STANDARD TREATMENT GUIDELINES

AND

ESSENTIAL MEDICINES LIST

FOR

SOUTH AFRICA

HOSPITAL LEVEL
ADULTS

2015 EDITION

Copies may be obtained from:
The Directorate: Affordable Medicines
Private Bag X828
Pretoria
0001
OR
Department of Health Website: http://www.health.gov.za/edp.php

First printed 1998
Second edition 2006
Third edition 2012
Fourth edition 2015

ISBN: 978-1-920031-95-4

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 drugs and other consequences.

Suggested citation:
Republic of South Africa. Essential Drugs Programme. Hospital level (Adults) Standard Treatment Guidelines and Essential Medicines List. 4th ed. Republic of South Africa: National Department of Health; 2015.

Published and funded by:
The National Department of Health, Pretoria, South Africa

FOREWORD

It gives me great pleasure to present the Fourth Edition, of the Adult Standard Treatment Guidelines (STGs) and Essential Medicines List (EML) for Hospital Level care.

The system for the selection of essential medicines in the South African public health sector is evolving as our country moves towards the implementation of National Health Insurance. The National Department of Health, through the National Drug Policy, remains committed to ensuring the availability and accessibility of good quality essential medicines that are effective, safe, and affordable and, the rational use thereof. The STGs and EML remains an important tool in achieving this goal.

These guidelines are as a result of a rigorous evidence based peer review process. Congratulations to the National Essential Medicines List and Adult Expert Review Committees and external stakeholders on a successful collaboration and revision. I commend their continued commitment to healthcare provision in South Africa.

Access to previous editions of the Adult Hospital Level STGs and EML was mainly paper-based. To strengthen access and implementation of the revised publication, the guideline will be supported by the development of a mobile application format. I believe that we should now leverage the capabilities of technology to facilitate efficient, point-of-care access to up-to-date medicine information.

Ensuring that guidelines become an integrated and useful part of health care remains a challenge. Implementation of the revised edition of the STGs and EML calls for cooperation between all sectors of health care providers.

It is the hope of the National Department of Health that the revised guidelines will contribute towards greatly improved quality of care for our citizens.

DR A MOTSOALEDI, MP
MINISTER OF HEALTH
DATE:

INTRODUCTION

Access to essential medicines is a fundamental component in ensuring equitable health care to all South African citizens. The Standard Treatment Guidelines (STGs) and Essential Medicines List (EML) provides a platform for equitable access to safe, effective, and affordable treatment options. It is thus my honour to introduce the 4th Edition of the Adult Hospital Level STGs and EML.

Essential medicines are selected through the review of available clinical evidence, considering efficacy, safety and affordability. The STGs provide guidance for the rational use of these essential medicines.

New features have been incorporated into the revised Adult STGs and EML for Hospital Level care. These include the level of evidence and supporting citations, new algorithms and a warnings and cautions for medicine use reference. Additionally, the revised edition of the STGs and EML will be available in mobile application format. This is intended to improve accessibility to all healthcare professionals at all levels of care, and allows health care professionals immediate access to up-to-date information and decision support at their fingertips.

The extensive use of antimicrobials has resulted in drug resistance that threatens to reverse the life-saving power of these medicines. The revised STGs and EML features a quick antimicrobial reference appendix supporting the initiative of antimicrobial stewardship. In addition, a more comprehensive care package for anaesthesiology, pain and intensive care is included.

The revised publication is the culmination of many months of intensive review by the National Essential Medicines List and Adult Expert Review Committees, as well as collaboration and peer review from various internal and external stakeholders including National Department of Health Programmes, Clinical Societies and Health Care Professionals.

It is envisaged that the STGs and EML will undergo continuous improvement through the contributions of users, and therefore users are encouraged to submit their comments and suggestions to the National Department of Health.

I am confident that the revised guidelines will contribute towards promoting rational medicine use, preventing the development of AMR and improving the quality and safety of health care.

MS MP MATSOSO
DIRECTOR-GENERAL: HEALTH
DATE:

ACKNOWLEDGEMENTS

We would like to convey our sincere gratitude and thanks to the Adult Expert Review Committee for their passion, dedication, technical expertise and commitment to this process. We thank you for sacrificing the time.
We also thank the various stakeholders (doctors, pharmacists, nurses, dieticians, professional societies and other health care professionals) for their comments and contributions with submission of appropriate evidence and technical medicine reviews. Your willingness to participate in this peer review consultative process was integral in producing this excellent edition. We look forward to continuous constructive engagement.

In particular, we would like to thank:

- The Chairperson of the Adult Expert Review Committee, Prof Parrish, for his tireless support, continued dedication and innovative ideas.
- The Vice Chairperson of the Adult Expert Review Committee, Prof Blockman, for his commitment and contribution to the process.
- Prof Maartens for his technical and editorial support.

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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 drugs 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 care in South Africa were based on the WHO guidelines for drawing up a national EDL. 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 THIS BOOK

Principles

The National Drug Policy makes provision for an Essential Drugs Program 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 recommended treatments provided in this book are guidelines only and are based on the assumption that prescribers are competent to handle patients with the relevant conditions presenting to their facilities.

All reasonable steps have been 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) has been designed as a progression in care from the current Primary Health Care (PHC) STGs and EML. A medicine is 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. Where a referral to a tertiary facility is recommended, the relevant medicines have either been reviewed or included in the tertiary level EML, or is in the process of being reviewed. Given that the PHC STGs and EML are reviewed prior to the Adult Hospital Level STGs, there may be a period when the two STGs are not always perfectly aligned.

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.

It is anticipated that each Province will review the EML and prevailing tenders to compile a formulary which:

» Lists formulations and pack sizes that will facilitate care in alignment with the STGs.
» Selects the preferred member of the therapeutic class based on cost.
» Implements formulary restrictions consistent with the local environment.
» Provides information regarding the prices of medicines.

Therapeutic classes are designated in the “Medicine treatment” section of the STGs followed by an example such as, HMGCoA reductase inhibitors (statins) e.g. simvastatin. These therapeutic classes have been designated where none of the members of the class offer a significant benefit over the other registered members of the class. Always consult the local formulary to identify the example from the therapeutic class that has been approved for use in your facility.

Navigating the book

It is important that you become familiar with the contents and layout of the book

in order to use the STGs effectively.

The International Classification of Diseases (ICD)-10 number has been included with the conditions to facilitate accurate recording of diagnoses. A brief description and diagnostic criteria are included to assist the medical officer to make a diagnosis. These guidelines also provide guidelines for referral of patients with more complex and uncommon conditions to tertiary facilities with the resources for further investigation and management.

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 the book. 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: a quick reference to dosing of antimicrobials for specific indications (Appendix I) and a section providing guidance on special considerations for specific medicines (Appendix II).

Furthermore, to promote transparency, in this fifth edition, revisions 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 xxxviii.

The section on Patient Education in Chronic Conditions aims to assist health workers to improve patient adherence and health, generally.

Glossary

Term:	***Description:***
16+6 gestation weeks	Second trimester:16 weeks and 6 days pregnant
Child Pugh score (A,B,C)	Prognostic scoring tool for chronic liver disease
Morbid obesity	Obesity sufficient to prevent normal activity or physiologic function, or to cause the onset of a pathologic condition; BMI ≥ 40 kg/m^2.
Renal failure	eGFR < 30 mL/minute.
Severe penicillin allergy	A history of anaphylaxis, urticaria or angioedema associated with beta-lactam antimicrobials.
Surgical prophylaxis	Prophylactic antibiotic therapy that reduces the risk of surgical site infection. In most instances a single antibiotic dose prior to the procedure is sufficient. Postoperative antimicrobial administration is not recommended for most surgeries as this selects for antimicrobial resistance.

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 the Medicines Control Council'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 at the back of the book.

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

THERAPEUTIC DRUG MONITORING (TDM)

Potentially toxic medicines, 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.

Lithium
Measure serum levels at about 12 hours after the last dose – e.g. in the morning before that day's first dose. Levels should be less than 1 mmol/L and should be checked regularly while on therapy, with more frequent monitoring in the elderly and frail.

Aminoglycosides
Peak levels will generally be adequate if dosing is adequate (e.g. gentamicin 5 mg/kg/day in a single daily dose) and are not recommended unless the organism has a high MIC or the patient is critically ill. Trough levels taken immediately before the next dose are valuable in identifying potential toxicity before it manifests as deafness or renal impairment. Aminoglycosides are relatively contraindicated in renal impairment.

Anti-epileptics
Levels 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 levels may be difficult to interpret – if in doubt, seek assistance from a clinical pharmacologist/pharmacokineticist.

PRESCRIPTION WRITING

Medicines should be prescribed only when they are necessary for treatments following clear diagnosis. Not all patients or conditions need prescriptions for medicine. 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 important during pregnancy where the risk to both mother and foetus must be considered.

All prescriptions should:

» be written legibly in ink by the prescriber with the full name 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 contact details of the prescriber e.g. name and telephone number.

In all prescription writing the following should be noted:

» The name of the medicine or preparation should be written in full using the generic name.
» No abbreviations should be used due to the risk of misinterpretation. Avoid the Greek mu (μ): write mcg as an abbreviation for micrograms.
» Avoid unnecessary use of decimal points and only use where decimal points are unavoidable. A zero should be written in front of the decimal point where there is no other figure, e.g. 2 mg not 2.0 mg or 0.5 mL and not .5 mL.
» Frequency: 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).
» State the treatment regimen in full:
  – medicine name and strength,
  – dose or dosage,
  – dose frequency,
  – duration of treatment,
    e.g. amoxicillin 500 mg 8 hourly for 5 days.
» 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.
» After writing a script, 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 and that the patient's name and folder number are on the prescription form. Only then sign the script, and as well as signing provide some other way for the pharmacy staff to identify you 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 CKD (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, ARVs, 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.
Ceftriaxone	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.
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	Anemia 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 the frail and elderly patient, 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.
Lyophilised plasma	An alternative to fresh frozen plasma, based on limited evidence of efficacy. Does not require crossmatch prior to infusion, can be stored at room temperature and is pathogen inactivated (via a solvent detergent inactivation procedure).
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.
Moxifloxacin	Restricted for use in MDR-TB and in cases of severe penicillin allergy for specific indications (i.e. Hospital-acquired pneumonia, bronchiectasis, lung abscess, community acquired pneumonia, aspiration pneumonia and empyema).
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.
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.
Antivenom	Never administer antivenom without being fully prepared to manage acute anaphylaxis.

