

S05.6 + (Y43.99)

DESCRIPTION

Infection of the ocular cavity is an emergency as it can cause blindness. This may occur secondary to bacteraemia (endogenous infection) or, more commonly, after penetrating ocular injury or surgery.
In patients with endogenous endophthalmitis blood cultures should be done and the source of infection identified and treated.
In patients with endophthalmitis after penetrating injury/surgery culture should be done on specimens of aqueous or vitreous humour.

MEDICINE TREATMENT

Refer immediately to an ophthalmologist.

Endogenous endophthalmitis

Specialist initiated, vitrectomy often required:

- Ceftriaxone, IV, 2 g daily for 7 days.

Adjust antibiotics according to culture and sensitivity results.

AND

- Ceftazidime, intravitreal, 2.25 mg.

AND *LoE:III*[iii]

- Vancomycin, intravitreal, 1 mg.

Administer using separate tuberculin syringes. *LoE:III*[iv]

Post-surgical endophthalmitis

Specialist initiated, vitrectomy often required:

- Ceftazidime, intravitreal, 2.25 mg.

AND

- Vancomycin, intravitreal, 1 mg.

Administer using separate tuberculin syringes.

In addition, if there is soft tissue involvement or as prophylaxis after a penetrating eye injury:

- Ciprofloxacin, oral, 750 mg 12 hourly for 7 days.

18.3 GLAUCOMA

H40.0-6/H40.8-9

DESCRIPTION

Glaucoma is characterised by damage to the optic nerve with associated visual field loss, for which raised intra-ocular pressure (IOP) is a primary risk factor. Glaucoma is classified as open-angle or angle-closure. Glaucoma may occur as a primary condition or secondary to other ocular conditions. The condition is usually bilateral, but may be unilateral or asymmetrical (especially with secondary causes).

Clinical features

Open-angle glaucoma:

» Mostly asymptomatic.
» History of gradual loss of vision in the affected eye or loss of visual field.
» Often suspected after seeing cupping of optic disc on routine fundoscopy or finding elevated intra-ocular pressure on screening.

Angle-closure glaucoma:

» Usually presents acutely with sudden onset of severe eye pain and redness, associated with nausea, vomiting and hemicranial headache.
» Loss of vision in the affected eye.
» Coloured haloes or bright rings around lights.
» Hazy-looking cornea.
» Fixed, semi-dilated pupil.
» Shallow anterior chamber.

» Severely elevated intra-ocular pressure. When measured with finger palpation, the affected eye feels hard, compared to the other eye.
» If intraocular pressure rises more slowly, the patients may be asymptomatic with gradual loss of vision.

MEDICINE TREATMENT

Open-angle glaucoma

Refer to an ophthalmology unit for diagnosis and initiation of treatment.

First line

ß-blocker:

- Non-selective β-blocker, e.g.:
- Timolol 0.25%, ophthalmic drops, instil 1 drop 12 hourly.

LoE:II[v]

OR

Selective β-blocker:

- Betaxolol 0.25–0.5%, ophthalmic drops, instil 1 drop 12 hourly.

LoE:III

Poor response despite adequate adherence:

ADD *LoE:II*[vi]

- Prostaglandin analogues, e.g.:
- Bimatoprost 0.01%, ophthalmic drops, instil 1 drop daily. *LoE:I*[vii]
  - As first line if patient has contra-indication to ß-blocker.
  - In place of ß-blocker if patient has intolerable side effects with ß-blocker or if there is no significant reduction in IOP with other medicines.
  - In combination with ß-blocker if there is significant reduction in IOP with ß-blocker.

Intolerance to prostaglandin analogue, or poor response:

- Alpha-agonist, e.g.:
- Brimonidine 0.15–0.2%, ophthalmic drops, instil 1 drop 12 hourly. *LoE:III*[viii]
  - Second line if patient allergic to prostaglandin analogue.
  - In place of prostaglandin analogue if there is no significant further reduction in IOP when adding prostaglandin analogue to ß-blocker.
  - In combination with ß-blocker and prostaglandin analogue if the patient still has progression of disease or target IOP is not reached.

Failure to respond:

Alternatives in consultation with a specialist:

Parasympathomimetic agent:

- Pilocarpine 1%, ophthalmic drops, instil 1 drop 6 hourly.

LoE:III

In severe cases, as a temporary measure before ocular surgery in consultation with a specialist:
Carbonic anhydrase inhibitor:
- Acetazolamide, oral, 250 mg 6 hourly. *LoE:II*[ix]

Angle-closure glaucoma (acute) H40.1 Institute initial therapy and then refer to an ophthalmology unit.

Try to achieve immediate reduction in IOP:
- Acetazolamide, oral, 500 mg immediately as a single dose.
  - Followed by 250 mg 6 hourly.

AND
- Timolol 0.25–0.5%, ophthalmic drops, instil 1 drop 12 hourly.

Also treat patient for associated pain and nausea. See sections 12.4.1: Perioperative analgesics and 12.6.5.2: Treatment of PONV.

Where those measures fail, for short-term use only:
- Mannitol, IV, 1.5–2 g/kg as a 20% solution over 30–60 minutes.

OR

Glycerol, oral, 1 g/kg of 50% solution as a single dose immediately.

REFERRAL
All to an ophthalmology unit.

18.4 HERPES ZOSTER OPHTHALMICUS
B02.2* + (G53.0*)

DESCRIPTION
Herpes zoster ophthalmicus occurs when the varicella-zoster virus reactivates in the trigeminal ganglion and passes down the ophthalmic division of the trigeminal nerve. Patients present with a painful vesicular rash in the trigeminal V1 area – vesicles on the tip of the nose indicate nasociliary branch involvement, which increases the risk of ocular involvement. A minority of patients may develop conjunctivitis, keratitis, uveitis, retinitis, and cranial nerve involvement (oculomotor or optic nerves). Permanent sequelae of ophthalmic zoster infection may include chronic ocular inflammation, loss of vision, and debilitating post-herpetic neuralgia. All patients should be offered HIV testing.

MEDICINE TREATMENT
- Aciclovir, oral, 800 mg 4 hourly while awake for 7–10 days.

Note: Treatment should be initiated within the first three days of onset of symptoms, except in HIV-infected patients who should be treated if there are active skin lesions.

LoE:III

Post-herpetic neuralgia:
Initiate treatment with adjuvant therapy (i.e. amitriptyline) early. *LoE:II*[x]
See section 26.1.4: Management of neuropathic pain (Post-herpetic neuralgia).

REFERRAL
» Vesicles on the tip of the nose.
» Fluorescein staining of cornea shows corneal/ulceration.
» Decreased vision.
» Red eye (uveitis or keratitis).
» Cranial nerve palsies.

18.5 KERATITIS

18.5.1 KERATITIS, HERPES SIMPLEX
B00.5† + (H19.1*)

DESCRIPTION
Acute unilateral painful red eye with visual blurring and decreased corneal sensation. Characteristic dendritic corneal ulcer seen on staining with fluorescein.

MEDICINE TREATMENT
- Aciclovir 3%, ophthalmic ointment inserted in the lower conjunctival sac five times per day at 4 hour intervals.
  - Continue for 3 days after ulcer has healed.

If aciclovir 3% ophthalmic ointment is unavailable:
- Aciclovir, oral, 400 mg five times daily for 10–14 days. *LoE:II*[xi]

Note: Topical corticosteroids are contraindicated for treating dendritic ulcers.

18.5.2 KERATITIS, SUPPURATIVE
H16.8

DESCRIPTION
Painful red eye with corneal lesion that stains with fluorescein and has creamy white appearance. Contact lenses are a major risk factor, especially for fungal infections. Have a high index of suspicion for fungal infection if HIV positive or there is a history of injury to eye with plant matter.

MEDICINE TREATMENT
Empiric therapy until culture results become available:
Bacterial infection:
- Fluoroquinolone ophthalmic drops, e.g.:
- Ciprofloxacin 0.3%, ophthalmic drops, instil 1 drop hourly for 3 days.

- Then reduce frequency to 1 drop 3–4 hourly.

LoE: III[xii]

Fungal infection:

- Natamycin 5%, ophthalmic drops, instil 1 drop 1–2 hourly for 3–4 days. (Specialist prescribed).
  - Then reduce frequency to 1 drop 3–4 hourly.
  - Continue for 14–21 days until resolution of infection.

REFERRAL

» Hypopyon (pus in the anterior chamber)
» No facilities for microscopy, culture and sensitivity.

18.6 RETINITIS, HIV CMV

H30.9 + (B20.2)

DESCRIPTION

Cytomegalovirus (CMV) retinitis is seen in advanced HIV infection, with CD4 count <100 cells/mm^3. The characteristic retinal appearance is that of necrosis, i.e. white exudates, and hemorrhages at the edges of the exudates. Visual loss is irreversible – the goal of therapy is to limit further loss.

MEDICINE TREATMENT

Limited CMV retinitis:

- Valganciclovir, oral, 900 mg 12 hourly for the first 3 weeks, then 900 mg daily until immune recovery (CD4 >100) and a minimum of 3 months of therapy with valganciclovir (if available).

LoE:I[xiii]

  - Monitor FBC weekly during induction, then monthly as valganciclovir can cause bone marrow suppression. Avoid concomitant zidovudine use.
  - Initiate ART 2 weeks after starting induction therapy.

If valganciclovir is not available:

- Ganciclovir, intravitreal, 2 mg once a week (specialist)
  - Once immune function has been restored with antiretroviral therapy (CD4 >100) and the features of active retinitis has cleared, maintenance ganciclovir can be stopped but monitor for recurrence.

REFERRAL

To ophthalmologist for confirmation of diagnosis.

18.7 UVEITIS

H20.0

DESCRIPTION

Inflammation of the uveal tract and adjacent structures. The commonest

form is acute anterior uveitis, which presents with pain and photophobia, variable loss of vision, circumcilliary injection, and a miotic pupil. Chronic uveitis may lead to cystoid macular oedema with decreased central acuity, cataract formation, and secondary glaucoma. Numerous systemic diseases can cause uveitis.

MEDICINE TREATMENT

- Cycloplegic agent, e.g.:
- Homatropine 2 %, ophthalmic drops, instil 1–2 drops 3–4 hourly.

OR

Atropine 1%, ophthalmic drops, instil 1 drop 12 hourly.

AND

LoE:III[xiv]

- Corticosteroids, e.g.:
- Dexamethasone 0.1%, ophthalmic drops, instil 1–2 drops 4–6 hourly.

LoE:III[xv]

REFERRAL

All, for management at an ophthalmology unit.

18.8 SURGICAL AND DIAGNOSTIC PRODUCTS

Ocular peri-operative pharmaceutical products

- Sodium hyaluronate 10 mg/mL
- Acetylcholine chloride (for intra-ocular irrigation)
- Sterile intraocular irrigating solution

Ocular diagnostic products

- Fluorescein 2%, ophthalmic drops
- Fluorescein ophthalmic strips
- Tropicamide 1%, ophthalmic drops
- Cyclopentolate 2 mg/mL ophthalmic drops (for cycloplegic refraction)
- Cyclopentolate 2 mg/mL and phenylephrine 10 mg/mL (for fundoscopic examination)
- Polyacrylic acid 2 mg/g ophthalmic gel (as coupling liquid for diagnostic contact lenses)

- **Local anesthetics used on the eye**
- Oxybuprocaine hydrochloride 0.4%

LoE:III[xvi]

Preparations for tear deficiency

- Hydroxypropyl methylcellulose 0.3–0.5%

18.9 DRY EYE

H04.1

DESCRIPTION

Dry eye occurs when there is inadequate tear volume or function.
The common symptoms include feelings of dryness, grittiness, burning and foreign body sensation, usually worse during the day. A stringy discharge, redness and transient blurring of vision are also common.
Allergic conjunctivitis should be excluded.

GENERAL MEASURES

The management of dry eye involves controlling the symptoms, since the disease is generally not curable.
Patients should be educated to avoid over the counter topical medications, many of which exacerbate dryness, and control their environmental factors (e.g. encourage frequent blinking during visually attentive tasks, avoid air conditioners or heating, use humidifiers).

MEDICINE TREATMENT

Tear substitutes:

- Hydroxypropyl methylcellulose, ophthalmic drops, 1 drop, 6 hourly.

OR *LoE:III*[xvii]

Lanolin, anhydrous liquid, ophthalmic ointment, at night.

LoE:III[xviii]

18.10 MEDICAL MANAGEMENT OF EYE INJURY

18.10.1 CHEMICAL BURN

This is a medical emergency.
See Primary Health Care Standard Treatment Guidelines and Essential Medicine List, 2018; section 18.3.1: Eye injury, chemical burn.

18.10.2 EYE INJURY: BLUNT/PENETRATING/ FOREIGN BODY

See Primary Health Care Standard Treatment Guidelines and Essential Medicine List, 2018; sections 18.3.2 Eye injury/foreign bodies and 18.3.3: Eye injury (blunt or penetrating).

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CHAPTER 19
POISONING

POISONS INFORMATION CENTRES

Poisons Information Helpline (national service)	24 hours/day, every day for poisons queries	0861 555 777
Red Cross War Memorial Children's Hospital Poisons Information Centre Email: poisonsinformation@uct.ac.za http://www.paediatrics.uct.ac.za/poisons-information-centre	Office Hours	(021) 658 5308
Tygerberg Poison Information Centre Email: toxicology@sun.ac.za www.sun.ac.za/poisoncentre	Office Hours	(021) 938 9596
University of the Free State Poison Control and Medicine Information Centre	24 hours/day	082 491 0160
Telephone numbers tested September 2019		

Access poison information at: https://www.afritox.co.za/

ENVENOMATION

Envenomation is an instance of poisoning by venom resulting from a bite or sting from an animal such as a snake, spider, scorpion, insect or marine life.

19.1 INSECT BITES AND STINGS

T63.4 + (X29.99/X23.99) + External Cause Code (V,W,X,Y)

DESCRIPTION

Toxicity due to insect bites and stings usually results in local effects only and systemic effects are rare. Occasionally, hypersensitivity reactions are encountered, varying from minor local inflammation to acute anaphylaxis.

Multiple bee stings can result in toxicity and may require ICU care.

GENERAL MEASURES

Allergic reactions may be acutely life threatening.
Patients with multiple stings may develop delayed systemic toxicity. Beware of premature discharge from the healthcare facility.

MEDICINE TREATMENT

Anaphylaxis: See section 20.1.2: Anaphylaxis/Anaphylactic Shock.

For pain:

- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

LoE:III

19.2 SNAKEBITES

T63.0 + (X20.99/W59.99)

DESCRIPTION

In the majority of snakebite incidents, the offending snake is not identified. The table below illustrates the three main envenomation syndromes seen in South Africa: cytotoxic, neurotoxic and haemotoxic.

Venom type	Cytotoxic	Neurotoxic	Mixed cytotoxic and neurotoxic	Haemotoxic
Snake species	Puff adder, Gaboon adder, spitting cobras(Mozambique, black-necked, zebra), stiletto snake, night adders, horned adders	Black and green mamba, non-spitting cobras (Cape, forest, snouted)	Rinkhals, Berg adder, Peringuey's adder, desert mountain adder, garter snakes, shield-nose snake, coral snake	Boomslang, vine snakes
Clinical features of envenomation	Pain, swelling, bruising, blisters, necrosis, regional lymphadenopathy, hypotension, coagulopathy, compartment syndrome	Pins and needles, metallic taste, visual disturbances, ptosis, drowsiness, sweating, drooling, dysphagia, progressive weakness, respiratory paralysis	Combined cytotoxic and neurotoxic features	Spontaneous bleeding (can present late >24 hours after bite), headaches, dizziness, fainting
Antivenom (when indicated)	Polyvalent antivenom for Puff adder, Gaboon adder and spitting cobras only	Polyvalent antivenom for all species	Polyvalent antivenom for rinkhals only	Boomslang monovalent antivenom for boomslang bites only

To view pictures for identification of snakes click on following hyperlink: http://www.cmej.org.za/index.php/cmej/article/view/2546/2581

GENERAL MEASURES

Most snake bites will not result in death.
Supportive and symptomatic management with/without antivenom is required.
Mechanical ventilation may be needed in some cases of neurotoxic envenomation.
Cases of haemotoxic envenomation may require fluid resuscitation including blood products.

MEDICINE TREATMENT

Cleanse wound:

- Chlorhexidine 0.05% in water.

Antibiotics are seldom needed, except for secondary infection:
T79.3+(X20.99/W59.99)

- Amoxicillin/clavulanic acid, oral, 875/125 mg 12 hourly for 5 days.

LoE:III[i]

Immunisation, primary or booster: (Z23.5)

- Tetanus toxoid vaccine, IM, 0.5 mL immediately.

In unimmunised or partially immunised patients:

- Tetanus immunoglobulin, human, IM, 250 units immediately.

Analgesia
For mild pain:

- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

OR

For severe pain:
ADD

- Morphine, IV, to a total maximum dose of 10 mg (See Appendix II, for individual dosing and monitoring for response and toxicity).
  - Opioids should be used cautiously in neurotoxic snakebite.

LoE:III

Note: The use of NSAIDs is not recommended due to the antiplatelet effect and the potential danger of renal failure in a hypotensive patient.

LoE:III[ii]

19.2.1 CYTOTOXIC AND NEUROTOXIC SNAKEBITE

T63.0 + (X20.99)

MEDICINE TREATMENT

Polyvalent antivenom
Used in some cytotoxic and neurotoxic envenomations, only when indicated

Obtainable from South African Vaccine Producers (tel: (011) 386-6063/2/78 or afterhours 0716809897 or 0828842971). See package insert for full details.

Note: *LoE:III*[iii]

» In most cases, patients do not need and should not be given antivenom.
» Adverse reactions to antivenom are common and may be severe. Pre-medication with adrenaline (epinephrine) may reduce the risk of severe adverse reactions to polyvalent snake antivenom.
» The dose of antivenom is the same for adults and children.
» Monitor for any deterioration in respiratory function as patients may need ventilation whether or not polyvalent antivenom has been given.
» Antivenom should be given as soon as possible, however administration may be considered even as late as 48-72 hours after the bite, if there is continued clinical deterioration indicating ongoing venom activity.

LoE:III[iv]

Indications for polyvalent antivenom:

» Signs of neurotoxicity.
» Positively identified puff adder, Gaboon adder, Mozambique spitting cobra or rinkhals bites AND evidence of progressive severe cytotoxicity.
» Unidentified snakebites and evidence of progressive severe cytotoxic envenomation i.e.:
  - swelling of whole hand or foot within 1 hour
  - swelling to the knee or elbow in less than 6 hours
  - swelling of the whole limb in less than 12 hours
  - swelling progression >2.5 cm per hour
  - a threatened airway due to swelling
  - evidence of complication e.g. compartment syndrome

Systemic evidence of severe cytotoxicity includes:

» shock
» haematological abnormalities: INR >1.5, Hb <8 g/dL, thrombocytopaenia (<100 x 10^9/L) or leucocytosis (>10 x 10^9/ L)
» arrhythmias (rare)

LoE:III[v]

Note: Polyvalent antivenom is ineffective against the venom of:

» night adders, berg adders and other smaller adders,
» boomslang, and
» vine/twig snakes.

Caution
Never administer antivenom without being prepared to manage acute anaphylaxis.

Administration and polyvalent antivenom dose:

- Pre-treat with adrenaline (epinephrine), SC, 0.25 mL of 1:1000 solution.

(Contraindicated in patients with IHD, stroke, uncontrolled hypertension and tachyarrhythmia). LoE:I[vi]

- Polyvalent snake antivenom, slow IV infusion.
  - 1 ampoule contains 10 mL antivenom. LoE:III[vii]
    - Cytotoxic snakebite: give 50 mL.
    - Neurotoxic snakebite: give 80–100 mL (and up to 200 mL in black mamba bites).
    - Mozambique spitting cobra bite: give 100 mL. LoE:III[viii]
  - Dilute in sodium chloride 0.9%, 100–200 mL.
  - Administer IV, over 30 minutes.
  - Reassess once the infusion is completed. A repeat dose may be given if there is ongoing progression of neurotoxic or cytotoxic features.

19.2.2 BOOMSLANG SNAKEBITE

T63.0 + (X20.99)

DESCRIPTION

Boomslang venom is haemotoxic. A consumptive coagulopathy usually sets in within 6–36 hours after the bite with hypofibrinogenaemia and bleeding.

In suspected boomslang bite, a whole blood clotting time is a useful bedside test, especially in rural areas. Place 5 mL of blood in a dry glass test tube and leave at room temperature for 20 minutes. Normal clotting time varies from 5–20 minutes. It is important to repeat these over a few days.

Other investigations include FBC, activated PTT, prothrombin time (INR), fibrinogen, D-dimer and monomers.

Note: Polyvalent antivenom is not effective in boomslang bite.

Boomslang monovalent antivenom

Indicated for all boomslang bites with evidence of haemotoxicity

Obtainable from South African Vaccine Producers (tel: +2711 386-6063/2/78 or afterhours 0716809897 or 0828842971). See full details in the package insert**.**

Caution
Never administer antivenom without being fully prepared to manage acute anaphylaxis.

- Boomslang monovalent antivenom, slow IV infusion, 20 mL diluted in 50–100 mL sodium chloride 0.9% or dextrose 5%, administered over 5–10 minutes. LoE:III[ix]
  - The dose of antivenom is the same for adults and children.
  - Spontaneous systemic bleeding should stop within 15–30 minutes and blood coagulability be restored within 6 hours, after administering

antivenom.
- o Re-evaluate regularly, and if after 6 hours there is ongoing evidence of coagulopathy, a repeat dose of 10 ml may be considered.

19.2.3 SNAKE VENOM IN THE EYE

S05.9 + (X20.99)

DESCRIPTION

Snake venom in the eye, particularly from various species of spitting cobras and rinkhals, can cause local cytotoxic effects. Clinical presentation ranges from periocular swelling and mild conjunctival and corneal inflammation, to frank corneal ulceration and perforation with eventual blindness.

MEDICINE TREATMENT

Instil local anaesthetic:

- Tetracaine 1%, ophthalmic drops, instill 1 drop into the affected eye(s) before irrigation.
- Irrigate the eye thoroughly for 15–20 minutes with water or sodium chloride, 0.9% to dilute or remove the toxin.
- Apply chloramphenicol ointment and cover the affected eye with an eye patch. *LoE:III*

Note: Do not instil polyvalent antivenom in the eye or give systemically.

LoE:III[x]

REFERRAL

Refer all patients to an ophthalmologist.

19.3 SCORPION ENVENOMATION

T63.2 + (X22.99)

DESCRIPTION

Medically important scorpions in Southern Africa are of the genus *Parabuthus* (*P. granulatus* and *P. transvaalicus*). These are large scorpions measuring 7–15 cm in length. Features useful in their identification are a relatively large tail and small pincers, so-called thick-tailed scorpions. Scorpions from the Scorpionidae family (e.g. Hadogenes, Opistophthalmus) are thin-tailed with large pincers.

To view pictures for identification of scorpions click on following hyperlink: http://www.cmej.org.za/index.php/cmej/article/view/2545/2580

A sting from thin-tailed scorpions is likely to result in local pain requiring analgesia only.

Clinical features of thick-tailed scorpion stings include:

Local effects:
» immediate and excruciating pain
» local paraesthesias and hyperaesthesia

Systemic effects:
» tremors, involuntary movements and fasciculations
» muscle pain, cramps, and weakness
» generalised paraesthesias and hyperaesthesia
» excessive sympathetic stimulation e.g. sweating, tachycardia
» excessive parasympathetic stimulation e.g. hypersalivation, vomiting and diarrhoea, priapism
» bulbar paralysis (dysphagia, dysarthria)
» respiratory difficulty/failure

GENERAL MEASURES

Observe all cases of thick-tailed scorpion stings for at least 12 hours.
Monitor respiratory function.
Ventilatory support may be required.

MEDICINE TREATMENT

Scorpion antivenom therapy is recommended only in cases presenting with systemic neurotoxic effects.

Obtainable from South African Vaccine Producers (tel: +2711 386-6063/2/78 or afterhours 0716809897 or 0828842971). See full details in the package insert**.**

- Scorpion antivenom, IV infusion, 10 mL diluted in 100 mL sodium chloride 0.9% or dextrose 5%, administered over 10 minutes.
  - Response to antivenom may be slow and a repeat dose may be needed.

LoE:III

CAUTION
Never administer antivenom without being prepared to manage acute anaphylaxis.

Immunisation, primary or booster: (Z23.5)
- Tetanus toxoid vaccine, IM, 0.5 mL immediately.

In unimmunised or partially immunised patients: (Z23.5)
- Tetanus immunoglobulin, human, IM, 250 units immediately.

Analgesia

For pain:
- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

LoE:III[xi]

Severe local pain:

- Lidocaine 1–2%, 2 mL: infiltrate affected area as a local anaesthetic.

LoE:III[xii]

Opiates increase the risk of respiratory depression and if required, should only be used with caution in severe uncontrolled pain.

LoE:III[xiii]

Severe muscle pain and cramps:

- Calcium gluconate 10%, bolus IV infusion, 10 mL over 10 minutes.
  - Repeat if needed, only once

Note: Effect may only last for 20–30 minutes and there is a limited amount that can be given.

LoE:III[xiv]

19.4 SPIDER ENVENOMATION

T63.3 + (X21.99)

DESCRIPTION

Local venomous spiders are divided into cytotoxic and neurotoxic groups.
To view pictures for identification of spiders click on following hyperlink:
http://www.cmej.org.za/index.php/cmej/article/view/2547/2582

Cytotoxic spider group

The cytotoxic group includes sac, violin and crab spiders.
Lesions may present with significant bite site necrosis, for which surgical debridement may be required. Bites can take weeks/months to heal.
Note: Antibiotics are reserved for secondary infection.

Neurotoxic spider group

The neurotoxic group is represented by the button spider (also known as widow spiders), genus *Latrodectus*. Black button spiders are more venomous than brown button spiders.

Features useful in the identification of the black button spider are:

» Black or dark brown colour.
» Variable red markings on the dorsal aspect of the abdomen, which diminish with age. It has no ventral markings.

Features of brown button spider:

» Light brown to creamy yellow to pitch black in colour
» Typical red-orange hourglass-shaped marking on the ventral surface of the abdomen.

Envenomation from black button spiders may cause:

» Immediate local burning pain and tender regional lymph nodes within an hour.

» Severe general muscle pain, cramps and rigidity especially of the large girdle muscles
  - Causes feeling of tightness of the chest and board-like rigidity of a non-tender abdomen.
  - Lasts for days to a week if antivenom is not given.
» Profuse sweating may be prominent.
» Diffuse paraesthesia, especially of the hands and feet.

GENERAL MEASURES

Observe all cases of potential neurotoxic spider bite for at least 24 hours.

MEDICINE TREATMENT

» Spider antivenom is only indicated for systemic symptoms of neurotoxicity in patients with button spider bites.
» Obtainable from South African Vaccine Producers (tel: +2711 386-6063/2/78 or afterhours 0716809897 or 0828842971). See full details in the package insert**.**

- Spider antivenom, IV infusion, 5–10 mL diluted in 50–100 mL sodium chloride 0.9% or dextrose 5%, administered over 5–10 minutes.

LoE:III[xv]

Caution
Never administer antivenom without being prepared to manage acute anaphylaxis.

Immunisation, primary or booster: (Z23.5)
- Tetanus toxoid vaccine, IM, 0.5 mL immediately.

In unimmunised or partially immunised patients: (Z23.5)
- Tetanus immunoglobulin, human, IM, 250 units immediately.

Analgesia

For mild pain:
- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

Severe muscle pain and cramps:
- Calcium gluconate 10%, bolus IV infusion, 10 mL over 10 minutes.
  - Repeat if needed.

Note: Effect may only last for 20–30 minutes and there is a limited amount that can be given.

LoE:III[xvi]

For secondary infection:
See section 4.2: Cellulitis and Erysipelas.

POISONING

DESCRIPTION

Frequently encountered poisonings in adults include:

- » analgesics
- » hydrocarbons
- » pesticides
- » anti-infectives
- » antihistamines
- » ethanol/alcohol
- » cardiodepressants
- » anticonvulsants
- » toxic alcohols e.g. methanol, ethylene glycol
- » sedatives, antidepressants and antipsychotics
- » iron
- » irritants and corrosives

Suspect intentional ingestion in adults.

DIAGNOSTIC CRITERIA

Clinical

Can be divided into ‘toxidromes”:

Cholinergic: e.g. organophosphates

- » salivation
- » lacrimation
- » urination
- » miosis (pinpoint pupils)
- » diarrhoea
- » vomiting
- » bronchorrhoea
- » bradycardia

Salicylism: e.g. aspirin

- » tachypnoea
- » metabolic acidosis
- » seizures
- » agitation
- » coma

Anticholinergic: e.g. antihistamines, amanita pantherina, atropine

- » fever
- » ileus
- » flushing
- » tachycardia
- » urinary retention
- » dry/warm skin
- » blurred vision
- » mydriasis (dilated pupils)
- » coma
- » hallucinations and seizures

Sedative-hypnotic: e.g. alcohol, benzodiazepines

- » obtundation or coma

Opiates: e.g. morphine

- » miosis (pinpoint pupils)
- » respiratory depression
- » bradycardia
- » hypotension.
- » decreased bowel sounds
- » hypothermia
- » altered (decreased) mental status

Dystonic reaction: e.g. haloperidol

- » torticollis
- » opisthotonus
- » intermittent spasms and tongue thrusting

Sympathomimetic: e.g. cocaine, amphetamines

- » hypertension
- » tachycardia
- » hyperthermia
- » agitation
- » sweating
- » dilated pupils

Sympathomimetic toxidrome partly resembles anticholinergic toxidrome, i.e. fight, flight and fright response, however the sympathomimetic toxic patient is sweaty as opposed to hot dry skin seen with anticholinergic toxicity.

Toxic alcohols: e.g. ethylene glycol, methanol

- » metabolic acidosis
- » increased osmolar and anion gap
- » visual disturbances (methanol)
- » depressed level of consciousness.
- » hypoglycaemia
- » convulsions
- » renal failure (ethylene glycol)

GENERAL MEASURES

It is very important to ascertain if a TOXIC DOSE has been taken BEFORE instituting any potentially harmful decontamination procedures in an asymptomatic patient.

Take a complete and accurate history, ascertain all relevant facts and do a complete clinical examination. A high index of suspicion is important.
Obtain a collateral history, especially for patients with impaired consciousness. A special effort should be made to obtain tablets, packets, containers, etc. to identify agents involved.

Stabilise the patient and monitor basic clinical parameters, i.e.:

- » blood pressure and heart rate
- » hydration
- » airway and ventilation
- » neurological status
- » temperature
- » glucose

Persistent or prolonged seizures may require medical management. Phenytoin should not be used in cases of poisoning due to substances known to be cardiotoxic e.g. tricyclic antidepressants, or where there is evidence of clinical cardiotoxicity.

Prevent physical injury in the restless - avoid excessive sedation.

Limit toxicology investigations to those that may influence/alter management. It is important to note the time after ingestion when blood was taken in order to correctly interpret results (e.g. paracetamol, iron levels).

LoE:III

DECONTAMINATION

Limit further exposure to poison for the patient and protect healthcare workers where necessary.

i. Topical exposure

In case of skin exposure, remove clothes and wash the body. Showering may be useful.
Remove eye contaminants, especially alkalis, acids and other irritants, by continuous irrigation of the eye with sterile water or normal saline for 15–20 minutes. Analgesic eye drops may be required to perform this adequately.

ii. Gut decontamination

Methods of gut decontamination include:

- Gastric lavage
- Activated charcoal administration
- Whole bowel irrigation

Gastric lavage

If deemed beneficial, it should only be performed by experienced staff and within 60 minutes of ingestion. *LoE:III*[xvii]

Can be considered for cases with:

» potentially life-threatening ingestions AND
» a protected airway i.e. fully awake and cooperative or intubated with a depressed level of consciousness.

Gastric lavage is contra-indicated after ingestion of corrosive substances and volatile hydrocarbons such as paraffin.

Technique:

Place patient in left lateral head down position
Insert orogastric tube if possible, with largest bore and rounded tip.
Insert 200ml warmed water or normal saline, and aspirate.
Continue until recovered solution is clear of particulate matter.

Activated charcoal

May reduce systemic absorption of a variety of poisonous substances. The greatest benefit is achieved if activated charcoal is given within one hour after ingestion; however where gastric emptying is delayed by certain substances, there may be a longer period of time in which it is effective. Activated charcoal must only be given in cases where the airway is protected; i.e. fully awake and cooperative patient or intubated with a depressed level of consciousness.

Repeated doses of activated charcoal (i.e. 50 g every 4 hours) are effective in enhancing elimination of substances that undergo enterohepatic circulation, e.g. carbamazepine, dapsone, phenobarbitone, quinine or theophylline overdose.

LoE:III[xviii]

Charcoal may be useful if these poisons are taken in toxic dose	Poisons where charcoal is ineffective and should not be given
» carbamazepine, barbiturates, phenytoin » dapsone, quinine » theophylline » salicylates » mushroom poisoning (Amanita phalloides) » slow release preparations » digoxin » beta-blockers » NSAIDs	» ethanol, methanol, ethylene glycol » brake fluid » petroleum products (e.g. petrol or paraffin) » iron salts » lead, mercury, arsenic » lithium » strong acids or alkalis » other corrosive agents (e.g. household detergents)

- Charcoal, activated, oral, 50 g (equivalent to 36 level medicine measures) diluted in 100 mL water.
  - When mixing, add a small amount of water to charcoal in a container.
  - Cap and shake container to make a slurry and then dilute further.

LoE:III[xix]

Whole bowel irrigation

Whole bowel irrigation can be done for potentially toxic ingestions of substances that are:

» not absorbed by activated charcoal (e.g. iron and lithium)
» sustained-release and enteric-coated products
» or for removal of illicit drugs in body packers

Patients must have a protected airway i.e. fully awake and cooperative or intubated with a depressed level of consciousness.

- Polyethylene glycol (PEG) balanced electrolyte solution, NGT,
  - 1500–2000 mL/hour.
  - Continue until rectal effluent is clear.

LoE:III[xx]

OTHER TREATMENT MODALITIES

Urinary alkalinisation (e.g. severe salicylate or tricyclic antidepressant poisoning)

Caution
This is a high risk procedure and should only be performed in consultation with a specialist.

Haemodialysis

Patients with symptomatically severe poisoning e.g. due to salicylates, lithium, ethylene glycol, methanol, ethanol and theophylline, may benefit from dialysis (http://www.extrip-workgroup.org/).
Refer patient to a hospital with dialysis facilities.

Antidotes

There are a limited number of antidotes for poisoning by certain substances, e.g. N-acetylcysteine for paracetamol, naloxone for opioids. Each antidote has specific criteria and indications for use.

Once medically stable:

Assess and manage intentional poisoning – self-harm or harm by others:

» take a history of circumstances around the poisoning, substance use and mental illness, and examine the mental state
» assess further suicide risk – see Primary Health Care STGs and EML, section 16.7: Suicide risk assessment.
» refer to social, psychological and/or psychiatric services

Assess and manage a substance use disorder

» quantify the amount of substance used and related harms, e.g. with

ASSIST (http://www.who.int/substance_abuse/activities/assist/en/) or DUDIT (https://paihdelinkki.fi/sites/default/files/duditmanual.pdf) rating scales and discuss with patient
» provide brief intervention with motivational interview
» refer for rehabilitation

REFERRAL
» Severely ill patient for ventilatory/circulatory support.
» Relevant diagnostic testing not available, e.g. paracetamol levels, acid/base assessment.
» Relevant medication/antidote not available.
» Dialysis/haemoperfusion required.

19.5 ANALGESIC POISONING

19.5.1 PARACETAMOL POISONING
T39.1 + (X40.99/X60.99/Y10.99)

DESCRIPTION
Liver damage, due to the depletion of glutathione and accumulation of toxic metabolites, can occur in any individual with paracetamol overdose. Patients with predisposing risk factors for hepatotoxicity ("high risk" patients, see below) may experience toxicity at lower ingested doses.

Clinical features
Gastrointestinal symptoms (anorexia, nausea, vomiting, malaise) predominate in the first 0.5-24 hours. Patients with normal or only slightly raised serum paracetamol levels usually continue to full recovery. In patients with significantly raised paracetamol levels, hepatic toxicity (right upper quadrant abdominal pain and tenderness, elevated bilirubin, raised liver enzymes, coagulation defects, hypoglycaemia, encephalopathy and metabolic acidosis) may manifest from 20-24 hours, peaking in severity at about 72-96 hours. Patients may make a full recovery in 5-7 days, or demise from hepatic failure, or less commonly, renal failure.

"High risk" patients include:
» Chronic alcoholism
» Chronic liver disease
» Use of enzyme-inducing medicines (e.g. carbamazepine, phenytoin, efavirenz, phenobarbitone, rifampicin etc.)
» Depletion of glutathione resources (e.g. malnutrition, starvation, AIDS, chronic illness, eating disorders etc.)
» Patients with recent illness, dehydration

Treatment:
The treatment of paracetamol overdose depends on the dose ingested and the time of presentation since ingestion. A serum paracetamol level is plotted on the nomogram to assess the risk for hepatotoxicity. Values which appear above the treatment line require the antidote N-acetylcysteine (NAC).

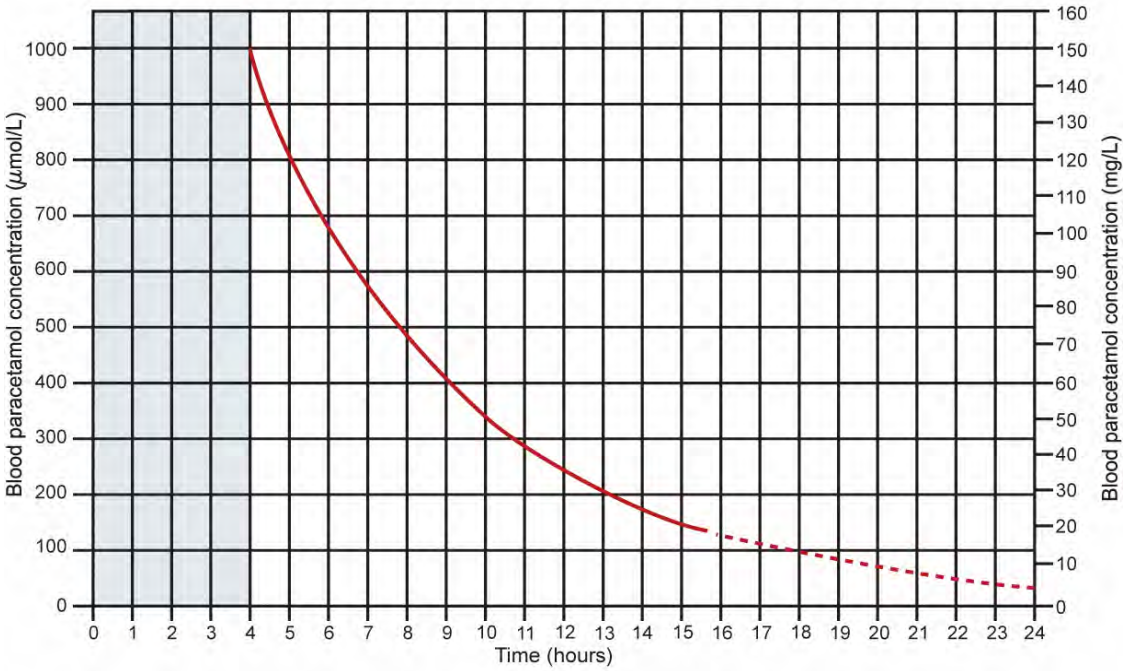
Acute single ingestion <8 hours post-ingestion:
Toxic dose defined as >200 mg/kg or 10 g (whichever is less).
Give activated charcoal if the patient presents within 1-2 hours of ingestion
Perform a serum paracetamol level 4 hours post-ingestion
If serum paracetamol level results will not be available before 8 hours post-ingestion, and the patient has taken a toxic dose, do not delay initiation of NAC. It can always be stopped if the serum level plotted on the nomogram does not indicate its continued use.

Acute single ingestion >8 hours post-ingestion:
Toxic dose defined as >200 mg/kg or 10 g (whichever is less).
Start NAC infusion if a toxic dose has been ingested or the patient shows clinical signs of toxicity.
Perform serum paracetamol level, INR and ALT.

Indications for continuing NAC infusion:
» serum paracetamol level above the treatment line on the nomogram
» serum paracetamol level under the treatment line but abnormal ALT
» more than 24 hours post-ingestion, measurable paracetamol level and/or abnormal ALT

Acute single ingestion with unknown time of ingestion
Manage as for >8 hours post-ingestion.

Paracetamol treatment nomogram



Source: Daly FF, Fountain JS, Murray L, Graudins A, Buckley NA; Panel of Australian and New Zealand clinical toxicologists. Guidelines for the management of paracetamol poisoning in Australia and New Zealand-explanation and elaboration. A consensus statement from clinical toxicologists consulting to the Australasian poisons information centres. Med J Aust. 2008 Mar 3;188(5):296-301.

LoE:III[xxi]

(Access the paracetamol nomogram tool on the EML Clinical Guide cellphone application).

Repeated supratherapeutic ingestion (RSTI):

This may occur in patients using repeated high doses of the same product or concurrent use of multiple paracetamol-containing products such as during an acute febrile illness or in patients with chronic pain.

RSTI toxic doses are defined as:

» >200 mg/kg or 10 g (whichever is less) over a single 24-hour period.
» >150 mg/kg or 6 g (whichever is less) per 24-hour period for the preceding 48 hours.
» >100 mg/kg or 4 g/day (whichever is less) per 24-hour period for more than 48 hours ***and*** patients have symptoms suggestive of liver injury.

MEDICINE TREATMENT

LoE:III[xxii]

N-acetylcysteine is the antidote of choice and should be given intravenously. Although it is more effective when given within 8 hours of ingestion of paracetamol, there may be benefit even if liver failure has developed.

Histamine may be released, which mimics an allergic reaction. If this occurs and the patient is stable, infusion may continue at a slower rate under antihistamine cover. In the presence of bronchospasm, stop the infusion.

- N-acetylcysteine, IV:
  - Initial infusion: 200 mg/kg in 500 mL 5% dextrose over 4 hours

- Second infusion: 100 mg/kg in 1000 mL 5% dextrose over 16 hours.
- Any further N-acetylcysteine is given according to the second infusion regimen.

LoE:III[xxiii]

If N-acetylcysteine, IV is unavailable:

- N-acetylcysteine, oral, 140 mg/kg, followed by 70 mg/kg 4 hourly for seventeen doses**.**

Note: Avoid giving activated charcoal if using oral N-acetylcysteine, as it will reduce systemic absorption of the antidote.

LoE:III[xxiv]

Further investigations and referral

Blood tests such as renal function, clotting profile, serum glucose and acid/base status should only be done where clinically indicated.

Patients who develop liver failure must be referred for further management and/or possible transplant.

19.5.2 SALICYLATE POISONING

T39.0 + (X40.99/X60.99/Y10.99)

DESCRIPTION

Mild to moderate toxicity:

» Nausea, vomiting, tinnitus, fever, tachypnoea and respiratory alkalosis

Severe toxicity:

» Metabolic acidosis, altered mental status, seizures, coma, non-cardiogenic pulmonary oedema.

Note: Wintergreen oils/ ointments contain 98 % methyl salicylate.

GENERAL MEASURES

» Assess severity with history, clinical examination and salicylate levels if possible.
» Correct hydration.
» Consider ICU admission for pulmonary and/or cerebral oedema.

MEDICINE TREATMENT

- Salicylates delay gastric emptying, therefore activated charcoal may be effective for a longer period than usual.
- Whole bowel irrigation maybe useful for enteric-coated or modified-release preparations.

LoE:III[xxv]

Treat acidosis and enhance renal excretion:

- Sodium bicarbonate, IV and urinary alkalinisation (blood pH 7.45-7.5 and urine pH 7.5–8.5) in consultation with specialist and arrange for transfer.

LoE:III

REFERRAL

Where acidosis does not respond to sodium bicarbonate, refer for haemodialysis. *LoE:III*[xxvi]

19.5.3. OPIOID POISONING

T40.2 + (X42.99/X62.99/Y12.99)

DESCRIPTION

Patients present with the triad of CNS depression, respiratory depression and constricted pupils. Non-cardiogenic pulmonary oedema can occur.

GENERAL MEASURES

Supportive management aimed at maintaining cardiorespiratory function.

Body packers/stuffers:

» Patients may ingest packages of heroin, and are at great risk of life-threatening toxicity in the event of rupture.
» Abdominal X-rays or CT scan may show packages.
» Conservative management is recommended, as any attempt at removal risks package rupture.
» Activated charcoal and whole bowel irrigation may aid in expelling packets.
» Surgery is reserved for those who develop obstruction or perforation.

MEDICINE TREATMENT

- Naloxone, IV, 0.4 mg immediately, in patients with significant respiratory depression.
  - Effectiveness is limited by a half-life (± 1 hour) that is shorter than most opioids; therefore repeated incremental doses may be needed at 2 to 3 minute intervals, followed by a naloxone infusion.
  - If there is no response after a maximum of 10 mg of naloxone is administered, the diagnosis of opioid-induced or partial opioid-induced toxicity should be questioned.
  - Consider intramuscular or subcutaneous administration, if the intravenous route is not available.
  - **Note:** Clinical response is measured by reversal of respiratory depression, as the level of CNS depression improves. Continuous monitoring is required for all patients who received naloxone.

LoE:III[xxvii]

19.6 ANTIDEPRESSANT POISONING

19.6.1. TRICYCLIC ANTIDEPRESSANT POISONING

T43.0 + (X41.99/X61.99/Y11.99)

DESCRIPTION

Patients can deteriorate rapidly. They may have:

Mild to moderate poisoning:

» Sedation
» Tachycardia
» Anticholinergic effects:
- delirium,
- dilated pupils,
- urinary retention, or
- dry mouth.

Severe Poisoning:

» QRS widening, ventricular dysrhythmias
» Coma
» Hypotension
» Seizures
» Pulmonary oedema

GENERAL MEASURES

Do a baseline ECG in all patients.

» ICU admission for ventilatory/circulatory support, when indicated. Be prepared to intubate symptomatic patients early.
» Discharge patients only when
- asymptomatic, or
- mild symptoms/signs of toxicity and ECG has normalised for 24 hours.

MEDICINE TREATMENT

Tricyclic antidepressants delay gastric emptying, therefore activated charcoal may be effective for a longer period than usual.

<u>Serum alkalinisation for all patients with:</u>

» ventricular dysrhythmias,
» prolonged QRS >100 msec
» hypotension unresponsive to fluids or
» seizures.

- Sodium bicarbonate, IV 1–2 mEq/kg as an 8.4% solution, as bolus doses to achieve a pH of 7.45–7.55 (Specialist consultation).
  - Monitor acid-base status, serum potassium and sodium.
  - If sodium bicarbonate is unavailable or fluid restrictions limit intake, consider hyperventilation of intubated patients.

LoE:III[xxviii]

In severe cases, inotropic support and anti-arrhythmics may be required (See section 3.3: Cardiac dysrythmias) in addition to serum alkalinisation.

Hypotension is due to myocardial dysfunction and alpha-adrenergic vasodilation; be careful not to fluid overload the patient.

LoE:III

For seizures or if sedation is required for restlessness:
Treat with benzodiazepines - see section: 14.4.1 Status epilepticus.
Note: Phenytoin should be avoided (due to potential cardiotoxicity).

LoE:III[xxix]

Note: The use of flumazenil is not recommended in any patient with mixed overdoses possibly including tricyclic antidepressants as it increases the risk of convulsions and dysrhythmias.

LoE:I[xxx]

19.7 IRON POISONING

T45.4 + (X44.99/X64.99/Y14.99)

DESCRIPTION

Iron is a commonly prescribed drug, especially in pregnancy, and in overdose causes initial gastrointestinal toxicity.
Patients may have a stage of “apparent recovery” 6–36 hours post-ingestion. This should not be confused with true recovery as patients may subsequently deteriorate.

Significant exposure may be associated with:
- » severe vomiting and diarrhoea
- » metabolic acidosis,
- » CNS depression,
- » hepatitis.
- » gastrointestinal haemorrhage
- » hypotension, shock
- » renal failure, and

Ferrous salt	Amount	Elemental iron
Ferrous sulphate	170 mg	±65 mg
Ferrous gluconate	300 mg	35 mg
Ferrous fumarate	200 mg	±65 mg

GENERAL MEASURES

Gastrointestinal decontamination by whole bowel irrigation is recommended:
- » if >60 mg/kg elemental iron has been ingested
- » if modified-release preparations ingested
- » undissolved tablets still visible on abdominal X-ray

Activated charcoal does not bind iron and is not indicated in isolated iron overdose.
Serum iron concentration should be measured 4–6 hours after ingestion and repeated every 6 hours until peak. The use of desferrioxamine interferes with the interpretation of further serum iron levels.
Give intravenous fluids for hypotension.

MEDICINE TREATMENT

Chelation therapy

Patients with serum iron levels <54 micromol/L and absence of symptoms >6 hours after overdose do not require chelation therapy.

Desferoxamine (deferoxamine) may be used for the following indications. If in doubt, consult the Poisons Information Helpline):

» Severe symptoms (altered mental status, hemodynamic instability, metabolic acidosis).
» Serum iron concentration >90 micromol/L.
» Peak serum iron concentration >60 micromol/L, AND persistent gastrointestinal symptoms.

- Desferoxamine (deferoxamine), IV infusion, 15 mg/kg/hour to a total of 80 mg/kg, i.e. given over about 6 hours. Beware of hypotension.
  - **Note:** Prolonged use >24 hours of high doses is associated with acute lung injury and should be avoided. However, in severe poisonings, additional doses may be required. *LoE:III*[xxxi]
  - Desferoxamine can be used in pregnant women. *LoE:III*[xxxii]

REFERRAL

Haemodialysis may be needed to remove desferoxamine-iron complexes in patients with renal insufficiency.

19.8 THEOPHYLLINE POISONING

T48.6 + (X44.99/X64.99/Y14.99)

DESCRIPTION

Patients present with:

» tachycardia and tachyarrhythmias,
» nausea and vomiting
» agitation
» seizures
» hyperventilation
» tremor
» profound hypokalaemia

GENERAL MEASURES

Monitor ECG and treat dysrhythmias.
Monitor and correct fluid status and electrolyte abnormalities.
Monitor theophylline concentrations, if available. Levels may continue to rise up to 24 hours after ingestion of modified release preparations.

MEDICINE TREATMENT

Vomiting is common: (R11)

- Metoclopramide, IV/oral, 10 mg 8 hourly as required.
- Activated charcoal. *LoE:III*
  - Multiple doses of activated charcoal enhance *LoE:III*[xxxiii]

elimination.

Correct hypokalaemia cautiously:
E87.6 + (T48.6/X44.99/X64.99/Y14.99)

- Potassium chloride, IV, maximal dose 40 mmol/L and maximal rate of 20 mmol/hour. *LoE:III*[xxxiv]

For seizures: R56.8 + (T48.6/X44.99/X64.99/Y14.99)
Treat with benzodiazepines - see section: 14.4.1 Status epilepticus.
Note: Phenytoin should be avoided (due to potential cardiotoxicity).
LoE:III[xxxv]

REFERRAL
In patients with symptoms of severe overdose (severe hypokalaemia, seizures, refractory hypotension, dysrhythmias, theophylline level >555 micromol/L (100 mg/L), refer for haemodialysis.
LoE:III[xxxvi]

19.9 SEDATIVE HYPNOTIC POISONING

19.9.1 BENZODIAZEPINE POISONING
T42.4 + (X44.99/X64.99/Y14.99)

DESCRIPTION
Patients present with depressed levels of consciousness, confusion, ataxia and dysarthria. Benzodiazepines are unlikely to cause significant respiratory depression unless co-ingested with alcohol or other CNS depressants.

However, in the elderly, the danger of respiratory depression with overdose exists.

Management is supportive and ventilation may be required.

Note: The use of flumazenil is not recommended in any patient with possible benzodiazepine poisoning as it increases the risk of convulsions and dysrhythmias. *LoE:I*[xxxvii]

19.9.2 LITHIUM POISONING
T43.9 + (X44.99/X69.99/Y14.99)

DESCRIPTION
Lithium toxicity mostly occurs with chronic therapy and may be precipitated by decreased excretion due to renal dysfunction, diuresis, dehydration, hyponatraemia or drug-drug interactions (e.g. NSAIDs, diuretics, ACE-inhibitors and ARBs).

Signs and symptoms include:

» nausea and vomiting
» diarrhoea
» nystagmus
» CNS symptoms: tremor, hyperreflexia, choreoathetoid movements, fasciculations, ataxia, agitation, confusion and lethargy

In severe toxicity:

» coma
» seizures
» dysrhythmias
» hypotension

GENERAL MEASURES

Whole bowel irrigation may be considered with a potentially toxic ingestion or ingestion of sustained-release products.

LoE:III[xxxviii]

Monitor:

» Vitals signs, mental status and urine output
» If available, do serial lithium levels 6 hourly until peaked and declining.
» Electrolytes and renal function.
» Fluid status: administer sodium chloride 0.9 % to maintain urine flow of 1–2 mL/kg/hour but prevent hypernatremia.
» Cardiac function and treat dysrhythmias (see chapter 3.3: Cardiovascular dysrhythmias).
» Thyroid function, in chronic toxicity.

MEDICINE TREATMENT

Correct electrolyte abnormalities: see section: 7.2 Major electrolyte abnormalities.

For seizures: R56.8 + (T43.9/X44.99/X69.99/Y14.99)
Treat with benzodiazepines - see section: 14.4.1 Status epilepticus.
Note: Phenytoin should be avoided (due to potential cardiotoxicity).

LoE:III[xxxix]

REFERRAL

Early referral for haemodialysis is indicated in severe lithium poisoning and in patients with renal impairment. Discuss with a specialist.

LoE:III[xl]

19.10 ISONIAZID POISONING

T37.1 + (X44.99/X64.99/Y14.99)

DESCRIPTION

Acute toxicity can present with the classic triad of seizures, metabolic acidosis and coma.
Seizures are generalised tonic-clonic and often refractory to standard anticonvulsant therapy.

GENERAL MEASURES

Supportive management aimed at preventing and managing complications.
Treat hyperthermia.

MEDICINE TREATMENT

For seizures:

- Pyridoxine, crushed tablets orally or via NGT in unconscious patient(s).
  - 1 g for every gram of isoniazid ingested (maximum of 5 g), or
  - 5 g for unknown amount ingested.

LoE:III[xli]

Benzodiazepines may be used as an interim measure to control seizures:

- Lorazepam, IV/IM, 4 mg, repeat once after 5–10 minutes, if necessary.

LoE:III[xlii]

OR

Diazepam, IV, 10 mg, not faster than 2 mg/minute, repeat once after 5–10 minutes if necessary.

OR

Clonazepam, IV, 2 mg, repeat once after 5–10 minutes if necessary.

OR

Midazolam, IM/IV 10 mg, repeat once after 5–10 minutes if necessary.

OR

Midazolam buccal, 10 mg using the parenteral formulation.

Phenytoin should not be used to control seizures in INH poisoning, as it does not have GABA agonist properties.

LoE:III[xliii]

REFERRAL

Uncontrolled seizures

19.11 CALCIUM CHANNEL BLOCKER AND BETA BLOCKER POISONING

T46.1

DESCRIPTION

Cardiovascular toxicity results in profound hypotension, bradycardia, decreased systemic vascular resistance and cardiogenic shock. Depressed level of consciousness and metabolic acidosis are consequent upon poor tissue perfusion. Hyperglycaemia and hypokalaemia may occur.
Patients who have co-ingested other cardiac medicines and those with pre-existing cardiac disease are at increased risk of morbidity.

The treatment of suspected cardiogenic shock in calcium channel blocker and beta blocker poisoning follows similar therapeutic principles. The

mainstay of treatment is high-dose insulin euglycaemia therapy and catecholamine infusions to improve inotropy and chronotropy.

LoE:III[xliv]

GENERAL MEASURES

Monitor vital signs, ECG and blood glucose.
Treat symptomatic patients in consultation with a specialist.

MEDICINE TREATMENT

» Caution is advised for all decontamination procedures as they increase vagal tone and may exacerbate bradycardia.
» Activated charcoal may be considered before the onset of symptoms.
» Whole bowel irrigation can be considered for ingestion of modified-release preparations.

LoE:III[xlv]

Treat hypotension: I95.9 + (T46.1/X44.99/X64.99/Y14.99)

- Sodium chloride, IV, 0.9%.

LoE:III[xlvi]

If hypotension not effectively controlled add:

- Calcium gluconate 10%, IV, 30–60 mL given over 15–30 minutes, with ECG monitoring.
  - This may be repeated a maximum of 4 times.

LoE:III[xlvii]

Treat bradycardia: R00.1 + (T46.1/X44.99/X64.99/Y14.99)

- Atropine, IV 0.5–1 mg every 2–3 minutes to a maximum of 3 mg.

LoE:III[xlviii]

Use vasopressors as needed, e.g. adrenaline (epinephrine) infusion for persistent hypotension (section 20.1: Cardiac arrest) or dobutamine for bradycardia (section 20.1.5: Cardiogenic shock).

REFERRAL

Refer for management with high dose insulin for resistant hypotension and bradycardia, in a high care or ICU setting.

LoE:III[xlix]

If glucose <10 mmol/L:

- Dextrose 50%, IV, 50 mL.

Followed by:

- Insulin, short acting, IV, 1 unit/kg.
  - Followed by 0.5 unit/kg/hour.
  - Titrate dose up until hypotension is corrected, to maximum 10 units/kg/hour.

Monitor and correct potassium and glucose.

LoE:III[l]

19.12 COTRIMOXAZOLE POISONING

T37.0

DESCRIPTION

In acute overdose, low toxicity expected. Symptoms include nausea and vomiting, dizziness, headache and neurological symptoms (such as drowsiness, confusion and mental depression). Other signs include bone marrow depression, haematuria and renal insufficiency. Hypersensitivity reactions may occur.

GENERAL MEASURES

Treatment is symptomatic and supportive.
Monitor FBC, electrolytes, glucose, hepatic and renal function in symptomatic patients.

19.13 ANTIRETROVIRAL AGENTS POISONING

T37.5

DESCRIPTION

Limited data is available regarding overdose of these medicines.
Toxicological effects are generally extensions of adverse effects.

GENERAL MEASURES

Monitor FBC, serum electrolytes, renal and liver function.
Monitor serum lipase in patients with abdominal pain.
Lactic acid and serum pH should be monitored in acidotic patients.

TREATMENT

There are no specific antidotes.
Treatment is symptomatic and supportive.

19.14 ILLICIT DRUGS

19.14.1 COCAINE POISONING

T40.5 + (X42.99/X65.99/Y12.99)

DESCRIPTION

Cocaine may be absorbed through any mucous membrane, smoked, ingested or injected intravenously.

Mild toxicity: euphoria, anxiety, altered mental status, tachycardia, mild hypertension

Moderate toxicity: agitation, paranoia, hallucinations, cardiac dysrhythmias
Severe toxicity: severe headache, seizure, hyperthermia, rhabdomyolysis, severe acidosis, vascular incidents (stroke, MI, intestinal ischaemia etc.), pulmonary oedema.

GENERAL MEASURES

Supportive management aimed at preventing and managing complications.
Cool patients with hyperthermia.
Raised serum creatinine kinase may indicate rhabdomyolysis or myocardial infarction.

Body packers/stuffers:
» Patients may ingest packages of cocaine, and are at great risk of life-threatening toxicity in the event of rupture.
» Abdominal X-rays or CT scan may show packages.
» Conservative management is recommended, as any attempt at removal risks package rupture.
» Activated charcoal and whole bowel irrigation may aid in expelling packets.
» Surgery is reserved for those who develop obstruction or perforation.

MEDICINE TREATMENT

For sedation and seizures: R56.8 + (T40.5/X42.99/X62.99/Y12.99)
Treat with benzodiazepines - see section: 14.4.1 Status epilepticus.
Note: Phenytoin should be avoided (due to potential cardiotoxicity).

LoE:III[li]

Delirium with severe agitation:
See section 20.8: Delirium with perceptual disturbances.

Arrhythmias:
See section 3.3: Cardiac dysrhythmias.

ß–blockers should not be used.

Severe hypertension:
See section 3.6.1: Hypertension, severe.

19.14.2 AMPHETAMINE DERIVATIVES POISONING

T43.6 + (X41.99/X61.99/Y11.99)

DESCRIPTION

These include:
» “Ecstasy”: 3,4-methylenedioxymethamphetamine (MDMA).
» “Ice” and “Eve”: 3,4-methylenedioxy-N-ethylamphetamine (MDEA).
» “Tik”: Methamphetamine.

Drug effects are due to the increased release of noradrenaline, dopamine and serotonin. Patients present with:

» hyperthermia, especially with MDMA
» tachycardia
» hypertension
» angina pectoris and myocardial infarction
» stroke
» hyperactivity
» sweating
» dilated pupils
» teeth grinding
» delirium
» tremors
» seizures and coma

Additional complications include:

» rhabdomyolysis
» hyperkalaemia
» acute tubular necrosis
» hyponatraemia
» dehydration

GENERAL MEASURES

Supportive management aims to maintain stable cardiorespiratory function.
Manage hyperthermia, hypoglycaemia, dehydration, and electrolyte abnormalities.

MEDICINE TREATMENT

For seizures: R56.8 + (T43.6/X41.99/X61.99/Y11.99)
Treat with benzodiazepines - see section: 14.4.1 Status epilepticus.
Note: Phenytoin should be avoided (due to potential cardiotoxicity).

LoE:III[iii]

Severe hypertension:
See section 3.6.1: Hypertension, severe.

Haemodialysis may be required for acute renal failure.

19.15 HYDROCARBON POISONING

T52.0

DESCRIPTION

Poisoning due to petroleum products, including paraffin, turpentine, petrol, mineral spirits. (This section does not include information on aromatic hydrocarbons (e.g. benzene, toluene, xylene) often used by glue sniffers to get high).

Clinical signs include:

» chemical pneumonitis,
» arrhythmias, and
» GIT effects,
» CNS effects.

GENERAL MEASURES

If contaminated, remove clothing and wash skin.
Do not induce emesis or attempt gastric emptying/lavage.

MEDICINE TREATMENT
Activated charcoal is of no value.
Observe and examine for chemical pneumonitis. Prophylactic antibiotics are not indicated.

19.16 INGESTION OF CAUSTIC SUBSTANCES
T54.3/T54.2

DESCRIPTION
Alkaline: Toilet bowl cleaners, drain cleaners, oven cleaners.
Acids: Various e.g. domestic descalers.
Depending on the concentration, caustic substances cause necrosis of the gut mucosa and underlying tissue resulting in possible strictures later.

GENERAL MEASURES
No activated charcoal, forced emesis or gastric lavage.
Rinse mouth with copious amounts of cold water.
Make patient nil by mouth and set up IV access.
If persistent vomiting, drooling or any difficulty in swallowing, patient may require endoscopic evaluation within 24-48 hours and possible surgical intervention. (Discuss with a specialist). *LoE:III*[liii]

19.17 ALCOHOLS

19.17.1 ETHANOL POISONING
T51.0 + (X45.99/X65.99/Y15.99)

DESCRIPTION
Acute poisoning usually presents with:
» nausea and vomiting,
» central nervous system depression,
» hypoglycaemia,
» hypothermia,
» hypokalaemia
» acidosis.
Consider other causes for the patient's condition, including hypoglycaemia and head trauma.

GENERAL MEASURES
Supportive management aimed at maintaining stable cardiorespiratory function.
Protect the airway (ventilation may be needed).
Manage hypothermia, hypoglycaemia, and electrolyte abnormalities.

MEDICINE TREATMENT

- Thiamine, IV, 100 mg in 1 L dextrose 5%.

19.17.2 ETHYLENE GLYCOL POISONING

T52.8 + (X46.99/X66.99/Y16.99)

DESCRIPTION

Ethylene glycol is the main component of motor vehicle radiator coolant/antifreeze and is occasionally found in brake fluid. It is also found in homemade toilet and drain cleaners.

Mild to moderate intoxication: Resembles alcohol intoxication, with nausea and vomiting, nystagmus, ataxia and somnolence.

Severe intoxication:
Associated with more severe CNS depression (coma, hypotonia, hyporeflexia) and high anion gap metabolic acidosis. Cardiovascular signs include tachycardia and hypertension. Calcium oxalate crystals cause renal failure and hypocalcaemia, which may manifest with prolongation of the QT interval or tetany.

Anion gap calculation = Na – (Cl + HCO3) (Normal = 8-16)

GENERAL MEASURES

Immediate consultation with the Poisons Information Helpline is important.
Early treatment with antidote may prevent formation of toxic metabolites.
Monitor blood gases and administer sodium bicarbonate
Early haemodialysis is the treatment of choice for severe poisoning with profound acidosis.

MEDICINE TREATMENT

Ethanol
Indications:
History of ingestion, plus any two of the following criteria:

» Arterial pH <7.3
» Serum bicarbonate <20 mmol/L
» Presence of urinary oxalate crystals (ethylene glycol only) or visual disturbances (methanol only) *LoE:III[liv]*

Dose:

- Ethanol 95% BP, oral,
  - Loading dose 1 mL/kg
  - Maintenance dose:
    - non-drinker: 0.125 mL/kg/hr
    - chronic drinker: 0.2 mL/kg/hr
  - Dilute the calculated ethanol volume to 20% (1:5) in any suitable liquid.

OR

- Ethanol 40% (gin, whiskey, vodka), oral
  - Loading dose: 2 mL/kg
  - Maintenance dose:
    - non-drinker: 25 mL/kg/hour
    - chronic drinker: 0.5 mL/kg/hour
  - Dilute the calculated ethanol volume to 20% (1:2) in any suitable liquid.

LoE:III[lv]

Note:

» If patients are not co-operative, administer ethanol via a nasogastric tube.
» Maintain ethanol levels of 1–1.3 g/L (100–130 mg/dL).
» The dose of ethanol needs to be increased if the patient is receiving concomitant haemodialysis.
» Several days of ethanol therapy may be required until clinical condition improves.

LoE:III[lvi]

Cofactor therapy:

- Thiamine, oral, 100 mg daily.

- Pyridoxine, oral, 100 mg daily.

LoE:III

Metabolic acidosis E87.2 + (T52.8/X46.99/X66.99/Y16.99)

- Sodium bicarbonate, IV, 50–100 mmol/L administered over 30–45 minutes**.**

Note:

» Rapid correction of acidosis may precipitate seizures in a hypocalcaemic patient. Correct severe or clinically evident hypocalcaemia.
» Monitor glucose levels and correct hypoglycaemia, if necessary.

LoE:III[lvii]

REFERRAL

Severe poisoning with profound acidosis for early haemodialysis.

19.17.3 METHANOL POISONING

T51.1

DESCRIPTION

No longer found in methylated spirits as methanol replaced with less toxic agents 10-20 years ago. Methanol may be found in stove or model fuels, or in antifreeze and windscreen washes. Methanol may result in an ethanol-like inebriation in the early phase.

Presentation:

» Ingestion of methanol results in initial mild inebriation (headache, confusion, nausea and vomiting) followed by an asymptomatic period.

» Later, toxic metabolite (formic acid) formation results in severe high anion gap metabolic acidosis, and retinal toxicity (with visual impairment to total blindness).

Anion gap calculation = Na – (Cl + HCO3) (Normal = 8-16)

MEDICINE TREATMENT

If acidotic or visual disturbances;

Start with immediate ethanol antidote therapy (See section 19.15.2: Ethylene glycol poisoning), and evaluate for urgent dialysis, if available.

LoE:III[lviii]

19.18 PESTICIDES AND RODENTICIDES

19.18.1 AMITRAZ POISONING

T44.6+ (X43.99/X63.99/Y13.99)

* Notifiable condition.

DESCRIPTION

Amitraz is a pesticide/insecticide which is an α_2-adrenergic agonist. It is usually formulated as a tick dip for dogs, cattle and sheep. Commercial formulations contain up to 20% of amitraz in organic solvents. Poisoning may occur when amitraz is ingested or absorbed via the skin or by inhalation.

Where the history is of an unspecified rat poison or pesticide ingestion, consider other active ingredients such as super-warfarin anticoagulants and organophosphates.

Patients with acute poisoning present with:

» impaired consciousness
» drowsiness
» vomiting
» hypotension
» constricted pupils or rarely, dilated pupils
» bradycardia
» respiratory depression
» hypothermia
» generalized seizures

Other complications include:

» hyperglycaemia
» glycosuria
» mild increase in transaminases

Patients usually regain consciousness within 24 hours.

Note: Amitraz poisoning can be confused with organophosphate poisoning; whilst amitraz causes central nervous system depression, bradycardia, miosis and respiratory depression, it does not cause excessive sweating and salivation, urinary and faecal incontinence or muscle fasciculation which are

seen with organophosphate poisoning. Furthermore, organophosphate toxicity results in reduced serum pseudocholinesterase levels.

GENERAL MEASURES

Decontamination of skin and clothes where applicable.
Supportive and symptomatic treatment to maintain patent airway, adequate respiration and circulation.
Mechanical ventilation may be needed in some cases.
Keep patient warm.

MEDICINE TREATMENT

- Activated charcoal, once patient is stabilised.

For severe bradycardia: R00.1 + (T44.6/X43.99/X63.99/Y13.99)
Manage with atropine - see section 3.3.3: Heart block (second or third degree). *LoE:III*

For seizures: R56.8 + (T44.6/X43.99/X63.99/Y13.99)
Treat with benzodiazepines - see section: 14.4.1 Status epilepticus.
Note: Phenytoin should be avoided (due to potential cardiotoxicity).

LoE:III[lix]

19.18.2 ORGANOPHOSPHATE POISONING

T60.0 + (X48.99/X68.99/Y18.99)
* Notifiable condition.

DESCRIPTION

Absorption occurs through the skin, when the agent is taken orally, or by inhalation.

Patients present with muscarinic and nicotinic manifestations of intoxication.

- Peripheral effects:
  - *Muscarinic overstimulation:* bradycardia, hypotension, salivation, lacrimation, vomiting, diarrhoea, increased bronchial secretions, bronchospasm and miosis (pin point pupils).
  - *Nicotinic overstimulation:* muscle weakness and fasciculations, tachycardia, hypertension, mydriasis (dilated pupils).
- Central effects: coma, confusion, convulsions

Diagnosis is supported by low serum pseudocholinesterase levels.

Intermediate syndrome can occur within 1-4 days after recovery from cholinergic crisis. Patients develop weakness or paralysis predominantly affecting the muscles of respiration (including the neck flexors and bulbar muscles) and proximal limb muscles, sparing the distal muscles. Cranial nerves may also be affected. Supportive care is the mainstay of therapy.
Refer if ventilatory support is unavailable. *LoE:III*[lx]

Where the history is of an unspecified rat poison or pesticide ingestion, consider other active ingredients such as super-warfarin anticoagulants and amitraz.

GENERAL MEASURES

Ensure use of personal protective equipment for staff – gloves, gowns and eye protection. If staff come into contact with body fluids, wash off immediately. *LoE:III*[lxi]

Decontamination procedures for the patient should only be done once the patient is fully resuscitated.

Remove patient's clothes and wash the body with soap and water. Place clothes in closed bags.

Maintain adequate ventilation and circulation. Ventilatory support in ICU may be required. Suction secretions frequently. If using suxamethonium for intubation, consider that metabolism may be delayed and prolonged respiratory support may be required. Use alternative agents if possible (See section 12.3: Muscle relaxants).

MEDICINE TREATMENT

- Activated charcoal, once patient is stabilised.

<u>For bronchorrhoea, bronchospasm or bradycardia:</u>

- Atropine bolus, IV, 2–5 mg,
  - Reassess after 3–5 minutes for evidence of atropinisation as indicated by reduced bronchial secretions, dry skin, increasing heart rate and blood pressure, and dilating pupils (note: pupil dilatation may be delayed) *LoE:II*[lxii]
  - Give repeated atropine boluses incrementally doubling the dose until adequate clinical response achieved, e.g. 2 mg, 4 mg, 8 mg, 16 mg etc.
    - If no clinical response, give double the dose.
    - If some response, give the same or reduced dose.
  - Follow with infusion. Calculate the total dose of atropine given as boluses (as described above). Give 10–20% of this dose per hour.
  - Reassess frequently and adjust atropine infusion as follows:
    - Bronchial secretions, bronchospasm or bradycardia recurs: increase dose.
    - Good control of bronchial secretions and signs of atropine overdose (tachycardia, mydriasis, agitation, pyrexia, reduced bowel sounds and urinary retention): decrease dose.
    - No recurrence of bronchial secretions and no signs of atropine overdose: reduce dose slowly.

Note: Do not stop atropine infusion abruptly, but wean over *LoE:III*[lxiii]

at least 24 hours. Tachycardia and mydriasis are not contraindications for giving atropine in the acute resuscitation setting.

For severe agitation:

- Diazepam, IV, 5–10 mg, immediately.
  - Repeat after 30–60 minutes if needed. *LoE:III*[lxiv]

REFERRAL

Refer if ventilatory support is unavailable.

19.18.3 PARAQUAT POISONING

T60.3 + (X48.99/X68.99/Y18.99)
* Notifiable condition.

DESCRIPTION

Paraquat poisoning causes multi-organ failure and is often fatal. Following oral ingestion, patients present with oral, oesophageal and gastric erosions with severe gastroenteritis. Multi-organ failure develops, particularly renal and respiratory failure, within 1–3 days. Patients surviving the initial phase usually develop pulmonary fibrosis.

GENERAL MEASURES

Supportive and symptomatic management to maintain patent airway, adequate respiration and circulation. Mechanical ventilation maybe needed in some cases. The mainstay of treatment is palliative care.

Note: High inspiratory fraction of inspired oxygen (FiO_2) may worsen pulmonary toxicity. Supplemental oxygen should only be provided if the patient is confirmed hypoxic.

MEDICINE TREATMENT

- Activated charcoal.

19.19 ANTICOAGULANT (WARFARIN AND RODENTICIDE SUPERWARFARIN) POISONING

T45.5 + (X44.99/X64.99/Y14.99)
* Notifiable condition – rodenticide superwarfarin poisoning

DESCRIPTION

Poisoning due to ingestion of warfarin and superwarfarins, e.g. rat poison and other vermin poisons.

Warfarin toxicity can occur with either acute overdose or unintentionally, during therapeutic use, whereby drug interactions increase warfarin

bioavailability (e.g. concomitant enzyme inhibitor), or concomitant anticoagulant drugs are administered (e.g. NSAIDS).
Bleeding is the main clinical presentation e.g. gastrointestinal or intracranial bleeding; however bleeding may be occult.
Superwarfarins are more potent than warfarin and may have a long duration of effect; small doses of concentrated formulations may cause significant anticoagulation.
Measure INR at baseline and 48 hours post ingestion, as the anticoagulant effect may be delayed by 1–2 days.

Where the history is of an unspecified rat poison or pesticide ingestion, consider other active ingredients such as amitraz and organophosphates.

GENERAL MEASURES

Resuscitation.
Stop warfarin in patients on therapy.

MEDICINE TREATMENT

For patients on warfarin therapy

INR 5 to 9 without bleeding:

» Stop warfarin
» Evaluate bleeding risk
- High risk patients: (history of bleeding, stroke, renal insufficiency, anaemia, hypertension).
  - Vitamin K_1 oral, 1–2.5 mg, for 1–2 days and monitor INR.
- Low risk patients: Monitor INR.

INR >9 without bleeding:

» Stop warfarin.
- Vitamin K_1 oral, 2.5–5 mg, for 1–2 days and monitor INR (response usually in 24 to 48 hrs).

» Resume warfarin therapy, at a lower dose.

Vitamin K_1 is available as a parenteral preparation only, but is safest given orally in anticoagulant poisoning.

LoE:I[lxv]

Elevated INR with significant bleeding: R58 + (T45.5/X44.99/X64.99/Y14.99)

» Stop warfarin.

- Lyophilised plasma, IV, 15 mL/kg.

OR

FFP 15 mL/kg.

LoE:III[lxvi]

LoE:II[lxvii]

Followed by:

- Vitamin K_1, IV,10 mg diluted in 100 mL sodium chloride 0.9% over 20 minutes and monitor for prophylaxis.

LoE:III[lxviii]

Note:

» In patients with prosthetic heart valves, high dose vitamin K is associated with increased resistance to warfarin and increased risk of thromboembolism. Treat as above, but monitor INR frequently to prevent overcorrection in consultation with a specialist.

» In all patients on therapeutic warfarin, a major overdose or bleeding episode should prompt careful review of the need for anticoagulation

» **If warfarin is indicated it should be re-instituted, once the INR is in the therapeutic range.**

Rodenticide ingestion - Superwarfarins

Do not given prophylactic vitamin K.

INR >4 or the patient is actively bleeding: *LoE:III*[lxix]

- Vitamin K_1 oral, 10–25 mg, daily may be required.

Vitamin K_1 is available as a parenteral preparation only, but is safest given orally in anticoagulant poisoning.

Treatment with vitamin K_1 may need to be prolonged for several months as superwarfarins are very long acting.

19.20 CARBON MONOXIDE POISONING

T58 + (X47.99/X67.99/Y17.99)

DESCRIPTION

Poisoning caused by accidental or intentional exposure to fires in poorly ventilated areas, combustion engines, faulty stoves and faulty heating systems.

Patients present with:

» dizziness
» headache
» seizures and other CNS symptoms
» nausea and vomiting
» metabolic acidosis (severe)
» high arterial carboxyhaemoglobin levels
» impaired level of consciousness
» tachycardia
» chest pain
» retinal haemorrhages
» respiratory alkalosis (mild)

Note: There may be a normal arterial PaO2, but low oxygen saturation on pulse oximetry. Neither are useful in assessing severity of carbon monoxide poisoning. Ideally, a blood gas sample should be sent for co-oximetry to specifically detect carboxyhaemoglobin levels.

GENERAL MEASURES

Remove patient from toxic environment.

Ventilation may be needed in deeply comatose patients.
Monitor ECG and neurological status.

MEDICINE TREATMENT

- Oxygen, 100%, via positive pressure facemask.