Prednisone taper	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.
Silver sulfadiazine	Do not use silver sulfadiazine if SJS/TEN is thought to be due to cotrimoxazole or other sulphonamide.
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.
Topical retinoids	Do not use in pregnant women.
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. PTT should be taken 4 hours after SC dose.
Valproate	Do not initiate valproate during pregnancy, or if a woman intends to fall pregnant, as it is associated with a higher teratogenic potential than the other first line anti-epileptic agents.
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, as indicated below.

Barriers that contribute toward poor adherence:

BARRIER	RECOMMENDED SUPPORT
Life style	
» It is often difficult to take multiple medications. » A busy schedule makes it difficult to remember to take the medication.	» Create a treatment plan with information on how and when to take the medications. » Use reminders such as cues that form part of the daily routine.

BARRIER	RECOMMENDED SUPPORT
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 maybe 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/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 a change in 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 whilst being encouraging regarding the impact of the negative aspects and offer support to deal with them if they occur.
» 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-medicine 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 the correct 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.
» Don't 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 (remember

side effects may be a problem here).

» 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 once the interval is decreased to 3 times a day there is a sharp drop in adherence with poor adherence to 4 times a day regimens.
» 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 implications.

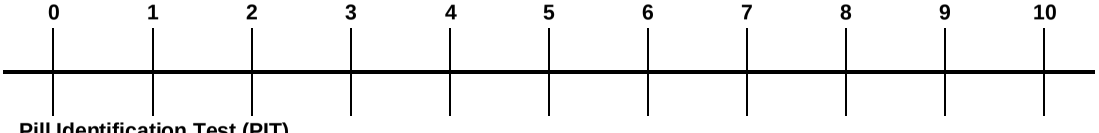
Patient Adherence Record

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

CHAPTER 1

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 emphasize 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 sulphate, 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

K57.9

DESCRIPTION

Colonic diverticulosis becomes increasingly common with age. 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 antibitoic 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, 1000/200 mg 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

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. 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

Weight reduction is recommended if overweight.
All patients with alarm symptoms, i.e. weight loss, haematemesis or melaena, dysphagia, or anaemia, 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:

- Lansoprazole, oral, 30 mg daily for 4 weeks. *LoE:I*[V]

Recurrence of symptoms

After endoscopic confirmation of disease:

- Lansoprazole, oral, 30 mg daily.
  - Decrease to omeprazole, oral, 10 mg daily after 4 weeks.

Barretts' oesophagitis

Restart PPI:

- 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 oesophagitis with PPIs reduces dysplasia or progression to malignancy.

REFERRAL

Discuss with a specialist for consideration of surgery in:

» 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.

1.1.4 HIATUS HERNIA

K44

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

1.1.5 INFLAMMATORY BOWEL DISEASE

K50.9/K51.9/K52.9

DESCRIPTION

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

REFERRAL

All patients with a potential diagniosis of Crohns disease or ulcerative colitis, should be discussed with a specialist.

1.1.6 PANCREATITIS, ACUTE

K85

DESCRIPTION

Acute inflammatory condition of the pancreas.
Intense local inflammation results in pain and local as well as systemic complications. DIC, metaboilic derangements and shock may occur.
Lipase assessment is useful to confirm the diagnosis
Renal function, electrolytes and calcium, can be used to determine severity.
Imaging is rarely needed.

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, psuedocyst, if required.

MEDICINE TREATMENT

For pain:

- 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

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

Antimicrobial therapy

The administration of prophylactic antibiotics is not necessary.

For abscess of the pancreas:

Broad spectrum IV antibiotics:

- Amoxicillin/clavulanic acid, IV, 1000/200 mg 8 hourly for 10 days, depending on clinical response.

LoE:III[VI]

1.1.7 PANCREATITIS, CHRONIC

K86.1

DESCRIPTION

Chronic inflammatory condition of the pancreas, 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.
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 12.12: 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.

1.1.8 PEPTIC ULCER

K27

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 inhibitor (PPI):

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

LoE:I[VII]

AND

<u>*H. pylori* eradication:</u>

- Amoxicillin, oral, 1 g 12 hourly for 7 days.
  OR
  <u>For severe penicillin allergy:</u>
  - Azithromycin, oral, 500 mg daily for 3 days.

LoE:I[VIII]

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.

Proton pump inhibitor (PPI):

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

LoE:II[IX]

Resistant disease

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

- Lansoprazole, oral, 30 mg daily. Specialist initiated.

LoE:III[X]

1.2 HEPATIC DISORDERS

1.2.1 HEPATITIS, NON-VIRAL

K70.1/K71/K75.4

* Notifiable 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: restrict protein if features of liver failure are present. Excessive protein restriction may accentuate catabolism.
Avoid alcohol.
Avoid other hepatotoxic agents.
Monitor blood glucose regularly because hypoglycaemia is common.

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

- FFP **or** lyophilised plasma. *LoE:II*[xi]

Routine administarion of parenteral vitamin K_1 is of unproven value.

MEDICINE TREATMENT

Hepatitis due to infections
Antibiotic therapy based on culture.

Alcohol-induced hepatitis

- Thiamine, oral, 100 mg daily

Other vitamins if indicated.

Drug-induced hepatitis
Stop all potentially hepatotoxic medication immediately, in consultation with a specialist.

Auto-immune hepatitis
Patients with persistent hepatitis, negative viral markers and no hepatotoxins. Biopsy and autoimmune markers are necessary to make the diagnosis.

If autoimmune hepatitis:

- Prednisone, oral, 0.5 mg/kg daily.
  - Taper dose to a suitable maintenance dose. (Refer to page xxvii for an example of a dose reduction regimen).

AND (on 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.

Refer timeously before extensive liver damage occurrs.

1.2.2 ACUTE LIVER FAILURE

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 preexisting liver disease. There are many causes, but the commonest are viral hepatitis, alcohol, drug-induced liver injury, or toxins.

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 administarion 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

K76.6

DESCRIPTION

The complications of portal hypertension are:

- » variceal bleeds
- » ascites and fluid overload
- » encephalopathy
- » spontaneous bacterial peritonitis in patients with ascites

GENERAL MEASURES

Ascites: sodium restriction, i.e. ≤ 2 g/day or ≤ 88 mmol/day.
Monitor weight regularly.
Bed rest.
Encephalopathy: low protein diet. Severe protein restriction may accentuate catabolism. Use increments of 20 g protein per day as tolerated.
Exclude infection, high protein load, occult bleed, sedatives and electrolyte disturbances.
Variceal bleeding: endoscopic sclerotherapy and/or banding.

MEDICINE TREATMENT

Ascites

- Single morning dose of oral spironolactone, oral 100 mg and furosemide, oral, 40 mg.
  - Increase the dose by 100 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 if eGFR < 30 mL/minute.

LoE:III[xii]

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

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

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

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

Look for preciptating factors : Sepsis, protein load, GIT bleed, overdiuresis, sedation

Oesophageal varices
To reduce the risk of bleeding:
- Carvedilol, oral, 12.5 mg 12 hourly for patients with Child Pugh A and 6.25 mg 12 hourly for Child Pugh B and C. Monitor pulse and BP. *LoE:II*[xv]

1.2.4 HEPATITIS, VIRAL

B19.9
* Notifiable disease

DESCRIPTION

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

1.2.4.1 HEPATITIS B, ACUTE

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:

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

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

HBsAg: hepatitis B surface antigen HBsAb: hepatitis B surface antibody
HBIG: hepatitis B immune globulin

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/B18.1/B19.1

DESCRIPTION

The hepatitis B virus (HBV) is commonly transmitted via sexual transmission, exposure to blood and other infectious body fluids, and vertically.
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.
Note that 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
1. 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.
2. 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.
3. Immune clearance	HBsAg positive HBeAg positive	>20000	Elevated	» Treatment required.
4. 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.

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 greater than 50 ml/min.

LoE:III[xvi]

AIMS OF TREATMENT

HBeAg-positive disease

» Sustained HBsAg loss due to therapy, with/without the development of anti-HBs, **and**
» Suppression of HBV DNA <2000 or undetectable levels, **and**

» Normalisation of ALT, **and**
» 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 <2000 or undetectable levels, **and**
» Normalisation of ALT.

MONITORING WHILST ON TENOFOVIR

Weeks 1 and 4 and every 12 weeks	ALT, INR
At inititiation of TDF, 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: HBeAg/ anti-HBe, HbsAg after anti-HBe seroconversion HBeAg-negative patients: HBsAg with persistently undetectable HBV DNA.
In HBeAg-positive patients: 12 months after HBeAg seroconversion	HBV DNA levels

Adapted from: Spearman CW, Sonderup MW, Botha JF, van der Merwe SW, Song E, Kassianides C, Newton KA, Hairwadzi HN. South African guideline for the management of chronic hepatitis B: 2013. S Afr Med J. 2013 May;103(5 Pt 2):337-49. http://www.ncbi.nlm.nih.gov/pubmed/23967497

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:** Longterm 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 COINFECTION)
B18.0/B18.1/B19.1 and B20
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, 1000/200 mg 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*[xvii]

1.2.7 ACUTE CHOLECYSTITIS AND ACUTE CHOLANGITIS

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 present:

» Elderly patients (older than 60 years of age)
» Co-morbidity
» Immune compromise

Acute cholecystitis and acute cholangitis

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

If unable to tolerate oral therapy:

- Amoxicillin/clavulanic acid, IV, 1000/200 mg 8 hourly.

REFERRAL

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

1.3 DIARRHOEA

1.3.1 CHOLERA

A00.9

*This is a notifiable disease.

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, 1 g immediately as a single dose.
  - Adjust antibiotic choice, according to the sensitivity of the isolate responsible for the local epidemic.

1.3.2 ACUTE INFLAMMATORY DIARRHOEA (DYSENTERY)

A03.9

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 500mg 12 hourly.

For uncomplicated dysentry in patients with no co-morbidity:

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

For uncomplicated dysentry 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 DIARRHOEA, ANTIBIOTIC-ASSOCIATED

A04.7

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.

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.
Surgery for bowel perforation.

MEDICINE TREATMENT

Loperamide is contraindicated as it may result in toxic megacolon.

<u>If diarrhoea does not settle on antibiotic withdrawal or if pseudomembranous colitis is present:</u>

- Metronidazole, oral, 400 mg 8 hourly for 10 days. *LoE:I*[xviii]

<u>Failure to respond to metronidazole after 5 days - consult a specialist and:</u>

ADD *LoE:III*[xix]

- Vancomycin, oral, 125 mg 6 hourly. (Give the parenteral formulation orally).

LoE:I[xx]

1.3.5 AMOEBIC DYSENTERY

A06

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[xxi]

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

A01.0

See section 9.9: Typhoid fever.

1.3.8 BACTERIAL PERITONITIS

K65

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) or normocytic anaemia (MCV 80 - 100 fL).