For seizures: R56.8 + (T58/X47.99/X67.99/Y17.99)
Treat with benzodiazepines - see section: 14.4.1 Status epilepticus.
Note: Phenytoin should be avoided (due to potential cardiotoxicity).

LoE:III[lxx]

Metabolic acidosis:
Metabolic acidosis shifts the oxygen-dissociation curve to the right and therefore aids in maintaining tissue oxygenation despite reduced haemoglobin carrying capacity. Metabolic acidosis should only be treated if profound and persistent, following standard treatment protocols.

Patients should be followed up after discharge for the persistence of neurocognitive symptoms.

19.21 HEAVY METAL POISONING

T56.1/T57.0/T56.8/T56.4/T56.0/T56.3

DESCRIPTION

This includes mercury, arsenic, gold, copper, lead poisoning, thallium etc. Inhalation of metal fumes and particles results in metal fume fever. This may be confused with an acute viral illness with fever, cough, sweating, myalgia, headache etc. The course of the illness is usually benign.

The management of heavy metal toxicity depends on the specific metal, route of exposure and length of time between exposure and clinical presentation of symptoms. Discuss all potential patients with the Poisons Information Helpline for further investigation, treatment options and possible referral.

Metal	Signs and symptoms
Copper salts	GIT irritation, hepatotoxicity and haemolysis.
Arsenic	Impairs cellular respiration, resulting in multi-organ dysfunction.
Mercury	Clinical effects depend on the route of exposure and type of mercury (inorganic versus organic).
Lead	Chronic toxicity more common. Affects nervous, gastrointestinal, renal and haematopoietic systems.
Gold	Deposition of immune complexes in kidneys and skin; mucus membrane inflammation
Thallium	Alopecia and painful ascending peripheral neuropathy.

LoE:III[lxxi]

19.22 POISONING WITH SUBSTANCES THAT CAUSE METHAEMOGLOBINAEMIA

D74.9 + (T46.3/X44.99/X64.99/Y14.99)

DESCRIPTION

Substances causing methaemoglobinaemia include nitrites, nitroglycerine, dapsone, mothballs (naphthalene), local anaesthetics, phenazopyridine, chlorates and anilines.

Nitrites are used to cure meat in the formal and informal butchery sector.

Patients present with:

» Deep cyanosis with only mildly reduced oxygen saturation,

» CNS depression, and

» arrhythmias.

Note: Methaemoglobinaemia causes patients to appear cyanosed with falsely high conventional pulse oximetry readings and normal PaO2. Blood gas analysis using co-oximetry is required to specifically measure methaemoglobin levels.

MEDICINE TREATMENT

- Oxygen via facemask.

In symptomatic cases or patients with high methaemoglobin values > 30%:

- Methylene blue (methylthionine chloride) 1% dilute solution, slow IV infusion, 1–2 mg/kg administered over 5 minutes.
  - Repeat in 1 hour and, if necessary, 4 hourly up to total of 7 mg/kg.
  - Side effects include precordial pain, restlessness and dyspnoea.
  - After administration of methylene blue, oxygen saturation may drop initially.

In life-threatening cases, not responding to methylene blue or if methylene blue is not available, exchange transfusion may be considered. Refer to the Poisons Information Helpline for advice on treatment and possible alternatives to methylene blue.

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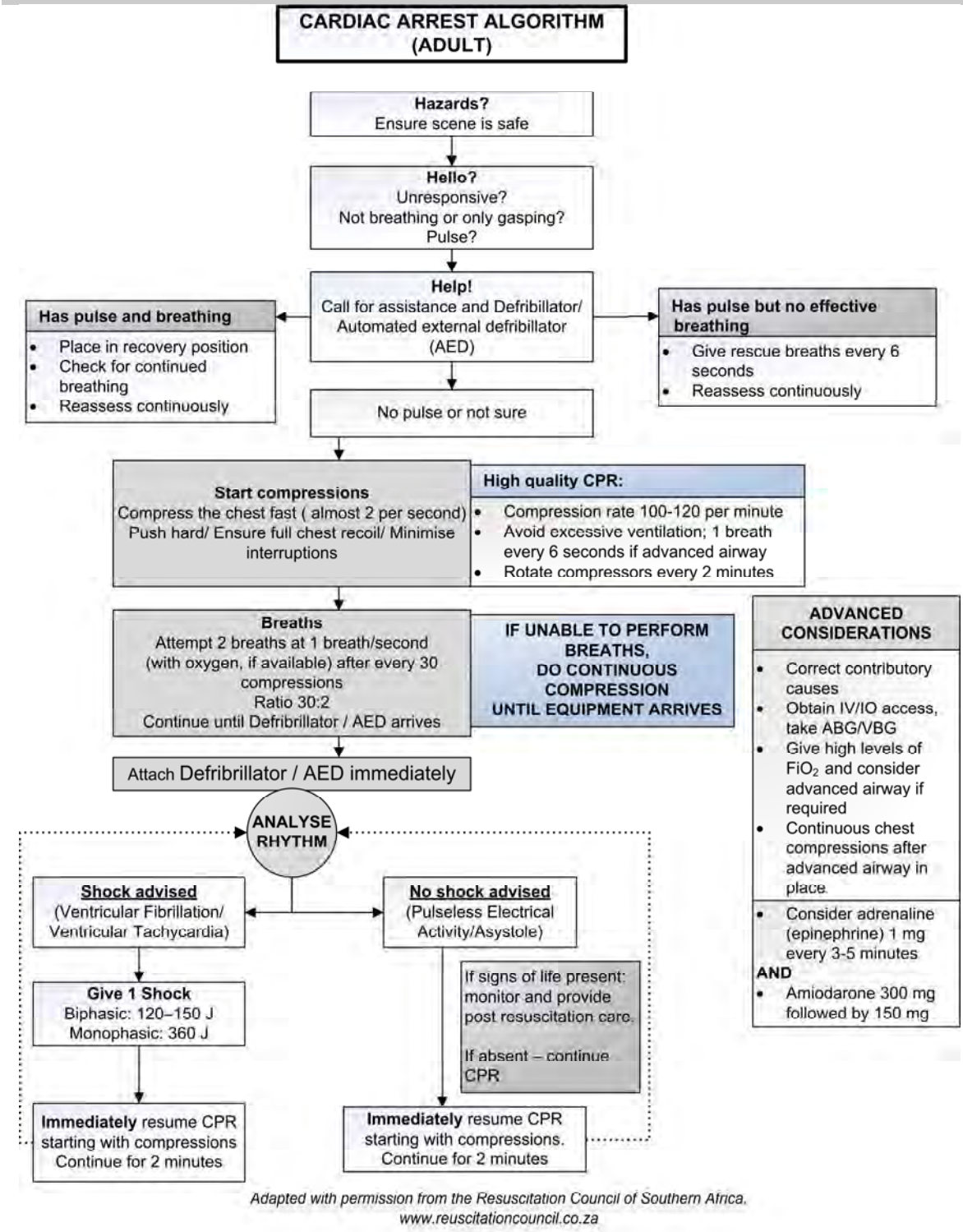
CHAPTER 20
EMERGENCIES AND INJURIES

CARDIAC ARREST – CARDIOPULMONARY RESUSCITATION



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www.reuscitationcouncil.co.za

Abbreviations: CPR = Cardiopulmonary Resuscitation; PEA = Pulseless Electrical Activity; VF = Ventricular Fibrillation; VT = Ventricular Tachycardia.

20.1 CARDIAC ARREST IN ADULTS

I46.0/I46.9

DESCRIPTION

Described as the loss of a heart beat and a palpable pulse, irrespective of the electrical activity captured on ECG tracing. Irreversible brain damage can occur within 2–4 minutes.

Clinical features include:
» sudden loss of consciousness, absent carotid pulses
» loss of spontaneous respiration

EMERGENCY TREATMENT

» Diagnose rapidly. After ensuring the safety of the scene, commence resuscitation as per acute adult cardiac arrest algorithm – as above
» Make a note of the time of starting resuscitation.
» Place the patient on a firm flat surface and commence resuscitation immediately.
» Call for skilled help and an automated external defibrillator (AED) or defibrillator.
» Initiate CAB (Circulation Airway Breathing) sequence of CPR (cardiopulmonary resuscitation).
» Where a defibrillator is not immediately available, a single powerful precordial thump is recommended for witnessed cardiac arrest.
» Document medication and progress after the resuscitation.

Cardiopulmonary resuscitation (CPR)

Circulation
» Check for carotid pulse for about 5 seconds.
» If there is no pulse or you are not sure, start with chest compressions at a rate of 100-120 compressions per minute. Push hard and allow full recoil of chest with minimum interruptions.

Airway and breathing
» To open the airway, lift the chin forward with the fingers of the one hand and tilt the head backwards with other hand on the forehead.
» **Note:** Do not do this where a neck injury is suspected – refer below for management of suspected neck injury.
» Do not do this where a neck injury is suspected – refer below for management of suspected neck injury
» Ensure airway is open throughout resuscitation.
» If there is no normal breathing, attempt 2 respirations with bag-valve-mask resuscitator and face mask.
» The administered breaths must cause visible chest rising in patient. If not, reposition and try again *once* and proceed to next step.
» Repeat the cycle of 30 compressions followed by 2 respirations for 5 cycles and then re-assess for a pulse.

» If advanced airway is placed, administer 1 breath every 6 second. Avoid excessive ventilation.
- Oxygenate with 100% oxygen.

Where neck injury is suspected:
» To open the airway, place your fingers behind the jaw on each side.
» Lift the jaw upwards while opening the mouth with your thumbs (jaw thrust).
» To open the airway, place your fingers behind the jaw on each side.
» Maintain in line cervical spine immobilisation.

Initiate fluids, IV/IO access
- Sodium chloride 0.9%. *LoE:I[i]*

If pulseless with shockable rhythm (ventricular fibrillation/tachycardia)
» Defibrillate, as indicated per algorithm.
» Immediately resume CPR. Starting with chest compression.
» Continue CPR for 2 minutes.
- Administer adrenaline (epinephrine) as per algorithm.
» Seek reversible cause of arrest.
» Continue CPR until spontaneous breathing and/or heart beat returns.
» For management of
» ventricular fibrillation or pulseless ventricular tachycardia that is unresponsive to defibrillation:
- Amiodarone, IV bolus, 300 mg, 2 minutes after adrenaline (epinephrine) dose.
  - Follow by a bolus of 10 mL sodium chloride 0.9%
  - Patient remains in a shockable rhythm following further 2 minutes of CPR, a defibrillation shock, another adrenaline (epinephrine) dose, and another 2 minutes of CPR (5 cycles of 30:2): Amiodarone, IV bolus, 150 mg.

LoE:I[ii]

If pulseless with non-shockable rhythm
» Immediately resume CPR. Starting with chest compression.
» Continue CPR for 2 minutes.
- Administer adrenaline as per algorithm.
» Seek reversible cause of arrest.
» Continue CPR until spontaneous breathing and/or heart beat returns.

Immediate emergency medicine treatment
Adrenaline (epinephrine) is the mainstay of treatment and should be given immediately, IV or intra-osseous, when there is no response to initial resuscitation or defibrillation.

- Adrenaline (epinephrine), 1:1 000, 1 mL, IV immediately, as a single dose. *LoE:I[iii]*
  - Flush with 5–10 mL IV of sterile water or sodium chloride, 0.9%.
  - Repeat every 3–5 minutes during resuscitation.

If no IV line is available:

- Adrenaline (epinephrine), intra-osseous (IO), 1:1000, 1 mL, via IO line. *LoE:III[iv]*
  - Flush with 5–10 mL of sterile water or sodium chloride 0.9%.
  - Repeat every 3–5 minutes during resuscitation.

» Assess continuously until the patient shows signs of recovery.
» Consider stopping resuscitation attempts and pronouncing death if:
  – further resuscitation is clearly clinically inappropriate, e.g. incurable underlying disease, all known reversible factors addressed or
  – no success after all the above procedures have been carried out for ≥ 30 minutes.
» Consider carrying on for longer especially when:
  – hypothermia and drowning, particularly in younger patients
  – poisoning or drug overdose or carbon monoxide poisoning

20.2 POST CARDIAC ARREST CARE

I46.0

DESCRIPTION

Post cardiac arrest care starts following successful CPR. During this time the patient is vulnerable to several processes, including:

» the underlying disease condition or injury causing the cardiac arrest
» post cardiac arrest haemodynamic instability
» post cardiac arrest brain injury
» the sequelae of global ischaemia and reperfusion.

Care should be aimed at reversing or minimising the above processes to optimise the likelihood of neurologically intact survival.

GENERAL MEASURES

The priorities of management post cardiac arrest include:

Determining the cause of cardiac arrest

» careful history and physical examination
» bedside tests such as 12-lead ECG, blood glucose, Hb, pulse oximetry, blood gases
» special investigations such as chest x-ray, eFAST, CT of the brain

Treating reversible conditions

This will be specific to the presentation and clinical findings.
Evidence of ST elevation myocardial infarction (STEMI) on ECG should prompt urgent treatment. See section 3.2.1: ST elevation myocardial infarction (STEMI).
Note: Prolonged CPR may be a contraindication to administration of thrombolytic or fibrinolytic agents. Consult a specialist to determine whether referral for

percutaneous intervention is possible.

Supportive care and prevention of complications

Airway

» Ensure that the airway is patent and protected.

» Endotracheal intubation may be required in patients that do not rapidly regain consciousness following return of spontaneous circulation.

Breathing

» Maintain oxygen saturation above 94%.

» Avoid hyperoxia by weaning the inspired oxygen concentration to the lowest percentage required to maintain the above saturation.

» Maintain PaCO2 within normal range in ventilated patients where feasible.

Circulation

» Correct hypovolaemia if present, with judicious IV fluids.

» Monitor response to fluids: pulse rate, BP, urine output, skin perfusion, development of basal crepitations.

» If hypotension persists despite fluid resuscitation, in the absence of ongoing blood loss, commence inotropes (e.g. adrenaline (epinephrine)).

» Aim to maintain mean arterial blood pressure (MAP) above 65 mmHg.

» If brain or spinal cord injury is suspected, it is reasonable to increase the target MAP to 80 mmHg.

Neurological care

» Position head up 30 degrees.

» Monitor for seizures. Treat promptly and load with an anti-epileptic agent if seizures occur.

Blood glucose control

» Maintain blood glucose between 8 and 10 mmol/L and avoid hypoglycaemic episodes.

LoE:III[v]

Temperature control

» Strictly avoid fever. Aim to control temperature below 36ºC in unconscious patients in the first 24 hours, using physical cooling methods e.g.: ice packs and fans, and antipyretics.

Deep vein prophylaxis

» Consider prophylaxis for venous thrombo-embolism, as required. See section 2.8: Venous thrombo-embolism.

LoE:I[vi]

MEDICAL TREATMENT

Hypoglycaemia

LoE:III[vii]

- Dextrose 50%, rapid IV injection, up to 50 mL.

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

Hypovolaemia

- Sodium chloride 0.9%, IV.

LoE:I[viii]

Hypotension (after volume correction)

- Adrenaline (epinephrine), IV infusion, start at 0.1 mcg/kg/minute titrated according to the response.
  - Dilute 10 mg i.e. 10 ampoules of adrenaline 1:1 000 in 1 L sodium chloride 0.9%.
  - Infuse according to weight and clinical response.
  - Infusion rate: mL/hour:

mcg/kg/minute	Weight in kg						
	50	**60**	**70**	**80**	**90**	**100**	**110**
0.1	30	36	42	48	54	60	66
0.2	60	72	84	96	108	120	132
0.3	90	108	126	144	162	180	198
0.4	120	144	168	192	216	240	264
0.5	150	180	210	240	270	300	330
0.6	180	216	252	288	324	360	396
0.7	210	252	294	336	378	420	462
0.8	240	288	336	384	432	480	528
0.9	270	324	378	432	486	540	594
1	300	360	420	480	540	600	660

LoE:III[ix]

Seizures

Treat seizures in post cardiac arrest, similar to management of status epilepticus. See section 14.4.1: Status epilepticus.

LoE:III[x]

Fever

- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

LoE:III[xi]

REFERRAL

» Following successful resuscitation cases should be discussed with a hospital with intensive care facilities for transfer.

» If evidence of myocardial infarction is present or if strongly suspected cases should be discussed with a cardiology service.

20.3 CARDIAC DYSRHYTHMIAS

See section 3.3: Cardiac dysrhythmias.

MEDICAL EMERGENCIES

Emergency health conditions are those requiring rapid intervention to avert death or disability, and those for which treatment delays of hours or less make interventions less effective. Concern that such a condition exists requires urgent assessment

20.4 ACUTE CORONARY SYNDROMES

See sections 3.2.1: ST elevation myocardial infarction (STEMI) and 3.2.2: Non-ST elevation myocardial infarction (NSTEMI) and Unstable angina (UA)

20.5 ASTHMA, ACUTE

See section16.1: Asthma, acute for the management of status asthmaticus.

20.6 ANGIOEDEMA

T78.3 + (Y34.99/Y57.9/Y14.99)

DESCRIPTION

Two major groups of angioedema should be differentiated: allergic angioedema forming part of a systemic reaction to an allergen, and non-allergic angioedema caused by bradykinin excess.

In allergic angioedema, features of allergy or anaphylaxis will often be present, including urticaria, bronchospasm, hypotension or gastrointestinal upset. Anaphylaxis should be treated urgently. See section 20.7: Anaphylaxis/anaphylactic shock.

Non-allergic angioedema is most commonly caused by ACE-inhibitors in susceptible individuals. It may also be caused by hereditary angioedema or acquired C1 esterase deficiency. Associated features of allergy are absent.

Symptoms

Swelling usually occurs around eyes and lips but may occur elsewhere.
Life-threatening airway obstruction can occur with angioedema of upper airways.

GENERAL MEASURES

Stop all suspected agents, e.g. ACE-inhibitor.
In case of angioedema with airway obstruction, early airway management is essential. If oedema is extensive or progressive, establish a definitive airway. The most skilled person available must handle airway interventions.
Avoid re-exposure to the offending agent and provide an alert bracelet.

MEDICINE TREATMENT

<u>In severe cases of hypersensitivity where airway obstruction may be imminent:</u>
Note: A definitive airway may be required before patient responds to medical treatment. Low threshold to surgical airway tracheostomy.

In cases where angioedema is part of anaphylaxis, treat as anaphylaxis.
See section 20.7: Anaphylaxis/Anaphylactic shock.

If urticaria and/or itch present (no imminent airway compromise):

- Hydrocortisone, IV, 100 mg as a single dose. *LoE:III*

AND

Promethazine, IV, 25–50 mg as a single dose.

OR

- Cetirizine, oral, 10 mg as a single dose. *LoE:III*

Severe ACE-inhibitor induced angioedema with threatened airway:

Note: A definitive airway may be required before patient responds to medical treatment. Low threshold to surgical airway tracheostomy.

- Lyophilised plasma, IV, 2 units. *LoE:III*

If lyophilised plasma is unavailable:

- FFP, IV, 2 units. *LoE:II*[xii]

Observe all cases until resolution.

20.7 ANAPHYLAXIS/ANAPHYLACTIC SHOCK

T78.2 + (Y34.99/Y57.9/Y14.99)

DESCRIPTION

An acute, potentially life-threatening hypersensitivity reaction.
The reaction usually starts within seconds to minutes after administration of, or exposure to a substance to which the individual has been sensitised.
Clinical manifestations range from mild urticaria and angioedema to upper airway obstruction, bronchospasm, hypotension, shock and death.
The reaction can be short-lived, protracted or biphasic, i.e. acute with recurrence several hours later.
Immediate reactions are usually the most severe and/or life threatening.

GENERAL MEASURES

Administer adrenaline (epinephrine) immediately (see below)
Cardiopulmonary resuscitation, if required.
Maintain an open airway. Intubate, if necessary.
Monitor all vital parameters (including pulse and blood pressure) closely.
Reassure and comfort the patient.
Patient counselling to prevent recurrence.
An alert bracelet should be worn at all times.

MEDICINE TREATMENT

- Adrenaline (epinephrine) 1:1000, 0.5 mL, IM, immediately into anterolateral thigh.
  - Repeat dose every 5 minutes, as required.

In cases of persistent hypotension or where multiple repeat doses are required:

- Adrenaline (epinephrine), IV infusion, start at 0.05 mcg/kg/minute titrated according to the response.
  - Dilute 10 mg i.e. 10 ampoules of adrenaline 1:1 000 in 1 L sodium chloride 0.9%.
  - Infuse according to weight and clinical response.
  - Infusion rate: mL/hour:

mcg/kg/minute	Weight in kg						
	50	**60**	**70**	**80**	**90**	**100**	**110**
0.05	15	18	21	24	27	30	33
0.1	30	36	42	48	54	60	66
0.2	60	72	84	96	108	120	132
0.3	90	108	126	144	162	180	198
0.4	120	144	168	192	216	240	264
0.5	150	180	210	240	270	300	330
0.6	180	216	252	288	324	360	396
0.7	210	252	294	336	378	420	462
0.8	240	288	336	384	432	480	528
0.9	270	324	378	432	486	540	594
1	300	360	420	480	540	600	660

LoE:III

AND

- Hydrocortisone, IV/IM, 200 mg, immediately as a single dose.

AND

Intravenous fluids

Establish an intravenous line:

- Sodium chloride 0.9%, IV.

LoE:I[xiii]

If bronchospasm:

- Oxygen if saturation <94%. *LoE:I[xiv]*

AND

Salbutamol, nebulisation, 5 mg.

- Nebulise continuously (refill the nebuliser reservoir every 20 minutes) at a flow rate of 6–8 L/minute.

AND *LoE: III[xv]*

- Ipratropium bromide, nebulisation 0.5 mg, added to salbutamol solution.

LoE: III[xvi]

If urticaria and/or itch present:

- Antihistamine, e.g.:
- Promethazine, IV 25–50 mg as a single dose.

OR

Cetirizine, oral, 10 mg as a single dose. *LoE:III*[xvii]

20.8 DELIRIUM WITH PERCEPTUAL DISTURBANCES

F05.0-1/F05.8-9/R45.1/R45.4-6

DESCRIPTION

Confusional states/delirium are characterised by altered consciousness, accompanied by impairments in orientation to time and place and seldom to person. Mental status may fluctuate. Disturbed behaviour may be present, e.g. agitation, hallucinations and paranoid ideation.

Note: Many acute medical emergencies can present as delirium, which may be misdiagnosed as an acute psychosis.

GENERAL MEASURES

» Investigations need to be done to exclude or diagnose an underlying medical problem, **the treatment of which is the primary management.**
» Ensure effective communication, re-orientation and reassurance.

MEDICINE TREATMENT

Treat underlying medical condition.

Acute management

For management for severe aggression and disruptive behaviour: see section 15.1: Aggressive disruptive behaviour in adults.

For agitated and acutely disturbed patient: *LoE:III*[xviii]

- Haloperidol, IM, 0.5–1 mg
  - This can be repeated in 30–60 minutes, if required and then 4 hourly to a maximum dose of 10 mg within 24 hours.
  - Monitor vital signs and beware of acute dystonia and neuroleptic malignant syndrome.
  - Dosing may vary according to clinical circumstances, e.g. lower doses in the elderly or where HIV infection or HIV-related dementia is known or suspected.

AND/OR

- Benzodiazepine, repeat as necessary, to achieve containment, e.g.:
- Lorazepam, IM, 1–4 mg.

OR

Clonazepam, IM, 0.5–2 mg.

OR

Diazepam, IV, 10 mg.

  - Switch to oral route once containment is achieved.

Note:

CAUTION
Benzodiazepines, especially diazepam IV, can cause respiratory depression.
Monitor patients closely.

» In the frail and elderly patient or where respiratory depression is a concern, reduce the dose by half. *LoE:III*[xix]
» The safest route of administration is oral followed by IM with the IV route having the highest risk of respiratory depression and arrest. Use the safest route wherever possible.
» Monitor vital signs closely during and after administration.
» Use haloperidol instead of benzodiazepines in patients with respiratory insufficiency.
» In the short-term, benzodiazepines can aggravate delirium.
» To avoid inappropriate repeat dosing allow at least 15–30 minutes for the medication to take effect. Repeated IM doses of benzodiazepines may result in toxicity owing to accumulation.
» Physical restraint worsens the outcomes of delirious patients: this is a last resort when all else has failed and is a short-term measure until chemical restraint has been achieved.

20.9 DIABETIC EMERGENCIES

See sections 8.6.1: Hypoglycaemia and 8.6.2: Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycaemic state (HHS).

20.10 PULMONARY OEDEMA, ACUTE

J81

DESCRIPTION

A life-threatening condition with abnormal accumulation of fluid in the lungs.
Common causes include acute decompensation of chronic underlying heart failure and acute renal failure (e.g. acute nephritis).
The acute decompensated heart failure patient appears extremely ill, restless, poorly perfused and sweaty, tachypnoeic, tachycardic, hypoxic, increased work of breathing, frothy sputum.

GENERAL MEASURES

Maintain open airway. Consider non-invasive positive pressure ventilation.
Position in Fowler's position, unless hypotensive or comatose.
Correct electrolyte disturbances.
Determine and correct any dysrhythmias.

MEDICINE TREATMENT

- Administer oxygen using face mask to deliver 40% oxygen at a rate of 6–8 L per minute.

Fluid overload suspected/detected:

- Furosemide, slow IV, 40 mg.
  - If response is adequate, follow with 40 mg in 2–4 hours.
  - If no response within 20–30 minutes: furosemide, IV, 80 mg.

Followed by:

- Nitrates, e.g.:
- Isosorbide dinitrate, SL, 5 mg repeat every 5–10 minutes, if necessary.
  - Monitor blood pressure. Do not administer if hypotensive.

OR *LoE:III*

- Glyceryl trinitrate, IV, 5–200 mcg/minute, titrated to response.
  - Start with 5 mcg/minute and increase by 5 mcg/minute every 5 minutes until response or until the rate is 20 mcg/minute.
  - If no response after 20 mcg/minute increase by 20 mcg/minute until response.
  - Flush the PVC tube before administering to patient. *LoE:III[xx]*
  - Monitor blood pressure carefully.

Volume of diluent	Glyceryl trinitrate 5 mg/mL	Concentration of dilution
250 mL	5 mL (25 mg)	100 mcg/mL
	10 mL (50 mg)	200 mcg/mL
	20 mL (100 mg)	400 mcg/mL
500 mL	10 mL (50 mg)	100 mcg/mL
	20 mL (100 mg)	200 mcg/mL
	40 mL (200 mg)	400 mcg/mL

Solution Concentration (mcg/mL)	100 mcg/mL solution	200 mcg/mL solution	400 mcg/mL solution
Dose (mcg/min)	Flow rate (microdrops/min = mL/hr)		
5	3	–	–
10	6	3	–
15	9	–	–
20	12	6	3
30	18	9	–
40	24	12	6
60	36	18	9
80	48	24	12
100	60	30	15
120	72	36	18
160	96	48	24
200	–	60	30

No fluid overload present:

Initiate nitrates, followed by furosemide.

If distressed, consider adding morphine:

- Morphine, IV. (See Appendix II, for individual dosing and monitoring for response and toxicity).

If hypotensive consider inotropic support, e.g.:

- Dobutamine, IV infusion, 5–20 mcg/kg/minute.
  - Dilute 1 vial (250 mg/20 mL) up to 50 mL with sodium chloride 0.9% or dextrose 5%. (Solution = 5 mg/mL or 5 000 mcg/mL)
  - Administer under constant ECG monitoring.
  - Rate of infusion in mL/hour: see weight-dose table in section 20.11.3: Cardiogenic shock.

20.11 SHOCK

20.11.1 HYPOVOLAEMIC SHOCK

20.11.1.1 NON-TRAUMA RELATED HYPOVOLAEMIC SHOCK

R57.1

DESCRIPTION

This happens when there is loss of intravascular fluid, e.g. severe diarrhoea and dehydration, haemorrhage or fluid shifts.

GENERAL MEASURES

Control obvious bleeding with direct pressure.
Insert one or two large bore IV catheters; peripheral lines are adequate.

MEDICINE TREATMENT

Non trauma related

- Sodium chloride 0.9%, IV, 1–2 L.

LoE:I[xxi]

Monitor blood pressure, pulse and clinical response.

20.11.1.2 TRAUMA-RELATED HYPOVOLAEMIC SHOCK

T79.4 + (R57.1 + Y34.99/Y57.9/Y14.99)

DESCRIPTION

Shock is inadequate perfusion of the vital organs. Clinically this may manifest with hypotension, tachycardia, weak pulses, clammy skin, pallor, altered mental state, poor urine output and elevated lactate.
The presence of shock in a patient with bleeding indicates that a significant volume of blood has already been lost.
The common traumatic sites of blood loss include the chest, abdomen, pelvis, long bone fractures and vascular injuries.

Major non-traumatic bleeds include gastrointestinal haemorrhage, ruptured ectopic pregnancy and obstetric haemorrhage.

GENERAL MEASURES

Control bleeding. Techniques may include:

» Direct, sustained pressure over the bleeding point.
» Use of tourniquets in exsanguinating limb haemorrhage, e.g. manual BP cuff or specialized tourniquet while awaiting transfer to theatre. (Do not use for longer than 6 hours).
» Tamponade techniques e.g. inflated Foley catheter in neck, axilla or femoral wounds.

Obtain large bore IV access, preferably two lines.
Prevent hypothermia.
Send blood sample to blood bank as early as possible for blood type and screening. Notify blood bank of possible massive transfusion.

MEDICINE TREATMENT

- Oxygen if saturation <94%. *LoE:I*[xxii]

Trauma related

- Sodium chloride 0.9%, IV. *LoE:I*[xxiii]

Consider blood products If more than 1 litre of fluid is needed, consider blood products:

» In cases of major bleeding, limit fluid volumes to less than 1.5 litres in total where possible. Replace acute blood loss with blood and blood products.
» Emergency blood should be used in unstable patients and when there will be significant delay in obtaining cross-matched blood from a blood bank.
» Rh typing is advised when possible.
  – Type O Rh negative blood should be reserved for women of childbearing age that are Rh negative or Rh status unknown.
  – Type O Rh positive blood may be given to Rh positive women of childbearing age, females >50 years of age or males regardless of Rh status.
» After 2 units of emergency blood, consider activation of massive transfusion protocol. See section 20.10.1.2.1: Massive transfusion.

20.11.1.2.1 MASSIVE TRANSFUSION

Z51.8

DESCRIPTION

A massive transfusion is the replacement of a patient's blood volume or 10 units over a 24-hour period, or replacement of half of that volume over 4 hours.

GENERAL MEASURES

Actively treat and prevent hypothermia.

When it is anticipated that large volumes of blood will be required, the replacement of platelets and clotting factors in addition to red blood cells is needed to prevent coagulopathy.

MEDICINE TREATMENT

Facilities without access to a blood bank:

- Lyophilised plasma, IV.
  - 1 unit for each unit of emergency blood transfused.

Arrange urgent transfer to a centre with blood bank and specialist services.

Facilities with access to a blood bank:

» Ensure that the blood bank receives an appropriate specimen as soon as the possible need for transfusion is identified.
» Notify the blood bank as soon as possible of the need for a massive transfusion and request a massive transfusion pack.

A massive transfusion pack will typically consist of:

- Red blood cells (RBCs), 6 units.

AND *LoE:III*

- Lyophilised plasma, IV.
  - 1 unit for each unit of emergency blood transfused.

OR

FFP, 6 units - thawed when requested.

AND

- Platelets, 1 mega-unit (normally 6 pooled donor units).
  - Aim to transfuse the above products in a 1:1:1 ratio, or as guided by laboratory parameters.
  - Send specimens for FBC and INR and continue to monitor.

Expedite definitive control of bleeding: *LoE:III*[xxiv]

- Tranexamic acid, IV, 1 g, infused over 10 minutes.
  - Followed with IV infusion, 1 g, over 8 hours. *LoE:I*[xxv]
  - Benefit is greatest if initiated in the 1st hour. Initiation of tranexamic acid more than 3 hours after the initial trauma may be harmful.

If patient responds initially and subsequently deteriorate, there may be an ongoing occult haemorrhage. If no response occurs, consider:

» Occult exsanguinating haemorrhage: intra-abdominal, retroperitoneal and intrapleural.
» Non-hypovolaemic shock: tension pneumothorax, myocardial contusion, cardiac tamponade or myocardial infarct.

20.11.2 DISTRIBUTIVE SHOCK

This happens when the blood vessels are abnormally dilated and presents with

a low blood pressure, tachycardia and warm peripheries. There are 3 causes of this type of shock:
» neurogenic shock,
» septic shock, and
» anaphylactic shock (see section: 20.7 Anaphylaxis/anaphylactic shock).

20.11.2.1 NEUROGENIC SHOCK

T09.3 + (Y34.99/R57.8)

DESCRIPTION

Occurs in spinal cord trauma when there is an interruption of the sympathetic chain causing vasodilatation.

GENERAL MEASURES

Check circulation, airway and breathing.
Spinal cord immobilisation.
Exclude other injuries that could cause low blood pressure.

MEDICINE TREATMENT

- Oxygen if saturation <94%. *LoE:I[xxvi]*
- Sodium chloride 0.9%, IV. *LoE:I[xxvii]*
  - Administer crystalloid in titrated boluses up to 1 litre.
- Adrenaline (epinephrine), IV infusion, start at 0.05 mcg/kg/minute titrated according to the response. *LoE:III*
  - Dilute 10 mg (10 ampoules) of adrenaline 1:1 000 in 1 L sodium chloride 0.9%.
  - Infuse according to weight and clinical response.
  - Infusion rate: mL/hour:

mcg/kg/minute	Weight in kg						
	50	**60**	**70**	**80**	**90**	**100**	**110**
0.05	15	18	21	24	27	30	33
0.1	30	36	42	48	54	60	66
0.2	60	72	84	96	108	120	132
0.3	90	108	126	144	162	180	198
0.4	120	144	168	192	216	240	264
0.5	150	180	210	240	270	300	330
0.6	180	216	252	288	324	360	396
0.7	210	252	294	336	378	420	462
0.8	240	288	336	384	432	480	528
0.9	270	324	378	432	486	540	594
1	300	360	420	480	540	600	660

20.11.2.2 SEPTIC SHOCK

R57.2

DESCRIPTION

Shock caused by a confirmed or suspected infection, with vasodilatation, increased capillary permeability, and decreased contractility of the heart.

GENERAL MEASURES

Check airway, breathing and circulation.

MEDICINE TREATMENT

- Oxygen if saturation <94%. *LoE:I[xxviii]*

Take blood culture (or any other tissue/body fluid), then administer appropriate parenteral broad spectrum antibiotics urgently, e.g.:

- Ceftriaxone, IV, 2 g daily. *LoE:II[xxix]*

Perform a fluid challenge for hypotension:

- Sodium chloride 0.9%, 500 mL boluses over 30 minutes, whilst monitoring clinical response until 30 mL/kg has been achieved.
  - Assess BP and pulse rate response. Response is defined by a good urine output (>0.5 mL/kg/hour) and adequate cerebral perfusion rather than an absolute BP value.

Balanced solutions may be appropriate in some patients (i.e. presentation with hyponatraemia, previous renal placement therapy): *LoE:I[xxx]*

- Balanced solution, e.g.:
- Ringer lactate, 500 mL boluses over 30 minutes, whilst monitoring clinical response, until 30 mL/kg has been achieved.
  - Assess blood pressure and pulse rate response. Response is defined by a good urine output (>0.5 mL/kg/hour) and adequate cerebral perfusion rather than an absolute blood pressure value.

Avoid over-hydrating as this could exacerbate hypoxia associated with adult respiratory distress syndrome.

If no haemodynamic response to early aggressive fluid resuscitation:

- Adrenaline (epinephrine), IV infusion, 0.05 mcg/kg/minute titrated according to the response.
  - Dilute 10 mg (10 ampoules) of adrenaline 1:1000 in 1 L sodium chloride 0.9%.
  - Infuse according to weight and clinical response. (Aim for target MAP 65 mmHg and urine output 0.5 mL/kg/hour).
  - See section 20.1.4.1: Neurogenic shock, for the infusion rate.

20.11.3 CARDIOGENIC SHOCK

R57.0

DESCRIPTION

Patients are hypotensive, cold and clammy and their pulse rate may be variable. Causes include an acute myocardial infarction, myocardial contusion, myocarditis, dysrhythmias, valvular heart disease, aortic dissecting aneurysm etc.
Consult with specialist and consider referring patients after initial emergency measures have been taken.

GENERAL MEASURES

Check circulation, airway and breathing.
ECG.
Treat the underlying cause, e.g.: MI, dysrhythmia, etc.

MEDICINE TREATMENT

- Oxygen if saturation <94%. *LoE:I*[xxxi]

A right ventricular myocardial infarction may respond to a fluid challenge:

- Sodium chloride 0.9%, IV. *LoE:I*[xxxii]
  - Administer 250–500 mL as a bolus and assess fluid responsiveness.
- Dobutamine, infusion, 5–10 mcg/kg/minute.
  - Dilute 1 vial (250 mg/20 mL) up to 50 mL with sodium chloride 0.9% or dextrose 5% (5 mg/mL or 5 000 mcg/mL).
  - Rate of infusion in mL/hour: *LoE:III*[xxxiii]

Dose mcg/kg/min	Weight (kg)									
	30	40	50	60	70	80	90	100	110	120
2	0.9	1.2	1.5	1.8	2.1	2.4	2.7	3	3.3	3.6
5	1.8	2.4	3	3.6	4.2	4.8	5.4	6	6.6	7.2
7.5	2.7	3.6	4.5	5.4	6.3	7.2	8.1	9	9.9	10.8
10	3.6	4.8	6	7.2	8.4	9.6	10.8	12	13.2	14.4

20.11.4 OBSTRUCTIVE SHOCK

R57.8

DESCRIPTION

Occurs when there is an obstruction to the filling of the right ventricle or an obstruction in blood flow. Clinical signs include hypotension, tachycardia, cold peripheries and distended neck veins.

Causes include:

- » cardiac tamponade,
- » acute pulmonary embolism, and
- » tension pneumothorax,
- » severe bronchospasm.

TREATMENT

Treat the cause.

Acute pulmonary embolism and cardiac tamponade require urgent consultation with a specialist and referral after initial emergency measures have been taken

20.12 STATUS EPILEPTICUS

See section 14.4.1: Status epilepticus

TRAUMA AND INJURIES

For trauma-related haemorrhage, presenting within 3 hours of injury, see section 20.1.3 Hypovolaemic shock.

20.13 ACUTE KIDNEY INJURY

See section 7.1.4: Acute kidney injury.

20.14 BITES AND STINGS

See chapter 19: Poisonings – envenomation.