2.2 ANAEMIA, IRON DEFICIENCY

D50.9

DESCRIPTION

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

Investigations

» Low MCV and MCH (mean cell Hb – hypochromia).
» 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 sulphate compound BPC, oral, 170 mg (± 65 mg elemental iron), 12 hourly.

- Do not ingest with tea, antacids or calcium supplements/milk.
- Doses should be taken on an empty stomach, but if gastrointestinal side effects occur doses should be taken with meals.
- Continue with treatment for 3 months once Hb has normalised to replace iron stores.

LoE:III[I]

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

For example during pregnancy:

- Ferrous sulphate compound BPC, oral, 170 mg (± 65 mg elemental iron), 12 hourly. *LoE:III[II]*

Consider the following if there is failure to respond to iron therapy:

» non-adherence,
» continued blood loss,
» wrong diagnosis
» malabsorption, and
» mixed deficiency; concurrent folate or vitamin B_{12} deficiency.

Parenteral iron

Parenteral iron is seldom required and may be associated with anaphylaxis.
Parenteral iron is **only** indicated when oral iron is:

» 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.

Use in consultation with a specialist.

- Iron, IV.
  - An initial total dose of 600 mg intravenous iron is usually adequate to raise the Hb.

OR

For patients requiring a single dose:

- Low molecular weight iron dextran.
  - Determine total dose of iron required (total dose should not exceed 20 mg/kg body weight).
  - 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[III]

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.

2.3 ANAEMIA, MEGALOBLASTIC
D53.1

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 (mean corpuscular volume) and MCH (mean corpuscular haemoglobin).
» Pancytopaenia in severe cases.
» Full blood count 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.

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.

Adjust management according to results.

Folic acid deficiency

- Folic acid, oral, 5 mg daily until haemoglobin 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 strength and improved sense of well-being.
» Reticulocytosis begins 3–5 days after therapy and peaks at about day 7.
» The 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

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 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.

2.4 ANAEMIA, CHRONIC DISORDER

D63

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).

2.5 ANAEMIA, HAEMOLYTIC

D59

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.

Investigations

» Evidence of haemolysis: anaemia, reticulocytosis, decreased haptoglobin, increased lactate dehydrogenase (LDH) and unconjugated hyperbilirubinaemia.
» Full Blood count 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.
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 page xxvii for an example of a dose reduction regimen). *LoE:III[IV]*
  - Glucocorticoids can be stopped when there is normalization of the haemoglobin and LDH. The patient should be monitored for recurrence following cessation of treatment.

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.

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

Immunosuppresive therapy is needed in some cases, initiated by specialists.
LoE:III[V]

2.6 ANAEMIA, APLASTIC

D61.9

DESCRIPTION

Pancytopenia due to a hypoplastic bone marrow.
Clinical features:
» pallor
» petechiae
» frequent or severe infections
» purpura
» bleeding

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).

Pancytopenia in HIV positive patients:

Full blood count (FBC) indicate different degrees of: anaemia, thrombocytopaenia and leucopaenia.

Most common causes include:
Direct effect of HIV, medication, secondary opportunistic infections, malignancies and nutritional deficiencies.

Investigations

» Full blood count smear.
» vitamin B12 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 persistence pancytopaenia) to exclude infiltration with opportunistic infections, malignancies, etc.

2.7 ANAEMIA, SICKLE CELL

D57

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.

To prevent venous thromboembolism:

- Unfractionated heparin, SC, 5000 IU 12 hourly.

OR

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

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

GENERAL MEASURES (CHRONIC MANAGEMENT)

Transfusion for severe anaemia should always be discussed with a specialist.

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.

2.8 FEBRILE NEUTROPENIA

D70

DESCRIPTION

Febrile neutropenia is conventionally defined as an absolute neutrophil count

of < 0.5 x 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.

This is a **medical emergency** as these patients can rapidly develop features of severe sepsis (multi-organ failure and/or hypotension).

GENERAL MEASURES

Treat the underlying cause of neutropenia, if applicable.
Withdraw any medication that may cause neutropenia.
Consider removing central IV line.

Take blood and other relevant cultures before starting antimicrobial therapy. 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:

- 3rd generation cephalosporin, e.g.:
- Ceftriaxone, IV, 1 g daily.

AND

- Gentamicin, IV, 6 mg/kg daily.

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, IV, 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

OR

- Cefepime, IV, 1 g 12 hourly.

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 > 0.5×10^9/L, continue for 2 days after fever has settled.
» If neutrophil count remains ≤ 0.5×10^9/L, continue for 7 days after fever has settled.

REFERRAL/CONSULTATION
All cases – consult with haematologist/oncologist.

2.9 MYELODYSPLASTIC SYNDROMES
D46

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.

2.10 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: Full Blood Count, 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.

2.10.1 HAEMOPHILIA A AND B, VON WILLEBRAND'S DISEASE

D66/7/8

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/centres.html

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

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 hospitalization.
  - Discuss all patients promptly with local haemophilia treatment centre.

LoE:III[VII]

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[VIII]

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:

- FFP, IV, 15 mL/kg.

OR

Lyophilised plasma, IV, 15 mL/kg.

LoE:II[ix]

HAEMOPHILIA WITH INHIBITORS

Refer for assessment and planning with a haematologist.

VON WILLEBRAND'S DISEASE

Mild bleeding

E.g. epistaxis and menorrhagia.

Antifibrinolytics, e.g.:

- Tranexamic acid, oral, 1 g 6 hourly.

Recurrent menorrhagia can also be treated effectively with oral contraceptives.

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.

2.11 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.
Goal of treatment: to reduce the risk of bleeding, not to normalize 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 page xxvii for an example of a dose reduction regimen). *LoE:III*
  - Although prednisone is also indicated for HIV-associated immune thrombocytopenia it is important that all these patients should be fast-tracked for ART.

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[x]

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

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

M31.1/D59.3

DESCRIPTION

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.

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 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 the coagulation profile (PT/PTT) is deranged.

TREATMENT

- In HIV-associated thrombotic thrombocytopenia, start combination antiretroviral therapy urgently.

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

OR

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

LoE:II[xi]

The use of platelet transfusions should be discussed with a specialist.

REFERRAL
All patients – discuss with a haematologist.

2.13 ACQUIRED COAGULATION DEFECTS

2.13.1 DISSEMINATED INTRAVASCULAR COAGULATION (DIC)
D65

DIC is a complication of an underlying condition and is characterized 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:
- FFP, IV, 15 mL/kg as initial dose.
  - Volume: ±280 mL/unit.

OR

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

LoE:II[xii]

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.

2.14 VENOUS THROMBO-EMBOLISM

I82

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

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

Acute treatment

Unfractionated or low molecular weight heparin started simulatenously 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 venous thrombosis and/or pulmonary embolism:

- 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

OR

- Low molecular weight heparin, e.g.:
- Enoxaparin, SC, 1 mg/kg 12 hourly.

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

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

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.

Prophylaxis

- Prophylaxis is indicated for most medical and surgical patients. Unfractionated heparin, SC, 5 000 units 12 hourly.

OR

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

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

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

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 hr of full therapeutic dose,
(Timing of anticoagulants for patients receiving anaesthesia: See section 12.8: Spinal (intrathecal) anaesthesia).
» renal insufficiency,
» coagulopathy, or
» uncontrolled hypertension.

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*[1]

GENERAL MEASURES

Lifestyle modification, especially smoking cessation, is essential and often has greater benefit 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

Indication for lipid lowering medication:

Secondary prevention (irrespective of baseline cholesterol levels):

» Established atherosclerotic disease, irrespective of cholesterol or triglyceride plasma concentrations:
  - ischaemic heart disease,
  - peripheral vascular disease, or
  - atherothrombotic stroke.

» Type 2 diabetics > 40 years of age, or diabetes for > 10 years, or cardiovascular disease, or chronic kidney disease (eGFR < 60 mL/minute) *LoE:I[II]*

OR

Primary prevention:

» A risk of MI of greater than 20% in 10 years (see table above).

▪ HMGCoA reductase inhibitors (statins) that lower LDL-cholesterol by at least 25%, e.g.:

• Simvastatin, oral, 10 mg at night. *LoE:I[III]*

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

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.

3.2.1 ST ELEVATION MYOCARDIAL INFARCTION (STEMI)

I21.0-I21.3

DESCRIPTION

Ischaemic chest pain that is ongoing > 30 minutes and associated with persistent ST elevation or new or presumed new left bundle branch block (LBBB). Repeat ECG regularly as clinically indicated.

MEDICINE TREATMENT

If hypoxic:

- Oxygen.

- Clopidogrel, oral, 75 mg daily for one month. *LoE:I[IV]*

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:III*

AND

Thrombolytic therapy (see table for time window below):

- Thrombolytic, e.g.:
- 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**. *LoE:I[IV]*
  - 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
» <u>For acute myocardial infarction with ST elevation or left bundle branch block</u> - if history of onset is less than 6 hours. (Beyond 6 hours treat as NSTEMI (see below), - if on-going ischaemic pain. *LoE:I*[VI]	» <u>Absolute:</u> - 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 - active bleeding or known bleeding disorder. » <u>Relative:</u> o refractory hypertension, o warfarin therapy, o recent retinal laser treatment, o subclavian central venous catheter, o pregnancy, o TIA in the preceding 6 months, o traumatic resuscitation.

Adjunctive 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).

<u>Pain not responsive to this dose may suggest ongoing unresolved ischaemia.</u>

- 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.

<u>For ongoing chest pain, control hypertension or pulmonary oedema:</u>

- 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

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) that lower LDL by at least 25%, e.g.:
- Simvastatin oral, 10 mg daily at night. *LoE:I*[VII]

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

- ACE-inhibitor, e.g.:
- Enalapril, oral 10 mg 12 hourly.

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.

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 high risk for progression to completer heart blocks.
» Myocardial infarction-related mitral regurgitation or ventricular septal defect (VSD).
» Contraindication to thrombolytic therapy (only if within the period for stenting).
» 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/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 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

<u>If hypoxic:</u>

- Oxygen.

LoE:I[VIII]

- Clopidogrel, oral, 300 mg.
  - 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:III

AND

Anticoagulation:

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

- Parenteral anticoagulation, e.g.:
- 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[ix]

To relieve spasm and pain and to reduce preload:

- 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 pain:

- Morphine, IV, to a total maximum dose of 10 mg (See Appendix II, for individual dosing and monitoring for response and toxicity).
  - Pain not responsive to this dose may suggest ongoing unresolved ischaemia.

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) that lower LDL by at least 25%, e.g.:
- Simvastatin oral, 10 mg daily at night. *LoE:I*[x]

If there is cardiac failure or LV dysfunction:

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

3.2.3 CHRONIC MANAGEMENT OF STEMI / NSTEMI / UA

I21.0-I21.3/ I21.4/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, oral.
  See section 3.4: Congestive cardiac failure.