20.15 BURNS

T30.0-3 + (T31.0-9/Y34.99

DESCRIPTION

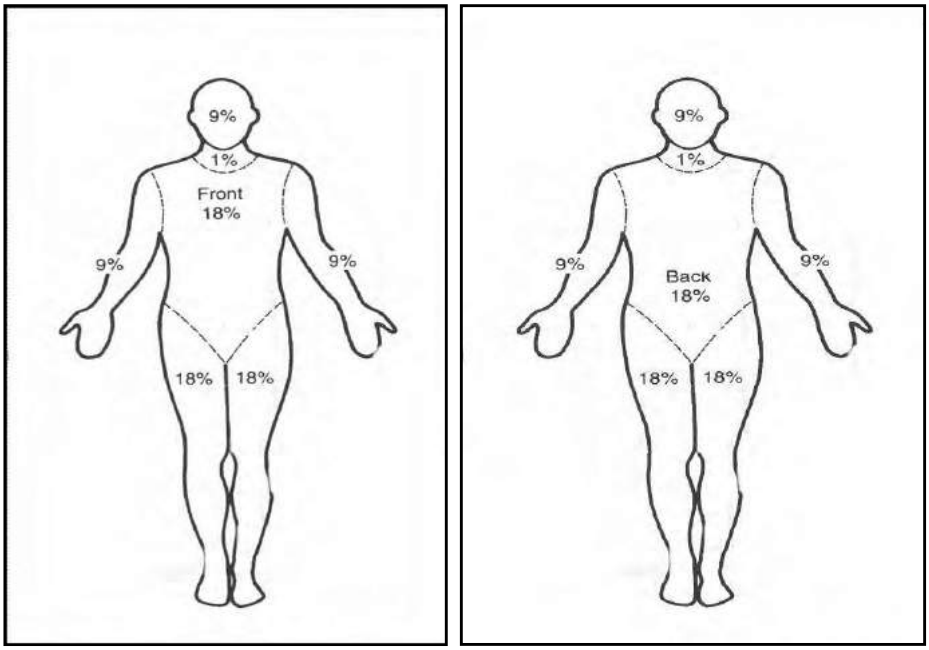
Skin and tissue damage caused by:

» exposure to extremes of temperature,
» contact with an electrical current,
» exposure to a chemical agent, and
» radiation.

ASSESSMENT OF BURNS

Depth of burn wound	SURFACE /COLOUR	PAIN SENSATION/HEALING
Superficial or epidermal	Dry, minor blisters, erythema	» Painful » Heals within 7 days
Partial thickness superficial or superficial dermal	Blisters, moist	» Painful » Heals within 10–14 days
Partial thickness deep or deep dermal	Moist white or yellow slough, red mottled	» Less painful » Heals within a month or more Generally needs surgical debridement and skin graft
Full thickness (complete loss of skin)	Dry, charred whitish, brown or black	» Painless, firm to touch » Healing by contraction of the margins (generally needs surgical debridement and skin graft)

The figures below are used to calculate body surface area %.
These diagrams indicate percentages for the whole leg/arm/head (and neck in adults) not just the front or back.
Children ≥8 years and adults



Source: Karpelowsky JS, Wallis L, Madaree A, Rode H; South African Burn Society. South African Burn Society burn stabilisation protocol. S Afr Med J. 2007 Aug;97(8):574-7. http://www.ncbi.nlm.nih.gov/pubmed/17966146

GENERAL MEASURES

» Assess airway, breathing
  – Look for signs of inhalational burn- history of hot gas, smoke, steam.
  – INTUBATE if significant airway obstruction present or WORSENING symptoms.
  – Intubation is necessary in the case of unconscious patients, hypoxic patients with severe smoke inhalation, or patients with flame or flash burns involving the face and neck if there is evidence of compromised airway patency.
  – Intubate early if burns are inhalational, or in the presence of pharyngeal burns with soft tissue swelling, as these patients frequently tend to develop respiratory failure.
  – Close monitoring is essential during the first 24-48 hours
  – If breathing is compromised because of tight circumferential trunk burns, consult with burn centre surgeons immediately. Urgent escharotomies may be required to facilitate chest expansion
» Assess circulation
  – Establish large-bore intravenous (IV) lines and provide resuscitation bolus fluid.
  – Reminder: IV lines may be placed through the burned area if necessary (suture to secure).

» Assess neurological state of the patient
» Assess for associated trauma related injuries
  – Secure the C–spine with an inline stabilising collar, when the mechanism of injury could indicate additional trauma.
  – Identify potential sources of internal bleeding.
  – Stop any external bleeding.
» Remove any sources of heat or chemicals. Removal constrictive clothing/accessories.
» Estimate percentage of total body surface area involved.
» Support vital organ function.
» Look for aggravating comorbidities, e.g. seizures, hyperkalaemia, renal failure.
» Assess need for decompression incisions: escharotomies
» Local wound care: Clean superficial burns can be managed by occlusive dressings. Deeper wounds may have to be excised and grafted.
» Rehabilitation involving physiotherapy and occupational therapy.

Burn injuries put patients into a hypermetabolic state which requires early and adequate nutritional support. Seek early guidance from local burns centre. See section 12.13.1: Nutritional support.

MEDICINE TREATMENT

Fluid replacement

Burns ≤10% Total Body Surface Area (TBSA):

- Oral rehydration solution.

Burns >10% of TBSA:

- Sodium chloride 0.9%, IV fluid for resuscitation, replacement and maintenance.

Calculation of fluid replacement

Replacement fluids for burns

» First 24 hours:

- Sodium chloride 0.9%, IV. *LoE:I*[xxxiv]
  - Calculate total fluid requirement in 24 hours:
    Total % burn x weight (kg) x 4 mL.
  - Give half this volume in the 1st 8 hours.
  - Administer remaining fluid volume in next 16 hours.

Note: If urine output is not adequate, increase fluids for the next hour by 50%. Continue at a higher rate until urine output is adequate, then resume normal calculated rate. Aim for urine output 0.5 mL/kg/hr.

Analgesia

Ensure adequate analgesia particularly at change of dressing, i.e.:

- Morphine, IV, to a total maximum dose of 10 mg (See Appendix II, for individual dosing and monitoring for response and toxicity).

AND

- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

Tetanus prophylaxis Z23.5

Tetanus toxoid vaccine, IM, 0.5 mL immediately.

Local Wound Care

» Melted plastic and tar can be removed with the topical application of liquid paraffin solution
» Wash burn wounds with soap and water or 1% chlorhexidine.
» Cool burns less than 3 hours old with cold tap water for at least 30 minutes and then dry the patient.
» Keep the wound clean and dress with sterile dressings.

For chemical burns

» Remove all clothing.
» Brush powdered chemicals off the wound
» Flush chemical burns for a minimum of 30 minutes using copious volumes of running water.
» Reminder: Never neutralise an acid with a base or vice versa.
» Determine what chemical (and what concentration) caused the injury.
» Ocular burns: T26.4 + (Y34.99)

- Sodium chloride 0.9% gentle eye washes or irrigations as soon as possible. Follow with an ophthalmology consultation

For electrical burns

» Differentiate between low-voltage (<1 000 v) and high-voltage (>1 000 v) injuries.
» Attach a cardiac monitor; treat life-threatening dysrhythmias as needed.
» Suspect compartmental syndrome, consider escharotomies.

Stress ulcer prophylaxis

Feeding patients provides protection against gastric ulcer developing and prophylaxis is not necessary in patients who are tolerating feeds.

Note: Pharmacokinetic parameters are altered in patients with severe burns, notably an increased volume of distribution. An appropriate loading dose should be given of certain medicines, e.g. aminoglycosides. Therapeutic drug monitoring (TDM) may inform dosing and should be requested, if available.

Discuss the following cases with a burns specialist:

» Burns >15% body surface area (BSA) or >10% BSA >50 years of age.
» Burns of face, hands, feet, genitalia, perineum or involving joints.
» Electrical burns, including lightning burns.
» Chemical burns.
» Inhalation injury or burns.
» Burns associated with major trauma.

» Circumferential burns.

20.16 EXPOSURE TO POISONOUS SUBSTANCES

See chapter 19: Poisoning.

20.17 EYE INJURIES

See section 18.10: Medical management of eye injury.

20.18 POST EXPOSURE PROPHYLAXIS

See section 10.5: Post-exposure prophylaxis.

20.19 SOFT TISSUE INJURIES

See Primary Health Care STGs and EML; section 21.3.7: Soft tissue injuries.

20.20 SPRAINS AND STRAINS

See Primary Health Care STGs and EML; section 21.3.8: Sprains and strains.

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CHAPTER 21
ONCOLOGIC EMERGENCIES

21.1 ONCOLOGICAL EMERGENCIES

Any acute, potentially morbid or life-threatening event directly or indirectly related to a patient's tumour or its treatment. Most oncological emergencies can be classified as metabolic, haematologic, structural, or side effects of chemotherapy agents or radiation therapy.

21.1.1 METABOLIC EMERGENCIES

21.1.1.1 HYPERCALCAEMIA OF MALIGNANCY

See section 8.9: Hypercalcaemia, including primary hyperparathyroidism

21.1.1.2 SYNDROME OF INAPPROPRIATE ANTIDIURETIC HORMONE (SIADH)

E22.2

DESCRIPTION

Patients present with: anorexia, nausea, vomiting, constipation, muscle weakness, myalgia, polyuria, polydipsia, neurologic symptoms (e.g. seizures, coma).

For management see section: 7.2.4 Hyponatraemia.

REFERRAL

Refer to Oncology Unit for management of underlying malignancy producing Antiduretic Hormone (ADH).

21.1.1.3 TUMOUR LYSIS SYNDROME

E88.3

DESCRIPTION

Rapid destruction of malignant cells can result in the release of cellular breakdown products and intracellular ions, causing potentially lethal metabolic derangements including acute renal failure.
Commonly seen in cancers with rapidly growing tumours and high tumour burdens, particularly acute leukaemias, chronic myeloid leukaemia and high-grade lymphoma, generally following chemotherapy.

Presentation: (Cairo-Bishop definition)

- azotaemia
- acidosis
- hyperphosphataemia >1.45 mmol/L
- hyperkalaemia >6.0 mmol/L
- hypocalcaemia <1.75 mmol/L

» uric acid >0.476 mmol/L

GENERAL MEASURES

There is an increased risk of arrhythmias.
Monitor urine output.
Monitor urine and electrolytes, creatinine and uric acid levels.

MEDICINE TREATMENT

Fluid resuscitation:

» IV hydration 2–3 L/m^2/day. The urine output needs to be monitored and maintained within 80–100 mL/m^2/hour.
» Diuretics are not indicated in patients with normal renal and cardiac function; and are contraindicated in patients with hypovolemia.

- Sodium chloride 0.9%, IV, 1000 mL 6–8 hourly.

If patient is hypernatraemic or fluid overloaded, consult a specialist.

LoE:III[i]

For control of uric acid:

- Allopurinol, oral, 100 mg 8 hourly.
  - Maximum dose: 300 mg 8 hourly.
  - Adjust dose to 50 mg 8 hourly, if eGFR <20 mL/minute.

LoE:III[ii]

Correct electrolyte imbalances:

» For hyperkalaemia, see section 7.2.1: Hyperkalaemia.
» For hypocalcaemia see section 8.10 Hypocalcaemia.

REFERRAL

Transfer to oncology unit.

21.1.2 HAEMATOLOGIC EMERGENCIES

21.1.2.1 FEBRILE NEUTROPENIA

See section 2.8: Febrile neutropenia.

21.1.2.2 HYPERVISCOSITY AND LEUCOSTATIC SYNDROMES

D78.9

DESCRIPTION

Hyperviscosity is seen in patients with Waldenström's macroglobulinemia and multiple myeloma, while leucostasis may be seen in patients with acute leukaemias and chronic myeloid leukaemia with high white cell counts. Sludging and decreased perfusion of the microvasculature and vascular stasis occur due to increased paraproteins or leucostasis.
Patients present with spontaneous bleeding, visual signs and symptoms, and

neurologic defects.

GENERAL MEASURES
Perform investigations: FBC, peripheral blood smear, serum protein electrophoresis (SPEP) and erythrocyte sedimentation rate (ESR).
Monitor urine, electrolytes and creatinine.

REFERRAL
Ensure adequate hydration and refer.

21.1.3 STRUCTURAL EMERGENCIES

21.1.3.1 EPIDURAL SPINAL CORD COMPRESSION
G95.2

DESCRIPTION
Seen in breast, lung, and prostate cancers, as well as multiple myeloma.
Patients present with new back pain that worsens when lying down, late paraparesis, late incontinence, and loss of sensory function.

GENERAL MEASURES
To evaluate level of neurologic function, perform a spinal x-ray or MRI if available.

MEDICINE TREATMENT
- Dexamethasone, IV, 16 mg immediately as a single dose.
  - Followed by 4 mg 6 hourly, until transfer.

LoE:III[iii]

REFERRAL
Urgent referral to tertiary services with oncology or neurosurgery services.

21.1.3.2 MALIGNANT PERICARDIAL EFFUSION
I31.3

DESCRIPTION
Seen in metastatic lung and breast cancer, melanoma, leukaemia, and lymphoma.
Patients present with dyspnoea, fatigue, distended neck veins, distant heart sounds, tachycardia, orthopnoea, narrow pulse pressure, pulsus paradoxus, or water-bottle heart.

Investigation
Trans-thoracic echocardiography.

GENERAL MEASURES

Management is dependent on the underlying aetiology and symptom progression.

Diagnostic and therapeutic pericardiocentesis:

» Immediate pericardiocentesis is mandatory for patients with tamponade.
» Send some of the fluid drained for microbiology and cytology.

REFERRAL

All patients for definitive therapy.

21.1.3.3 SUPERIOR VENA CAVA SYNDROME

I87.1

DESCRIPTION

Superior Vena Cava (SVC) obstruction may be seen in lung cancer, germ cell tumours, lymphomas, thyroid carcinomas, and metastatic mediastinal tumours. Indwelling central venous catheters may cause SVC syndrome due to venous thrombosis.

Patients present with: cough, dyspnea, dysphagia, facial oedema, or upper extremity swelling or discoloration, with development of collateral venous circulation.

GENERAL MEASURES

Histological diagnosis is essential for definitive management.

Head elevation and supplementary oxygen.

MEDICINE TREATMENT

Maintain normovolaemia.

- Sodium chloride 0.9%, IV, 1000 mL 8 hourly.
- Corticosteroids may be considered in consultation with a specialist.

REFERRAL

Refer for histological diagnosis, and further management.

21.2 SIDE EFFECTS FROM ONCOLOGY TREATMENT AGENT

21.2.1 DIARRHOEA

Refer to section 1.3.3: Diarrhoea, acute non-inflammatory.

21.2.2 EXTRAVASATIONS

T80.8

DESCRIPTION

Chemotherapeutic agents are classified as vesicants (can cause necrosis), non-vesicants, and irritants.
Patients present with pain and erythema at infusion site, swelling, necrosis, contractures.

GENERAL MEASURES

Limb elevation.

MEDICINE TREATMENT

Long term

Small localised area of erythema at the catheter insertion site will usually resolve without antibiotic therapy.

In patients with larger areas of erythema and tenderness extending beyond the insertion site, where secondary infection is suspected:

- Clindamycin, oral, 450 mg 8 hourly for 5 days. *LoE:III*[iv]

Catheter related infections

If patients with peripheral or central venous catheter infections are systemically unwell they should be treated as a venous catheter-related systemic blood infection.
Microbiologic specimen (for speciation and sensitivity).

REFERRAL

All patients to oncological department where chemotherapy was administered.

21.2.3 CONSTIPATION

See section 24.1.2: Constipation.

21.3 SIDE EFFECTS FROM RADIATION AND CHEMOTHERAPY

21.3.1 RADIATION AND CHEMOTHERAPY RELATED MUCOSITIS

K12.3

DESCRIPTION

An inflammatory reaction where shallow ulcerative lesions occur on mucosal surfaces.

GENERAL MEASURES

Avoid irritants (e.g.: smoke, alcohol and hot spicy food).
Ensure adequate fluid intake e.g.: 2 L/day.
Modify diet to include soft or pureed foods.
Use lip care e.g. petroleum jelly, as required.
Keep dentures clean and snug fitting. If loose, refer to dentist.
Ensure adequate mouth care:

» Clean teeth with soft toothbrush or clean cloth.
» Avoid dental flossing.
» Rinse and gargle regularly, at a minimum after every meal.

Simple mouth rinse:

- ½ teaspoon salt
- 3 teaspoons sodium bicarbonate
- 1 L of filtered or previously boiled water.
  (Discard this mixture after 3 days).

LoE:III^{v}

MEDICINE TREATMENT

Adequate pain control. See section 25.2: Analgesia for acute non-surgical pain.

21.3.2 WET DESQUAMATION OF SKIN

R23.4

DESCRIPTION

Acute toxicity of skin that occurs during radiation treatment and up to 2-3 weeks after completion of the radiation.
Few or even no skin care products are effective to prevent or reduce acute radiotherapy skin reactions.

GENERAL MEASURES

Keep skin clean and apply paraffin gauze dressings daily.
Avoid friction and trauma from clothes, weather, etc.
Prevent infection.
Encourage good nutrition.
Encourage smoking cessation.

MEDICINE TREATMENT

Adequate pain control. See section 25.2: Analgesia for acute non-surgical pain.

21.3.3 RADIATION- OR CHEMOTHERAPY-INDUCED PNEUMONITIS

J70.0

DESCRIPTION

Radiation pneumonitis is inflammation of the lung caused by radiation therapy to the chest. It mostly develops 1–6 months after treatment.
Chemotherapy-induced pneumonitis is inflammation of the lung caused by various chemotherapy agents. It mostly develops on treatment.
Symptoms include: fever, dry cough, chest congestion, shortness of breath, and chest pain.
The differential diagnosis includes infectious pneumonitis, pulmonary embolism, and tumor recurrence.

GENERAL MEASURES

Symptoms generally resolve within 7–10 days following cessation of treatment.
Maintain hydration.

MEDICINE TREATMENT

For symptomatic subacute pneumonitis:

- Corticosteroids (intermediate-acting) e.g.:
- Prednisone 1 mg/kg daily for 2–4 weeks at a maximum daily dose of 40–60 mg, and then taper slowly over 3–12 weeks. Refer to Appendix II for an example of a dose reduction regimen. *LoE:III*[vi]

REFERRAL

All patients with symptomatic pneumonitis.

21.3.4 RADIATION PROCTITIS

K62.7

DESCRIPTION

An inflammatory process of the rectal mucosa that can present acutely (immediately after the initiation of radiation therapy or up to 3 months after) or chronically (8-12 months after completion of therapy). The acute process is usually self-limiting.

Symptoms include diarrhoea, nausea, cramps, tenesmus, urgency, mucus discharge, and minor bleeding.
Severe complications include bleeding, strictures, perforation, fistula, and bowel obstruction.

Diagnosis
Suspect radiation proctitis when there has been previous radiation to the pelvis.
On colonoscopy/sigmoidoscopy, pallor, friability, telangiectasia are seen localised to the area that was exposed to radiation. Do not biopsy.
Exclude other causes, e.g.: malignancy, infection, or inflammatory bowel disease.

REFERRAL
All patients to a radiation oncology centre.

21.3.5 RADIATION- OR CHEMOTHERAPY-INDUCED CYSTITIS
N30.4

DESCRIPTION
Symptoms include dysuria, frequency, nocturia, recurrent haematuria, and recurrent urinary tract infection.

GENERAL MEASURES
Increase fluid intake.
Urine microscopy, culture and sensitivity to exclude/confirm an infection.
High dose cyclophosphamide and ifosfamide may cause severe cystitis due to excretion of acrolein into bladder.
Acute cystitis is usually self-limiting and resolves in one to two weeks after completing radiation therapy. If symptoms continue, cystoscopy with biopsy is indicated.

REFERRAL
All patients.

21.4 SIDE EFFECT FROM CHRONIC PAIN MEDICATION

21.4.1 CONSTIPATION
See section 26.1.3: Treatment of adverse effects of chronic opioid use.

21.4.2 NAUSEA & VOMITING
See section 26.1.3: Treatment of adverse effects of chronic opioid use.

21.4.3 DEPRESSION
See section 24.2.3: Depression.

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CHAPTER 22
MEDICINES USED FOR DIAGNOSIS

22.1 DIAGNOSTIC CONTRAST AGENTS AND RELATED SUBSTANCES

Medication used in diagnostic radiology includes:
Barium sulphate suspension.

- Non-ionic contrast media, e.g.:
  - iohexol, or
  - iopamidol, or
  - iopromide, or
  - ioversol.

SAFETY
The overall rate of adverse reactions is estimated to be less than 1 in 100[i] when using non-ionic contrast media and serious allergic reactions are even less common (about 1 in 2000[ii]). Contrast media-associated fatality is rare, estimated to be 2 per million injections.[iii]

Management of any reaction depends on it's severity. Life-threatening acute cardiopulmonary collapse should be treated according to guidelines for cardiopulmonary resuscitation. See chapter 20: Emergencies and injuries.
Moderate and severe reactions may be associated with bronchospasm and wheeze, stridor, hypotension, and loss of consciousness. Stop the infusion of the contrast agent and start treatment as for anaphylaxis including adrenaline, oxygen (if indicated), intravenous fluids, and antihistamines. See sections 20.6: Angioedema and 20.7: Anaphylaxis/anaphylactic shock.

Iodine allergy: (Z91.0)
Patients allergic to iodine are at an increased risk of adverse drug reactions when exposed to iodine-containing contrast media and patients who report previous allergic reactions to contrast agents should be carefully evaluated as to the need for the investigation. If the investigation is considered essential, the patient should be pre-treated with steroids and antihistamines before proceeding.

- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 50 mg given 13 hours, 7 hours, and 1 hour before the procedure. *LoE:II*[iv]

Contrast-Induced Nephrotoxicity (CIN) is an important consideration; it may result in permanent renal impairment with significant effects on longevity. This is particularly important in an environment with limited access to renal replacement therapy. Before referring any patient for an

investigation involving contrast use, carefully weigh up the individuals' potential risk of CIN against potential benefits (the likelihood of detecting a condition for which a significant therapeutic intervention is available).

CIN is variously defined as either a 25% or a 50% rise on pre-contrast creatinine levels, or an absolute creatinine increase of more than 25 micromol/L. CIN is rare in individuals with normal renal function[v,vi] .

Factors that increase the risk of CIN include: diabetes, pre-existing renal impairment, age >75 years, anaemia, cardiac failure, hypotension and the volume of contrast media injected[vii,viii].

The probability of developing a 25% rise in creatinine after cardiac catheterisation in patients given 200 mL of non-ionic contrast media is linked to co-morbidity[vii]:

CIN risk	None	Anaemia	>75 yrs	CCF or low BP	>1 risk factor
No diabetes					
eGFR>60	7.5%	7.5%	7.5%	15%	15%
eGFR 40–60	7.5%	15%	15%	15%	15%
eGFR 20–40	7.5%	15%	15%	15%	25%
eGFR<20	15%	15%	25%	25%	25%
Diabetes					
eGFR>60	7.5%	15%	15%	15%	25%
eGFR 40–60	15%	15%	15%	25%	25%
eGFR 20–40	15%	25%	25%	25%	25%
eGFR<20	15%	25%	25%	25%	55%

The probability of needing dialysis after cardiac catheterisation is correlated with the risk of CIN[vii]:

CIN risk	7.5%	15%	25%	55%
Dialysis risk	0.04%	0.12%	1.1%	13%

Reducing the risk of developing CIN

There is no clear evidence that any specific medication is protective against the development of CIN. However, meticulous attention to fluid balance is important in patients at higher risk, as dehydration increases the risk of CIN.

Patients on metformin should be monitored for deterioration in renal function post procedure, as there is a small risk of precipitating lactic acidosis. In high risk patients it may be advisable to omit metformin for 48 hours after contrast injection while monitoring serum creatinine.

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CHAPTER 23
SEDATION

23.1 SEDATION

DESCRIPTION
Sedation aims to reduce some combination of anxiety, agitation and pain while the patient retains control of airway, breathing and blood pressure.

23.1.1 PROCEDURAL SEDATION AND ANALGESIA

Procedural sedation and analgesia is a technique that uses medications to allow patients to tolerate unpleasant medical, interventional or diagnostic procedures.
It is a brief intervention, unlike sedation in intensive or palliative care. It is commonly used in emergency units, dentistry and for certain endoscopic and gynaecological procedures.
The information described does not apply to:
» Patients receiving inhaled anaesthetics.
» Patients receiving analgesia for pain without sedation.
» Patients receiving sedation to manage behavioural emergencies.
» Patients who are intubated.

GENERAL MEASURES
Procedural sedation is a continuum: ranging from minimal sedation (anxiolysis), moderate sedation/analgesia, deep sedation/analgesia, to general anaesthesia.

Deep sedation/analgesia includes the dissociative state caused by medicines like ketamine. It is often difficult to predict levels of sedation and therefore clinicians undertaking procedural sedation should be adequately trained in this technique. The clinician should have a detailed understanding of the risks and benefits of all the medicines used. Further the clinician should be competent in resuscitation, airway management and assisted ventilation.

Procedural sedation should only be performed in an area with adequate light, space and fully functional and adequate observation, monitoring and resuscitation equipment.

Besides the clinician performing the procedure, there must be one other trained health care provider present responsible for observing the patient, assisting with resuscitation if necessary and monitoring the patient. The trained health care provider should observe the patient until the patient is ready for discharge.

Patient monitoring and details of the types and amounts of all medicines used must be recorded for each procedure. After the procedure the patient's fitness to leave the observation area should be formally assessed and recorded.
Sedation level:

Sedation				General anaesthesia
Depth	**Minimal**	**Moderate**	**Deep**	
Other aims	**Anxiolysis**	**Analgesia**		
Examples	Nitrous oxide **OR** benzodiazepine	Opioid **AND** benzodiazepine	Opioid **AND** benzodiazepine **OR** propofol **OR** etomidate	
Response to stimuli	Verbal	Purposefully to verbal or tactile	Purposefully only after repeated/painful	Unrousable
Airway intervention	Not required	Not usually needed	May be needed	Requires assistance
Breathing	Normal	Usually normal (spontaneous ventilation adequate)	May need assistance	Requires assistance /positive pressure ventilation
BP/Pulse	Normal	Usually normal/ maintained		May need support
Monitoring	Intermittent review of vital signs	Continuous pulse oximetry and heart rate, intermittent BP and respiratory rate. Continuous ECG if CVS disease or sedation with more than one agent		As for any general anaesthetic
Cognitive Function or level of conscious	Impaired	depressed		Loss of consciousness

LoE:III[i]

Ketamine

Ketamine administration leads to a dissociative state (patients may not be able to speak coherently or respond purposefully to verbal commands) and provides both sedation and analgesia. Used on its own, it rarely requires airway intervention or affects breathing, but may cause hypertension and tachycardia because of sympathetic stimulation.

LoE:III[ii]

MEDICINE TREATMENT

Patient characteristics and required depth and/or duration of sedation lead to differences in dosing requirements; the doses listed serve only as a guide, and incremental further dosing may be required depending on clinical response.

Minimal sedation and anxiolysis (no analgesic effect required)

Oral sedation may be appropriate for certain procedures.

Initial dose (further dose increments may be necessary – consult full prescribing information for each agent to determine maximum safe dosages, and reduce doses in the frail and elderly):

- Diazepam, IV, 0.1 mg/kg. (In a 60 kg patient, give boluses of 2 mg every minute; may require up to 10 mg).

OR *LoE:II*[iii]

Midazolam, IV, 0.05 mg/kg. (In a 60 kg patient, give boluses of 1 mg every minute; may require up to 3 mg).

OR

Nitrous oxide, inhaled 20 to 50%, in oxygen (will also provide some analgesia).

Benzodiazepines may cause respiratory depression; monitor accordingly.

Moderate sedation and analgesia

If analgesia is required, one of the above is usually combined with an opioid. However, ketamine has analgesic activity and can be used on its own, or combined with a benzodiazepine. The opioids may cause respiratory depression; monitor accordingly.

Initial doses:

- Fentanyl, IV, 0.25 mcg/kg.
  - Titrate to effect and repeat dose every five minutes until desired level of analgesia has been achieved.

OR *LoE:III*[iv]

Morphine, IV, 0.1 mg/kg, in increments of 2 mg every 5 minutes.

OR

Ketamine, IV, 0.5 mg/kg (the addition of a benzodiazepine is often recommended to reduce the incidence/severity of phenomena such as hallucinations and dreaming, but the benefit of this is unclear).

- Repeat doses of 0.5 mg/kg as required, every 5 to 10 minutes. *LoE:III*[v]

OR

Nitrous oxide, 20–50% inhaled, in oxygen.

LoE:III[vi]

Other agents for moderate sedation

Propofol on its own provides moderate sedation for short procedures (e.g. endoscopy), but without analgesia:

- Propofol, IV, 0.5 mg/kg, repeated as 0.25 mg/kg boluses every 5 minutes as required. Specialist consultation. *LoE:III*[vii]

Etomidate is a short-acting agent like propofol, but is more likely to cause myoclonus. It has minimal haemodynamic effects and a reliable onset of action, but no analgesic effect and is more commonly used for emergency unit procedures, rather than endoscopies.

- Etomidate, IV, 0.1 mg/kg. *LoE:III*[viii]
  - Repeat doses of 0.05 mg/kg every 5 minutes, as required.

Deep sedation and analgesia
This is usually achieved with either higher doses of medications used for moderate sedation, or by combining an opioid, a benzodiazepine, and either propofol or etomidate.

When agents are combined, lower doses may be adequate. Always have another health care provider monitoring the patient and resuscitation equipment present.

Supplemental analgesia
Simple analgesics can be given before or after the procedure as appropriate:

- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

AND/OR

- NSAID, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with meals after the procedure.

Other routes (e.g. rectal or intramuscular) may be appropriate for certain indications and medications.

Reversal Agents must be available as medicine doses for sedation/analgesia are highly variable as are patient's age, concurrent medication and medical conditions. Supportive management is aimed at maintaining cardiorespiratory function.

For opioid toxicity:

- Naloxone, IV, 0.08 mg immediately. *LoE:III*[ix]
  - Repeat doses as required at 2 minute intervals.
  - Maximum total dose is 10 mg.

23.1.2 SEDATION IN INTENSIVE CARE

Indications for sedation in intensive care need to be defined for each patient, and may include one or more of: anxiolysis, analgesia, agitation control, or to help patients tolerate uncomfortable situations or procedures (e.g. intubation and ventilation). Sedation requirements fluctuate rapidly and warrant regular review. Individualised sedation objectives should be clearly defined, and level of sedation regularly recorded. Sedation protocols that recognise the need for dose minimisation, weaning and sedation interruptions probably improve outcomes.

LoE:II[x]

Adequate pain control is often more efficacious than sedatives for reducing agitation. Delirium should be considered, and managed appropriately. The doses listed apply to ventilated patients in whom short term respiratory depression is not a concern.

Short term sedation (less than 24 hours)

- Midazolam, IV infusion, 0.05–0.2 mg/kg/hour.

OR

Propofol, IV infusion, 0.5 mg/kg/hour.

Note: Propofol does have cardiovascular effects; benzodiazepines are preferred.

LoE:III[xi]

Longer term sedation (expected 72 hours or more)

- Lorazepam, IV, 0.1 mg/kg/hour.

OR

Midazolam, IV, 0.2 mg/kg/hour.

Note: Lorazepam (0.1 mg/kg/hour) is as effective (and as easy to wean) as midazolam 0.2 mg/kg/hour) but is more difficult to titrate. Due to high fat solubility, midazolam also becomes 'long acting' after infusions of more than 24 hours.

Supplemental analgesia:

Analgesia can be added to any of the above regimens:

- Morphine, IV infusion, 0.1–0.2 mg/kg/hour.

OR

- Fentanyl, IV infusion, 1 mcg/kg/hour (also becomes long acting after prolonged infusion due to fat solubility.)

LoE:III[xii]

23.1.3 SEDATION IN PALLIATIVE CARE

See section 24.5: Sedation in palliative care.

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CHAPTER 24
MEDICINES USED IN PALLIATIVE CARE

PALLIATIVE CARE

Palliative care is an approach that improves the quality of life of patients and their families facing problems associated with life-threatening illness, regardless of whether or not they also receive life-prolonging treatment. It requires a multidisciplinary approach and aims to address physical, psychosocial, and spiritual problems.

Life threatening illnesses are where death is expected to be a direct consequence of the specified illness.
Analysis of available evidence suggested 11 common symptoms occurring in the advanced stages and end of life stages: anorexia, anxiety, constipation, delirium, depression, diarrhoea, dyspnoea, fatigue, nausea and vomiting, pain and respiratory tract secretions.
All symptoms should be managed by a multi-disciplinary team to ensure a holistic approach.

Note: Please be advised that the recommendations in this chapter are directed at treating common symptoms associated with end-of-life care (acute and sub-acute) - a component of palliative care. The approach to end-of-life care may differ from supportive palliative care. Refer to relevant sections for supportive palliative care, e.g. section 15.3.1: Depressive disorders.

Always refer to the latest National Guidelines on Palliative Care.

For management of pain in palliative care see chapter 26: Pain.

24.1 GASTROINTESTINAL CONDITIONS

24.1.1 ANOREXIA AND CACHEXIA

R63.0/R63.4/R64 + (Z51.1)

DESCRIPTION

Anorexia/cachexia syndrome is a complex metabolic process found in many end-stage illnesses. It is characterised by loss of appetite, weight loss and muscle wasting, and cannot be fully reversed by conventional nutritional support. It may impact significantly on the quality of life of patients, leading to increased anxiety and distress for both patients as well as family.

GENERAL MEASURES

Reduced food and fluid intake is expected at the end of life, and treatment of anorexia and weight loss may not be appropriate if these symptoms are not having a direct impact on quality of life. This should be explained to caregivers and family.

Management of anorexia and weight loss includes identification and, if appropriate, treatment of possible underlying cause(s). It may include the use of pharmacological and non-pharmacological treatment approaches.

Identify reversible problems that may contribute to or exacerbate anorexia/ cachexia including:

- Pain, nausea, heartburn, dyspnoea, gastritis, depression, constipation anxiety dysphagia, medication and fatigue
- Oral problems e.g. dry mouth, ulcers, candidiasis, etc.
- Odours e.g. fungating lesions, cooking smells, incontinence etc.
- Delayed gastric emptying due to local disease, autonomic neuropathy with early satiety and vomiting of undigested foods

If appropriate, moderate exercise must be encouraged, along with pacing of activities and good sleep hygiene.

Nutritional advice includes eating small amounts of enjoyable food frequently.

MEDICINE TREATMENT

If the anorexia and/ cachexia contributes significantly to decreased quality of life and the patient has a short life expectancy.

- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral, 0.5 mg/kg (e.g. 20–30 mg) daily.
  - The effect may be rapid but usually decreases after 3–4 weeks.
  - If there is no benefit after 1 week, stop the treatment.

LoE:III[i]

If symptoms of reflux or gastritis: see section 1.1.3: Gastro-oesophageal reflux disease.

If gastroparesis is present, see section 8.7.1 Diabetic neuropathies.

24.1.2 CONSTIPATION

K59.0 + (Z51.1)

DESCRIPTION

Constipation is the passage of small, hard faeces infrequently and with difficulty. Individuals vary in the weight they give to the different components of this definition when assessing their own constipation and may introduce other factors, such as pain and discomfort when defecating, flatulence, bloating or a sensation of incomplete evacuation. Constipation may also be secondary to other conditions e.g. dehydration, immobility poor diet, anorexia, tumour compressing bowel wall or hypercalcaemia.

GENERAL MEASURES

Ensure privacy and comfort to allow a patient to defecate normally.
Increase fluid intake within the patient's limits.
Encourage activity and increased mobility within the patient's limits.
Anticipate the constipating effects of pharmacological agents such as opioids, anticholinergic agents (e.g. tricyclic antidepressants), antacids, iron, 5HT3 antagonists and provide laxatives prophylactically.

MEDICINE TREATMENT

The combination of a softener and stimulant laxative is generally recommended, and the choice of laxatives should be made on an individual basis.

- Sennosides A and B, oral, 13.5 mg, 1 tablet at night.
  - In resistant cases increase to 2 tablets.

AND/OR *LoE:III[ii]*

Lactulose, oral, 15–30 mL 12–24 hourly. *LoE:III[iii]*

Severe constipation in patients who are unable to swallow:

- Bisacodyl, rectal, 10 mg suppository daily.

OR *LoE:III[iv]*

Glycerine (glycerol), rectal, 1.698 mL/2.4 g suppository when necessary. *LoE:III*

If these therapies are not effective, other options could be considered.

Note: Manual removal should only be undertaken if the patient has received adequate pain relief and sedation, if relevant.

REFERRAL/CONSULTATION

If bowel obstruction is suspected refer/consult for appropriate radiological investigations and, if appropriate, surgical interventions.

24.1.3 DIARRHOEA

A09.0/A09.9/K52.2/K52.9 + (Z51.5)

See Primary Health Care chapter: Medicines for palliative care: section 22.1.2: Diarrhoea.

24.1.4 NAUSEA AND VOMITING

R11 + (Z51.5)

GENERAL MEASURES

Treat the underlying cause and rehydrate the patient.
Reversible causes include medication, hypercalcemia, constipation, uraemia, gastritis, gastroenteritis, coughing and infections.
Manage odours e.g. cooking smells and fungating wounds.

MEDICINE TREATMENT

Treat the underlying cause.

- Metoclopramide, oral/IM/IV, 10 mg 8 hourly, 30 minutes before a meal.

<u>If metoclopramide is ineffective or contra-indicated (i.e. inoperable bowel obstruction):</u>

- Haloperidol, oral, 1.5–5 mg daily.

OR *LoE:III*[v]

Haloperidol, SC/IM/IV

- Initiate 0.5 mg 12 hourly.
- Titrate to a maximum dose of 5 mg 8 hourly. *LoE:III*[vi]

<u>Drug-induced parkinsonism:</u> *LoE:III*[vii]

ADD

- Anticholinergic agent, e.g.:
- Orphenadrine, oral, 50–150 mg daily according to individual response
  - Usual dose: 50 mg 8 hourly.
  - Maximum dose: 150 mg daily.
  - Use with caution in the elderly as it may cause confusion and urinary retention.

Note: Anticholinergic medicines (e.g. orphenadrine) should not be added prophylactically to antipsychotics to prevent extrapyramidal side effects.

<u>If haloperidol is ineffective/ inoperable bowel obstruction:</u>

- Promethazine, IM/IV, 12.5–25 mg, 4–6 hourly. *LoE:III*[viii]

Corticosteroids can decrease cerebral oedema: See section: 14.12.1 Brain oedema due to tumours and inflammation.

REFERRAL

Refer to the appropriate discipline if the underlying cause can be reversed e.g. bowel obstruction - refer to a surgeon.
Consult a palliative care trained doctor if the vomiting persists.

24.2 NEUROPSYCHIATRIC CONDITIONS

24.2.1 ANXIETY

F40.0-2/F40.8-9F41.3/ F41.8-9/F42.0-2/F42.8-9 + (Z51.1)

DESCRIPTION

Anxiety is defined as the apprehensive anticipation of future danger or misfortune accompanied by a feeling of dysphoria or somatic symptoms of tension. Anxiety is characterised by excessive feelings of fear apprehension and worry. Anxiety may be associated with symptoms of depression, poor concentration, insomnia, irritability, panic attacks, sweating, tremor and nausea. It is a common symptom in Palliative Care and the complex multi-

causative nature of anxiety in patients with life threatening illnesses always require a multimodal approach.

GENERAL MEASURES

Address any contributing factors such as pain and dyspnoea. Consider other underlying conditions that may mimic anxiety e.g. electrolyte imbalance, hyperthyroidism, hypoxia, arrhythmias and many medicine side effects.
Assess for depression or any other previous psychiatric illness.
Include the caregivers
Ensure the patient and caregivers have received the desired amount of information around the nature of the disease, treatment, side-effects and outcomes.