REFERRAL

» Patients with a diagnosis of NTSEMI 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 should be referred to a cardiology service for angiography and revascularization therapy, provided that personnel and facilities are available that will allow diagnostic coronary angiography and revascularization by means of percutaneous intervention or coronary bypass surgery within 7 days of the index event. 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).

» 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-I20.9

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 daily. *LoE:III*

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

- Atenolol, oral, 50–100 mg daily.
  - Titrate to resting heart rate of approximately 60 beats/minute.

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

Step 2

ADD

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

Step 3

ADD

- Organic nitrates, e.g.:
- Isosorbide dinitrate, oral, 20–40 mg.
  - Taken at 8:00 and 14:00 as this provides a nitrate-free period to prevent tolerance.
  - Modify for night shift workers.
- HMGCoA reductase inhibitors, e.g.:
- Simvastatin, oral, 10 mg at night. *LoE:I*[xii]

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

I25.0

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.

LoE:III

- HMGCoA reductase inhibitors, e.g.:
- Simvastatin, oral, 10 mg daily.
  Therapy should be initiated together with appropriate lifestyle modification. See section 3.1: Ischaemic heart disease and atherosclerosis, prevention.

LoE:I[xiii]

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

I47.1

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-I48.9

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 fibrillations.

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 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

» If patient has a score of one, use either aspirin or warfarin. When 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:

- 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 are:
    - the elderly,
    - patients with renal dysfunction,
    - hypokalaemia, and
    - patients with lean body mass. *LoE:II*[xiv]

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 left ventricular dysfunction).

LoE:III[xv]

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 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: do 3 monthly monitoring.

– INR < 1.5 or > 3.5: do monthly monitoring.

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:

- 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*[XVI]

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*[XVII]

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:

- 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.

3.3.1.2 ATRIAL FLUTTER

I48

Atrial rate > 250 beats/minute with no flat baseline.
Can be difficult to recognise if 2:1 atrioventricular (AV) block, as the first of the 2 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 beats per minute) and make the dysrhythmia more obvious.

GENERAL MEASURES

Synchronised 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 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.

MEDICINE TREATMENT

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.
  - 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 DC shock.

Note: Adenosine is contraindicated when atrial flutter is the obvious diagnosis, administration of adenosine can precipitate 1:1 conduction at ventricular rates 250–360 beats per minute 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:

- Verapamil, oral, 40–120 mg 8 hourly. *LoE:III*[xviii]

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

I47.1/I47.2

DESCRIPTION

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

3.3.2.1 REGULAR WIDE QRS TACHYCARDIAS

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).

GENERAL MEASURES

CPR.

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
Never give verapamil or adenosine IV to patients with a wide QRS tachycardia as this may precipitate ventricular fibrillation. *LoE:III*[xix]

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

- 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.
  - Titrate to maintenance dose of 200–400 mg daily. Consult specialist before instituting long term (>than 1week) therapy.

  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 as thyroid abnormalities may develop.
- Ophthalmological examination every 6 months.

3.3.2.2 SUSTAINED (> 30 SECONDS) IRREGULAR WIDE QRS TACHYCARDIAS

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 beats per minute, treat as for atrial fibrillation. See section 3.3.1: Narrow QRS complex (supraventricular) tachycardias.

If the rate is > 170 beats per minute, 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

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 (>than 1week) therapy.

Precautions:

- If on warfarin, halve the dose of warfarin and monitor INR closely, until INR is stable.

- Avoid concomitant digoxin.
- Monitor thyroid function every 6months as thyroid abnormalities may develop.
- 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, 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)

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

Cardioversion/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 www.sads.org.uk/**drugs**_to_avoid.htm).
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 beats per minute (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.
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:

- 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 beats per minute after resuscitation and stabilization.
» 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

I49.8

DESCRIPTION

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

Sinus bradycardia < 50 beats per minute 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

I45.5

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 damage to the heart.

Potentially reversible causes include:

» anaemia
» thyroid disease
» valvular heart disease
» constrictive pericarditis
» hypertension.
» 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.
Influenza immunization.
Salt restriction.
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*[xx]

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 these agents in appropriate doses.
Digoxin has been shown to improve symptoms and reduce hospitalisation only. *LoE:I*[xxi]

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.

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.

- **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*[xxii]

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[xxiii]

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[xxiv]

Digoxin

Patients remaining symptomatic after the above-mentioned agents (Specialist consultation):

- 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 are:
    - the elderly
    - patients with renal dysfunction
    - hypokalaemia
    - patients with lean body mass

LoE:II[xxv]

Anticoagulants

Heparin: for DVT prophylaxis.

For patients admitted to hospital, unless contraindicated:

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

OR

LoE:II[xxvi]

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

LoE:I[xxvii]

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

Anti-dysrhythmic medicines

See section 3.3: Cardiac Dysrhythmias.

Only for potentially life-threatening ventricular dysrythmias.

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.

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 left bundle branch block (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

I09.1

GENERAL MEASURES

Bed rest.

Early surgical intervention in acute fulminant and prosthetic valve endocarditis is often indicated. Surgery should also be considered 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:

- 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[xxviii]

Empiric therapy

Native valve	• Benzylpenicillin (penicillin G), IV, 5 million units 6 hourly for 4 weeks **AND** • Gentamicin, IV, 1.5 mg/kg 12 hourly for 2 weeks If staphylococcal infection is suspected (acute onset): **ADD** • Cloxacillin, IV, 3 g 6 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.

* All cases of prosthetic valve endocarditis should be referred.

Directed therapy (native valve)

Streptococcal	
Fully susceptible to penicillin MIC: < 0.2mg/L	• Benzylpenicillin (penicillin G), IV, 5 million units 6 hourly for 4 weeks.
Moderately susceptible MIC: 0.12–0.5 mg/L	• Benzylpenicillin (penicillin G), IV, 5 million units 6 hourly for 4 weeks. **AND** • Gentamicin, IV, 1.5 mg/kg 12 hourly for 2 weeks.
Moderately resistant MIC: 0.5–4mg/L Enterococci and Abiotrophia spp. (nutritionally variant streptococci)	• Benzylpenicillin (penicillin G), IV, 5 million units 6 hourly for 4 weeks. **AND** • Gentamicin, IV, 1.5 mg/kg 12 hourly for 4 weeks. Six weeks of therapy may be required in cases with a history of > 3 months, or mitral or prosthetic valve involvement.
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.
Enterococcal	
Fully susceptible to penicillin MIC: < 4mg/L	• Benzylpenicillin (penicillin G), IV, 5 million units 6 hourly for 4 weeks.

Resistant to penicillin MIC ≥4mg/L **or** significant β-lactam allergy **and** Sensitive to vancomycin MIC: ≤4 mg/L	Refer.
Staphylococcal (cloxacillin/methicillin sensitive)	
S. aureus	• Cloxacillin, IV, 3 g 6 hourly for 4 weeks. If necessary, add: • Gentamicin, IV, 6 mg/kg daily for the first 3–5 days. The benefit of adding an aminoglycoside has not been established. In the rare occurrence of a penicillin sensitive staphylococcus, penicillin should be used in preference to cloxacillin.
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.

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
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:
- 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[xxix]

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).

Target organ damage:
» left ventricular hypertrophy,
» hypertensive retinopathy
» microalbuminuria, or
» elevated creatinine level.

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 albumin:creatinine ratio. Repeat yearly.
» If haematuria > 1+, investigate further.
» If glycosuria, exclude diabetes mellitus.
» If known diabetic, HbA_{1c}.
» 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).
» 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.
» 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.

Note:

» Check adherence to antihypertensive therapy.
» 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

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.
» Start antihypertensive therapy immediately (together with lifestyle modification) if there are 3 or more risk factors, target organ damage and/or associated clinical conditions.

BP 160-179/100-109 mmHg, < 3 risk factors, no target organ damage or associated clinical conditions:

» Lifestyle modification for 3–6 months.

» Start antihypertensive therapy with a combination of two medicines if target BP not achieved.
» Start antihypertensive therapy immediately (together with lifestyle modification) if there are 3 or more risk factors, target organ damage and/or associated clinical conditions.

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

Initial antihypertensive medicine:
- Low dose thiazide diuretic e.g.:
- Hydrochlorothiazide, oral, 12.5 mg daily.

If target BP is not reached after one month despite adequate adherence (or immediately in patients with BP 160-179/100-109 mmHg), add one of the following: ACE-inhibitor or calcium channel blocker.

- ACE-inhibitor, e.g.:
- Enalapril, oral, 10 mg daily.

OR

- Long-acting calcium channel blocker, e.g.:
- Amlodipine, oral, 5 mg daily.

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 not reached after one month despite adequate adherence, add a β-blocker.

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

If target BP is not achieved after one month despite adequate adherence, increase the dose of medication, one medicine every month, to their maximal levels: enalapril 10 mg 12 hourly, amlodipine 10 mg daily and hydrochlorothiazide 25 mg daily.

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 ACE-inhibitor
Diabetes type 1 or 2 with/without evidence of microalbuminuria or proteinuria	ACE- inhibitor, usually in combination with a diuretic
Chronic kidney disease	ACE-inhibitor, usually in combination with a diuretic
Isolated systolic hypertension	Hydrochlorothiazide Calcium channel blocker
Pregnancy	See Chapter 6: 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.

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

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

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

REFERRAL

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

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 2nd measurement is still elevated at the same level, start oral therapy using 2 medicines together, one of which should be low dose hydrochlorothiazide. The 2nd 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

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.

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 2 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.

- 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

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).

- 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.

3.7 RHEUMATIC HEART DISEASE

I09.9

DESCRIPTION

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

GENERAL MEASURES

Acute stage of rheumatic fever: bed rest and supportive care.

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MEDICINE TREATMENT

Acute rheumatic fever

For eradication of streptococci in throat:

- Benzathine benzylpenicillin (depot formulation), IM, 1.2 million units 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*[xxxi]

OR

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

Severe penicillin allergy:

- Macrolide, e.g.:
- Azithromycin, oral, 500 mg daily for 3 days. *LoE:I*[xxxii]

For arthritis and fever:

- NSAIDs, 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*[xxxiii]

- Benzathine benzylpenicillin (depot formulation), IM, 1.2

million units 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 *LoE:III*[xxxiv]

Phenoxymethylpenicillin, oral, 250 mg 12 hourly.

- Severe penicillin allergy:
- 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 should be discussed with a specialist for possible valve surgery.

» Pregnancy.

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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

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 characterized 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

- Benzoyl peroxide 5%, gel, apply in the morning to affected areas as tolerated.
  - Wash off in the evening.
  - If ineffective and tolerated, increase application to 12 hourly.