MEDICINE TREATMENT

A multi-disciplinary team approach is recommended (including a spiritual carer).

Acute management of anxiety:

<u>For an acute episode or intense prolonged anxiety:</u>

- Benzodiazepine, e.g.:
- Diazepam, oral, 2.5–5 mg as a single dose.
  - Repeat if required up to 12 hourly. *LoE:III*[ix]
  - Duration of therapy: up to 2 weeks, taper off to zero within 6 weeks.
  - Avoid if liver function impaired.

OR *LoE:III*[x]

- Lorazepam, oral, 0.5–1 mg, immediately.
  - Repeat as necessary to control symptoms. *LoE:III*[xi]
  - Tablets may be crushed and administered sublingually. *LoE:III*[xii]

<u>Patient unable to take oral medication/ terminal sedation required:</u>
See section 24.5: Sedation in palliative care.

CAUTION

Benzodiazepines, especially diazepam IV, can cause respiratory depression.
Patients with liver dysfunction require lower doses.
Monitor patients closely. *LoE:III*[xiii]
In the short-term, benzodiazepines can aggravate delirium.

» In frail and elderly patients or where respiratory depression is a concern, reduce the dose by half. *LoE:III*[xiv]
» The safest route of administration is oral with the IV route having the highest risk of respiratory depression and arrest. Use the safest route wherever possible.
» Monitor vital signs closely during and after administration.

» Use haloperidol instead of benzodiazepines in patients with respiratory insufficiency.
» To avoid inappropriate repeat dosing allow at least 15–30 minutes for the medication to take effect. Repeated IM doses of benzodiazepines may result in toxicity owing to accumulation.

- SSRI e.g.:
- Citalopram, oral. *LoE:I*[xv]
  - Initiate at 10 mg daily for 2 weeks.
  - Then increase to 20 mg daily.

OR *LoE:I*[xvi]

Fluoxetine, oral.
- Initiate at 20 mg every alternate day for 2 weeks
- Increase to 20 mg daily after 2–4 weeks
- Delay dosage increase if increased agitation/panicked feelings occur.

LoE:III[xvii]

Note: Effect of SSRIs are only apparent after 2–3 weeks of treatment, so they should be reserved for patients where end-of-life is not imminent.

REFERRAL
Poor response to treatment.

24.2.2 DELIRIUM
F02.0-4/F02.8/F03/F05.0-1/F05.8-9 + (Z51.5)

DESCRIPTION
Delirium (confusion) is very common in the terminal stages of advanced disease and is associated with a short prognosis. When treatment of the underlying cause(s) of delirium is not possible or unsuccessful, pharmacological management is necessary. Causal treatment may not be indicated in patients with limited prognosis and pharmacological symptomatic therapy has to be initiated without delay.

GENERAL MEASURES
Assess for underlying causes e.g. infection or electrolyte imbalance.
Remove factors that can agitate the patient (e.g. full bladder, thirst, pain, constipation, medicines such as opioids, steroids, benzodiazepines, withdrawal of medicines, dehydration, liver or renal impairment and cerebral tumour).
Reduce polypharmacy.
Where appropriate, ensure adequate fluid and nutritional intake (not indicated in the pre-terminal stage).
Mobilise early when appropriate.
Monitor for sensory deficits and manage accordingly e.g. using hearing aids.

Keep the family involved and informed. Provide tools of care such as how to orientate and reassure the patient.

MEDICINE TREATMENT

- Haloperidol, oral/SC/IV, 0.5 mg 8 hourly.
  - Titrate dosage up as required and use the minimum dose that controls the symptoms.

LoE:III[xviii]

In the elderly or where there is no response or resistance to haloperidol:

ADD

- Lorazepam, oral, 0.5–1 mg 2–4 hourly as required.
  - Tablets may be crushed and administered sublingually.

LoE:III[xix]

OR *LoE:III*[xx]

Patients unable to swallow:

- Midazolam, SC/IV, 0.5–5 mg immediately.
  - Titrate up slowly.
  - Lower doses are indicated for patients with liver dysfunction.

LoE:III[xxi]

24.2.3 DEPRESSION

F32-3/F32.8-.9/F33.0-4/F33.8-9/F34.1 + (Z51.5)

DESCRIPTION

Depression is characterized by persistent feelings of extreme sadness and low mood associated with loss of interest in activities and inability to experience pleasure. There are often associated biological features of significant changes in appetite and weight, disturbed sleep, fatigue and poor concentration.

Diagnosis of major depression in a terminally ill patient often relies more on the psychological or cognitive symptoms (worthlessness, hopelessness, excessive guilt and suicidal ideation) than the physical/somatic signs (weight loss and sleep disturbance) described in depression in patients who are not terminally ill. The key indicators of depression in the terminally ill are persistent feelings of hopelessness and worthlessness and/or suicidal ideation.

Demoralisation is a phenomenon where hope and meaning is lost and where patients wish to hasten their death because they cannot foresee any future pleasure.

GENERAL MEASURES

Exclude physical reversible causes e.g. hypothyroidism, hyperthyroidism, or hypercalcaemia.

MEDICINE TREATMENT

- SSRI, e.g.:
- Citalopram, oral.
  - Initiate at 10 mg daily for 2 weeks.
  - Then increase to 20 mg daily.

OR *LoE:III*[xxii]

<u>If sedation is required:</u>

- Amitriptyline, oral, at bedtime.
  - Start with: 25 mg, increase by 25 mg/day at 3–4 day intervals.
  - Dose range: 75–150 mg daily.

Note: Effect of SSRIs are only apparent after 2-3 weeks of treatment, so they should be reserved for patients where end-of-life is not imminent.

24.2.4 FATIGUE

R53 + (Z51.5)

DESCRIPTION

Fatigue is defined as a subjective feeling of tiredness, weakness or lack of energy. The pathophysiology is not fully understood but will be multifactorial in most palliative care patients, including disease- and treatment-related causes. Fatigue may be severe, distressing and persistent, regardless of adequate amounts of sleep and rest.

GENERAL MEASURES

Treat underlying causes such as anaemia, depression, and infections.
Encourage aerobic exercises, where appropriate.
Ensure that the multidisciplinary team assists with activity pacing, assisted devices where indicated, and diet.

MEDICINE TREATMENT

Note: Because of limited evidence, consideration of steroids in palliative care should be restricted to use in the terminally ill with fatigue and a specific short-term treatment goal.
Fatigue can also protect patients at the end of life from physical and emotional distress.

- Corticosteroids (intermediate-acting) e.g.:
- Prednisone, oral 0.5 mg/kg (e.g.:15–30 mg) daily, for 1 week.

LoE:III[xxiii]

24.3 PAIN

See chapter 26: Pain.

24.3.1 CHRONIC CANCER PAIN

See section 26.1.2: Analgesia for chronic cancer pain.

24.3.2 NEUROPATHIC PAIN

See section 26.1.4: Neuropathic pain.

24.4 RESPIRATORY CONDITIONS

24.4.1 DYSPNOEA

R06.0+ (Z51.5)

DESCRIPTION

Dyspnoea is the subjective unpleasant sensation of being unable to breathe adequately (breathlessness). Dyspnoea is a complex multidimensional symptom with physical, psychological, and emotional dimensions, especially anxiety. The intensity of dyspnoea is generally not related to the oxygen saturation.

Look for reversible causes, e.g. infection, pulmonary embolism, pleural effusion, bronchospasm and anxiety

The aim should always be to address the cause. However, in end stage disease symptomatic treatment is indicated.

GENERAL MEASURES

Ideally, include a physiotherapist and occupational therapist for pulmonary rehabilitation and to teach patients pursed lip breathing, pacing of activities, relaxation techniques, and positioning.

The use of a fan may reduce the sensation of dyspnoea.

Treat the underlying cause (e.g. antibiotics for underlying respiratory infection) wherever possible.

MEDICINE TREATMENT

- Morphine syrup, oral.
  - Starting dose: 2.5–5 mg, 4 hourly as required, titrating up slowly.

<u>Dyspnoea associated with hypoxaemia</u>

- Oxygen.

24.4.2 RESPIRATORY SECRETIONS

R06.0 + (Z51.5)

DESCRIPTION

Excessive respiratory tract secretions (also referred to as death rattle), is used to describe a rattling noise produced by accumulated secretions in the airway which oscillate in time with inspiration and expiration. Generally, respiratory secretions occur in patients who are extremely weak and close to death.

GENERAL MEASURES

Change position of the patient.
Explain to caregivers and relatives that the patient is not distressed by the secretion. Patients are not conscious that they are unable to clear secretions. Minimal oropharyngeal suctioning is required.

MEDICINE TREATMENT

- Hyoscine butylbromide, SC/IM, 20 mg.
  - Increase dose to effect to maximum of 120 mg.

LoE:III[xxiv]

24.5 SEDATION IN PALLIATIVE CARE

Y47.9 + (Z51.5)

Sedation in palliative care has unique objectives, and tolerance for some adverse effects may be greater than in other situations. There is also an emphasis on avoiding parenteral medication. Palliative sedation should be undertaken by clinicians experienced in the process and the advice of an expert should be sought where necessary. Sedation should only be started after discussion with, and with the consent of, the patient and/or family (when the patient is unable to consent).

The aim of sedation in palliative care is to ameliorate refractory suffering and not to hasten death.
Palliative care medication addresses symptoms such as pain, dyspnoea, nausea and depression. Managing many of these symptoms involves the use of medications which may have sedative properties. Palliative sedation involves the additional use of medication where sedation is the primary objective, and is appropriate only after standard care has proven unsuccessful.

GENERAL MEASURES

Pain must always be the first symptom to be excluded.
Always look for reversible causes of symptoms prior to prescribing sedation such as dehydration, hypoxia, concurrent synergistic sedative medicines, hypercalcaemia, renal failure, or infection.
Caution should be exercised and palliative care prescription examined for possible drug-drug interactions, prior to commencing sedation (or escalating doses of sedative medicines).
Dose escalation may be considered only if there is evidence of inadequate sedation.

MEDICINE TREATMENT

Dosing in frail, elderly patients should be titrated to effect.

- Lorazepam, oral, 0.5 mg 4 hourly.

- Tablets may be crushed and administered sublingually.

OR LoE:III[xxv]

Haloperidol, oral, 0.5 mg 4 hourly.

Patient unable to take oral medication or terminal sedation required:

- Midazolam, SC/IV:
  - Initial dose: 1–5 mg as needed
  - Titrate to effect.

LoE:III[xxvi]

24.6 END OF LIFE CARE

Z51.1

DESCRIPTION

Patients can be defined as being terminal when there is irreversible decline in functional status prior to death. It is essential during this time to ensure the ethical management of the dying phase and to minimise distress for the patient, family and fellow health care professionals by using a biopsychosocial and spiritual approach.

Signs of dying:

» The patient may gradually spend more time sleeping during the day and at times will be difficult to rouse.
» There may be decreased need for food and drink.
» The patient may become increasingly confused about time, place and identity of friends and family.
» Arms and legs may become cool to the touch and the undersides of the body may become darker in colour.
» Loss of control of bowel and bladder may occur.
» Urine output may decrease.
» Saliva and mucus may collect at the back of the throat as the swallowing and cough reflexes diminish. This sometimes causes a noise known as the “death rattle”.
» Vision and hearing may decrease.
» Breathing patterns may become irregular, with longer intervals between breaths.

GENERAL MEASURES

Communication is at the centre of care. The following aspects should be addressed:

» Honest, direct, compassionate and culturally sensitive information about the prognosis.
» Evaluation of the patient and family resources and needs, especially spiritual needs.
» Decision making on place of death as many patients want to go home.
» Education about patient care.

» Emergency contact details, especially if the patient wants to go home.
» Compassionate information about symptoms that might develop and how to manage them.
» Nutrition and hydration.

Discontinue all non-essential, futile procedures and medicines e.g. discontinue 4-hourly blood pressure measurements and vitamin tablets.
Ensure medicines are prescribed for symptom management and prescribe medicine when needed to pre-empt common symptoms during the terminal phase using the appropriate route of administration:
» Pain (see section above)
» Nausea and vomiting (see section above)
» Respiratory secretions (see section above)
» Agitation /restlessness/delirium (see section above)

Discuss feeding and hydration with the family. If the decision is to hydrate and/ feed, ensure gentle hydration and monitor oedema, especially in patients with hypoalbuminaemia. Hydration does not improve quality of life, survival, or symptom burden at the end of life, and should not be given as routine management. Rather offer sips of water if the patient is able to swallow.

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CHAPTER 25

SEXUALLY TRANSMITTED INFECTIONS

SEXUALLY TRANSMITTED INFECTIONS MANAGED AT SECONDARY LEVEL OF CARE

These guidelines apply to patients who are referred from primary healthcare centres for further investigation and management of **persistent** STI symptoms or syndromes that have not improved or resolved and are still present 7 days after administration of standard first-line syndromic therapy.

25.1 MALE URETHRITIS SYNDROME (MUS)

A64 + N34.1

Male urethritis/ visible urethral discharge that persists despite appropriate syndromic management should be investigated for suspected ceftriaxone-resistant gonorrhea. Referral letter from PHC should include all relevant information (including HIV status, treatment history and partner notification and management).

INVESTIGATIONS

- » It is essential to confirm ceftriaxone-resistant gonorrhea.
- » All NHLS standard laboratory forms must include the following information:
  - – Name and contact details (cellphone number + email address) of requesting healthcare worker.
- » Genital specimen collection and test requests (to confirm presence of any STI pathogens and if *Neisseria gonorrhoeae* present, and determine ceftriaxone susceptibility):
  - – *Materials:* Two Dacron swabs (wire shaft, slender tip); Amies transport medium (all obtained from local NHLS laboratory).
    - > Urethral swab 1: Gently insert 2cm into the urethral meatus, and rotate for 5-10 seconds. Place this swab immediately into Amies transport medium.
    - > Test request: Transport on ice to local NHLS laboratory as soon as possible, preferably within 24 hours for *Neisseria gonorrhoeae* culture and sensitivity testing. (Contact laboratory for directions on transport of specimens).
    - > Presumptive diagnosis: Persistent urethritis due to possible ceftriaxone-resistant gonorrhea.
    - > Urethral swab 2: Gently insert 2cm into urethral meatus, and rotate for 5-10 seconds. Place in a sterile universal container or tube, cut off the wire shaft and close the container.

> *Test request:* transport on ice to NICD STI reference laboratory as soon as possible for PCR genital discharge pathogens.
> Presumptive diagnosis: Persistent urethritis due to possible ceftriaxone-resistant gonorrhea.

MEDICINE TREATMENT

Persistent urethral discharge after 7 days confirmed on examination, pending results:

- Ceftriaxone, IM, 1 000 mg immediately as a single dose.
  - Dissolve ceftriaxone 1 g in 3.6 mL lidocaine 1% without adrenaline (epinephrine).

LoE: III[i]

AND

LoE: III[ii]

- Azithromycin, oral, 2 g as a single dose.

LoE: III[iii]

Severe penicillin allergy: Z88.0

- Gentamicin, IM, 6 mg/kg, IM as a single dose. (See Appendix II for guidance on prescribing).

AND

LoE: III[iv]

- Azithromycin, oral, 2 g as a single dose.

Ask patient to return in two weeks for follow-up of laboratory results and further clinical evaluation. Treat accordingly.

25.2 VAGINAL DISCHARGE SYNDROME (VDS)

B37.3/N76.0/N89.8

Abnormal vaginal discharge that persists despite appropriate syndromic management should be investigated. Referral letter from PHC should include all relevant information (including HIV status, treatment history and partner notification and management).

INVESTIGATIONS

» All NHLS standard laboratory forms must include the following information:
  – Name and contact details (cellphone number + email address) of requesting healthcare worker.
» Genital specimen collection and test requests (to confirm presence of STI pathogens and if *Neisseria gonorrhoeae* is present, and determine ceftriaxone susceptibility):
  – *Materials:* One cotton-tip swab (plastic shaft); two Dacron swabs (plastic shaft, slender tip); Amies transport medium (all obtained from local NHLS laboratory). Insert speculum to visualize cervix.
  – *Endocervical swab 1:* Gently insert Dacron swab 2cm into the endocervical canal, and rotate for 5-10 seconds. Place this swab immediately into Amies transport medium.

  - *Test request:* Transport on ice to local NHLS laboratory as soon as possible, preferably within 24 hours for *Neisseria gonorrhoeae* culture & sensitivity testing.
  - *Presumptive diagnosis:* Persistent cervicitis due to possible ceftriaxone-resistant gonorrhea.
- *Endocervical swab 2*: Gently insert Dacron swab 2cm into the endocervical canal, and rotate for 5-10 seconds. Place in sterile universal container or tube, break off plastic shaft and close the container.
  - *Test request:* Transport on ice to NICD STI Reference laboratory as soon as possible for PCR genital discharge pathogens.
  - *Presumptive diagnosis:* Persistent cervicitis/vaginal discharge due to possible ceftriaxone-resistant gonorrhea.
- *Vaginal swab1*: Gently insert cotton-tip swab into the vagina and then dip swab in the poster fornix fluid. Place swab in sterile universal container or tube, break off plastic shaft and close the container.
  - *Test request:* Transport to local NHLS laboratory as soon as possible for M/C/S - for bacterial vaginosis; *Candid*a culture and sensitivity testing.
  - *Presumptive diagnosis:* Persistent vaginal discharge due to bacterial vaginosis or candidiasis.

MEDICINE TREATMENT

Persistent cervicitis confirmed on speculum examination, pending results:

- Ceftriaxone, IM, 1 g immediately as a single dose.
  - Dissolve ceftriaxone 1 g in 3.6 mL lidocaine 1% without adrenaline (epinephrine). *LoE: III[v]*

AND *LoE: III[vi]*

- Azithromycin, oral, 2 g as a single dose.

If metronidazole, oral was not given at PHC prior to referral administer:

- Metronidazole, oral, 2 g as a single dose. *LoE: III[vii]*

Severe penicillin allergy: Z88.0

- Gentamicin, IM, 6 mg/kg, IM as a single dose. (See Appendix II for guidance on prescribing).

AND *LoE: III[viii]*

- Azithromycin, oral, 2 g as a single dose.

If metronidazole, oral was not given at PHC prior to referral administer:

- Metronidazole, oral, 2 g as a single dose. *LoE: III[ix]*

Ask patient to return in two weeks for follow-up of laboratory results and further clinical evaluation. Treat accordingly.

25.3 GENITAL ULCER SYNDROME (GUS)

A60.9/A51.0

Genital ulcer disease that persists despite appropriate syndromic management should be investigated. Referral letter from PHC should include all relevant information (including HIV status, treatment history and partner notification and management).

INVESTIGATIONS

» All NHLS standard laboratory forms must include the following information:
  – Name and contact details (cellphone number + email address) of requesting healthcare worker.
» Genital specimen collection and test requests:
  – Materials: Two cotton-tip swabs (plastic shaft); one Dacron swab (wire shaft); glass slide, slide box (all obtained from local NHLS laboratory)
  – Cotton swab 1: Prior to taking specimen, roll a cotton-tip swab across the lesion gently to remove exudates from secondary infection and/ or debris in a way that minimizes bleeding. Discard cotton swab.
  – Cotton swab 2: Roll a second cotton-tip swab over the base of the ulcer, including the ulcer edges. Make a thin smear by rolling evenly over the centre of a labelled-glass slide to the size of a R2 coin. Air dry slide and place in slide box. Discard cotton swab.
  – Dacron swab: Collect material from base of ulcer lesion; place swab in sterile universal container or tube and cut off wire shaft. Close container.
    > *Test request:* Transport glass slide and Dacron swab on ice to NICD STI Reference laboratory as soon as possible for microscopy for Donovanosis and PCR genital ulcer pathogens.
    > *Presumptive diagnosis:* Persistent genital ulcer disease
» Venous blood specimen: 5 mL in serum separator tube for syphilis serology – send to local NHLS laboratory.

MEDICINE TREATMENT

Ask patient to return in two weeks for follow-up of laboratory results and further clinical evaluation. Treat accordingly, but note that syphilis does not require re-treatment if benzathine penicillin was used to treat GUS.

If the syndromic treatment at PHC used doxycycline instead of benzathine penicillin and syphilis is detected on PCR, treat with:

- Benzathine benzylpenicillin, IM, 2.4 MU immediately as a single dose.
  - Dissolve benzathine benzylpenicillin, IM, 2.4 MU in 6 mL lidocaine 1% without adrenaline (epinephrine).

LoE: III^{x}

Recurrent herpes

For frequent recurrences of herpes simplex (i.e. ≥4 episodes of clinically apparent reactivations per year), suppressive antiviral therapy may be considered.

- Antiviral (active against herpes simplex) e.g.: *LoE: II*[xi]
- Aciclovir, oral, 400 mg 12 hourly.
  - Review annually for ongoing suppressive therapy.

LoE: III[xii]

REFERRAL

If ulcer PCR results for STI pathogens are inconclusive and genital ulceration persists, refer to specialist for genital ulcer biopsy and histopathological examination to exclude a non-infectious cause, which includes cancer.

25.4 BUBO

A58

Buboes that persist despite appropriate syndromic management should be investigated. Referral letter from PHC should include all relevant information (i.e. HIV status, treatment history and partner notification and management).

INVESTIGATIONS

» All NHLS standard laboratory forms must include the following information:
  – Name and contact details (cellphone number + email address) of requesting healthcare worker.

» Genital specimen collection and test requests:
  Materials: One Dacron swab (wire shaft); 21-gauge sterile needle and syringe; two sterile universal containers or tubes (all obtained from local NHLS laboratory).

  1. If genital ulcer is present:

  – Dacron swab: Collect material from base of ulcer lesion; place swab in sterile universal container or tube and cut off wire shaft. Close container.
    > *Test request:* Transport Dacron swab on ice to NICD STI reference laboratory as soon as possible for PCR for chancroid and LGV.

  2. If genital ulcer is absent:

  – After topical disinfection, insert 21-gauge needle into bubo and aspirate pus into syringe. Transport pus in two sterile tubes/ containers to laboratory.
    > *Test request:* send one tube on ice to NICD STI reference laboratory as soon as possible for PCR for chancroid and Lymphogranuloma Venereum (LGV).
    > *Test request:* send one tube to local NHLS laboratory for bacterial M/C/S.
  – *Presumptive diagnosis:* Persistent bubo unresponsive to syndromic management.

MEDICINE TREATMENT

- Doxycycline 100 mg, oral 12 hourly for 21 days.

LoE: III[xiii]

Note: Follow-up until there is complete resolution of symptoms. Fluctuant buboes may require frequent needle aspiration to prevent rupture – review every 72 hours, as necessary.

For laboratory-confirmed diagnosis of LGV:

- Doxycycline 100 mg, oral 12 hourly for more than 21 days may be required for complete resolution of disease.

LoE: III[xiv]

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CHAPTER 26
PAIN

26.1 PAIN, CHRONIC

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage. The relationship between pain (a subjective experience) and tissue damage (which may be assessed directly by others) is moderated by socio-cultural context as well as the nervous system.

The goals of pain management include pain reduction and improved function, sleep, and well-being. Family members play an important part in the patient's treatment and should be included where possible.

Measure care outcomes by evaluating pain severity, quality of life, and functionality, e.g. Pain, Enjoyment and General Activity (PEG) scale, http://www.med.umich.edu/1info/FHP/practiceguides/pain/PEG.Scale.12.2016.pdf

26.1.1 ANALGESIA FOR CHRONIC NON-CANCER PAIN

ASSESSEMENT OF CHRONIC NON-CANCER PAIN

A biopsychosocial assessment is necessary to inform effective pain management.

Ascertain the aetiology and perpetuating factors and manage accordingly. Note that there may be overlap between different aetiologies, and condition-specific pain management may be required.

» Nociceptive pain, e.g. osteoarthritis (see section 13.3); rheumatoid arthritis (see section 13.1); gout (see section 13.4); spondylarthritis (see section 13.5); chronic post-surgical or injury pain; visceral pain, e.g. chronic pancreatitis; chronic cancer pain (see section 26.1.2); endometriosis (see section 5.4).
» Neuropathic pain (see section 26.1.4).
» Fibromyalgia and irritable bowel syndrome (see PHC STGs and EML, section 2.12).
» Mental illness, e.g. mood disorders (depression and bipolar disorder), anxiety, post-traumatic stress disorder (see chapter 15: Mental health conditions), somatic symptoms, and related disorders.
» Substance use disorders, including over the counter analgesics, opioids, benzodiazepines, and alcohol.

Ascertain the patient's beliefs about their pain and hopes of care. Common issues to address are:

» Idealised nature of reality, e.g. that life must be pain-free.

» That pain means exercise and physical activity must be avoided.
» Catastrophic thinking regarding the pain.
» A need to be unwell to be cared for by others.
» Fear of work and responsibility, for various reasons.
» Stigma, with denial of mental illness or interpersonal conflict.

Social stressors, trauma, interpersonal conflict or violence may predispose to and perpetuate chronic pain.

GENERAL AND SUPPORTIVE MEASURES

Patients with chronic pain should be treated with a biopsychosocial approach, according to findings of a comprehensive assessment. Note that those with greater subjective pain complaints may also be at higher risk of an opioid use disorder.

» Validate the pain experienced and manage with empathy.
» Educate regarding the cause of pain, prognosis (including that pain may not be fully relieved), and realistic expectations regarding pain reduction.
» Establish goals of care with the patient and select a measure of effectiveness e.g. Pain, Enjoyment and General Activity (PEG) scale, http://www.med.umich.edu/1info/FHP/practiceguides/pain/PEG.Scale.12.2016.pdf
» Treat the underlying physical cause of pain. Refer for specialist care (e.g. rheumatologist, orthopaedic surgeon) where necessary.
» Treat underlying or comorbid mental illness.
» Manage substance use, refer to SANCA/ rehabilitative services.
» Encourage physical activity; refer to Physiotherapy and Occupational Therapy (OT).
» Address self-esteem, motivation, daily function, and social skills; refer to OT.
» Address social stressors and interpersonal conflicts; refer to social worker, counselling services, psychologist, social welfare organisations, NGOs (e.g. FAMSA, http://famsa.org.za, or if there is domestic violence, POWA, https://www.powa.co.za)

LoE:III[i]

MEDICINE TREATMENT

Paracetamol, ibuprofen and tramadol may be used alone or in combination according to the severity of the pain.

Mild/moderate pain:

- Paracetamol, oral, 1 g 4–6 hourly when required.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum daily dose: 4 g in 24 hours.

- NSAID, e.g.: *LoE:I*[ii]
- Ibuprofen, oral, 400 mg 8 hourly with meals.
  - May be used in combination with paracetamol or opioids.

CAUTION

Avoid long-term use of NSAIDs (e.g. ibuprofen) as they are associated with an increased risk of arterial thrombosis, renal impairment and gastrointestinal bleeding.

Concomitant use of more than one oral NSAID has no additional clinical benefit and only increases toxicity.

Use of all NSAIDs is associated with increased risks of gastrointestinal bleeding, renal dysfunction, and cardiovascular events (stroke and myocardial infarction).

NSAIDs should be used judiciously at the lowest effective dose for the shortest duration. Explore and manage exacerbating factors for pain. See section 26.1: Chronic pain.

Do not use NSAID in pregnancy or while breastfeeding.

In high-risk patients: i.e. patients > 65 years of age, or with a history of peptic ulcer disease, or on concomitant warfarin, aspirin or corticosteroids:

ADD *LoE:III*[iii]

- PPI, e.g.:
- Lansoprazole, oral, 30 mg daily.

Severe pain:

- Tramadol, oral, 50–100 mg 4–6 hourly.
  - Warn patient of adverse effects and addiction potential. Advise not to operate machinery/drive initially and after dosage increases.
  - Evaluate response to treatment using a rating scale at 2 weeks, and every following 4 weeks: **taper and stop tramadol if not reducing pain.**
  - In patients with uncontrolled pain the dose can be increased to a maximum of 100 mg (2 x 50 mg) 6 hourly.
  - Improved effect when given with paracetamol. *LoE:III*[iv]

CAUTION

» Tramadol causes respiratory depression and may be fatal in overdose.
» Avoid concurrent prescribing of opioid pain medication, benzodiazepines or other respiratory depressants.
» After a period of no treatment, re-initiate at 25 mg. Treat overdose as in section 19.5.3. Opioid poisoning.
» Avoid use in those at high risk of opioid addiction (a personal or family history of any substance use disorder, comorbid mental illness, high levels of subjective pain and younger people).
» Inhibits reuptake of noradrenaline and serotonin – increases risk of seizures, of serotonin syndrome, and mania or hypomania. Avoid use in at-risk groups (e.g. epilepsy, head injury, if taking antidepressants, bipolar disorder). Educate the patient, optimise treatment of primary condition, avoid polypharmacy and monitor closely.
» Other adverse effects include constipation, dry mouth, drowsiness, confusion.

LoE:III[v]

OR

- Morphine syrup (Mist morphine), oral.
  - Starting dose: 10–15 mg (maximum 0.2 mg/kg) 4 hourly.
  - Elderly or frail patients: 2.5–5 mg oral (maximum 0.1 mg/kg) 4 hourly.
  - Increase dose by 50% every 24 hours if pain control is inadequate.
  - Reduce the dosing interval if there is regular breakthrough pain.
  - **Increase the dosing interval in patients with renal or liver impairment.**

When stable on morphine syrup, the morphine syrup can be changed to an equivalent dose of long- acting, slow release morphine:

- Morphine, long-acting, oral, 12 hourly.
  - Available in tablets of 10 mg, 30 mg and 60 mg
  - Duration of action 12 hours.
  - Dose according to previous morphine syrup requirement: e.g. a patient whose pain is controlled by 6 doses of morphine syrup 10 mg per 24 hours (i.e. 60 mg morphine per day) can be converted to slow release morphine tablets, 30 mg 12 hourly, oral.
  - Maximum dose for non-cancer pain is usually 60 mg 12 hourly.

Note:

» When morphine is used for chronic non-cancer pain, discuss potential side-effects with the patient, the maximum dose of opioids that will be prescribed and anticipated duration of treatment.
» Avoid in patients with history of alcohol or other drug addiction, where possible.

26.1.2 ANALGESIA FOR CHRONIC CANCER PAIN

The term “cancer pain” also includes pain due to terminal illness.
The same steps as given in section 26.1.1: Analgesia for chronic non-cancer pain should be followed with the following exceptions:

- Morphine:
» There is no maximum dose of morphine that may be needed.
» Concerns regarding addiction should not compromise adequate pain control with opioids when used to treat terminal illnesses.
» For terminally ill patients on slow release morphine, it is advisable to still prescribe morphine syrup for breakthrough pain or for painful procedures.

Note:
» Opioid–induced hyperalgesia is defined as increasing pain sensitivity in patients chronically exposed to opioids without any new causes for pain. Increasing doses of morphine paradoxically result in increased pain, often with features of neuropathic pain such as hyperalgesia or allodynia.
» It can be managed by switching to methadone, in consultation with a specialist familiar with the use of this agent. *LoE:III*[vi]

Bisphosphonates may be considered for metastatic bone pain – refer to the Tertiary and Quaternary EML (specialist management/consultation).

26.1.3 TREATMENT OF ADVERSE EFFECTS OF CHRONIC OPIOID USE

Y45.0

Constipation:
Patients on chronic opioids should routinely be prescribed a laxative.

- Sennosides A and B, oral, 13.5 mg, 1–2 tablets at night.
  - Contraindicated in patients with potentially obstructive lesions.

LoE:III[vii]

In patients with potentially obstructive lesions:

- Lactulose, oral, 10–20 mL 12 hourly.

LoE:III[viii]

Nausea and vomiting:

- Metoclopramide, oral/IM/slow IV, 10 mg 8 hourly (See section 12.7.5.2 treatment of PONV).

OR

Promethazine, oral, 10 mg 8 hourly. *LoE:III*

OR

- Ondansetron, oral, 8 mg 12 hourly.

26.1.4 NEUROPATHIC PAIN

G62.9/G50.0

DESCRIPTION

Defective functioning of nerves, which may involve both peripheral nerves (peripheral neuropathy) and cranial nerves. Different patterns are noted, i.e. polyneuropathy, mononeuritis multiplex, and mononeuropathy, each of which may be caused by axonal degeneration or demyelination or a combination of the above. Clinical features may be predominantly of a sensory, sensorimotor or motor nature.

Important causes of a predominantly sensory neuropathy include:

» alcohol,
» diabetes,
» HIV infection,
» thiamine deficiency, vitamin B12 deficiency, (although the latter more commonly presents as subacute combined degeneration of the cord),
» medicines (e.g. isoniazid, stavudine, metronidazole, amiodarone)

Important causes of a predominantly motor neuropathy include:

» Acute Inflammatory Demyelinating Polyradiculoneuropathy (AIDP – also known as Guillain-Barrè syndrome),
» Chronic Inflammatory Demyelinating Polyradiculoneuropathy (CIDP),
» acute porphyrias

GENERAL MEASURES

If there is a history of rapid progression, particularly in patients with features suggestive of AIDP, (e.g. rapid progression with stabilisation within 4 weeks) admit the patient and monitor vital capacity carefully with spirometry, as intubation and ventilatory support may be required.

Manage the cause where possible.

Specialised nursing care and dedicated physiotherapy may be indicated. If not managed appropriately, chronic cases may develop contractures, weakness affecting gait, and chronic bedsores, and they may become wheel chair-bound.

Encourage activity, with referral to OT and physiotherapy.

Address psychosocial stressors and enhance perceived social support, and refer to social worker as required.

Treat comorbid mental illness (see chapter 15: Mental health conditions).

Assess outcome of treatment with objective measures of function, e.g. Pain, Enjoyment and General Activity (PEG) scale.
http://www.med.umich.edu/1info/FHP/practiceguides/pain/PEG.Scale.12.2016.pdf

MEDICINE TREATMENT

Most cases respond to management of the underlying disease process or removal of the aetiological agent.

In addition to the analgesics for chronic nociceptive pain (see section 12.13.1 Analgesia for chronic non-cancer pain), anti-neuropathic pain medicines to stabilise affected sensory nerves can be used.

- Amitriptyline, oral, 10 mg, two hours before usual sleep time.
  - Titrate up to 75 mg (to a maximum of 200 mg) at night if needed. *LoE:II*[ix]
  - In the elderly: 10–25 mg daily, increasing gradually up to 50–100 mg daily, if required and tolerated. A single bedtime dose is optimal for most patients. *LoE:III*[x]
  - Use regularly, as takes 2–6 weeks for maximal effect. *LoE:III*[xi]

Post-herpetic neuralgia

Initiate treatment with adjuvant amitriptyline therapy early. *LoE:II*[xii]

<u>If no response after 2-4 weeks or amitriptyline is contraindicated:</u>

ADD/REPLACE WITH

- Carbamazepine, oral, 100–200 mg 12 hourly for 2 weeks.
  - If response is inadequate, increase the dose every 2 weeks to a maximum dose of 600 mg 12 hourly.
  - Monitor for possible drug interactions in patients on ART. *LoE:II*[xiii]

Note: Aciclovir is not beneficial in treating post-herpes zoster neuropathy.

Isoniazid–induced polyneuropathy

- Pyridoxine, oral 75 mg daily for 3 weeks.
  - Follow with 25–50 mg daily.

Trigeminal neuralgia (G50.0)

Sudden, usually unilateral, severe, brief, stabbing, recurrent episodes of pain in the distribution of one or more branches of the trigeminal nerve.

- Carbamazepine, oral 100 mg 12 hourly, initial dose.
  - Increase dose slowly. Doses of up to 1 200 mg daily may be required.
  - After exacerbation, reduce to maintenance dose of 400–800 mg daily. *LoE:III*[xiv]

REFERRAL

For neuropathic pain unresponsive to these medicines, refer patient to an experienced pain clinician.

26.2 ANALGESIA FOR ACUTE NON-SURGICAL PAIN

26.2.1 MEDICAL CONDITIONS ASSOCIATED WITH SEVERE PAIN

R52.9

There are numerous medical conditions associated with severe acute pain e.g. myocardial infarction, renal colic, sickle-cell crisis and intra-articular haemorrhage due to haemophilia.
The analgesic treatment for these conditions is as for patients with acute post-operative pain (see section 12.4.2: Postoperative pain in the recovery room).
Patients should be monitored for respiratory and cardiovascular depression when IV opioids are administered.
Patients already on opioids for chronic pain, who experience an acutely painful event, may be opioid tolerant and require higher IV opioid boluses in order to control their pain.

26.2.2 ACUTE PAIN DUE TO GASTROINTESTINAL COLIC

R10.84

- Hyoscine butylbromide, IV/oral, 10 mg 8 hourly.

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The list of antimicrobial medicines, below, excludes antiretroviral medicines.
It is important to refer to the text of the standard treatment guidelines for detailed information of specific medicines for specific indications (i.e. duration of therapy, if used in combination with other antibiotics, prescriber level, etc.).

ACICLOVIR

4.5: Atopic eczema/dermatitis, eczema herpeticum (if patient is unable to swallow due to odynophagia):

- **Aciclovir, IV, 5 mg/kg 8 hourly for 7 days.**

9.12: Varicella (chickenpox), complicated, 9.13: Zoster (Shingles – with secondary dissemination or neurological involvement), 14.6.2: Viral meningoencephalitis:

- **Aciclovir, IV, 10 mg/kg 8 hourly.**

18.5.1: Keratitis, herpes simplex:

- **Aciclovir, ophthalmic ointment 3%, applied into lower conjunctival sac, five times daily.**

9.12: Varicella (chickenpox), complicated, 9.13: Zoster (Shingles), 18.4: Herpes zoster ophthalmicus:

- **Aciclovir, oral, 800 mg five times a day or 4 hourly while awake.**

4.5: Atopic eczema/dermatitis, eczema herpeticum; 18.5: Keratitis; 25.3: Genital ulcer syndrome (GUS):

- **Aciclovir, oral, 400 mg 8 hourly for 7 days or five times a day for 10-14 days or 12 hourly.**

AMIKACIN

9.1.3: Hospital-Acquired Pneumonia (HAP), 9.1.4: Urinary tract infections, catheter associated, 10.1.1: Management of selected antiretroviral ADRs - drug-induced liver injury:

- **Amikacin, IV, 15 mg/kg daily**.

AMOXICILLIN

6.12: Preterm Labour (PTL) AND Preterm Prelabour Rupture of Membranes (PPROM), 16.4: Chronic obstructive pulmonary disease (COPD):

- **Amoxicillin, oral, 500 mg 8 hourly for 5 days***.*

1.1.8: Peptic ulcer, H. pylori +ve:

- **Amoxicillin, oral, 1 g 12 hourly for 7 days.**

3.5: Endocarditis, infective, prophylaxis:

- **Amoxicillin, oral, 2 g one hour before dental procedure.**

16.6: Pneumonia, community acquired (uncomplicated), 17.4: Otitis media, acute

- **Amoxicillin, oral, 1 g 8 hourly.**

AMOXICILLIN/CLAVULANIC ACID

1.1.2: Diverticulosis, 1.2.5: Liver abscess, pyogenic, 1.2.7: Acute cholecystitis and acute cholangitis, 1.3.8: Bacterial peritonitis, 4.7: Leg ulcers, complicated, 5.3: Pelvic inflammatory disease (PID), 5.8.4: Septic miscarriage, 6.18: Postpartum fever, 6.21.2: Urinary tract infection in pregnancy: acute pyelonephritis, 8.7.1: Diabetic neuropathies, 16.3: Bronchiectasis, 16.4: Chronic obstructive pulmonary disease (COPD), 16.5: Lung abscess, 16.6: Pneumonia, community acquired, 16.7: Pneumonia, aspiration, 16.8: Empyema, 17.1: Epiglottis, 17.4: Otitis media, acute, 17.8: Abscess, Peritonsillar, 19.2: Snakebites: secondary infection:

- **Amoxicillin/clavulanic acid 875/125 mg, oral, 12 hourly.**

1.2.7: Acute cholecystitis and acute cholangitis, 1.1.2: Diverticulosis: cannot take oral medicines, 1.1.6: Pancreatitis acute: abscess of the pancreas, 1.2.5: Liver Abscess, pyogenic , 1.3.8: Bacterial peritonitis, 5.8.4: Septic miscarriage, 6.18: Postpartum Fever, 8.7.3: Diabetic foot ulcers: severe infection, 16.5: Lung abscess, 16.7: Pneumonia, aspiration, 16.8: Empyema, 17.8: Abscess, peritonsillar:

- **Amoxicillin/clavulanic acid, IV, 1.2 g 8 hourly.**

AMPHOTERICIN B

9.1.1: Intravascular catheter infections, candidaemia:

- **Amphotericin B, IV, 0.7 mg/kg daily.**

2.2: Febrile neutropenia, 10.2.4.2: Symptomatic, non-meningeal Cryptococcosis 10.2.4.3: Cryptococcal meningitis: , 14.6.1.2.2: Cryptococcal meningitis, HIV-uninfected:

- **Amphotericin B, slow IV infusion, 1 mg/kg daily.**

AMPICILLIN

16.6: Pneumonia, community acquired:

- **Ampicillin, IV, 1 g 6 hourly.**

3.5: Endocarditis, infective, prophylaxis, if patient cannot take oral medicines:

- **Ampicillin, IV/IM, 2 g one hour before dental procedure.**

14.6.1: Meningitis: Listeria monocytogenes meningitis:

- **Ampicillin, IV, 3 g 6 hourly for 21 days.**

AZITHROMYCIN

3.7: Rheumatic heart disease, prophylaxis of recurrent disease, severe penicillin allergy:

- **Azithromycin, oral, 250 mg daily.**

11.4: Antibiotic prophylaxis:

- **Azithromycin, 500 mg, IV, as a single dose.**

16.6: Pneumonia, community acquired (severe pneumonia):

- **Azithromycin, 500 mg, slow IV (over not less than 60 minutes) daily for 3 days.**

1.1.8: Peptic ulcer, severe penicillin allergy, 3.7: Rheumatic heart disease, acute rheumatic fever - severe penicillin allergy, 4.2: Cellulitis and erysipelas – severe penicillin allergy, 4.3: Impetigo – severe penicillin allergy, 6.12: Preterm Labour (PTL) AND Preterm Prelabour Rupture of Membranes (PPROM) - severe penicillin allergy, 10.2.8: Mycobacteriosis - disseminated non tuberculous, 16.3: Bronchiectasis - severe penicillin allergy, 16.4: Chronic obstructive pulmonary disease (COPD) - severe penicillin allergy, 17.1: Epiglottitis - severe penicillin allergy, 17.4: Otitis media, acute - severe penicillin allergy:

- **Azithromycin, oral, 500 mg daily for 3 days.**

9.10: Tick bite fever, in pregnancy:

- **Azithromycin, oral, 500 mg 12 hourly for 3 days.**

5.3: Pelvic Inflammatory Disease (PID) - stage I, 5.3: Pelvic Inflammatory Disease (PID), stage II-IV: chlamydia (also for severe penicillin allergy), 5.10: Sexual Assault (STI prophylaxis), 7.3.4: Prostatitis (acute bacterial prostatitis), 13.2: Arthritis, Septic and osteomyelitis, acute , 13.5.1: Arthritis, reactive: 10.4.2: Non occupational post exposure prophylaxis, sexual assault and inadvertent exposure:

- **Azithromycin, oral, 1 g as a single dose.**

5.3: Pelvic Inflammatory Disease (PID)-stage I, severe penicillin allergy, 10.5.2: Non occupational post exposure prophylaxis, sexual assault, 25.1: Male urethritis syndrome (MUS), 25.2: Vaginal discharge syndrome (VDS):

- **Azithromycin, oral, 2 g as a single dose.**

BENZATHINE BENZYLPENICILLIN

3.7: Rheumatic heart disease, prophylaxis:

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

3.7: Rheumatic heart disease, acute rheumatic fever:

- **Benzathine benzylpenicillin (depot formulation), IM, 1.2 mu as a single dose.**

6.8: Syphilis, asymptomatic well baby:

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

25.3: Genital ulcer syndrome (GUS):

- **Benzathine benzylpenicillin (depot formulation), IM, 2.4 mu immediately as a single dose.**

6.8: Syphilis, mother:

- **Benzathine benzylpenicillin (depot formulation), IM, 2.4 mu weekly for 3 doses.**

BENZYL PENICILLIN

6.8: Syphilis, symptomatic baby:

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

17.8: Abscess, peritonsillar:

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

9.9: Tetanus:

- **Benzylpenicillin (penicillin G), IV, 5 MU 6 hourly for 10 days.**

3.5: Endocarditis, infective – empiric therapy and directed therapy for native valve:

- **Benzylpenicillin (penicillin G), IV, 5 MU 6 hourly for 4 weeks.**

14.6.1: Meningitis (meningococcal meningitis – confirmed meningococcal disease only), 14.6.1: Meningitis (pneumococcal meningitis):

- **Benzylpenicillin (penicillin G), IV, 20–24 MU daily in 4–6 divided doses for 10 days.**

14.6.3: Meningovascular Syphillis:

- **Benzylpenicillin (penicillin G), IV, 20 MU daily in 4–6 divided doses for 10 days.**

CEFALEXIN

4.2: Cellulitis and erysipelas:

- **Cefalexin, oral, 500 mg 6 hourly for 5 days.**

CEFAZOLIN

11: Cardiac surgery, 11: Endoscopic gastrointestinal procedures, 11: Gastrointestinal surgery, 11: General surgery, 11: Neurosurgery , 11: Obstetrics/ gynaecology surgery, 11: Orthopaedic surgery , 11: Otorhinolaryngology/ Head and neck surgery: severe beta lactam allergy, 11: Plastic and reconstructive surgery, 11: Thoracic surgery, 11: Urology, 11: Vascular surgery:

- **Cefazolin, IV, 1-3 g as a single dose.**

4.2: Cellulitis and erysipelas, 4.4: Furuncles and abscesses, 9.1.2: Surgical wound infections:

- **Cefazolin, IV, 1 g 8 hourly.**

3.5: Endocarditis, infective – empiric therapy and directed therapy for native valve, 13.2: Arthritis, Septic and osteomyelitis, acute:

- **Cefazolin, IV, 2 g 8 hourly.**

CEFEPIME

2.2: Febrile neutropenia; 9.1.3: Hospital-acquired pneumonia (HAP):

- **Cefepime, IV, 2 g 12 hourly.**

CEFTAZIDIME

18.2: Endophthalmitis, bacterial (endogenous endophthalmitis and post-surgical endophthalmitis):

- **Ceftazidime, intravitreal, 2.25 mg.**

CEFTRIAXONE

5.3: Pelvic Inflammatory Disease (PID), stage I, 5.10: Sexual assault, 7.3.4: Prostatitis, associated urethritis, 10.5.2: Non occupational post exposure prophylaxis, sexual assault and inadvertent exposure, 13.5.1: Arthritis, reactive:

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

1.3.2: Acute inflammatory diarrhoea (dysentery) , , 1.3.8: Bacterial peritonitis, 17.1: Epiglottitis, 2.2: Febrile neutropenia, 5.3: Pelvic Inflammatory Disease (PID), stage II-IV, 6.2.1.2: Pyelonephritis, acute, 7.3.2: Urinary tract infection (UTI), acute pyelonephritis: impaired renal function, 13.2: Arthritis, septic and osteomyelitis, acute, 17.1: Epiglottitis, 25.1: Male urethritis syndrome (MUS) , 25.2: Vaginal discharge syndrome (VDS):

- **Ceftriaxone, IV, 1 g, daily.**

9.11: Typhoid fever (enteric fever), 14.6.1: Meningitis, 14.6.4: Brain abscess, 14.6.5: Antimicrobial use in patients with head injuries, penetrating brain injuries, 17.3: Sinusitis, bacterial, complicated, 17.6: Mastoiditis:

- **Ceftriaxone, IV, 2 g 12 hourly.**

16.3: Bronchiectasis, 18.2: Endophthalmitis, bacterial, 16.6: Pneumonia, community acquired, patients >65 years, comorbid disease, 16.6: Pneumonia, community acquired, severe pneumonia,20.11.2.2: Septic shock, 9.1.3: Hospital-Acquired Pneumonia (HAP), no risk factors for MDR infection, 9.1.2: Surgical wound infections: female uro-genital tract, open GIT surgery:

- **Ceftriaxone 2 g, IV, daily.**

CHLORAMPHENICOL

18.10.1: Chemical burn, 19.2.3: Snake venom in the eye:

- **Chloramphenicol 1%, ophthalmic ointment, applied 6 hourly.**

18.1.3: Conjunctivitis, bacterial:

- **Chloramphenicol 1%, ophthalmic ointment, applied 8 hourly.**

11: Ophthalmic surgery:

- **Chloramphenicol 0.5% ophthalmic drops, instil 1 drop 2–4 hourly for 24 hours prior to surgery.**

CIPROFLOXACIN

17.5: Otitis media, chronic, suppurative:

- **Ciprofloxacin 0.3%, ophthalmic drops, 3–4 drops instilled into the ear**

every 8 hours for 7 days after mopping.

18.1.3: Conjunctivitis, bacterial, 18.5.2: Keratitis, suppurative:

- **Ciprofloxacin 0.3%, ophthalmic drops.**

14.6.1: Meningitis, nasopharyngeal carriage eradication, 14.6.1: Meningitis, prophylaxis of contacts:

- **Ciprofloxacin, oral, 500 mg immediately as a single dose.**

1.3.1: Cholera, 1.3.2: Acute inflammatory diarrhoea (dysentery) , 1.3.8: Bacterial peritonitis, 5.3: Pelvic inflammatory disease (stage II-IV) – severe penicillin allergy, 5.8.4: Septic miscarriage, severe penicillin allergy, de-escalation therapy, 7.3.2: Urinary tract infection (complicated community acquired UTI) , 7.3.2: Urinary tract infection (UTI), acute pyelonephritis: de-escalation therapy, 7.3.4: Prostatitis, 9.1.4: Urinary tract infections, catheter associated, 9.11: Typhoid fever (enteric fever), chronic carriers, 9.11: Typhoid fever (enteric fever), following ceftriaxone IV, based on culture sensitivity results,10.2.7: Cystoisosporiasis, cotrimoxazole allergy

- **Ciprofloxacin, oral, 500 mg 12 hourly.**

16.3: Bronchiectasis, pseudomonas infection, 17.7.1: Otitis externa, necrostising, 18.2: Endophthalmitis, bacterial, prophylaxis/soft tissue injury:

- **Ciprofloxacin, oral, 750 mg 12 hourly for 7 days.**

9.10: Tick bite fever, cannot take oral medicines:

- **Ciprofloxacin, IV, 400 mg 8 hourly.**

CLINDAMYCIN

4.2: Cellulitis and erysipelas, severe penicillin allergy, 4.4: Furuncles and abscesses, severe penicillin allergy, 5.3: Pelvic Inflammatory Disease (PID), stage II-IV: severe penicillin allergy, 5.8.4: Septic miscarriage, severe penicillin allergy, 9.1.2: Surgical wound infections, severe penicillin allergy, 17.8: Abscess, peritonsillar, severe penicillin allergy, 13.2: Arthritis, septic and osteomyelitis, acute, severe penicillin allergy:

- **Clindamycin, IV, 600 mg 8 hourly.**

3.5: Endocarditis, infective, prophylaxis: severe penicillin allergy (if patient cannot take oral), 11: Cardiac surgery, severe penicillin allergy, 11: Endoscopic gastrointestinal procedures: severe penicillin allergy, 11: Gastrointestinal surgery: severe penicillin allergy, 11: General surgery: severe penicillin allergy, 11: Neurosurgery: severe penicillin allergy, 11: Obstetrics/ gynaecology surgery: severe penicillin allergy, 11: Orthopaedic surgery: severe penicillin allergy, 11: Otorhinolaryngology/Head and neck surgery: severe penicillin allergy, 11: Plastic and reconstructive surgery: severe penicillin allergy, 11: Thoracic surgery: severe penicillin allergy, 11: Urology: severe penicillin allergy, 11: Vascular surgery: severe penicillin allergy:

- **Clindamycin, IV, 600 mg as a single dose.**

3.5: Endocarditis, infective, prophylaxis, severe penicillin allergy:

- **Clindamycin, oral, 600 mg one hour before the procedure.**

8.7.3: Diabetic foot ulcers, severe penicillin allergy:

- **Clindamycin, oral, 150-450 mg 8 hourly.**

4.2: Cellulitis and erysipelas: severe penicillin allergy, 4.4: Furuncles and abscesses: severe penicillin allergy, 4.5: Atopic eczema/dermatitis: severe penicillin allergy, 5.3: Pelvic Inflammatory Disease (PID), stage II-IV: severe penicillin allergy, de-escalation therapy, 5.8.4: Septic miscarriage, severe penicillin allergy, de-escalation therapy,, 9.1.1: Intravascular catheter infections, erythema beyond catheter site, 9.1.2: Surgical wound infections, severe penicillin allergy, de-escalation therapy, 13.2: Arthritis, septic and osteomyelitis, acute: severe penicillin allergy, 17.8: Abscess, peritonsillar, 21.2.2: Extravasations:

- **Clindamycin, oral, 450 mg 8 hourly.**

3.5: Endocarditis, infective, prophylaxis, severe penicillin allergy:

- **Clindamycin, oral, 600 mg one hour before the dental procedure.**

10.2.9: Pneumocystis pneumonia, cotrimoxazole intolerance, unsuccessful cotrimoxazole desensitisation:

- **Clindamycin, oral, 600 mg 8 hourly for 21 days.**

CLOTRIMAZOLE

4.10: Fungal infections, yeast and dermatophytes:

- **Clotrimazole 1%, topical, apply 8 hourly until clear of disease (i.e. for at least 2 weeks after the lesions have cleared).**

COTRIMOXAZOLE

7.3.3: Recurrent UTI, prophylaxis:

- **Cotrimoxazole 80/400 mg, oral, 1 tablet at night.**

10.2.2: Opportunistic infection prophylaxis, with cotrimoxazole, 10.2.7: Cystoisosporiasis, secondary prophylaxis, 10.2.9: Pneumocystis pneumonia, secondary prophylaxis, 10.2.10: Cerebral toxoplasmosis, secondary prophylaxis:

- **Cotrimoxazole, oral, 160/800 daily.**

10.2.9: Pneumocystis pneumonia: <60kg:

- **Cotrimoxazole, oral, 240/1200 6 hourly for 21 days.**

10.2.10: Cerebral toxoplasmosis:

- **Cotrimoxazole 320/1600, oral, 12 hourly for 28 days, followed by 240/1200 tablets 12 hourly for 3 months.**

10.2.7: Cystoisosporiasis:

- **Cotrimoxazole 320/1600, oral, 12 hourly for 10 days.**

10.2.9: Pneumocystis pneumonia, >60kg:

- **Cotrimoxazole 320/1600 mg, oral, 6 hourly for 21 days.**

10.2.9: Pneumocystis pneumonia, if vomiting:

- **Cotrimoxazole, IV, 6 hourly.**
  - < 60 kg 240/1200 mg.
  - > 60 kg 320/ 1600 mg.

DAPSONE

10.2.9: Pneumocystis pneumonia, if primaquine not available:

- **Dapsone, oral, 100 mg daily for 21 days.**

10.2.9: Pneumocystis pneumonia, secondary prophylaxis, cotrimoxazole intolerant:

- **Dapsone, oral, 100 mg daily for at least 6 months.**

DOXYCYCLINE

4.1: Acne, inflammatory (moderate):

- **Doxycycline, oral, 100 mg daily for 3 months.**

9.10: Tick bite fever, 16.4: Chronic obstructive pulmonary disease (COPD) – severe penicillin allergy:

- **Doxycycline, oral, 100 mg 12 hourly for 5 or 7 days.**

9.3: Brucellosis:

- **Doxycycline, oral, 100 mg 12 hourly for 6 weeks.**

25.4: Bubo:

- **Doxycycline, oral, 100 mg 12 hourly for 21 days (or more for laboratory-confirmed diagnosis of LGV).**

ECHINOCANDIN

9.1.1: Intravascular catheter infections (specialist motivation).

ERTAPENEM

9.1.2: Surgical wound infections (gram-negative organism):

- **Ertapenem, IV, 1 g daily.**

ETHAMBUTOL

16.11.1: INH monoresistant TB:

- **Ethambutol, oral, 15 mg/kg daily for 6-9 months.**

10.2.8: Mycobacteriosis - disseminated non tuberculous:

- **Ethambutol, oral, 15–20 mg/kg daily.**

10.1.1: Management of selected antiretroviral ADRs: drug-induced liver injury:

- **Ethambutol, oral, 800 - 1200 mg daily.**

FLUCLOXACILLIN

13.2: Arthritis, septic and osteomyelitis, acute:

- **Flucloxacillin, oral, 1 g 6 hourly (after 2 weeks of IV cloxacillin therapy in patients with good clinical response to complete the 4 weeks treatment).**

4.2: Cellulitis and erysipelas, 4.3: Impetigo , 4.4: Furuncles and abscesses, 4.5: Atopic eczema/dermatitis (infected eczema), 9.1.2: Surgical wound infections , 9.13: Zoster (Shingles)- if there is suspected associated bacterial cellulitis:

- **Flucloxacillin, oral, 500 mg 6 hourly.**

FLUCONAZOLE

4.10: Fungal infections, dermatophyte hair and nail infections; immunocompomised with extensive skin infection, 4.10: Fungal infections, onychomycosis:

- **Fluconazole, oral, 200 mg weekly.**

10.2.3: Candidiasis of oesophagus/trachea/bronchi, 10.2.4.1: Asymptomatic cryptococcosis, CrAg positive, maintenance therapy, 10.2.4.2: Symptomatic, Non-Meningeal Cryptococcosis, maintenance therapy, 10.2.4.3: Cryptococcal meningitis, maintenance therapy, 14.6.1.2.2: Cryptococcal meningitis, HIV-uninfected:

- **Fluconazole, oral, 200 mg daily.**

10.2.3: Candidiasis of oesophagus/trachea/bronchi, if vomiting or unable to swallow:

- **Fluconazole, IV, 200 mg daily.**

14.6.1.2.2: Cryptococcal meningitis, HIV-uninfected:

- **Fluconazole, oral, 400 mg daily for 8 weeks.**

9.1.1: Intravascular catheter infections, candidaemia,10.2.4.1: Asymptomatic cryptococcosis, CrAg positive, consolidation phase , 10.2.4.2: Symptomatic, Non-Meningeal Cryptococcosis, consolidation phase , 10.2.4.3: Cryptococcal meningitis, consolidation phase , 14.6.1.2.2: Cryptococcal meningitis, HIV-uninfected:

- **Fluconazole, oral, 800 mg daily**

10.2.4.1: Asymptomatic cryptococcosis, CrAg positive, induction therapy , 10.2.4.2: Symptomatic, Non-Meningeal Cryptococcosis, induction therapy , 10.2.4.3: Cryptococcal meningitis, induction therapy:

- **Fluconazole, oral, 1200 mg daily**

FOSFOMYCIN

6.21.1: Cystitis (in pregnancy), 7.3.2: Urinary tract infection (UTI):

- **Fosfomycin 3 g, oral, as a single dose.**

GANCICLOVIR

10.2.6: Cytomegalovirus (CMV), HIV:

- **Ganciclovir, IV, 5 mg/kg 12 hourly.**

18.6: Retinitis, HIV CMV:

- **Ganciclovir, intravitreal, 2 mg once a week.**

GENTAMICIN

3.5: Endocarditis, infective, empiric therapy (prosthetic and native valve); staphylococcal directed therapy; streptococcal directed therapy (native valve):

- **Gentamicin, IV, 1.5 mg/kg 12 hourly.**

3.5: Endocarditis, infective, enterococcal directed therapy (native valve):

- **Gentamicin, IV, 1 mg/kg 8 hourly.**

7.3.2: Urinary tract infection (UTI):

- **Gentamicin, IM, 5 mg/kg as a single dose**

14.6.1: Meningitis: Listeria monocytogenes meningitis:

- **Gentamicin, IV, 5 mg/kg daily for 7 days (may be prolonged if response is poor).**

2.2: Febrile neutropenia, 3.5: Endocarditis, infective, 5.3: Pelvic Inflammatory Disease (PID), stage II-IV: severe penicillin allergy, 5.8.4: Septic miscarriage (severe penicillin allergy), 6.21.2: Pyelonephritis, acute, in pregnancy, 7.3.2: Urinary tract infection (UTI), acute pyelonephritis: normal renal function, 8.7.3: Diabetic foot ulcers – severe penicillin allergy, 9.3: Brucellosis, 11: Gastrointestinal surgery: severe penicillin allergy, 11: Obstetrics/ gynaecology surgery: severe penicillin allergy, 11: Urology procedures: severe penicillin allergy, 25.1: Male urethritis syndrome (MUS), 25.2: Vaginal discharge syndrome (VDS):

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

IMIPENEM

2.2: Febrile neutropenia (if fever develops after 48 hours of admission – also consider local susceptibility patterns):

- **Imipenem/cilastin, IV, 500/500 mg 6 hourly.**

9.1.3: Hospital-Acquired Pneumonia (HAP), with risk factors, Ventilator Associated Pneumonia (VAP):

- **Imipenem/cilastin, IV, 1000/1000 mg 8 hourly (except CNS infections or known epileptics).**

ISONIAZID

10.1.1: Management of selected antiretroviral ADRs, drug-induced liver injury, 10.2.1: Isoniazid preventive therapy (IPT):

- **Isoniazid, oral 300 mg daily.**

LEVOFLOXACIN

10.1.1: Management of selected antiretroviral ADRs, drug-induced liver injury, 16.11.1: Isoniazid monoresistant TB:

- **Levofloxacin 750–1000 mg daily.**

MEROPENEM

2.2: Febrile neutropenia:

- **Meropenem, IV, 1 g 8 hourly.**

14.6.1: Meningitis, 9.1.3: Hospital-Acquired Pneumonia (HAP), with risk factors, VAP, CNS infections/seizures:

- **Meropenem, IV, 2 g 8 hourly.**

METRONIDAZOLE

1.3.4: Diarrhoea, antibiotic associated, 6.12: Preterm labour (PTL) and preterm prelabour rupture of membranes (PPROM) , 14.6.4: Brain abscess:

- **Metronidazole, oral, 400 mg 8 hourly**

1.1.8: Peptic ulcer, H. pylori +ve, 5.3: Pelvic Inflammatory Disease (PID), stage I::

- **Metronidazole, oral, 400 mg 12 hourly for 7 days.**

1.2.6: Liver abscess, amoebic, 1.3.5: Amoebic dysentery:

- **Metronidazole, oral, 800 mg 8 hourly for 10 days.**

1.3.6: Giardiasis, 5.10: Sexual assault , 10.5.2: Non occupational post exposure prophylaxis, sexual assault and inadvertent exposure, 25.2: Vaginal discharge syndrome (VDS):

- **Metronidazole, oral, 2 g.**

11: Gastrointestinal surgery, 11: Obstetrics/ gynaecology surgery, 11: Otorhinolaryngology/ Head and neck surgery, 11: Urology, 11: Thoracic surgery; 11: Vascular surgery:

- **Metronidazole, IV, 500 mg, as a single dose.**

1.3.4: Clostridum difficile diarrhoea, 5.3: Pelvic Inflammatory Disease (PID), stage II-IV, 9.1.2: Surgical wound infections, female uro-genital tract, open GIT surgery, 9.9: Tetanus , 14.6.4: Brain abscess:

- **Metronidazole, IV, 500 mg, 8 hourly.**

MOXIFLOXACIN

9.1.3: Hospital-Acquired Pneumonia (HAP), severe penicillin allergy, 16.3 Bronchiectasis if pseudomonas infection is suspected, severe penicillin allergy, 16.5: Lung abscess, severe penicillin allergy 16.6: Pneumonia, community acquired, severe penicillin allergy, 16.7: Pneumonia, aspiration, severe penicillin allergy, 16.8: Empyema, severe penicillin allergy:

- **Moxifloxacin, IV, 400 mg daily, until patient apyrexial for 24 hours.**

9.1.3: Hospital-Acquired Pneumonia (HAP), severe penicillin allergy, 10.1.1: Management of selected antiretroviral ADRs, 16.3 Bronchiectasis if pseudomonas infection is suspected, severe penicillin allergy, 16.5: Lung abscess, severe penicillin allergy 16.6: Pneumonia, community acquired, severe penicillin allergy, 16.7: Pneumonia, aspiration, severe penicillin allergy, 16.8: Empyema, severe penicillin allergy:

- **Moxifloxacin, oral, 400 mg daily.**

NATAMYCIN

18.5.2: Keratitis, suppurative, fungal infection:

- **Natamycin 5%, ophthalmic drops.**

NITROFURANTOIN

6.21.1: Cystitis (pregnancy); 7.3.2: Urinary tract infection (UTI):

- **Nitrofurantoin, oral, 100 mg 6 hourly for 5 days.**

PHENOXYMETHYLPENICILLIN

3.7: Rheumatic heart disease, prophylaxis:

- **Phenoxymethylpenicillin, oral, 250 mg 12 hourly.**

3.7: Rheumatic heart disease, acute rheumatic fever:

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

6.8: Syphilis, penicillin desensitisation:

- **Phenoxymethylpenicillin, IV, 250 mg/5 mL.**

PIPERACILLIN/TAZOBACTAM

2.2: Febrile neutropenia, 9.1.2: Surgical wound infections, 9.1.3: Hospital-Acquired Pneumonia (HAP), with risk factors, Ventilator Associated Pneumonia (VAP), CNS infections/seizures:

- **Piperacillin/tazobactam, IV, 4.5 g 8 hourly.**

PROCAINE PENICILLIN

6.8: Syphilis, symptomatic baby:

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

PYRAZINAMIDE

10.1.1: Management of selected antiretroviral ADRs, drug-induced liver injury, 16.11.1: INH monoresistant TB:

- **Pyrazinamide, oral, 25 mg/kg daily.**

RIFABUTIN

10.1: Antiretroviral therapy, TB treatment for patients on ATV/r or darunavir when rifampicin is contraindicated:

- **Rifabutin, oral, 150 mg daily.**

RIFAMPICIN

3.5: Endocarditis, infective, 9.3: Brucellosis:

- **Rifampicin, oral, 7.5 mg/kg 12 hourly for 6 weeks.**

16.11.1: INH monoresistant TB:

- **Rifampicin, oral, 10 mg/kg daily.**

10.1.1: Management of selected antiretroviral ADRs, drug-induced liver injury; <60kg:

- **Rifampicin, oral 450 mg daily.**

10.1.1: Management of selected antiretroviral ADRs, drug-induced liver injury:

- **Rifampicin, oral 600 mg daily.**

RIFAMPICIN/ISONIAZID

16.9: Tuberculosis, pulmonary, continuation phase: 30-37kg, 16.10: Tuberculosis, pleural, continuation phase: 30-37kg:

- **Rifampicin/isoniazid, oral, 300/150 mg, daily for 4 months.**

16.9: Tuberculosis, pulmonary, continuation phase: 38-54kg, 16.10: Tuberculosis, Pleural, continuation phase: 38-54kg:

- **Rifampicin/isoniazid, oral, 450/225 mg, daily for 4 months.**

16.9: Tuberculosis, pulmonary, continuation phase: >55kg, 16.10: Tuberculosis, Pleural, continuation phase: >55kg:

- **Rifampicin/isoniazid, oral, 600/300 mg, daily for 4 months.**

RIFAMPICIN/ISONIAZID/PYRAZINAMIDE/ETHAMBUTOL

16.9: Tuberculosis, pulmonary, initial phase: 30-37kg, 16.10: Tuberculosis, Pleural, initial phase: 30-37kg, 16.11.1: Isoniazid monoresistant TB (single medicines unavailable): 30-37kg:

- **Rifampicin/isoniazid/pyrazinamide/ethambutol, oral, 300/150/800/500 mg, daily for 2–6 months.**

16.9: Tuberculosis, pulmonary, initial phase: 38-54kg:16.10: Tuberculosis, Pleural, initial phase: 38-54kg, 16.11.1: Isoniazid monoresistant TB (single medicines unavailable): 38-54kg:

- **Rifampicin/isoniazid/pyrazinamide/ethambutol, oral, 450/225/1200/825 mg, daily for 2–6 months.**

16.9: Tuberculosis, pulmonary, initial phase:55-70kg, 16.10: Tuberculosis, Pleural, initial phase:55-70kg, 16.11.1: Isoniazid monoresistant TB (single medicines

unavailable):55-70kg:

- **Rifampicin/isoniazid/pyrazinamide/ethambutol, oral, 600/300/1600/1100 mg, daily for 2–6 months.**

16.9: Tuberculosis, pulmonary, initial phase:71kg and over, 16.10: Tuberculosis, Pleural, initial phase:71kg and over, 16.11.1: Isoniazid monoresistant TB (single medicines unavailable): >71kg:

- **Rifampicin/isoniazid/pyrazinamide/ethambutol, oral, 750/3755/2000/1375 mg, daily for 2–6 months.**

TENOFOVIR

1.2.4.2: Hepatitis B, chronic (non-HIV co-infection):

- **Tenofovir, oral, 300 mg daily.**

VALGANCICLOVIR

10.2.6: Cytomegalovirus (CMV), 18.6: Retinitis, HIV CMV:

- **Valganciclovir, oral, 900 mg 12 hourly for 3 weeks, then 900 mg daily until until immune recovery (CD4 >100 cells/mm^3).**

VANCOMYCIN

1.3.4: Clostridum difficile diarrhoea:

- **Vancomycin, oral, 125 mg 6 hourly. (Give the parenteral formulation orally).**

18.2: Endophthalmitis, bacterial:

- **Vancomycin, intravitreal, 1 mg.**

3.5: Endocarditis, infective:

- **Vancomycin, IV, 20 mg/kg 12 hourly.**

2.2: Febrile neutropenia, IV, skin infection, 9.1.1: Intravascular catheter infections, S. aureus infection, 9.1.2: Surgical wound infections, MRSA:

- **Vancomycin, IV, 30 mg/kg as a loading dose. Follow with 20 mg/kg/dose 12 hourly.**

AMIKACIN, IV

- Amikacin, IV, 15 mg/kg daily.
  - If BMI is >40 kg/m^2 use ideal body weight* + 40% of the difference between ideal and actual body weight).
  - In severe sepsis or septic shock, a loading dose of 25 mg/kg should be given (irrespective of renal function).
  - If eGFR is 40–60 mL/minute, adjust maintenance dose to 15 mg/kg every 36 hours (check trough amikacin level and give the next dose when level <5 mg/L).
  - Maximum daily dose 1.5 g, usually for a maximum of 10 days.
  - Amikacin is potentially nephrotoxic and ototoxic – monitor creatinine three times per week and discontinue if vestibular or cochlear symptoms develop. Regular audiometry is essential with longer term use in patients with drug-resistant TB.
  - Therapeutic drug monitoring: pre-dose amikacin trough levels after the third dose. Aim for a trough level of <5 mg/L.
    - Normal renal function: do not wait for the amikacin level before giving the next dose. The level should be used to adjust the dose for the next day if applicable.
    - Impaired renal function: wait for the amikacin level and give the next dose when level <5 mg/L.
    - In obese patients or in patients with resistant Gram-negative bacteria also measure peak concentrations (0.5–1 hours after infusion). Aim for peak >30 mg/L (or ten times higher than the MIC for resistant organisms).

      ** ideal body weight calculator:* https://www.mdcalc.com/ideal-body-weight-adjusted-body-weight

AMIODARONE, ORAL

- Amiodarone, oral, 800 mg daily for 7 days.
  - Then 600 mg daily for 3 days.
  - Hypotension may occur, especially during the loading dose phase
  - Titrate to maintenance dose of 200–400 mg daily.
  - May cause hypothyroidism or thyrotoxicosis - monitor thyroid function every 6 months.
  - Monitor for pulmonary symptoms and perform baseline CXR before starting long-term therapy and annually thereafter to monitor for interstitial pulmonary fibrosis.

AMOXICILLIN/CLAVULANIC ACID, ORAL

- Amoxicillin/clavulanic acid, oral, 875/125 mg (containing 875 mg amoxicillin trihydrate and 125 mg clavulanic acid) 12 hourly.
  - When treating pneumonia in areas where there is a confirmed high prevalence (≥ 5%) of *Streptococcus pneumoniae* with intermediate resistance to penicillin : dose 8 hourly

ADD: Amoxicillin 1 g, oral, daily between the amoxicillin/clavulanic acid doses (i.e. 8 hours after the morning dose of amoxicillin/clavulanic acid).

AMOXICILLIN/CLAVULANIC ACID, IV

Amoxicillin/clavulanic acid IV is not suitable for intramuscular or subcutaneous administration.

- Amoxicillin/clavulanic acid, 1.2 g powder vials for intravenous injection containing amoxicillin sodium equivalent to 1 g of amoxicillin and potassium clavulanate equivalent to 200 mg clavulanic acid.
  - **Dosage Recommendation:** Amoxicillin/clavulanic acid, 1.2 g, IV, 8 hourly.
  - **Directions for use:**
    - Powder vials for injection can be reconstituted by dissolving in 20 mL water for injection.
    - Reconstituted vials can be administered intravenously by injection over 2 minutes or slow intravenous infusion over
    - For intravenous infusion, the reconstituted vial should be further diluted with the desired volume of a suitable infusion fluid (e.g. Sodium chloride 0.9%, 100 mL).
    - 30 minutes.
    - **The contents of the vials must be used within 20 minutes.**
  - **Precautions:**
    - Allergy to penicillins.
    - Drug-induced cholestatic hepatitis may occur, typically a few weeks after starting therapy. Use with caution in patients with evidence of hepatic dysfunction.
    - Dosage adjustments required in renal impairment:
      - CrCl >70 mL/minute: no dose adjustment required.
      - CrCl 10–30 mL/minute: 1.2 g as a single dose followed by 600 mg 12 hourly.
      - CrCl <10 mL/minute: 1.2 g as a single dose followed by 600 mg daily.

AMPHOTERICIN B, IV

- Amphotericin B, IV, 0.7–1 mg/kg daily, dose and duration of therapy depend on indication for use and infecting organism.
  - Reconstitue in 5% dextrose water only (as incompatibile with saline solution).
  - Administer over a period of 2–6 hours.
  - Ensure adequate hydration to minimise the risk of nephrotoxicity.

Monitoring

- Serum potassium, magnesium and creatinine (baseline and twice weekly). Monitoring of serum potassium and creatinine should occur more frequently in neutropenic patients (3 times a week).
- Monitor haemoglobin (baseline and weekly).

- Careful attention to fluid monitoring of intake and output.
- For management of hypokalaemia, see section 7.2.2: Hypokalaemia.

Management of elevated creatinine

If creatinine increases by ≥2 fold from baseline value, either omit an amphotericin B dose, or increase pre-hydration to 1 litre 8 hourly.

- Once improved, restart at 0.7 mg/kg daily and consider alternate day amphotericin B.
- If creatinine remains elevated i.e. ≥2 fold from baseline value, discontinue amphotericin B and continue with fluconazole, oral, 800 mg daily (for fungal infections known to be responsive to fluconazole, e.g. *Cryptococcus*).
  (Adapted from: WHO. Rapid advice: diagnosis, prevention and management of cryptococcal disease in HIV-infected adults, adolescents and children: Prevention, monitoring and management of amphotericin B toxicity. 2011 [Online] [Accessed March 2016] http://www.ncbi.nlm.nih.gov/books/NBK299520/pdf/Bookshelf_NBK299520.pdf

CEFEPIME, IV

- Cefepime IV/IM, 1–2 g 12 hourly.
  - Renal adjusted dosing:
    - eGFR >50 mL/minute: 100% of daily dose
    - eGFR 10–50 mL/minute: 50–100% of daily dose
    - eGFR <10 mL/minute: 25–50% of daily dose
      (Source: *Bennet, WM. Drug prescribing in renal failure. Fifth edition*).

CLINDAMYCIN, IV

- Clindamycin IV, 600 mg, 8 hourly (maximum of 4.8 g/day)
  - Dilute the contents of the vial in 100 mL of diluent prior to infusion.
  - Infuse over 20 minutes.
  - **Note:** Rapid infusion can cause flushing, pain, thrombophlebitis, hypotension and cardiopulmonary arrest.

DIGOXIN, ORAL

- Digoxin, oral, 0.125 mg daily, adjust according to rate response, if in atrial fibrillation, and trough plasma level.
  - Digoxin trough plasma levels (before the morning dose) should be maintained between 0.6–1 nmol/L. Monitor after 7 days and periodically thereafter.
  - Patients at high risk of digoxin toxicity are:
    - the elderly,
    - patients with renal dysfunction,
    - hypokalaemia, and
    - patients with low lean body mass.

GENTAMICIN, IV

- Gentamicin, IV, 5–6 mg/kg once daily.
  - If BMI is >40 kg/m^2 use ideal body weight* + 40% of the difference between ideal and actual body weight.
  - Administer slowly over 3 minutes or infused over 20–30 minutes up to 2 hours, diluted in 5% dextrose or 0.9% sodium chloride solution.
  - For streptococcal endocarditis: 1.5 mg/kg 12 hourly (in combination with penicillin).
  - Renal impairment dosage adjustment (eGFR <60 mL/minute):
    - Administer 3–4 mg/kg loading dose and adjust further dosing according to plasma concentrations.
  - Gentamicin is potentially nephrotoxic and ototoxic – monitor creatinine three times per week and discontinue if vestibular or cochlear symptoms develop.
  - Therapeutic drug monitoring: Sample after the third dose;
    - Draw trough concentrations immediately before dose; peak concentrations 0.5–1.0 hours after dosing from the drip-free arm.
    - Therapeutic ranges: Peak >8 mcg/ml, trough <1 mcg/ml
    - Reduce the dose per kg or consider omitting a dose if concentration is supratherapeutic. If the plasma concentration is subtherapeutic but the patient has signs of toxicity, change to an alternative agent.

      ** ideal body weight calculator:* https://www.mdcalc.com/ideal-body-weight-adjusted-body-weight

LABETALOL, IV

- Labetalol, IV infusion, 2 mg/minute to a total of 1–2 mg/kg.
  - Initial dose: 2 mg/minute
  - Titrate to response up to 300 mg total cumulative dose (e.g. discontinue after 2.5 hours of 2 mg/minute).
  - Usual total dose required is 50–200 mg (1–2 mg/kg).
  - Commence an oral antihypertensive regimen as soon as the infusion is discontinued.