  Avoid contact with eyes, mouth, angles of the nose and mucous membranes. *LoE:III*[f]

OR

Topical retinoids
Indicated in non-inflammatory acne and where benzoyl peroxide alone is ineffective.

The main action is to control comedone formation.
Introduce topical retinoids gradually as a night-time application to limit skin irritant effects, as thery are not photo-stable and degrade when exposed to sunlight.

Do not use topical retinoids in pregnant women.

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

Moderate Acne:
Topical treatments as above
AND

<u>For inflammatory acne:</u>

- Doxycycline, oral, 100 mg daily for 3 months.
  - Review patient after 3 months of treatment. *LoE:III[II]*
  - Take with meals.
  - Do not take it with iron preparations and antacids.

Women who need oral contraception and have inflammatory acne can be initiated on a cyproterone acetate containing combined oral contraceptive pill.

- Cyproterone acetate 2 mg plus ethinyl estradiol 35 mcg, oral, provided that there is no personal or family history of breast cancer or thrombosis.

LoE:I[III]

For all severe cases discuss with a dermatologist

4.2 CELLULITIS AND ERYSIPELAS

L03.9/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.

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

OR
- Paracetamol, oral, 1 g 4–6 hourly when required to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum dose: 4 g in 24 hours.

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

- Cloxacillin, IV, 1 g 6 hourly.

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

Severe penicillin allergy:
- 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.

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

Non-urgent
» To surgeon for non-response.

4.3 IMPETIGO
L01.0

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

- Macrolide, e.g.:
- Azithromycin, oral, 500 mg daily for 3 days.

LoE:III[IV]

4.4 FURUNCLES AND ABSCESSES

L02.9

DESCRIPTION

Localised bacterial skin infection of hair follicles (furuncle/boil) or dermis (abscess), usually with *S. aureus***.**
The surrounding skin becomes:

» swollen, » red,
» hot , and » tender to touch.

Note: Boils in diabetic, 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.
The treatment of choice for small furuncles is moist hot compress.
Large fluctuant lesions should be treated with incision and drainage.
Systemic antibiotics are used only as indicated below.

MEDICINE TREATMENT

Antibiotic therapy

Systemic antibiotics are seldom necessary, except if there are:
Facial abscess, or if the abscess is associated with tender draining lymph nodes, fever, or extensive surrounding cellulitis.
Antibiotics should usually be given for 5–10 days, depending on clinical response.

- Cloxacillin, IV, 1 g 6 hourly.

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

Severe penicillin allergy:
- Clindamycin, IV, 600 mg 8 hourly.

When there is clinical improvement, change to:
- Clindamycin, oral, 450 mg 8 hourly.

4.5 ATOPIC ECZEMA/ DERMATITIS

L30.9

DESCRIPTION

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

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

To relieve skin dryness:

- Aqueous cream topical, to wash or bath.
- Emulsifying ointment (UE), topical, applied daily to dry areas as a moisturiser. *LoE:III[v]*

Creams are preferred to ointments on opening or oozing lesions and in intertriginous folds.
Moisturising soap, creams and ointments, as described above, should continue permanently as maintenance, even if the dermatitis is controlled.

Mild eczema

- Topical corticosteroids, e.g.:
- Hydrocortisone 1%, topical, applied 12 hourly to body and daily to 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 12 hourly for 7 days to the affected areas.
  - Apply sparingly to face, neck and flexures. *LoE:III[vi]*

If non-responsive:
Refer for dermatologist opinion.

- Prednisone, oral, for a maximum period of two 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.

LoE: III[i]

Infected eczema
This is usually due to staphylococcal infection.

Antibiotic therapy

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

Severe penicillin allergy:
- 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.
Therapy should be initiated without delay:
- Aciclovir 400 mg, oral, 8 hourly for 7 days.

LoE:III[vii]

If patient is unable to swallow due to odynophagia:
- Aciclovir, IV, 5 mg/kg/dose, 8 hourly for 7 days.

LoE:III[viii]

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
L51.9/L51.1/L51.2

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

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

Stevens-Johnson Syndrome (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. sulphonamides, non-nucleoside reverse transcriptase inhibitors (especially nevirapine), anti-epileptics (phenytoin, phenobarbitone, carbamazepine, lamotrigine), allopurinol, laxatives (phenolphtalein).

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

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.

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 sulphonamide.

Mucous membranes:

Regular supervised oral, genital and eye care to prevent adhesions and scarring.
Two-hourly mouth washes with bland mouth wash, e.g. glycothymol.
Examine daily for ocular lesions and treat 2-hourly with eye care and lubricants (methylpropylcellulose drops or ointment) 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. This 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 12.13.3 Analgesia for acute non-surgical pain).

REFFERAL/CONSULTATION

Discuss with a specialist, if considering re-initiation of medicine treatment.

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 with:

- Gauze moistened with sodium chloride 0.9%.

LoE:I[ix]

For exudative, infected wounds:

- Povidone-iodine 5% cream, topical apply daily.

4.8 PSORIASIS

L40.9

DESCRIPTION

This is an inflammatory condition of the skin and joints of unknown aetiology. Scaly red, 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.

Local plaques

For maintenance:

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

For flares:

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

LoE:III[x]

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.

LoE:III[xi]

For flares:

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

REFERRAL

» Indequate response to topical treatment.
» Severe disease, especially if joint involvement.

4.9 URTICARIA

L50.9

DESCRIPTION

A transient itchy inflammatory skin and mucosal condition recognised by a wheal and flare reaction. There are many causes. In most chronic cases the precipitant for the urticaria is never found. Lesions due to insect 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

L50.9

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:

- 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

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:

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

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[xii]

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.

Anogaenital warts:

» Pap smear should be done in women.
» Screen for other STIs.

MEDICINE TREATMENT

Cutaneous warts

Treatment seldom indicated.

Anogenital warts

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

  Podophyllin is a cytotoxic agent.
  Avoid systemic absorption.
  Contraindicated in pregnancy.

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

N94.6

DESCRIPTION

Lower abdominal pain that starts with the onset of menstruation, and subsides after menses have ended. 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:

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

OR *LoE:III[I]*

- Paracetamol, oral, 1 g 4–6 hourly when required to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum dose: 4 g in 24 hours.

LoE:III

For dysmenorrhoea caused by endometriosis:

ADD

- A 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

N91.0–N93.9

GENERAL MEASURES

All women over 45 years of age should have a transvaginal ultrasound and endometrial sampling.

Actively exclude organic causes, e.g. fibroids, for abnormal uterine bleeding.

MEDICINE treatment

Dysfunctional uterine bleeding implies that no organic cause is present.

Arrest of acute haemorrhage

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

<u>For women in the reproductive years:</u>

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

OR

As alternative to combined oral contraceptives:

Progestin only:

- 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 meals. *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>

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

ADD

<u>For dysmenorrhoea and abnormal bleeding:</u>

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

REFERRAL
Refer for surgical procedures as dictated by the diagnosis.

5.3 PELVIC INFLAMMATORY DISEASE (PID)
N73.9

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

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

Stage	Manifestations
Stage I	» cervical motion tenderness and/or uterine tenderness and/or adnexal tenderness
Stage II	» as stage 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 IUDs.

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 4–6 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:

- 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:

- 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:

- Clindamycin, IV, 600 mg 8 hourly.

AND

- Gentamicin, IV, 6 mg/kg daily.

Continue intravenous therapy until there is definite clinical improvement (within 24-48 hours). Thereafter, change to:

- Clindamycin, oral, 450mg 8 hourly.

AND

- Ciprofloxacin, oral, 500 mg 12 hourly to complete 10 days' therapy.

AND

To treat chlamydia: *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

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 meals. *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/N91.1

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 normal menses.

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

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.
» Prolactin level.
» Mid-luteal (day 21) progesterone assay: > 30 nmol/L suggests adequate ovulation.
» Laparoscopy and/or hysterosalpingography (Specialist supervision).

MEDICINE TREATMENT
Treat the underlying disease.

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

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

5.8 MISCARRIAGE
O00–O08

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

5.8.1 SILENT MISCARRIAGE OR EARLY FETAL DEATH
O02.0

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

5.8.2 INCOMPLETE MISCARRIAGE IN THE FIRST TRIMESTER

O02.1

GENERAL MEASURES

Counselling.
Evacuation of the uterus after ripening the cervix.

MEDICINE TREATMENT

Before MVA, to ripen the cervix:

- Misoprostol, oral/PV, 400 mcg as a single dose.

Medical evacuation:

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

5.8.3 MIDTRIMESTER MISCARRIAGE (FROM 13–22 WEEKS GESTATION)

O03.4

GENERAL MEASURES

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

MEDICINE TREATMENT

If no cervical dilatation:

- Misoprostol, PV, 400 mcg immediately.

Follow with:

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

Warning
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.

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:
- 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
O03.87

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:
- Clindamycin, IV, 600 mg 8 hourly.

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

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

AND
- Ciprofloxacin, oral, 500 mg 12 hourly.

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)

O04

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.

Summary of Choice of Termination of Pregnancy Act
Women eligibility

1st trimester (< 13 weeks): on request.

Second trimester (13 to 20 weeks): If doctor is satisfied that pregnancy was from rape or incest, or there is risk of fetal abnormality or risk to mother's physical or mental health or social or economic circumstances.

More than 20 weeks: Doctor and second doctor or registered midwife are satisfied that there is danger to the mothers' life, 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

1st trimester (< 13 weeks): doctor, midwife or registered nurse with appropriate training.

Second trimester (13 to 20 weeks), onwards: doctor responsible for decision and prescription of medication. Registered nurse/midwife may administer medication according to prescription.

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

5.9.1 GESTATION, 1ST TRIMESTER (< 13 WEEKS)

O04

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*[XV]

MEDICINE TREATMENT

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

Routine analgesia for vacuum aspiration:

- Pethidine, IM, 1 mg/kg 30 minutes before aspiration procedure, to a maximum of 100 mg. *LoE:III*[XVI]

OR

- Morphine, IM, 0.1 mg/kg 30 minutes before aspiration procedure, to a maximum of 10 mg (Doctor initiated). *LoE:III*[XVII]

Do not give intravenous benzodiazepines and parenteral opioid analgesics concurrently.

Conscious sedation - see chapter 23: Sedation.

Alternatively, consider paracervical block.

Oral analgesia as required for 48 hours:

- Paracetamol, oral, 1 g 4–6 hourly when required to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum dose: 4g in 24 hours.

AND

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

Medical TOP:
An alternative to MVA:

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

LoE:III

Followed 24–48 hours later by:

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

Note: Bleeding may persist for up to 1 week.

After administration of mifepristone, start:

- Paracetamol, oral, 1 g 4–6 hourly when required to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum dose: 4g in 24 hours.