LITHIUM, ORAL

- Lithium, oral, 250 mg 12 hourly.
  - Usual dose range: 200–500 mg/dose 12 hourly.
  - May be given as a single total daily dose at night to improve adherence and to protect renal function.
  - Measure serum concentrations at steady state (i.e. after 5 days) at about 12 hours after the last dose.
  - Lithium has a narrow therapeutic window. The therapeutic range is 0.4–0.8 mmol/L for maintenance therapy, and 0.8–1.0 mmol/L in mania.
  - If levels are sub-therapeutic and the patient is adherent increase the daily dose by 250 mg and repeat trough plasma levels after 5 days.

- Maintain therapeutic blood levels of lithium for as long as the patient is on lithium. Monitor lithium levels and renal function at least monthly for the first 3 months of therapy.
- Monitor lithium levels 6 monthly once stable levels have been achieved, together with serum creatinine, sodium and potassium.
- Check TSH (for lithium-induced hypothyroidism) and serum calcium (for lithium-induced hyperparathyroidism) before starting treatment and annually thereafter.
- Beware of combining lithium with ACE-inhibitors, NSAIDs and thiazide diuretics, as they all potentiate the risk for lithium toxicity.
  Pregnancy - Lithium has been associated with congenital abnormalities in the newborn with first trimester exposure. Risk-benefit assessment required for indication of maternal use during pregnancy.

METFORMIN, ORAL

- Metformin, oral, 500 mg twice 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.
  - Monitor renal function.
  - Dose-adjust in renal impairment as follows:
    - eGFR > 60 mL/minute: Normal daily dose (see above).
    - eGFR < 60 mL/minute: Half of the daily dose.
    - eGFR < 30 mL/minute: Stop metformin.
  - Contra-indicated in:
    - renal impairment i.e. eGFR < 30 mL/minute,
    - uncontrolled congestive cardiac failure,
    - severe liver disease,
    - patients with significant respiratory compromise, or
    - peri-operative cases.
  - Drug-drug interaction with dolutegravir (DTG): DTG may increase the serum concentration of metformin. Limit maximum dose of metformin to 1000 mg daily if concomitant use with DTG.

MORPHINE, IV

- Morphine, IV, to a maximum dose of 10 mg.
  - Morphine, IV, 3–5 mg as a single dose then further boluses at intervals of 5–10 minutes and monitor all vitals closely.
  - Dilute 10 mg up to 10 mL with sodium chloride 0.9%.
  - Repeat after 4 hours if necessary.
  - Monitor response to pain and effects on respiration and blood pressure.
  - Onset 5–10 minutes. Duration of action 4-5 hours.

PHENYTOIN, IV

- Phenytoin, IV, 20 mg/kg diluted in sodium chloride 0.9% **(not dextrose)** administered not faster than 50 mg/minute, with cardiac monitoring.
  - Mixing instructions: For preparation of the infusion, the contents of a vial of phenytoin should be well mixed in 0.9% sodium chloride at a concentration of less than 4 g/L and be completely administered within 1 hour of mixing to avoid precipitation.
  - Cardiac monitoring should be done during the infusion.
  - If dysrhythmias occur, interrupt the infusion temporarily and reintroduce slowly, once rhythm becomes stable.
  - Continue with, IV, 5 mg/kg/day (300 mg daily for most adults).

POTASSIUM CHLORIDE, IV

Must always be diluted before infusion.

- Potassium chloride, IV, diluted in 1 L sodium chloride 0.9%.
  - Rapid infusion of potassium chloride can cause fatal dysrhythmias.
  - Infusion rates > 20 mmol/hour are very irritable to peripheral veins.
  - Potassium chloride 15% for intravenous use contains 20 mmol K+ per 10 mL ampoule.
  - Potassium chloride infusion – see diabetes section for the administration of potassium infusion in DKA (Section 8.6.2: Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycaemic state (HHS)).
  - Non DKA; Dilute potassium chloride in a non-glucose containing solution (e.g. 0.9% sodium chloride) to a concentration not exceeding 40 mmol/L. Maximum rate of infusion should not exceed 20 mmol/ hour.
  - As large volumes of solution may need to be given, monitor the patient for fluid overload.
  - For preparation of the infusion, the contents of an ampoule of potassium chloride should be well mixed in 0.9% sodium chloride.

An example prescription might be: '*dilute two 10 ml ampoules of 20 mmol KCl in 1 litre of 0.9% sodium chloride, and mix thoroughly. Infuse at a rate of 125 ml/hour, and repeat 8 hourly (i.e. give three litres of the solution containing 40 mmol KCl per litre as a constant infusion over a 24 hour period)*'.

PREDNISONE, ORAL

Prednisone tapering - generally required after prolonged use (i.e. >1 week)

- Example of a dose reduction regimen: for an initial dose of 60 mg daily, reduce initial dose by 2/3, and continue as follows:
  - » 40 mg/day in week 2,
  - » 25 mg/day in week 3,
  - » 20 mg/day in week 4,
  - » 15 mg/day in week 5,
  - » 10 mg /day in week 6 and

» thereafter 5 mg daily for 1 week and then discontinue.

Note: Weaning should be adjusted according to clinical context. If control deteriorates on weaning return to the previous effective dose.

VANCOMYCIN, IV

- Vancomycin, IV, 30 mg/kg as a loading dose. Follow with 20 mg/kg/dose 12 hourly. Duration depends on the organism & site of infection: for methicillin-resistant *Staphylococcus aureus* duration is 2 weeks after first negative blood culture, or 4 weeks for complicated infections (e.g. endocarditis).
  - The rate of infusion should not exceed 1 g/hour (i.e. at least 2 hours for a 2 g infusion).
  - **Note:** Rapid infusion can cause flushing, pain, thrombophlebitis, hypotension and cardiopulmonary arrest.
  - Weigh patients and estimate eGFR (see chapter 7: Nephrological/ urological disorders).
  - See table for dosing interval and measurement of trough concentrations.
  - Aim for trough concentration of 10–20 mcg/mL except in osteitis or endocarditis or if MIC > 1 when trough should be 15–20 mcg/mL.
  - If trough is too low, increase dose (specialist consultation if unsure how much to increase) and/or shorten dose interval to 8 hourly.
  - If trough too high increase dosing interval (specialist consultation if unsure how much to increase).
  - Vancomycin is not significantly removed by conventional intermittent haemodialysis. Dosing and monitoring as for those with eGFR <25 mL/minute.

Dosing intervals and when to measure trough concentrations of vancomycin:

eGFR (mL/minute)	**Dosing interval (hours)**	**Measurement of trough concentrations**
>80	12	Before 3rd dose
50-79	24	Before 3rd dose
35-49	36	Before 2nd dose
25-34	48	Before 2nd dose
<25 **or** haemodialysis **or** CAPD	When trough level <15	3 days after loading dose

(Adapted with permission from Groote Schuur hospital's protocol).

WARFARIN, oral

- Warfarin, oral, 5 mg daily adjusted to maintain INR between 2 and 3.
  - o *Warfarin interactions:*
    A large number of medicines interact with warfarin leading to under- or over-anticoagulation, and careful evaluation of all new medicines, herbal and over-the counter products is critical. This includes (but is not an exhaustive list):
    - Medicines altering platelet function e.g. NSAIDs, aspirin, clopidogrel, etc.
    - Food or medicines altering vitamin K synthesis e.g. antibiotics.
    - Medicines interfering with warfarin metabolism e.g. efavirenz, rifampicin, macrolide antibiotics, simvastatin, phenytoin, carbamazepine, etc.
    - Grapefruit juice.

Unless INR is markedly out of range the modest adjustments recorded below should be followed:

Initiation

Warfarin initiation dosing protocol (week 1) with INR target: 2–3		
Day therapy	**INR Value**	**Total daily dose**
Day 1		5 mg daily (2.5 mg daily for high sensitivity)
2 to 3 days after initiation	< 1.5 1.5 – 1.9 2.0 – 2.5 > 2.5	5–7.5 mg daily 2.5–5 mg daily 2.5 mg daily Hold warfarin and recheck INR next day
2 to 3 days after last INR check	< 1.5 1.5 – 1.9 2.0 – 3.0 > 3.0	7.5–10 mg daily 5–10 mg daily 2.5–5 mg daily Hold warfarin and recheck INR in1–2 days

Frequency of INR monitoring after initiation of warfarin	
Check INR	
Every 2–3 days	Until INR within therapeutic range on 2 consecutive INR checks
Then every week	Until INR within therapeutic range on 2 consecutive INR checks
Then every 2 weeks	Until INR within therapeutic range on 2 consecutive INR checks
Then every 4 weeks	When dose is stable, check monthly

Maintenance

Warfarin maintenance dosing protocol to maintain an INR 2-3:

INR<1.5	INR: 1.5-1.9	INR: 2.0-3.0	INR: 3.1-4.0	INR: 4.1-5	INR: 5.1-9.0	INR>9.0
Extra Dose. Increase **weekly** dose 10%.	Increase **weekly** dose 5%.	No change.	Decrease **weekly** dose 5%.	Withhold 1 dose. Decrease **weekly** dose 10%.	*Withold 2 doses. Decrease **weekly** dose 20%.	Admit.

*History and examination to exclude bleeding. Admit persons with additional risks for bleeding.

Frequency of INR monitoring for maintenance of warfarin	
Check INR	
Every 3–5 days	If start/stop interacting medication, change in diet, change in activity level or other change that could affect INR.
Every 1–2 weeks	If dose needed adjustment by 5–10%.
Every 4 weeks	If maintained on same stable dose < 6 months.
Every 6–8 weeks	If maintained on same stable dose ≥ 6 months.

MEDICINES AND BIRTH DEFECTS

Some medicines are known to cause abnormal fetal development resulting in fetal death or babies born with birth defects. Some of these effects may happen very early in pregnancy, within the first 6 weeks of gestation, before most patients realise they are pregnant. It is therefore important that women who are in their reproductive age and are prescribed any teratogenic medicine should be made aware of the risk and placed on reliable contraception. Some medicines can cause fetal damage in the second or third trimester.

Where possible, stop teratogenic medicines before a pregnancy is planned and prescribe suitable alternatives.

Any medicine that is prescribed during pregnancy must be carefully evaluated, and risk versus benefit should be assessed before use. Refer to prescriber information for details regarding risks in pregnancy. .

Refer pregnancies exposed to teratogenic medicines during the first trimester for a detailed fetal anomaly scan.

The table below lists some commonly used medicines that are associated with birth defects.

MEDICINES	ADVERSE FETAL EFFECTS	*LoE*
Androgens	Masculinisation of the developing female fetus can occur.	*III*[i]
ACE- inhibitors/ ARBs	Fetal hypotension resulting in fetal kidney hypoperfusion and anuria, with fetal growth restriction and demise.	*III*[ii]
Anticonvulsants:		
Carbamazepine	Increases the risk of facial dysmorphology, neural tube defects, cardiovascular defects, and urinary tract defects.	*II*[iii]
Phenytoin	Increases the risk of fetal hydantoin syndrome, consisting of facial dysmorphology, cleft palate, ventricular septal defect, and growth and intellectual disability.	
Valproic acid	Increases the risk of spina bifida, facial dysmorphology, autism, atrial septal defect, cleft palate, hypospadias, polydactyly, craniosynostosis, limb abnormalities, neurodevelopmental problems (approximately 40%) and autism[iv].	

[i] Androgens:Wilkins L. Masculinization of female fetus due to use of orally given progestins. JAMA. 1960 Mar 5;172(10):1028–32. https://jamanetwork.com/journals/jama/article-abstract/327726

[ii] Hanssens M, Keirse MJ, Vankelecom F, Van Assche FA. Fetal and neonatal effects of treatment with angiotensin-converting enzyme inhibitors in pregnancy. Obstet Gynecol. 1991 Jul;78(1):128–35. https://www.ncbi.nlm.nih.gov/pubmed/2047053

[iii] Anticonvulsants: Weston J, Bromley R, Jackson CF, Adab N, Clayton-Smith J, Greenhalgh J, Hounsome J, McKay AJ, Tudur Smith C, Marson AG. Monotherapy treatment of epilepsy in pregnancy: congenital malformation outcomes in the child. Cochrane Database Syst Rev. 2016 Nov 7;11:CD010224. https://www.ncbi.nlm.nih.gov/pubmed/27819746

[iv] Valproic acid – caution in pregnancy: European Medicines Agency - Pharmacovigilance Risk Assessment Committee. Assessment report EMA/198940/2018 - valproate exposure in pregnancy, 8 February 2018.

Antidepressants	SSRIs should in general be continued during pregnancy and breastfeeding. There is uncertainty in the evidence, but potential complications may include an increased risk of birth defects, postpartum haemorrhage, premature birth and low birth weight.	*III*[v]
Carbimazole	Increased risk of birth defects in the first trimester and at high daily doses of ≥15 mg.	*III*[vi]
Dolutegravir	There is an increased risk of neural tube birth defects involving the brain, spine, and spinal cord; if used within the first 6 weeks of pregnancy.	*III*[vii]
Efavirenz	No increased prevalence of birth defects detected and in a large multi-cohort analysis or from a South African exposure registry.	*I*[viii]
Lithium	First trimester exposure is associated with an increased risk of birth defects.	*II*[ix]
Macrolide	In a large population-based cohort study, when compared to penicillin, first trimester macrolide exposure was associated with increased risk of cardiovascular malformations, and macrolide exposure in any trimester was associated with increased risk of genital malformations. The majority of macrolide exposures in	*III*[x]

http://www.ema.europa.eu/docs/en_GB/document_library/Referrals_document/Valproate_2017_31/Position_provided_by_CMDh/WC500250221.pdf

Valproic acid – caution in pregnancy: Meador K, Reynolds MW, Crean S, Fahrbach K, Probst C. Pregnancy outcomes in women with epilepsy: a systematic review and meta-analysis of published pregnancy registries and cohorts. Epilepsy Res. 2008 Sep;81(1):1-13. https://www.ncbi.nlm.nih.gov/pubmed/18565732

[v] Antidepressants: ACOG Committee on Practice Bulletins--Obstetrics. ACOG Practice Bulletin: Clinical management guidelines for obstetrician-gynecologists number 92, April 2008 (replaces practice bulletin number 87, November 2007). Use of psychiatric medications during pregnancy and lactation. Obstet Gynecol. 2008 Apr;111(4):1001–20. https://www.ncbi.nlm.nih.gov/pubmed/18378767

Antidepressants: National Institute of Clinical Excellence: National Clinical Guideline Number 192: Antenatal and postnatal mental health – clinical management and service guidance, April 2018. https://www.nice.org.uk/guidance/cg192/evidence/full-guideline-pdf-4840896925

[vi] Carbimazole: Bowman P, Vaidya B. Suspected Spontaneous Reports of Birth Defects in the UK Associated with the Use of Carbimazole and Propylthiouracil in Pregnancy. J Thyroid Res. 2011;2011:235130. https://www.ncbi.nlm.nih.gov/pubmed/21922050

[vii] Dolutegravir: Raesima MM, Ogbuabo CM, Thomas V, Forhan SE, Gokatweng G, Dintwa E, et al. Dolutegravir Use at Conception - Additional Surveillance Data from Botswana. N Engl J Med. 2019 29;381(9):885–7. https://www.ncbi.nlm.nih.gov/pubmed/31329378

[viii] Efavirenz: Mehta UC, van Schalkwyk C, Naidoo P, Ramkissoon A, Mhlongo O, Maharaj NR, et al. Birth outcomes following antiretroviral exposure during pregnancy: Initial results from a pregnancy exposure registry in South Africa. South Afr J HIV Med. 2019;20(1):971. https://www.ncbi.nlm.nih.gov/pubmed/31616571

Efavirenz: Martinez de Tejada B, European Pregnancy and Paediatric HIV Cohort Collaboration Study Group. Birth Defects After Exposure to Efavirenz-Based Antiretroviral Therapy at Conception/First Trimester of Pregnancy: A Multicohort Analysis. J Acquir Immune Defic Syndr. 2019 01;80(3):316–24. https://www.ncbi.nlm.nih.gov/pubmed/30570524

Efavirenz: Zash R, Holmes L, Diseko M, Jacobson DL, Brummel S, Mayondi G, Isaacson A, Davey S, Mabuta J, Mmalane M, Gaolathe T, Essex M, Lockman S, Makhema J, Shapiro RL. Neural-Tube Defects and Antiretroviral Treatment Regimens in Botswana. N Engl J Med. 2019 Aug 29;381(9):827-840. https://www.ncbi.nlm.nih.gov/pubmed/31329379

[ix] Lithium: Munk-Olsen T, Liu X, Viktorin A, Brown HK, Di Florio A, D'Onofrio BM, et al. Maternal and infant outcomes associated with lithium use in pregnancy: an international collaborative meta-analysis of six cohort studies. Lancet Psychiatry. 2018 Aug;5(8):644-652. https://www.ncbi.nlm.nih.gov/pubmed/29929874

[x] Fan H, Gilbert R, O'Callaghan F, Li L. Associations between macrolide antibiotics prescribing during pregnancy and adverse child outcomes in the UK: population based cohort study. BMJ. 2020 Feb 19;368:m331. https://www.ncbi.nlm.nih.gov/pubmed/32075790

	this study (93%) were to erythromycin, but a class effect cannot be ruled out. Macrolides should only be prescribed in pregnancy when clearly indicated.	
Methotrexate	Pregnancy loss, growth restriction, microcephaly, intellectual disability.	*III*[xi]
Contraceptive agents and sex steroids (progestin)	There is no risk for congenital defects if contraceptive agents were used inadvertently during the first trimester. Very high doses of androgen hormone-derived progestin may produce masculinisation if used before 13 weeks of pregnancy.	*II*[xii]
Prednisone	Prednisone does not represent a major teratogenic risk in humans at therapeutic doses, but there is an increased risk (about 3-fold) for cleft palate.	*II*[xiii]
Retinoids	Oral formulation is associated with increased risk of CNS, cardioaortic, ear, and clefting defects. Topical administration is very unlikely to have teratogenic potential because teratogenic serum levels cannot be attained by topical exposure to retinoids.	*III*[xiv]
Tetracyclines (e.g. docycycline)	Produces bone and teeth staining; it does not increase the risk of any malformations but should not be used during pregnancy.	*III*[xv]
Warfarin	Early exposure during pregnancy can result in nasal hypoplasia, intrauterine growth restriction and miscarriage. CNS malformations can occur in late pregnancy exposure because of bleeding. In women with new generation prosthetic heart valves taking warfarin daily at a dose of ≤5mg, the risk of serious teratogenesis is small and warfarin may be safely continued in the first trimester being discontinued prior to delivery to avoid intracranial bleeding in the newborn (substituted with heparin).	*II*[xvi]

ACE-inhibitor: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; LoE: level of evidence; DS-TB: drug-sensitive tuberculosis; RHZE: rifampicin/isoniazid/pyrazinamide/ethambutol; CNS: central nervous system

[xi] Methotrexate: Kozlowski RD, Steinbrunner JV, MacKenzie AH, Clough JD, Wilke WS, Segal AM. Outcome of first-trimester exposure to low-dose methotrexate in eight patients with rheumatic disease. Am J Med. 1990 Jun;88(6):589–92. https://www.ncbi.nlm.nih.gov/pubmed/2189302

[xii] Contraceptive agents and sex steroids (progesterone): Raman-Wilms L, Tseng AL, Wighardt S, Einarson TR, Koren G. Fetal genital effects of first-trimester sex hormone exposure: a meta-analysis. Obstet Gynecol. 1995 Jan;85(1):141–9. https://www.ncbi.nlm.nih.gov/pubmed/7800312

[xiii] Prednisone: Park-Wyllie L, Mazzotta P, Pastuszak A, Moretti ME, Beique L, Hunnisett L, et al. Birth defects after maternal exposure to corticosteroids: prospective cohort study and meta-analysis of epidemiological studies. Teratology. 2000 Dec;62(6):385–92. https://www.ncbi.nlm.nih.gov/pubmed/11091360

[xiv] Retinoids: Heckel S, Favre R, Weber P, Dellenbach P. [Teratogenicity of retinoids. A case and review of the literature]. J Gynecol Obstet Biol Reprod (Paris). 1993;22(1):43-7.https://www.ncbi.nlm.nih.gov/pubmed/8463566

Retinoids: Jick SS, Terris BZ, Jick H. First trimester topical tretinoin and congenital disorders. Lancet. 1993 May 8;341(8854):1181–2. https://www.ncbi.nlm.nih.gov/pubmed/8098078

[xv] Tetracycline (e.g. docycycline): Wormser GP, Wormser RP, Strle F, Myers R, Cunha BA. How safe is doxycycline for young children or for pregnant or breastfeeding women? Diagn Microbiol Infect Dis. 2019 Mar;93(3):238–42. https://www.ncbi.nlm.nih.gov/pubmed/30442509

[xvi] Warfarin: Steinberg ZL, Dominguez-Islas CP, Otto CM, Stout KK, Krieger EV. Maternal and Fetal Outcomes of Anticoagulation in Pregnant Women With Mechanical Heart Valves. J Am Coll Cardiol. 2017 Jun 6;69(22):2681–91. https://www.ncbi.nlm.nih.gov/pubmed/28571631

EXTEMPORANEOUS COMPOUNDING

Compounding is the process where a pharmacist or other registered person prepares, mixes, combines, packages or labels a medicine for an individual patient.

Medicines compounded, or prepared "extemporaneously", are unlicensed medicines and not subject to Medicines Regulatory Authority oversight. Thus, assumptions cannot be made regarding quality and stability of these compounded products relative to licensed medicines.

In terms of Section 22C(5) of the Medicines and Related Substances Act, 1965 (Act No. 101 of 1965), "*No person shall compound or dispense a medicine unless he or she is authorised thereto in terms of the Pharmacy Act, 1974, is a veterinarian or is the holder of a licence as contemplated in subsection (1) (a)*." This license may be granted by the Director-General to a medical practitioner, dentist, practitioner, veterinarian, nurse or other person registered under the Health Professions Act, 1974 (Act No. 56 of 1974).

Pharmacists or other registered persons should only engage in extemporaneous preparation when all routes of timely procurement have been exhausted (medicine cannot be sourced locally or globally; suitable therapeutic alternatives are not available or the medicine is not available from an authorised specialised compounding facility), or if the appropriate formulation or strength of the medicine is no readily available.

Extemporaneous preparations should be compounded by a pharmacist or other registered person in accordance with the Medicines and Related Substances Act, 1965 (Act No. 101 of 1965), as amended (adhering to minimum standards relating to premises, facilities and equipment) and at a facility that is licenced according to the Pharmacy Act.

Section 3 of the General Regulations to the Medicines and Related Substances Act, 2017, provides the conditions for compounding a medicine. In terms of Section 3(1) of the Regulations:
"*A pharmacist or other person licensed in terms of section 22C(1)(a) of the Act to compound a medicine for sale in terms of section 14(4) of the Act, shall only compound a quantity that is intended to be used by a patient for no more than 30 consecutive days from the date of compounding: Provided that the date of compounding and the statement "Use within 30 days" are clearly indicated on the label*."

Standard operating procedures will assist to minimise risk regarding calculation errors, inappropriate validation of the preparation, microbial contamination, stability and storage of the compounded product, labelling errors, patient

acceptability and the health and safety of personnel involved in compounding – appropriately aligned with Good Pharmacy Practice regulations.

Labelling should contain batch number, date of preparation, expiry date, the statement “Use within 30 days”, and all relevant labelling specific to the preparation. Relevant record-keeping should be maintained.

Standardised formulas have been provided for the following essential medicines that have supply constraints:

MORPHINE, ORAL SOLUTION

- Morphine, oral solution:
    - 1 mg/mL (0.1%)
    - 5 mg/mL (0.5%)
    - 20 mg/mL (2%)

Declaration:
Active ingredient: Morphine hydrochloride/sulphate 1 mg/mL; 5 mg/mL; 20 mg/mL
Dosage form: Oral solution
Excipients: Benzoic acid, propylene glycol, sorbitol, purified water

Formula:

	1 mg/mL	**5 mg/mL**	**20 mg/mL**
Morphine hydrochloride/sulphate	50 g	250 g	1000 g
Benzoic acid solution 5%*	100 mL	100 mL	100 mL
Sorbitol 70%	1500 mL	1500 mL	1500 mL
Sterile water, add to	5000 mL	5000 mL	5000 mL

(Smaller volumes can be formulated - calculate proportions).

Preparation:
Dissolve the morphine in approximately 2000 mL of the purified water. Dissolve the benzoic acid solution 5% in this solution. Add the 70% sorbitol solution and a sufficient quantity of purified water to a volume of 5000 ml and mix well.

Quality requirements
Identity: as stated under the section "Declaration", above.
Content of morphine hydrochloride: 90–110% of the declared amount, calculated as the pure substance.
pH: ≤ 4
Appearance: The solution is clear and almost free of visible particles.

Storage: Glass amber bottle, below 25 °C with an expiry date of 1 month.

**To make the benzoic acid 5% solution:* Dissolve the benzoic acid in the propylene glycol, adding the hot purified water to a volume of 1000 mL.

Benzoic acid	50 g
Propylene glycol	750 mL
Sterile water, heated to ±60°C, add to	1000 mL

Storage: Glass amber bottle, below 25 °C with an expiry date of 1 month.

Note: Commercial preparation of methyl parahydroxybenzoate, propyl hydroxybenzoate, alcohol and purified water[i] could be considered as the diluent for morphine, oral solution, if available.

PODOPHYLLIN, TOPICAL SOLUTION

- Podophyllin 20% in compound benzoin tincture BP, 100 mL.

Active ingredient: Podophyllin 200 mg/mL
Dosage form: Topical solution
Excipients: Compound Benzoin Tincture BP

Formula

Podophyllin resin BP	20 g
Compound benzoin tincture BP, add to	100 mL

Preparation

1. Weigh out the podophyllin resin, and place in 100 mL amber glass bottle (previously dried out with a few drops of 70% alcohol).
2. Add compound benzoin tincture to 100 mL and mix well.
3. Decant 10 mL in an amber glass bottle for a treatment course and label appropriately.

Storage: Glass amber bottle, below 25 °C with an expiry date of 6 months.

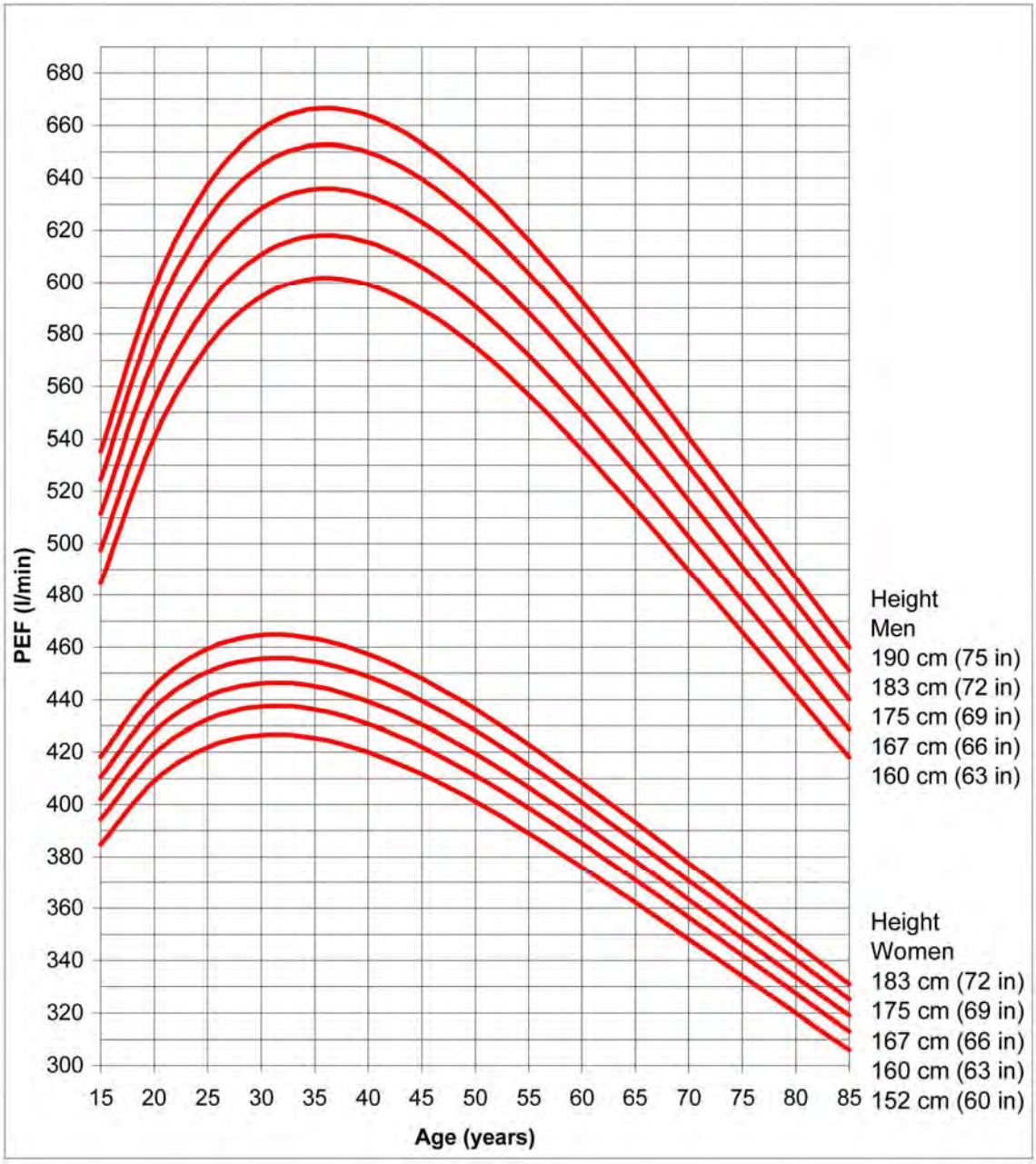
Quality requirements

Identity: as stated under the section "Declaration", above.
Content of podophyllin: 90–110% of the declared amount, calculated as the pure substance.
Appearance: The solution is clear and almost free of visible particles.
Label: Appropriately labelled for external use only.

[i] Commercial preparation formulated in accordance with the World Health Organisation. Model formulary: Morphine formulations on the Essential Medicines List for Children.
http://www.who.int/selection_medicines/committees/expert/19/applications/Morphine_2_2_C_NF.pdf

PEAK EXPIRATORY FLOW RATES

Peak expiratory flow in normal adult subjects



Adapted with permission from
Nunn AJ Gregg I, Br Med J 1989:298;1068-70
and Clement Clarke International.

CALCULATING % PREDICTED PEAK FLOW RATE

- Take the best of 3 of the patient's observed peak flow rate:
  e.g. 200, 180, 190 performed – so take 200.
- Find the patient's sex, age and height predicted value from the nomogram.
  e.g. 440 for a woman of age 25 years and height 167 cm
- Divide patient's observed peak flow rate over their predicted peak flow rate:
  e.g. 200/440 = 0.45
- Multiply by 100:
  e.g. 0.45X100 = 45%

So, in this example, the patient's observed peak flow rate is 45% of predicted.

CALCULATING PEAK FLOW VARIABILITY

There are a number of methods for calculating PEF variability.

One method is described below:

- Subtract the lowest from the highest reading.
- Divide by the highest reading.
- Multiply by 100.

So, in this example, where a patient has readings of 300 to 400, the variability is 25%. If these readings were taken before and after a test dose of salbutamol, asthma is diagnosed. (See sections 16.1 Asthma, acute and 16.2 Asthma, chronic persistent).

ASTHMA CONTROL TEST™

This is a validated measure of clinical asthma control that can be completed by the patient (after initial instruction) at each visit to the clinic prior to consultation. A value of ≥19 suggests adequate asthma control.

Online version of the test is accessible at: https://www.asthmacontroltest.com/

Reference: Nathan RA, Sorkness CA, Kosinski M, Schatz M, Li JT, Marcus P, Murray JJ, Pendergraft TB. Development of the asthma control test: a survey for assessing asthma control. J Allergy Clin Immunol. 2004 Jan;113(1):59-65. http://www.ncbi.nlm.nih.gov/pubmed/14713908

GUIDELINES FOR THE MOTIVATION OF A NEW MEDICINE ON THE NATIONAL ESSENTIAL MEDICINES LIST

Section 1: Medication details

» Generic name.
A fundamental principle of the Essential Drug Programme is that of generic prescribing. Most clinical trails are conducted using the generic name.

» Proposed indication.

» There will usually be many registered indications for the medication. However, this section should be limited to the main indication which is supported by the evidence provided in section 2.

» Prevalence of the condition in South Africa

» This information is not always readily available. However, it is an important consideration in the review of a proposed essential medicine.

» Prescriber level.

» Here the proposed prescriber level should be included. If more than one level is proposed each relevant box should be ticked.

Section 2: Evidence and motivation

» Estimated benefit:

- Effect measure: this is the clinical outcome that was reported in the clinical trial such as BP, FEV, CD_4, VL etc.
- Risk benefit: this should reported in the clinical trial and, in most cases, includes the 95% confidence level (95% CI). Absolute risk reduction, also termed risk difference, is the difference between the absolute risk of an event in the intervention group and the absolute risk in the control group.
- Number Need to Treat (NNT): gives the number of patients who need to be treated for a certain period of time to prevent one event. It is the recipr ocal of the absolute risk or can be calculated using the formula below.

Calculations

	Bad outcome	**Good outcome**	**Total patients**
Intervention group	*a*	*c*	*a + c*
Control group	*b*	*d*	*b + d*

Measure	**Equation**
Absolute risk:	$[b/(b+d)] - [a/(a+c)]$
Number needed to treat	$\dfrac{1}{[b/(b+d)] - [a/(a+c)]}$
Relative risk	$[a/(a+c)] \div [b/(b+d)]$
Odds ratio	$\dfrac{[a/(a+c)] \div [c/(a+c)]}{[b/(b+d)] \div [d/(b+d)]} = (a/c) \div (b/d)$

Reference - Aust Prescr 2008;31:12–16)

» Motivating information (**Level of evidence based on the SORT system**):
  - The National Essential Medicine List Committee has endorsed the adoption of the SORT system for categorising levels of evidence. This system[1] contains only three levels:

Level I	Good quality evidence	Systematic review of RCTs with consistent findings High quality individual RCT
Level II	Limited quality patient orientated evidence	Systematic review of lower quality studies or studies with inconsistent findings Low quality clinical trial Cohort studies Case-control studies
Level III	Other	Consensus guidelines, extrapolations from bench research, usual practice, opinion, disease-oriented evidence (intermediate or physiologic outcomes only), or case series

A: Newer product: for most newer products, level 1 evidence such as high quality systematic reviews or peer-reviewed high quality randomised controlled trials should be identified and referenced in the space provided.

B: Older products: many of these products were developed prior to the wide use of randomised controlled trials. However, there may be level 1 evidence where the product was used as the control arm for a newer product. If no level 1 evidence can be identified, then level II data from poorer quality controlled trials or high quality observational studies should be referenced in the space provided.

» Cost considerations:
  - Where a published reference supporting the review of cost is available comments should be made regarding its applicability to the South African public sector environment.
  - Possible unpublished information that can be included:
    - Cost per daily dose or course of therapy – for long term or chronic therapy such as hypertension the usual daily dose should be calculated (Dose x number of times a day) and converted into the number of dosing units e.g. tablets. This is then used to calculate the cost per day. For medications used in a course of therapy such as antibiotics this is then multiplied by the number of days in the course of therapy.

[1] *Ebell MH, Siwek J, Weiss BD, et al. Strength of recommendation taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. Am Fam Physician. 2004;69:550-6.*

- Cost minimisation is used where there is evidence to support equivalence and aims to identify the least costly treatment by identifying all the relevant costs associated with the treatment.
- Cost-effectiveness analysis is used to compare treatment alternatives that differ in the degree of success in terms of the therapeutic or clinical outcome. By calculating a summary measurement of efficiency (a cost-effectiveness ratio), alternatives with different costs, efficacy rates, and safety rates can be fairly compared along a level playing field.

Where any of these have been performed tick the relevant block and send as an attachment with all the calculations. If possible, the spread sheet should be supplied electronically.

Section 3: Motivator's Details

The receipt of all submission will be acknowledged. In addition, all decisions with supporting arguments will be communicated where appropriate. This section therefore forms a vital link between the motivator and the decision making process.

DEPARTMENT OF HEALTH
Republic of South Africa

Motivation form for the inclusion of a new medication on the National Essential Medicines List

Section 1: Medication details			
Generic name (or International Non-proprietary Name):			
Proposed indication:			
Prevalence of condition (based on epidemiological data, if any):			
Prescriber level			
Primary Health Care 1	Medical Officer 2	Specialist 3	Designated Specialist 4

Section 2: Evidence and motivation			
2.1 Estimated benefit			
Effect measure			
Risk difference (95% CI)			
NNT			
2.2: Motivating information (Level of evidence based on the SORT system)			
A. Newer product: High quality systematic reviews or peer-reviewed high quality randomised controlled trials (Level I)			
Author	Title		Journal ref
B. Older product with weaker evidence base: Poorer quality controlled trials or high quality observational studies (Level II)			
Author	Title		Journal ref
2.3: Cost-considerations			
Have you worked up the cost?	YES		NO
	Daily cost	Cost minimisation	Cost-effectiveness analysis
Other relevant cost information if available:			
Author	Title		Journal ref
2.4: Additional motivating comments.			

Section 3: Motivator's Details	
Name:	**Date submitted:**
Qualification:	**Registration number:**
PTC motivation: Y/N	**PTC Details:**
PTC Chair:	**PTC Chair signature:**

GUIDELINES FOR ADVERSE DRUG REACTION REPORTING

National Pharmacovigilance Programme

The South African Health Products Regulatory Authority (SAHPRA) has a responsibility to ensure the safety, efficacy and quality of all medicines used by the South African public. The National Pharmacovigilance Programme is coordinated by the SAHPRA and has a dedicated Unit, The National Adverse Drug Event Monitoring Centre (NADEMC), in Cape Town, which monitors the safety of all registered medicines in South Africa.

What is Pharmacovigilance?

Pharmacovigilance is defined as the science and activities concerned with the detection, assessment, understanding and prevention of adverse reactions to medicines (i.e. adverse drug reactions or ADRs). The ultimate goal of this activity is to improve the safe and rational use of medicines, thereby improving patient care and public health.

What is an Adverse Drug Reaction (ADR)?

SAHPRA defines an Adverse Drug Reaction (ADR) as a response to a medicine which is noxious and unintended, including lack of efficacy, and which occurs at any dosage and can also result from overdose, misuse or abuse of a medicine.

Who should report Adverse Drug Reactions?

All health care workers, including doctors, dentists, pharmacists, nurses and other health professionals are encouraged to report all suspected adverse reactions to medicines (including vaccines, X-ray contrast media, traditional and herbal remedies), especially when the reaction is not in the package insert, potentially serious or clinically significant.

What happens to a report?

All ADR reports are entered into a national ADR database. Each report is evaluated to assess the causal relationship between the event and the medicine. A well-completed adverse drug reaction/product quality form submitted could result in any of the following:

» additional investigations into the use of the medicine in South Africa;
» educational initiatives to improve the safe use of the medicine;
» appropriate package insert changes to include the potential for the reaction, and
» changes in the scheduling or manufacture of the medicine to make it safer.

The purpose of ADR reporting is to reduce the risks associated with the use of medicines and to ultimately improve patient care.

Will reporting have any negative consequences on the health worker or the patient?

An adverse drug reaction report does not constitute an admission of liability or that the health professional contributed to the event in any way. The outcome of a report, together with any important or relevant information relating to the reaction, will be sent back to the reporter as appropriate. The details of a report are stored in a confidential database. The names of the reporter or any other health professionals named on a report and that of the patient will be removed before any details about a specific adverse drug reaction are used or communicated to others. The information is only meant to improve the understanding of the medicines used in the country.

Is the event possibly an ADR?

The following factors should be considered when an adverse drug reaction is suspected:

1. What exactly is the nature of the reaction? (*Describe the reaction as clearly as possible and where possible provide an accurate diagnosis.*)
2. Did the reaction occur within a reasonable time relationship to starting treatment with the suspected medicine? *(Some reactions occur immediately after administration of a medicine while others take time to develop.)*

3. Is the reaction known to occur with the particular medicine as stated in the package insert or other reference? *(If the reaction is not documented in the package insert, it does not mean that the reaction cannot occur with that particular medicine.)*
4. Did the patient recover when the suspected medicine was stopped? *(Some reactions can cause permanent damage, but most reactions are reversible if the medication is stopped.)*
5. Did the patient take the medicine again after the reaction abated (i.e. rechallenge). If so, did the same reaction occur again? *(In most situations it is not possible or ethical to rechallenge the patient with the same medicine. If such information is available or if such a rechallenge is necessary, recurrence of the event is a strong indicator that the medicine may be responsible.)*
6. Can this reaction be explained by other causes (e.g. underlying disease/s; other medicine/s; toxins or foods)? *(It is essential that the patient is thoroughly investigated to decide what the actual cause of any new medical problem is. A medicine-related cause should be considered, when other causes do not explain the patient's condition.)*

What types of reactions should be reported?

The following adverse drug reactions should be reported:

- All ADRs to newly marketed drugs or new medicines added to the EML
- All serious reactions and interactions
- ADRs that are not clearly stated in the package insert.
- All adverse reactions or poisonings to traditional or herbal remedies

Report even if you are not certain that the medicine caused the event.

What Product Quality Problems should be reported?

The following product quality problems should be reported:

- suspected contamination;
- questionable stability;
- defective components;
- poor packaging or labeling;
- therapeutic failures.

How can ADRs be prevented from occurring?

Some ADRs are unavoidable and cannot be prevented. However, most ADRs can be prevented by following the basic principles of rational use of medicines.

How are adverse drug reactions reported?

An Adverse Drug Reaction/Product Quality Report Form is enclosed in this book and should be completed in as much detail as possible before returning it by fax or post to any of the addresses provided below. Additional forms can be obtained by contacting the MCC at these addresses. Report forms may also be accessed via the following website: https://www.sahpra.org.za/

1. The Registrar of Medicines

South African Health Products Regulatory Authority (SAHPRA), Private Bag X828
Pretoria, 0001
Tel: (021) 842 7609/10; E-mail: adr@sahpra.org.za

2. The National Adverse Drug Event Monitoring Centre (NADEMC)

C/o Division of Pharmacology, University of Cape Town,
Observatory, 7925
(021) 447 1618; Fax: (021) 448 6181

SAHPRA
SOUTH AFRICAN HEALTH PRODUCTS REGULATORY AUTHORITY

ADVERSE DRUG REACTION (ADR)/PRODUCT QUALITY PROBLEM REPORT FORM (PUBLIC AND PRIVATE SECTOR) (Including Herbal Products)

Reporting Health Care Facility/Practice					
Tel: 012 842 7609/10 (SAHPRA) 021 447 1618 (NADEMC) **Fax:** 021 448 6181 **E-mail:** adr@sahpra.org.za	Facility/Practice				
	District		Tel		
	Province		Fax		

Patient Details									
Patient Initials		File/Reference Number			Date of Birth/Age				
Sex	□ M □ F □ Unk	Race		Weight (kg)		Height (cm)		Pregnant?	□ N □ Y
Allergies				Estimated Gestational Age at time of reaction					

Suspect Medicine(s) [Medicines suspected to have caused the ADR]							
Trade Name [Generic Name if Trade Name is unknown]	Route	Dose (mg) and Interval	Date Started/Given	Date Stopped	Reason for use	Batch Number	Expiry Date

All other Medicines Patient was taking at time of reaction [Including over-the-counter and herbal products]							
Trade Name [Generic Name if Trade Name is unknown]	Route	Dose (mg) and Interval	Date Started/Given	Date Stopped	Reason for use	Batch Number	Expiry Date

Adverse Drug Reaction/Product Quality Problem			
Date and time of onset of reaction		Date reaction resolved/duration	

Please describe Adverse Reaction/Product Quality Problem: (kindly add as much clinical information as possible)

Intervention(tick all that apply)	**Patient Outcomes (tick all that apply)**
□ No intervention	□ ADR recovered/resolved□ recovering/resolving
□ Intervention unknown	□ not recovered/not resolved
□ Patient Counselled/non-medical treatment	□ Patient Died: Date of death: _____
□ Discontinued Suspect Drug; **Replaced with**: _____	□ Impairment/Disability □ Congenital Anomaly
□ Decreased Suspect Drug Dosage; **New Dose**: _____	□ Patient Hospitalised or Hospitalisation prolonged
□ Treated ADR - with: _____	□ Life Threatening □ Other: _____
□ Referred to Hospital: **Hospital Name**_____	□ ADR reappeared after restarting suspect drug/similar drug (rechallenge)?: □ N □ Y □ Not done □ Unknown
□ Other Intervention (e.g. dialysis): _____	

Laboratory Results			**Additional Laboratory Results**		
Lab Test	**Test Result**	**Test Date**	**Lab Test**	**Test Result**	**Test Date**

Co-morbidities/Other Medical Condition(s)

Reported by			
Name		E-mail	
Designation	□ Nurse □ Pharmacist □ Doctor □ Other:	Telephone	
Date reported:		Signature	

THIS ADR REPORT IS NOT A CONFIRMATION THAT THE REPORTER OR THE SUSPECT MEDICINE(S) CAUSED THE ADR **V5.0 05/19**

ADVICE ABOUT VOLUNTARY REPORTING

Report adverse experiences with:
- medications (drugs, vaccines and biologicals)
- medical devices (including in-vitro diagnostics)
- complementary / alternative medicines (including traditional, herbal remedies, etc.)

Please report especially:
- adverse drug reactions to newly marketed products
- serious reactions and interactions with all products
- adverse drug reactions which are not clearly reflected in the package insert.

Report Product Quality Problems such as:
- suspected contamination
- questionable stability
- defective components
- poor packaging or labelling
- therapeutic failures

Report even if:
- you're not certain the product caused the event
- you don't have all the details

Important numbers:

Investigational Products and Product Quality Problems:
- phone: (012) 842-7609/10 or 082 256 2626/083 387 3358
- email: mlungisi.wondo@sahpra.org.za

Adverse Events Following Immunisation:
- phone: (012) 395 9461/063 6996 114
- email: marione.schonfeldt@health.gov.za

Confidentiality: Identities of the reporter and patient will remain strictly confidential.

Your support of the South African Health Products Regulatory Authority's adverse drug reaction monitoring programme is much appreciated. Information supplied by you will contribute to the improvement of medicine safety and therapy in South Africa.

DISEASE NOTIFICATION PROCEDURES

The disease reporting system in South Africa is based on government law (the Health Act, Act No. 61 of 2003), together with regulations on the reporting of specific diseases to the Local, Provincial and/or National Health Department.

Who should notify

The first health care professional to come into contact with a patient presenting with one of the prescribed Notifiable Medical Conditions (NMCs) is required by law to notify. This may include clinic personnel, infection control nurses, other hospital staff or private medical practitioners. In the event of deaths (or cases) in the community, a member of the community is obliged to notify the event.

Which diseases to notify

Currently 33 broad medical conditions are currently notifiable in South Africa (see List of Notifiable Medical Condition). Some conditions (e.g. tuberculosis and viral hepatitis) have been divided into various components, resulting in more than 40 notifiable medical conditions.

Notifiable medical conditions have been sub-divided into two categories according to type of disease:

Category 1 NMC: Requires immediate reporting by the most rapid means available upon clinical or laboratory diagnosis followed by a written or electronic notification to the Department of Health, within 24 hours of diagnosis by health care providers, private health laboratories or public health laboratories.

Any health care professional identifying even a single case of a disease (presumptive or laboratory confirmed) contained in the Category 1 should make an immediate notification directly to the designated local health officer through fax or telephonically as rapidly as possible (within 24 hours). The local health officer must report to the Provincial health officer and/or to the National Department of Health. Where it is applicable, laboratory confirmation should be obtained at the earliest opportunity and also reported to the designated health office. After reporting through a telephone/fax, it is still required of the health care provider to send a complete GW17/5 form to the designated local health authority within five days after telephonic reporting.

Category 2 NMC: Requires reporting through a written or electronic notification to the Department of Health, within 7 days of diagnosis by health care providers, private health laboratories or public health laboratories.

The notification system is based on clinical notifications and, therefore, all suspected cases of a notifiable condition must be notified immediately.

Reporting a Notifiable Disease during an outbreak
During an outbreak of a notifiable disease, report all cases by phone, email or fax. Daily reporting by health facilities should be maintained through an Outbreak Case Line Listing Form as well through the notification form (GW17/5) to the local health authority that must report to the provincial health officials and the National Department of Health.

Priority Reporting of MDR & XDR-TB
Tuberculosis (TB) is one of 33 medical conditions, which is notifiable in terms of the National Health Act (Act 61 of 2003). The Directorate: Epidemiology and Surveillance have instituted a priority reporting for MDR and XDR TB. This means that all health care facilities, public and private, including clinics, hospitals, laboratories, general practitioners and private specialist doctors, are required to report all cases of MDR and XDR TB to the Department of Health within 24 hours.

How to notify
The initial notification of a medical condition is done on a case-based form (*GW 17/5*) with the relevant details by the health personnel e.g., clinic personnel, infection control nurses, other hospital staff, public or private medical practitioners. Initial notification makes tracing as easy as possible, since a disease notification demands action (follow-up) at the peripheral level.
The GW17/5 form makes provision for the notification of cases as well as deaths. Any person contracting a notifiable disease and then dies from the disease should be notified twice: first as a **"CASE"** and then later as a **"DEATH".** This will ensure that when estimating the **"Case Fatality Rate"** (CFR%), all deaths in the numerator are also included in the denominator. Depending on the structural organization of the province, the completed **GW 17/5** forms is sent to the relevant local health authority, district health office or the provincial office.

Electronic reporting can also be done via the NMC mobile or web based APP.

National Department of Health
Cluster: Health Information, Evaluation & Research (HIER)
Directorate: Epidemiology & Surveillance
Private Bag X828
PRETORIA
0001
Tel: 012 395 8150/1

National NMC contact details:
Helpline: 072 621 3805
Fax no: 086 639 1638
Sms/whatsup line (for copy/photograph submissions): 072 621 3805
Email address: NMCsurveillanceReport@nicd.ac.za

List of Notifiable Medical Conditions

Category 1: *Immediate notification (within 24 hours) of diagnosis*
Acute flaccid paralysis
Acute rheumatic fever
Anthrax
Botulism
Cholera
Diphtheria
Food borne disease outbreak*
Haemolytic uraemic syndrome (HUS)
Listeriosis
Malaria
Measles
Meningococcal disease
Pertussis
Plague
Poliomyelitis
Rabies (human)
Respiratory disease caused by a novel respiratory pathogen**
Rift valley fever (human)
Smallpox
Viral haemorrhagic fever diseases***
Yellow fever

Category 2: *Notification within seven days of diagnosis*
Agricultural or stock remedy poisoning
Bilharzia (schistosomiasis)
Brucellosis
Congenital rubella syndrome
Congenital syphilis
Haemophilus influenzae type B
Hepatitis A
Hepatitis B
Hepatitis C
Hepatitis E
Lead poisoning
Legionellosis
Leprosy
Maternal death (pregnancy, childbirth and puerperium)
Mercury poisoning
Soil transmitted helminths
Tetanus
Tuberculosis: pulmonary
Tuberculosis: extra-pulmonary
Tuberculosis: multidrug-resistant (MDR-TB)
Tuberculosis: extensively drug-resistant (XDR-TB)

INDEX OF CONDITIONS

INDEX OF MEDICINES

Italics indicates a therapeutic class. Therapeutic classes are designated in the "Medicine treatment" sections of the STGs which provide classes of medicines followed by an example of each class. Additional medicines in the class that has been reviewed and approved by NEMLC is listed in the Therapeutic Interchange database – available on the National Department of Health website at: http://www.health.gov.za/index.php/standard-treatment-guidelines-and-essential-medicines-list/category/286-hospital-level-adults

ABBREVIATIONS

3TC	lamivudine	M	molar
ab	antibody	m2	square metre
ABC	abacavir	MAC	minimum alveolar concentration
ACE-inhibitor	angiotensin converting enzyme inhibitor	MAP	mean arterial pressure
ACR	albumin creatinine ratio	mcg	microgram
ACTH	adrenocorticotropic hormone	MCH	mean corpuscular haemoglobin
ADH	antidiuretic hormone	MCV	mean corpuscular volume
ADR	adverse drug reaction	MDEA	3,4-methylenedioxy-N-ethylamphetamine ("Ice", "Eve")
AED	automated external defribillator	MDI	metered dose inhaler
AIDP	acute inflammatory demyelinating polyradiculoneuropathy	MDMA	3,4-methylenedioxymethamphetamine ("Ecstacy")
AIDS	Acquired Immune Deficiency Syndrome	MDR-TB	multi-drug resistant tuberculosis
AKI	acute kidney injury	MERS	Middle East Respiratory Syndrome
ALP	alkaline phosphatase	MERS-CoV	Middle East Respiratory Syndrome Coronavirus
ALT	alanine aminotransferase	mg	milligram
AMH	anti-mullerian hormone	MHCA	Mental Health Care Act No. 17 of 2002
aPTT	activated partial thromboplastin time	MHCU	mental health care user
ARB	Angiotensin receptor blocker	MI	myocardial infarction
ART	antiretroviral therapy	MIC	Minimum Inhibitory Concentration
AST	aspartate aminotransferase	mL	millilitre
ATV/r	atazanavir/ritonavir	mm3	Cubic millimetre
AUB	abnormal uterine bleeding	mmHg	Millimeters mercury
AV	atrioventricular	mmol	millimole
AZT	zidovudine	mOsm	milliosmole
β-hCG	beta human chorionic gonadotropin	MRI	magnetic resonance imaging
β-blocker	beta-receptor blocker	MRSA	Methicillin reistant *Staphyloccal aureus*
β2-agonist	beta2-receptor blocker	MTB	*Mycobacterium tuberculosis*
BD	bipolar disorder	MU	million units
BMI	body mass index	MUS	male urethritis syndrome
BP	blood pressure	MVA	manual vacuum aspiration
BPRS	Brief Psychiatric Rating Scale	Na	sodium
bpm	beats per minute	NAC	N-acetylcysteine
BSA	body surface area	NaCl	sodium chloride
Ca	calcium	NCD	non-communicable disease
CAB (sequence)	circulation airway breathing (sequence)	NDMR	non-depolarising muscle relaxant
CCF	congestive cardiac failure	NEMLC	National Essential Medicines List Committee
CD	crohn's disease	NERD	non-erosive reflux disease
CD4	cluster of differentiation 4 (T-cells)	ng	nanogram
CHC	community health centre	NGO	non-government organisation
CHD	coronary heart disease	NGT	nasogastric tube
CIDP	chronic inflammatory demyelinating polyradiculoneuropathy	NHLS	National Helath Laboratory Services
CIN	contrast induced nephrotoxicity	NICD	National Institute of Communicable Diseases
CKD	chronic kidney disease	NICE	National Institute for Health and Care Excellence
cm	centimetre	NMA	normetanephrine
CMV	cytomegalovirus	nmol	nanomole
CNS	cental nervous system	NRTI	nucleoside reverse transcriptase inhibitor

COPD	chronic obstructive pulmonary disease	NNT	number needed to treat
CPAP	continuous positive airway pressure	NPH insulin	Neutral Protamine Hagedorn insulin
CPR	Cardio-pulmonary resuscitation	NRS	numeric rating scale
CrAg	cryptococcal antigen	NSAID(s)	non-steroidal anti-inflammatory drug(s)
CrCl	creatinine clearance	NSTEMI	non-stress test
CRP	c-reactive protein	NSTEMI	non-ST elevation myocardial infarction
CSF	cerevrospinal fluid	NTD	neurotubular defect
CT	computerized tomography	NVP	nevirapine
CTG	cardiotocography	NYHA	New York Heart Association (functional classification)
CVD	cardiovascular disease	OOWS	objective opioid withdrawal scale
CXR	chest x-ray	ORS	oral rehydration solution
DBP	diastolic blood pressure	OT	occupational therapy
DC	direct current	PaCO2	partial pressure of carbon dioxide in arterial blood
DILI	drug-induced liver injury	PaO2	partial pressure of oxygen in arterial blood
DIC	disseminated intravascular coagulation	PAIR	percutaneous aspiration injection of helminthicidal agent and re-aspiration
dL	decilitre	PANSS	Positive and Negative Syndrome Scale
DKA	diabetic ketoacidosis	PCA	patient controlled analgesia
DMARD	disease-modifying anti-rheumatic drug	PCI	percutaneous coronary intervention
DNA	deoxyribonucleic acid	PCR	protein creatinine ratio/polymerase chain reaction
DTG	dolutegravir	PCV13	polyvalent conjugated vaccine (13-valent)
DU	duodenal ulcer	PEA	pulseless electrical activity;
DVT	deep venous thrombosis	PEF	peak expiratory flow
EC	emergency contraception	PEG	polyethylene glycol
ECG	electrocardiogram	PEG (scale)	pain, enjoyment and general activity (scale)
ECT	electroconvulsive therapy	PEP	post exposure prophylaxis
EEG	electroencephalogram	pH	acidity (partial pressure of hydrogen)
EFV	efavirenz	PHC	primary health care
EFW	estimated fetal weight	PI	protease inhibitor
e.g.	example	PID	pelvic inflammatory disease
eGFR	estimated Glomerular Filtration Rate	PLHIV	people living with HIV
ELISA	enzyme-linked immunosorbent assay	PMTCT	prevention of mother to child transmission
E or EMB	ethambutoal	PO4	phosphate
EML	essential medicines list	PONV	postoperative nausea and vomiting
EPI	expanded programme on immunisation	PPG	post prandial plasma glucose
EPO	erythropoietin	PPH	post-partum haemorrhage
ESR	erythrocyte sedimenattion rate	PPI	proton pump inhibitor
ESRD	end-stage renal disease	PPROM	preterm prelabour rupture of membranes
FAMSA	Families South Africa	PROM	prelabour rupture of membranes at term
FBC	full blood count	PPS23	pneumococcal polysaccharide vaccine (23-valent)
FDC	fixed dose combination	PT	Prothrombin time
FEV1	forced expiratory volume in 1 second	PTH	parathyroid hormone
FFP	fresh frozen plasma	PTL	preterm labour
FH	familial hyperlipidaemia	PTT	prolonged partial thromboplastin time
FiO2	fraction of inspired oxygen	PV	per vagina (vaginal route)
FPG	fasting plasma glucose	PZA or Z	pyrazinamide
FSH	follicle stimulating hormone	RA	rheumatoid arthritis
FTA-ABS	fluorescent treponemal antibody	RAAS	Renin-angiotensin-aldosterone system

	absorption
FTC	emtricitabine
FVC	forced vital capacity
g	gram
G6PD	glucose-6-phosphate dehydrogenase
GDM	gestational diabetes mellitus
GGT	gamma-glutamyl transferase
GI(T)	gastrointestinal (tract)
GORD	gastro-oesophageal reflux disease
GU	gastric ulcer
GUS	genital ulcer syndrome
H or INH	isoniazid
Ham-D	Hamilton Depression Rating Scale
HAP	hospital-acquired pneumonia
Hb	haemoglobin
HbA1c	haemoglobin A1c
HBeAg	hepatitis B e antigen
HBIG	hepatits B immunoglobulin
HbS	sickle haemoglobin
HBsAb	hepatitis B surface antibody
HBsAg	hepatitis B surface antigen
HbSS	sickle cell haemoglobin
HBV	hepatitis B virus
HCl	hydrochloric acid
HCO3	bicarbonate
HCV	hepatitis C virus
HCW	healthcare workers
HCTZ	hydrochlorothiazide
HDL	high density lipoprtein
HE	hepatic encephalopathy
HELLP syndrome	haemolysis, elevated liver enzymes, low platelet count syndrome
Hep B	hepatitis B
HHS	hyperglycaemic hyperosmolar syndrome
HIV	human immunodeficiency virus
HMGCoA	3-hydroxy-3-methyl-glutaryl-coenzyme A (statin)
H2O	water
HR	heart rate
HSV	herpes simplex virus
HT	hormone therapy
ICS	inhaled corticosteroid
ICU	intensive care unit
IgG	immunoglobulin G
IgM	immunoglobulin M
IHD	ischaemic heart disease
IM	intramuscular
INR	international normalized ratio
InSTI	integrase inhibitor
IOP	intraocular pressure
RAL	raltegravir
R or RIF	rifampicin
RBC	red blood cell
Rh	Rhesus
RH	rifampicin/isoniazid combination
RHZE	rifampicin/isoniazid/pyrazinamide/ethambutol combination
RNA	rheumatoid factor
RPR	rapid plasma reagin
RRT	renal replacement therapy
RSTI	repeated supratherapeutic ingestion
RUT	rapid urease test
SABA	short-acting beta2 agonist
SANCA	South African Nursing Council
SAPS	South African Police Services
SBGM	self-blood glucose monitoring
SBP	systolic blood pressure
SC	subcutaneous
SIADH	syndrome of inappropriate antidiuretic hormone (SIADH)
SJS	Stevens-Johnson Syndrome
SL	sublingual
SLE	systemic lupus erythematosus
SPEP	serum protein electrophoresis
SSRI	selective serotonin re-uptake inhibitor
STEMI	ST elevation myocardial infarction
STD/ STI	sexually transmitted disease/infection
STG	standard treatment guideline
SVC	superior vena cava
T3	triiodothyonine
T4	thyroxine
TB	tuberculosis
TBM	tuberculosis meningitis
TBSA	total body surface area
TCA	tricyclic antidepressants
TDD	total daily dose
TDF	tenofovir
TEN	Toxic Epidermal Necrolysis
TFT	thyroid function test
TIA	transient ischaemic attack
TIP	transjugular intrahepatic portosystemic
TOD	target organ damage
TOP	termination of pregnancy
TP	Treponema pallidum
TPHA	Treponema pallidum haemagglutination assay
TPN	total parenteral nutrition
TPT	tuberculosis preventive therapy
TSH	thyroid stimulating hormone
TTP-HUS	thrombotic thrombocytopenic purpura-Haemolytic uraemic syndrome

IRIS	immune reconstitution inflammatory syndrome	UA	unstable angina
ITP	Immune thrombocytopenia	UDV	unit dose vial
iu	international units	ULN	upper limit of normal
IUCD	intrauterine contraceptive device	UE	ung emulsificans (emulsifying ointment)
IV	intravenous	UTI	urinary tract infection
J	Joule	v	volt
K	potassium	VAP	ventilator-associated pnwumonia
kg	kilogram	VDRL test	venereal disease research laboratory test
KS	Kaposi Sarcoma	VDS	vaginal discharge syndrome
L	litre	VF	ventricular fibrillation
LABA	long-acting beta2 agonist	VHF	viral haemorrhagic fevers
LAM (urine test)	lipoarabinomannan (urine test)	VL	viral load
LBBB	left bundle branch block	VSD	ventricular septal defect
LDH	lactate dehydrogenase	VTE	Venous thromboembolism
LDL (-C)	low density lipoprotein (-cholesterol)	VT	ventricular tachycardia
LGV	Lymphogranuloma Venereum	VWF	von Willebrand factor
LH	luteinising hormone	VZIG	varicella-zoster immunoglobulin
LMWH	low molecular weight heparin	WCC	white cell count
LNG	levonorgestrel	WHO	World Health Organisation
LP	lumbar puncture	WHO DAS	WHO Disability Assessment Schedule
LPA	line probe assay	WOCP	women of childbearing potential
LoE	level of evidence	WPW	Wolf-Parkinson-White
LPV/r	lopinavir/ritonavir	XDR-TB	extensively drug-resistant tuberculosis
LV	left ventricular	YMRS	Young Mania Rating Scale

DECLARATION OF INTERESTS

Selection of medicines for the essential medicines list requires measures to ensure that the best possible assessment of scientific evidence is achieved in an independent environment, free of either direct or indirect pressures. Thus, to assure the credibility of the process, it is necessary to avoid situations in which financial or other interests may unduly influence decision-making.

All members of the NEMLC, Adult Hospital Level Technical Expert Review Committee and co-opted experts were required to make formal declarations of interest on application and at the start of each meeting. Guidance for declaring, assessing and handling conflicts of interests is outlined in the NEMLC conflict of interest policy, accessible at: http://www.health.gov.za/index.php/national-essential-medicine-listcommittee-nemlc. The following specific declarations were noted and managed during the development of the Adult Hospital Level STGs and EML:

Adult Hospital Level Committee (2017-2020)	
Dr A Black (Chair: March 2017-March 2019)	Astra Zeneca: Attendance and accommodation to attend Pulmonology Update in Cape Town; Pfizer: Sponsorship to attend Pneumococcal weekend summit in Cape Town; Bristol Meyers Squib Foundation: Pro rata fee for training on Lung Cancer screening and diagnosis, as part of a Lung Cancer screening and Diagnosis grant.
Dr H Dawood (Chair: April 2019-2020)	MSD: Attendance of SAASP meetings and ESCMID 2018 conference; Aids Clinical Trial Group (Crytptococcal meningitis): Investigator for trial A 5225; Adcock Ingram: Speaker for HIV discussion for GPs, 2017; Pfizer South Africa: SA Pneumococcal disease summit: 2017, 2018; IDEAL Summit, 2018; Advisory Committee for Cef/taz; Novartis South: Speaker fees, 2015; The Infectious Diseases Society of Southern Africa (IDSSA): President elect, 2018; HPCSA Research Ethics Committee member; The HIV Prevention Trials Network (HPTN): HPTN077, AMP: investigator of records; The South African HIV Clinicians Society: Cryptococcal meningitis management guidelines; Biomerieux workshop.
Dr E Bera (Vice Chair)	National Committee for Confidential Enquiry into Maternal Deaths (NCCEMD): Guideline development: Hypertension in Pregnancy, June 2018
Prof R Coetzee	MSD: SAASP meetings and workshop.
Prof PJC Commerford	McMaster University (PHRI)/ Bayer: Together with spouse, run COMPASS in South Africa and remunerated by PHRI (COMPASS tests rivaroxaban); GlaxoSmithKline: Served on steering committee of the trials evaluating fondaparinux (OASIS) in CV disease and was a co-author on some of the papers. My institution received payment for conducting the studies; Novartis: Speakers fee and travel sponsorship for chairing a meeting on heart failure; Pfizer: Sponsored meeting in Cape Town and provided speaker fees for chairing.
Prof GS Gebhardt	Royal College of Obstetricians and Gynaecologists (RCOG): Sponsorship for congress attendance; HAIN Life Science: Partner works for HAIN Lifescience involved in TB diagnostics; Abbvie: Support to Province in Perinatal conference (support for conference and not for self); SA-Medical Research Council: Sponsor Accommodation sponsored for Cochrane workshop.; National Committee for Confidential Enquiry into Maternal Deaths (NCCEMD): Hypertension in Pregnancy Guidelines (2018); Maternity Care Guidelines

Dr R Griesel (resigned)	UCT: Involved in drafting the initial motivation for fondaparinux, submitted to the Western Cape PTC.
Dr Y Hookamchand (resigned)	Janssen Pharmaceutica: Honoria for Pain Internship and Community service officer training 2017; Sponsorship registration and accommodation: PAIN2016, WIP2015; MundiPharma: Sponsored Tea and Lunch At Pain CSO & Intern Training 2016, 2017.
Dr L Robertson	Sanofi Aventis: Lunch and attend price sensitivity meeting on public sector cost of amisulpiride; Speaker honorarium donated to the Society for Mental Health and Deafness via South African Society of Psychiatrists (SASOP); Lundbeck: Lunch - January 2019; Astra Zeneca: Lunch 25 July 2017; Dr Reddy's Laboratories: Annual sponsorship for congress attendance and accommodation, 2014 – 2019; Janssen Pharmaceutica: Meeting to discuss training and other support of community psychiatry; Various pharmaceutical companies: Sponsorship to the SASOP; Various pharmaceutical companies: Sponsorships to the South African Orthopaedic Association (Spouse is a member).
Dr A Sherriff	National Department of Health: Breast cancer control policy, 2017; South African Society of Radiation Oncologists Board: President of College of Radiation Oncologists; Roche Products: Sponsorship to attend breast cancer congress; Oncology trial involvement: Ecufs: 104/2011 – Trastusamab vs Pertuzumab adjuvant yherapy in patients with HER-2 positive primary breast cancer, Ecufs: 100/2014 – Veliparib in HER-2 neg metastatic or locally advanced unresesctable BRCA breast cancer, Ecufs: 225/2015 – Pembrolizumab evaluating biomarkers in advanced solid tumours, Ecufs 226/2015 – Pembrolizumab in colorectal cancer, Ecufs: 17/2015 – BI695502 in advanced nonsquamus non-small cell lung cancer, Ecufs 227/2015 – ABT414 for gioblastoma.
Dr AS Rossiuw	Boehringer Ingelheim: Conference sponsorship (ESOC 2017, Prague) and honorarium (training and workshop: Integrated care pathway, Thrombolysis in Eastern Cape). Honararium received in 2018 for conference attendance, training and workshops as well as steering committee; Sanofi Aventis: Honorarium received in 2015 and 2018 for workshop attendance and training (including workshop on the approach to management of epilepsy); Bayer: Attended product launch of rivaroxaban; SA-Medical Research Council: Grant for pilot research.
Dr S Takuva	Sanofi Pasteur/GlaxoSmithKline Biologicals/Novartis: Medical Monitor/Safety Physician for a number of studies using Pfizer's / GSK Biologicals'/ Novartis' experimental products (vaccines for HIV) in Phase 1/2a/ 2b and 3 trials - position funded through a grant to the HVTN from the NIH and Gates Foundation; Janssen Pharmaceutica (Johnson and Johnson): Conduct periodically training for clinicians and non-clinicians on HIV vaccinology and immunology. No speaker fees received.
Ad hoc technical support to the Committee	
Dr J Nel	AbbVie: consultation on study relating to antiretrovirals; Mylan: consultation on antiretroviral regimens; Helen Joseph Hospital: Research on cryptococcal meningitis;
Dr L Weich	Rickett Benkiser & Equity Pharmaceuticals: sponsorship of snacks for patient open day 2011-2014; Adcock Critical Care & Equity Pharmaceuticals: sponsorship of snacks for patient open day 2011-2014; The South African HIV Clinicians Society: Cryptococcal meningitis management guidelines.
Secretariat to the Adult Hospital Level Committee	
Ms TD Leong	ISPOR-SA: Sponsorship and honorarium for ISPOR-SA 2019 conference.

National Essential Medicines List Committee (2017-)	
Dr G Reubenson (Vice Chair)	Aspen, GlaxoSmithKline, Pfizer, Sanofi: Speaker fees and conference support (local and international).
Dr A Black (resigned)	See above
Prof S Boschmans	Spouse employed by Aspen Pharmacare.
Dr H Dawood	See above
Prof K Cohen	Non-commercial entity: Co-author of journal article on the use of IPT in HIV-infected pregnant women, submitted to NEMLC.
Dr R de Waal	Non-commercial entity: Co-author of journal article on the use of IPT in HIV-infected pregnant women, submitted to NEMLC.
Mr A Gray:	Non-executive director of Jembi Health Systems
Dr G Grobler	Sanofi, Dr Reddy's Laboratories: Sponsored meetings in 2019
Dr T Kredo	SA- Medical Research Council: Receipt of grants.
Prof G Maartens	GlaxoSmithKline: Advisory Board for Dolutegravir clinical therapy; Non-commercial entity: Co-author of journal article on the use of IPT in HIV-infected pregnant women, submitted to NEMLC.
Ms N Makalima	Haemophilia Medical and Scientific Advisory Council meeting (7-8 November 2019): conference and travel sponsorship
Prof M Mendelson (resigned)	MSD, Pfizer, GSK, Galderma, PharmaDynamics: Honoraria for non-product related education on antibiotic stewardship; Pfizer: Advisory board: influenza vaccine; MSD: Travel grants to attend ESCMID 2013, 2014, 2015, 2016
Prof P Ruff	Wits University Health Consortium: Clinical trial funding and honoraria from various pharmaceutical companies involved in oncology trials and funds are directed to Wits Health Consortium.
Mr R Wiseman	Liberty Health: Employed by Liberty Health
Secretariat to the National Essential Medicines List Committee	
Ms TD Leong	See above

Funding

- Discovery Health: commissioned Levnorgestrel IUS economic evaluation.
- United States Agency for International Development (USAID) through The USAID funded Global Health Supply Chain - Technical Assistance program: commissioned Flucytosine economic evaluation.

USEFUL NUMBERS AND URL LINKS

POISONS INFORMATION CENTRES

Poison Information Helpine	0861555 777
Red Cross War Memorial Children's Hospital Poisons Information Service	0216585308 Email: poisonsinformation@uct.ac.za http://www.paediatrics.uct.ac.za/poisons-information-centre
Tygerberg Poison Information Centre	0219388596 www.sun.ac.za/poisoncentre
University of the Free State Poison Control and Medicine Information Centre	082491 0160
Information on poisons	https://www.afritox.co.za/

COMMUNICABLE DISEASES

COVID-19 hotline	Clinicians: 080011131 Public: 080002999 http://www.nicd.ac.za/ https://sacoronavirus.co.za/
Rabies hotline (NICD)	082883 9920
Viral Haemmorhagic Fever outbreak hotline (NICD)	082883 9920
South African Vaccine Producers	0113866063/2/00
National notifiable medical conditions surveillance	Helpline: 0726213805 Fax: 0866391638 Email: NMCSurveillanceReport@nicd.ac.za

MEDICINE INFORMATION CENTRES

Medicine Information Centre (Cape Town)	0214066829 0861100531
Amayeza Info Centre	011678 2332
National HIV Healthcare Worker Hotline	0800 212 506 0214066782

DEPARTMENT OF HEALTH

National Department Health website	www.health.gov.za
Essential Drugs Programme	www.health.gov.za/edp.php Email:SAEDP@health.gov.za
Third line ART applications	Email: TLART@health.gov.za
Medicine stock availability reporting	Email: stockalert@health.gov.za
Adverse drug reporting:	The National Adverse Drug Event Monitoring Centre (NADEMC): 021 4471618 Fax: 021448 6181 South African Health Products Regulatory Authority (SAHPRA) 012 842 7609/10 adr@sahpra.org.za
Central Chronic Medicine Dispensing and Distribution (CCMDD)	012 395 8988 012 395 8362 Email: nhiccmddadmin@health.gov.za

USEFUL NUMBERS AND URL LINKS

OTHER NUMBERS

Women abuse helpline	0800150150
Child line	0800055555
South African Police Services Crime Stop	086010111
National Human Trafficking Helpline	0800222777
Suicide helpline	0800567567

MISCELLANEOUS

Antiretroviral pregnancy registry	http://www.APRegistry.com/
Antiretroviral therapy: drug-drug interactions	https://www.hiv-druginteractionslite.org/checker http://www.mic.uct.ac.za/
Asthma control test™	https://www.asthmacontroltest.com/
BMI-based CVD risk tool	https://www.framinghamheartstudy.org/fhs-riskfunctions/cardiovascular-disease-10-year-risk/#
COPD: Modified Medical Research Council (mMRC) dyspnea scale calculator	https://www.mdcalc.com/mmrc-modified-medical-research-council-dyspnea-scale `
Dietary phosphate restriction	https://www.kidney.org/
ECG analysis: Reference guide	ECG APPtitude: http://q-r.to/baoxer ECG ONLINE: http://ecgonline.uct.ac.za
eGFR calculator	https://www.kidney.org/professionals/KDOQI/gfr_calculator
Haemophilia centres	http://www.haemophilia.org.za/treatment-centres/
Ideal weight calculator	https://www.mdcalc.com/ideal-body-weight-adjusted-body-weight
Hyponatraemia: Infusion rate calculator	https://reference.medscape.com/calculator/hyponatremia-correction-infusate-rate
Mental health conditions: support groups	www.SADAG.org www.SAFMH.org.za
NSTEMI: Risk stratification calculators	TIMI: http://www.mdcalc.com/timi-risk-score-for-uanstemi/ Grace Risk Score: http://www.mdcalc.com/grace-acs-risk-and-mortality-calculator/
Opioid withdrawal: Objective opioid withdrawal scale (OOWS)	https://medicine.yale.edu/sbirt/OOWS_251773_284_5_v1.pdf
Pain (chronic): Rating scale to measure pain severity, quality of life, and functionality	Pain, Enjoyment and General Activity (PEG) scale: http://www.med.umich.edu/1info/FHP/practiceguides/pain/PEG.Scale.12.2016.pdf
Potassium deficit calculator	http://www.medicinehack.com/2011/07/hypokalemia-potassiumreplacement.html
QT prolongation: Medicines causing QT prolongation	https://www.sads.org.uk/drugs-to-avoid/?doing_wp_cron=1585301751.3996679782867431640625
Renal impairment: Medicines requiring dose adjustment in renal impairment	http://www.globalrph.com/index_renal.htm
Scorpion identification	http://www.cmej.org.za/index.php/cmej/article/view/2545/2580
Spider identification	http://www.cmej.org.za/index.php/cmej/article/view/2547/2582
Substance use disorder: rating scales	ASSIST: http://www.who.int/substance_abuse/activities/assist/en/ DUDIT:

	https://paihdelinkki.fi/sites/default/files/duditmanual.pdf
Valproate: acknowledgement of risk form	https://www.sahpra.org.za/documents/f150bf3f6.28_Valproate_Annual_Risk_Acknowledgement_Form_Dec18_v1.pdf
Vertigo: benign paroxysmal positional vertigo diagnosis	Dix-Hallpike test: https://www.youtube.com/watch?v=8RYB2QlO1N4 Epley manoeuvre: https://www.youtube.com/watch?v=jBzID5nVQjk
VTE: Risk assessment tools	Padua Prediction Score: https://www.mdcalc.com/padua-prediction-score-risk-vte IMPROVE VTE risk score: https://www.outcomes-umassmed.org/IMPROVE/risk_score/vte/index.html Geneva risk score: https://www.mdcalc.com/geneva-risk-score-venous-thromboembolism-vte-prophylaxis
Water deficit calculator	http://www.nephromatic.com/water_deficit.php