ADD
After expulsion is complete:

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

5.9.2 GESTATION, SECOND TRIMESTER (13 TO 20 WEEKS)

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

GENERAL MEASURES

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

MEDICINE TREATMENT

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

- Misoprostol, PV, 3 hourly to a maximum of 5 doses
  - 13 to 16^{+6} weeks: 400 mcg, PV.
  - 17 to 20 weeks: 200 mcg, PV.

LoE:III[XVIII]

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

LoE:III[XIX]

Followed 24–48 hours later by:

- Misoprostol, PV, 400–800 mcg as a single dose.
  - Then, misoprostol, PV, 400 mcg 3 hourly for 5 doses at gestation 13–16^{+6} weeks.
    OR
  - Misoprostol, PV, 200 mcg 3 hourly for 5 doses at gestation 17–20 weeks.

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

Warning
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.

Analgesia
- 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.

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

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

5.10 SEXUAL ASSAULT
Y05

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:

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

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

OR LoE:I[xx]

- Copper IUD, e.g.:
- Cu T 380A, within 5 days of unprotected intercourse.

LoE:I[xxi]

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. LoE:III[xxii]

AND

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

HIV post-exposure prophylaxis (PEP)

See section10.4.2: Non occupational post exposure prophylaxis, sexual assault and inadvertent exposure.

5.11 URINARY INCONTINENCE

N81.9

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 replacement therapy (HT)

This is 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).

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.

Sequentially opposed therapy:

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

OR

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

Equivalent doses to medroxyprogesterone acetate:

- Norethisterone acetate, oral, 1 mg daily from day 11–21.
- Cyproterone acetate, oral, 1 mg daily from day 11–21.

Continuous combined therapy, e.g.:

- Conjugated equine estrogens, oral, 0.3–0.625 mg plus medroxyprogesterone acetate, oral, 2.5–5mg daily.

OR

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

Note:

» Start at the lowest possible dose to alleviate symptoms. The need to continue 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 are recommended.

Uterus absent (post hysterectomy)

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.

REFERRAL

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

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CHAPTER 6
OBSTETRICS

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

6.1 ANAEMIA IN PREGNANCY

O99.0

DESCRIPTION

Haemoglobin (Hb) <11 g/dL. Anaemia in pregnancy is most commonly due to iron deficiency. Hb levels in pregnancy should be routinely checked on-site at the first antenatal visit, and again at 28 weeks and 36 weeks. Treatment of anaemia is generally recommended when the Hb falls below 10 g/dL.

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

- Ferrous sulphate compound BPC, oral, 170 mg (± 65 mg elemental iron) daily.

AND *LoE:III*

- Folic acid, oral, 5 mg daily.
    - Continue with iron and folic acid supplementation during lactation.

Iron deficiency (Hb <10g/dL)

- Ferrous sulphate compound BPC, oral, 170 mg (± 65 mg elemental iron) 12 hourly. *LoE:I*[II]
    - 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

If there is no response to oral iron, and iron deficiency is confirmed, review adherence to oral iron, and consider:

- Iron, IV.
    - An initial dose of 600 mg intravenous iron is usually adequate to raise the Hb to acceptable levels.

- Administration varies with the type of parenteral iron preparation. Consult the package insert for total dose iron infusion. (Iron sucrose, for example, is administered as follows: 200 mg iron in 200 mL sodium chloride IV, over 30 minutes, given on alternate days until the total dose has been given).
- 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

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, from 24 weeks gestation onwards:

» Women of Indian ethnic origin.
» BMI >35 kg/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[III]*

- 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-, 1-hour and 2- hour 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:III[IV]

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 regimen

Use intermediate acting insulin at bedtime (with a bedtime snack) to maintain preprandial levels and short acting insulin with all 3 meals to maintain the post prandial levels.

Starting dose may be based on previous insulin requirements, if known, or empiric starting dose:

- Insulin, intermediate acting, 12 units at bedtime with a bedtime snack.
- Insulin, soluble, short acting 8 units 30 minutes before each of the three main meals (breakfast, lunch and supper).

Adjust insulin dosage daily according to blood glucose profiles, until control is adequate. *LoE:III*

Where the above recommended regimen is not feasible

Twice-daily regimen with biphasic insulin.

Empiric starting dose if previous insulin requirements are not known:

- Insulin, biphasic.
  - Daily dose: 0.5 units/kg/day, two thirds 30 minutes before breakfast and one third 30 minutes before *LoE:III*

supper.
- Titrate to achieve target blood glucose as above.

During labour:
Monitor serum glucose hourly.
Stop subcutaneous insulin.
Administer short acting insulin to maintain physiological blood glucose levels.

- Insulin, short acting, continuous IV infusion, 20 units plus 20 mmol potassium chloride in 1 L dextrose 5% at an infusion rate of 50 mL/hour, i.e. 1 unit of insulin/hour
  - If blood glucose < 4 mmol/L, discontinue insulin.
  - If >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, and
» congenital abnormalities.

Postpartum management
Contraception
Tubal ligation should be considered.
Consider:
- Low-dose combined contraceptive in well-controlled cases.
- Progestogen-only preparation or intra-uterine contraceptive device if planning to breastfeed.

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
O75.4

All women with heart disease require referral for specialist evaluation and risk assessment. The risk is particularly high in women with mechanical

valves, Eisenmenger's syndrome or pulmonary hypertension. Termination of pregnancy (TOP) is an option for women with severe heart disease if recommended by a specialist.

GENERAL MEASURES

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 section, unless there are obstetric reasons for surgery.

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 is indicated include:
  – Vaginal delivery in the presence of suspected infection.
  – Caesarean section.
  – 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.

MEDICINE TREATMENT

Indications for full anticoagulation during pregnancy (high risk):

» valvular disease with atrial fibrillation
» mechanical prosthetic heart valves

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

First trimester

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

OR

- Unfractionated heparin, SC, 15 000 units 12 hourly.
  - Adjust the dose to achieve a mid-target 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 2.5–3.5 for mechanical valves, and 2–3 for atrial fibrillation.

After 36 weeks until delivery

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

OR

- Unfractionated heparin, SC, 15 000 units 12 hourly.
  - Adjust dose with aPTT to keep it 2 – 3 x control.
  - Stop heparin on the morning of elective Caesarean section (6 hours before scheduled surgery) or when in established labour, and re-start 6 hours after vaginal delivery or 12 hours after Caesarean section, as long as there is no concern that the patient is bleeding.

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

Prophylaxis for venous thromboembolism

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

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

OR *LoE:I[V]*

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

LoE:I[VI]

Cardiac failure

See section 3.4: Congestive Cardiac Failure.

Treatment is as for non-pregnant women, except that **ACE-inhibitors and ARBs are contra-indicated.**

If a vasodilator is needed:

- Hydralazine, oral, 25 mg 8 hourly.
  - Maximum dose: 200 mg daily.

AND

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

Delivery

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

In women with NYHA grade II dyspnoea or more, consider the use of furosemide:

- Furosemide, IV, 40 mg with delivery of the baby.
  - Monitor for 48 hours thereafter for pulmonary oedema.

6.4 HYPERTENSIVE DISORDERS IN PREGNANCY

O15.9

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.

Mild to moderate pre-eclampsia:

A diastolic BP of 90-109 mmHg and/or systolic BP of 140-159 mmHg, with ≥1+ proteinuria; and no organ dysfunction.

Severe pre-eclampsia:

» Acute severe hypertension (diastolic BP of 110 mmHg and/or systolic > 160 mmHg) and ≥ 1+ proteinuria.

OR

» Any degree of hypertension & proteinuria with evidence of organ dysfunction (renal dysfunction, raised liver enzymes, thrombocytopaenia).

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[VII]

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

AND/OR

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

Hypertensive emergency

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[VIII]

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 200 mL 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[IX]

Delivery

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

LoE:III[X]

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
For women at high risk of pre-eclampsia, e.g. pre-eclampsia in a previous pregnancy, chronic hypertension, diabetes, antiphospholipid syndrome or SLE, from 12 weeks gestation onwards:

- Aspirin, oral, 75–150 mg daily with food.

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

6.5 SEVERE PRE-ECLAMPSIA AND ECLAMPSIA

O15

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.

MEDICINE TREATMENT

If necessary:

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

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

Treatment

In high-care setting:

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

Follow with:

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

Where infusion pumps are not available:

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

Follow with:

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

Stop magnesium sulphate if knee reflexes 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 sulphate loading dose administration:

- Magnesium sulphate, 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

O10.9

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 ≥ 37 weeks duration, or
» in the presence of maternal or fetal compromise, e.g. poor SFH growth and oligohydramnios, etc.

MEDICINE TREATMENT

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

6.7 HIV IN PREGNANCY

O98.7

For comprehensive information on the care of HIV-infected pregnant women, refer to the current National consolidated guidelines for the prevention of mother-to-child transmission of HIV (PMTCT) and the management of HIV in children, adolescents and adults, April 2015.

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 every 3 months throughout pregnancy, at labour/delivery, at the 6-week EPI visit and 3 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 mothers should be educated during the antenatal period about the benefits

of breastfeeding.

The patient should have a TB symptom screen at each visit, with further TB investigations if any of the answers to the screening questions are positive.

Patients should be screened and treated for syphilis and other STIs, in line with basic antenatal care.

Lifelong ART should be initiated in all pregnant or breastfeeding women on the same day of diagnosis regardless of CD4 count or infant feeding practice.

Adequate support and counselling, particularly addressing ART adherence, should be given.

Women with unwanted pregnancies < 20 weeks' gestation should be assisted 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.

» If standard first-line ART is contraindicated, these patients are considered to have high-risk pregnancies and require urgent referral to HIV/ART services.
Administer:

- AZT, oral 300 mg 12 hourly, until alternative combination ART can be initiated.

» Perform a baseline ALT and serum creatinine at commencement of ART.

» Tenofovir should not be used in pregnant women with a calculated creatinine clearance or eGFR of < 60 mL/minute or a serum creatinine ≥ 85 µmol/L (the latter is a more sensitive measure of renal impairment in pregnancy).

» Partner testing and routine cervical cancer screening should be done.

FIRST-LINE ART REGIMENS		
1st ANC visit		
All pregnant women not on ART (any gestational age). **AND** All breastfeeding women not on ART.	• 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).	If there is a contraindication to the FDC, start AZT immediately and refer patient for individual medicines. Contraindication to TDF: renal insufficiency. Contraindication to EFV: active psychiatric illness.

Pregnant women currently on ART	Continue current ART regimen.	Do a VL as soon as pregnancy is confirmed. Pregnant women with confirmed 2nd or 3rd line ART regimen failures should not breastfeed their infants, if they can safely formula feed.
2nd ANC visit (1 week later)		
Creatinine ≤ 85 micromol/L	Continue FDC: TDF+FTC+EFV	
Creatinine > 85 micromol/L (TDF is contraindicated)	Stop FDC: TDF+FTC+EFV. Replace TDF with ABC: • ABC, oral, 600 mg daily.	High-risk pregnancy: refer urgently for alternate triple therapy within 2 weeks with dose adjustment if indicated and investigation of renal dysfunction.
Active psychiatric illness (EFV may be contraindicated. Consult an HIV specialist and/or psychiatrist)	• TDF, oral, 300 mg daily. **AND** • FTC, oral, 200 mg daily **AND** • NVP, oral, 200 mg daily for 2 weeks, then 200 mg 12 hourly (**OR** LPV/r 400/100 mg 12 hourly).	CD4 < 250 • Replace EFV with NVP, oral 200 mg daily for 2 weeks, then 200 mg 12 hourly. ○ Do an ALT test before starting NVP. NVP should not be used in women with elevated ALT. ○ If ALT elevated, replace EFV with LPV/r, oral, 400/100 mg 12 hourly. CD4 ≥ 250 • Replace EFV with LPV/r, oral, 400/100 mg 12 hourly.

LoE:III[xi]

Caesarean Section:

All pregnant women, including HIV infected pregnant women should receive a single dose of antibiotic prophylaxis (See chapter 11: Surgical

antibiotic prophylaxis).
Women with the following risk factors are at higher risk of infection post Caesarean section:
» Advanced immunosuppression.
» Prolonged rupture of membranes.
» Multiple vaginal examinations (> 5 PVs).
» Second stage CS.
Monitor carefully and treat infection appropriately.

HIV infected pregnant women in labour not on ART:
- NVP, oral, 200 mg as a single dose.

AND
- TDF, oral, 300 mg as a single dose.

AND
- FTC, oral, 200 mg as a single dose.

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

6.8 SYPHILIS
A53.9

DIAGNOSTIC CRITERIA
Positive syphilis serology (RPR titre ≥16).

GENERAL MEASURES
Inform contact(s).

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

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

Severe penicillin allergy
For penicillin sensitive pregnant women: penicillin desensitisation.
(See page xxviii 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 05 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 250mg/ 5mL = 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 I.V. use).

OR

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

6.9 JAUNDICE IN PREGNANCY

O26.6

DESCRIPTION

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

Pregnancy-specific causes include:

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

» hyperemesis gravidarum.

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

6.10 HYPEREMESIS GRAVIDARUM
O21.9

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

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

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

MEDICINE TREATMENT
Correct electrolyte imbalance with IV fluids.

- Pyridoxine, oral, 25 mg 8 hourly.

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.

6.11 PRETERM LABOUR (PTL) AND PRETERM PRELABOUR RUPTURE OF MEMBRANES (PPROM)
O60/O42

DESCRIPTION
Preterm: < 37 weeks gestation.
Most problems occur at < 34 weeks' gestation.
Confirm ruptured membranes by sterile vaginal speculum.

Preterm labour confirmed by regular uterine contractions with progressive cervical changes.

GENERAL MEASURES

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

MEDICINE TREATMENT

If gestation < 34 weeks:

Pre-hydrate before administration of nifedipine:

- Sodium chloride 0.9%, IV, 200 mL.

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*[xii]

  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:

- Betamethasone, IM, 12 mg, 2 doses 12 hours apart. *LoE:I*[xiii]

If betamethasone is not available:

- Dexamethasone, IM, 8 mg, 3 doses 8 hours apart. *LoE:III*[xiv]

Note: Corticosteroids are maximally effective from 24 hours after administration of the first dose. Therefore give as soon as possible following diagnosis of PTL or PPROM.

Antibiotic therapy

Indicated routinely for ruptured membranes and only selectively for preterm labour with intact membranes at high risk of infection.

- Amoxicillin, oral, 500 mg 8 hourly for 5 days.

AND

- Metronidazole, oral, 400 mg 8 hourly for 5 days. *LoE:I*[xv]

Severe penicillin allergy:

- Azithromycin, oral, 500 mg daily for 3-5 days

AND *LoE:III*[xvi]

- Metronidazole, oral, 400 mg 8 hourly for 5 days.

Prepare for appropriate care of preterm infant.

REFERRAL

» Fetus requiring neonatal intensive care, e.g. weight <1.5 kg or gestation < 32 weeks.
» Fetus requiring specialised treatment after birth, e.g. surgery.
» Severely ill mother.

6.12 SUPPRESSION OF LABOUR FOR FETAL DISTRESS

O62.9

DESCRIPTION

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

MEDICINE TREATMENT

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

LoE:I[xvii]

6.13 LABOUR INDUCTION

O80

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

GENERAL MEASURES

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

Cervix favourable and confirmed HIV-uninfected mother

Artificial rupture of the membranes.

Cervix unfavourable

Extra-amniotic Foley catheter with/without saline infusion: recommended if attempts at ripening the cervix with prostaglandins fail.
Pass a Foley catheter with 30 mL bulb through cervix with sterile technique.
Inflate bulb with 50 mL water or sodium chloride 0.9%.
Tape catheter to thigh with light traction.
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 favourable

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

- Oxytocin, IV, 2 units in 200 mL sodium chloride 0.9%
  - Start at an infusion rate of 12 mL/hour (i.e. 2 milliunits /minute). 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	16	96
210	20	120

Note:

» 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.

Cervix unfavourable

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[xviii]

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.

OR

- Misoprostol, oral, 20 mcg 2 hourly until in labour, or up to 24 hours.
  - Oral misoprostol may be given as freshly made-up solution of one 200 mcg tablet in 200 mL water, i.e. 1 mcg/mL solution. Give 20 mL of this solution 2 hourly.
  - Stop misoprostol administration when in established labour.
  - Maximum 24 hours.
  - If no response, consider induction with 50 mL bulb Foley catheter with or without extra-amniotic saline infusion.
  - Never use oxytocin and misoprostol simultaneously.
  - Misoprostol and other prostaglandins are contraindicated in women with previous Caesarean sections and in grand multiparous women.

Note:

» Misoprostol in larger doses than indicated here for labour induction at term, may cause uterine rupture.
» Only to be prescribed by a doctor experienced in Maternal Health.
» A non-stress test to be done an hour after each new dose of 4-hourly during misoprostol administration.

6.14 LABOUR PAIN, SEVERE

GENERAL MEASURES

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

MEDICINE TREATMENT

- 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[xix]

Titrate dose and dose frequency according to pain.
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:

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

Postpartum and post-episiotomy pain

- Paracetamol, oral, 1 g 4–6 hourly when required to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum dose: 4g in 24 hours.

OR

- 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[xx]

6.15 DEHYDRATION/KETOSIS IN LABOUR

E86

DESCRIPTION

Subclinical dehydration is often missed in labour.

GENERAL MEASURES

Encourage adequate oral fluid intake.

MEDICINE TREATMENT

Mild dehydration

Give oral fluids.

Moderate/severe dehydration

Administer intravenous fluids, e.g.:

- Sodium chloride 0.9%, IV, 250 mL/hour.

Re-evaluate hydration hourly.

6.16 POSTPARTUM FEVER

O75.2

DESCRIPTION

During delivery the woman's protective barrier against infections is temporarily reduced and this may lead to infections.
The cause of fever may be a serious complication.
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.

6.17 POSTPARTUM HAEMORRHAGE

O72

DESCRIPTION

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

GENERAL MEASURES

Bimanual compression of the uterus.
Ensure delivery of placenta.
Check for local causes of bleeding.
Balloon tamponade of the uterine cavity should be considered if the patient is to be transferred to another facility.

MEDICINE TREATMENT

Prevention

Active management of the 3rd stage of labour:

- Oxytocin, IM, 10 units.

AND

Controlled cord traction.

Treatment

Resuscitate.
Put up two IV lines.

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

If necessary:

ADD

- Ergometrine, IM, 0.2–0.5 mg.

OR

- Oxytocin, IM, 5 units.

AND

- Ergometrine, IM, 0.5 mg.
  - Repeat ergometrine as needed up to a maximum of 1 mg in 24 hours.

- Avoid ergometrine in women with hypertension or cardiac disease, except in severe cases where the benefit is considered to outweigh the risk (discuss with a specialist).

For non-responding cases:

- Dinoprost 5 mg/mL, intramyometrial.
  - Dilute 1 mL to 10 mL.
  - Give 2 doses of 1 mL of dilute solution at different sites.
- Tranexamic acid 1 g, IV, slowly over 10 minutes.

In settings where oxytocin had NOT been administered as prophylaxis at birth:

- Misoprostol, sublingual, or rectal, 600 mcg as a single dose.

LoE:I[xxi]

6.18 THE RHESUS NEGATIVE WOMAN

O36.0

GENERAL MEASURES

Maternal serum antibodies absent

Prevention

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

MEDICINE TREATMENT

After a termination of pregnancy (TOP), miscarriage, ectopic pregnancy or amniocentesis:

- Anti-D immunoglobulin, IM, 100 mcg.

After external cephalic version:

- Anti-D immunoglobulin, IM, 100 mcg.

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

- Anti-D immunoglobulin, IM, 100 mcg.

If a large feto-maternal transfusion is suspected:

- Anti-D immunoglobulin, IM, 300 mcg for every 30 mL transfusion.
  - Maximum dose: 1 200 mcg.

AND

Do a maternal blood Kleihauer test.

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

Maternal serum antibodies present
Consult a specialist.

6.19 URINARY TRACT INFECTION (UTI) IN PREGNANCY

6.19.1 CYSTITIS

N30

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; protein and/or blood may also be detected.

GENERAL MEASURES

Encourage oral fluid intake.
Midstream urine for microscopy, culture and sensitivity.

MEDICINE TREATMENT

Empiric treatment (nitrites positive **OR** leukocytes positive on dipstick):

- Amoxicillin/clavulanic acid 875/125 mg, oral, 12 hourly for 5 days.

Severe penicillin allergy:

- Fosfomycin 3 g, oral, as a single dose.

LoE:III[XXII]

REFFERAL/CONSULTATION

No response to treatment, or resistant organism on culture.

6.19.2 PYELONEPHRITIS, ACUTE

N10

DESCRIPTION

This condition is more serious and may result in preterm labour.
Features of pyelonephritis include:

» temperature ≥38°C
» 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 2 urine specimens are negative to confirm eradication.

REFFERAL/CONSULTATION

» Failure to respond to antibiotics.
» Impaired renal function.
» Abnormal urinary tract

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CHAPTER 7
NEPHROLOGICAL/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)

N18.9

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 or haematuria
  - increased serum creatinine or low eGFR
  - small kidneys on ultrasound
  - abnormalities renal biopsy

eGFR calculator online access:
https://www.kidney.org/apps/professionals/egfr-calculator

Common causes of CKD include:

» hypertension
» polycystic kidney disease
» glomerular disease (idiopathic, hepatitis B and C, systemic lupus erythematosus, etc.)
» diabetes mellitus
» HIV/AIDS

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.

Staging of kidney disease

Stage/ glomerular filtration rate (mL/minute/1.73m^2)	**Description**	**Action** Includes actions from preceding stages	**Frequency of follow up of kidney disease in a stable patient**
Stage 0 or eGFR > 90	» At increased risk of CKD e.g.: – diabetes mellitus – hypertension – glomerular disease – HIV	» Screening for CKD and CVD. » CKD and CVD risk reduction. » Treat hypertension, diabetes, HIV.	» Annual urine dipstix. » Annual measurement of potassium, creatinine and eGFR.
Stage 1 or eGFR > 90	» Kidney damage with normal eGFR.	» Diagnose and treat comorbid conditions. » Slow progression. » CVD risk reduction.	» Annual urine dipstix. » Annual measurement of potassium, creatinine and eGFR.
Stage 2 or eGFR 60–89	» Kidney damage with mild ↓ eGFR	» Investigate cause. » Develop care plan. » Monitor progression.	» Annual urine dipstix » Annual measurement of potassium, creatinine and eGFR
Stage 3 or eGFR 30–59	» Moderate ↓ eGFR	» Evaluate and treat for complications.	» Frequency of monitoring must increase when approaching Stage 4 or when eGFR shows rapid decline. » 3-6 monthly: clinical assessment. » 3-6 monthly testing of Hb, urea,

			creatinine, potassium, calcium, phosphate.
Stage 4 or eGFR 15–29	» Severe ↓ eGFR	» Refer for consideration of renal replacement therapy.	» 3 monthly clinical assessment. » 3 monthly testing of Hb, urea, creatinine, potassium, calcium, phosphate, PTH.
Stage 5 or ESRD or eGFR < 15 or on dialysis	» Kidney failure requiring renal replacement therapy » End Stage Renal Disease (ESRD)	» Refer for consideration of renal replacement therapy, i.e. dialysis or transplant if uraemia present.	<u>ON RRT:</u> » Monthly testing of Hb. » 3 monthly clinical assessment. » 3 monthly testing of urea, calcium, creatinine, PTH, potassium, HIV phosphate, and Hepatitis B.

GENERAL MEASURES

» Address cardiovascular disease risk factors. See section 3.1 Ischaemic heart disease and atherosclerosis, prevention.
» Limit salt intake.
» Limit dietary protein intake to 0.6 g/kg/day
» Avoid nephrotoxic medicines like NSAIDs.
» 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 protein creatinine ratio of > 0.1 g/mmol.
  - If urine dipstick less than 1+, request albumin creatinine ratio.

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

The ideal targets are: protein creatinine ratio < 0.03 g/mmol or albumin creatinine ratio (ACR) < 2.2 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.
  - 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[I]

If an ACE-inhibitor is not tolerated due to intractable cough:

- Consider an angiotensin II receptor blocker (ARB), e.g.:
- Losartan, oral,

LoE:III[II]

  - Start with 50 mg daily and titrate to 100 mg daily, if tolerated.
  - ARBs are contra-indicated following ACE-inhibitor-associated angioedema.

LoE:I[III]

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: 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/minutes.

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[IV]

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, to prevent calcium deposition in vessels and tissue which aggravates vascular disease.

Restrict dietary phosphate intake. (Dietitian consultation)
https://unckidneycenter.org/files/kidney-health-library-files/renaldiet_phosphorus.pdf

Patients with CKD stage 3–5, not on dialysis:

Hyperphosphataemia and/or hypocalcaemia:

- Calcium carbonate, oral, equivalent to elemental calcium, 500 mg 8 hourly with meals, increase to 1 g 8 hourly with meals, if hyperphosphatemia persists.

Hypocalcaemia and low or normal serum phosphate:

- Calcium carbonate, oral, equivalent to elemental calcium, 500 mg 8 hourly between meals, increase to 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 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:

- Calcitriol, oral, 0.25–4 mcg daily. Specialist initiated.

LoE:III

Anaemia associated with CKD in patients on dialysis programmes

Patients on chronic haemodialysis or peritoneal dialysis are often anaemic due to iron deficiency and deficiency of erythropoietin.

- Iron, elemental, oral. See section 2.2 Anaemia, iron deficiency
  - If no response consider parenteral iron.

AND

- Erythropoietin, SC/IV.

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.

CONSULT WITH A SPECIALIST AT THE LOCAL REFERRAL CENTRE

» CKD stage 3 and above.
» Unknown cause of kidney failure.
» Rapid deterioration in renal function.
» Resistant hypertension despite appropriate medication and adherence.
» All ESRD patients who may qualify for long term dialysis programs. See section 7.1.7: Renal replacement therapy.

7.1.2 GLOMERULAR DISEASE AND NEPHRITIC SYNDROME

N01.9/N03.9

DESCRIPTION

Acute glomerulonephritis presents with one or more of the following: haematuria, proteinuria, an acute decrease in eGFR, fluid retention, and hypertension.

GENERAL MEASURES

» Give oxygen, and nurse in semi-Fowlers 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.
  - Avoid unnecessary intravenous fluids.

If hypertension present:
Diastolic BP > 100 mmHg or systolic BP is >150 mmHg:

- Amlodipine, oral, 5 mg as a single dose.

AND

- Hydrochlorothiazide, oral, 25 mg (if eGFR ≥ 30 mL/min).

OR

Furosemide, oral, 40–80 mg (if eGFR < 30 mL/min).

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.: protein:creatinine ratio >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 protein creatinine ratio:
» initially – weekly
» when discharged – monthly, until stable
Monitor potassium frequently for patients on ACE-inhibitors and/or diuretics.

MEDICINE TREATMENT
Management should be guided by a specialist.

CONSULTATION/REFERRAL
All patients.

7.1.4 ACUTE KIDNEY INJURY
N17.9

DESCRIPTION
Acute kidney injury (AKI) is generally detected by an increase in the serum creatinine and/or a decrease in urine output.
Kidney injury may be due to a combination of factors.

GENERAL MEASURES
A detailed history and good clinical examination is necessary to identify potentially reversible causes.
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 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 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 0.5%, solution, nebulised.
  - Dilute 1 mL in 4 mL of sodium chloride 0.9%.

These are short term measures. Patients should then either 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

Some patients do not recover kidney function and should be treated as CKD.

7.1.5 RENAL REPLACEMENT THERAPY

Z49

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

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 and cramps.
Severe symptoms: rhabdomyolysis, paralysis, dysrhythmias, diaphragmatic weakness.
It is usually due to gastro-intestinal (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.
  - Titrate 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):

- Potassium chloride, oral, 600 mg, 1-2 tablets 8 hourly.
  - Titrate to response to therapy.
  - Maximum daily dose: 6 g.
  - Each 600 mg potassium chloride tablet contains 8 mmol of potassium chloride.
  - Continue treatment until the serum potassium concentration is persistently above 3.5 mmol/L and symptoms or signs have resolved.

LoE:III[V]

For severe symptomatic hypokalaemia:

- Potassium chloride, IV, 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.
  - Potassium chloride 15%, 10 mL ampoule contains 20 mmol of potassium.

LoE:III[VI]

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.

If not responding to therapy, check for hypomagnesaemia.

7.2.3 HYPERNATRAEMIA

E87.0

DESCRIPTION

A serum sodium level > 145 mmol/L.

» Mild to moderate symptoms: Lethargy, weakness, irritability
» Severe symptoms: Convulsions, coma

It is usually due to inadequate water intake (decreased thirst sensation or unable to drink water) or to gastro-intestinal (vomiting, diarrhoea) or renal losses (diabetes insipidus, osmotic diuresis, furosemide) of water.

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:

- 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[vii]

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 per hour

7.2.4 HYPONATRAEMIA

E87.1

DESCRIPTION

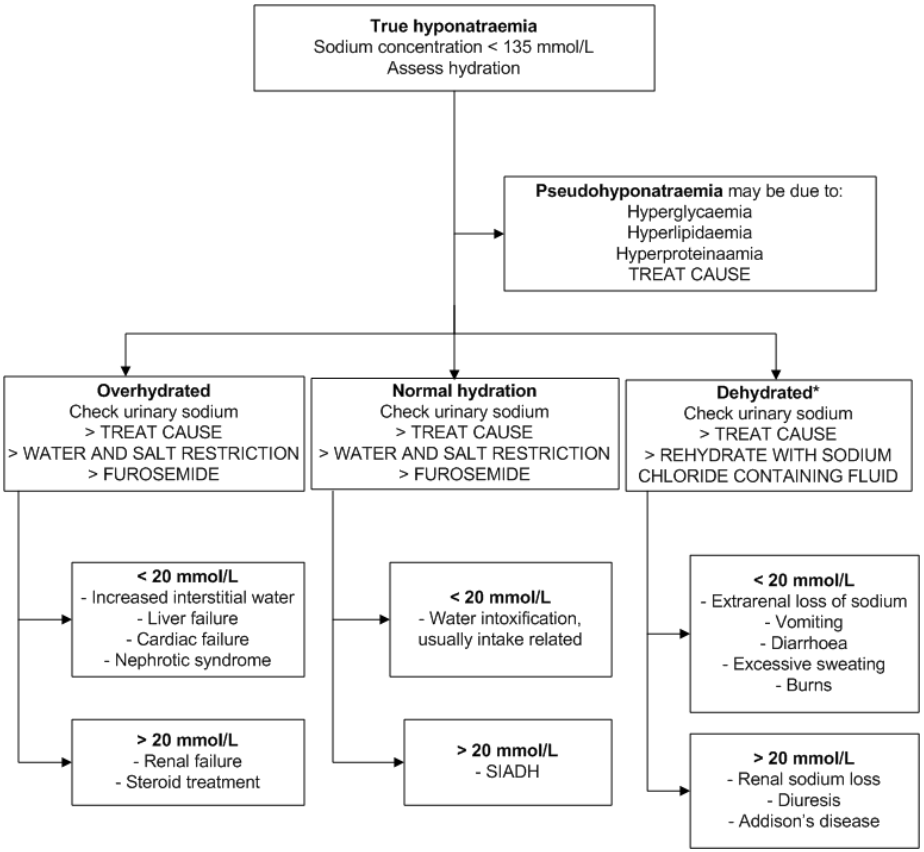
A serum sodium level < 135 mmol/L.

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[VIII]

In the absence of fluid overload:

Consult with a specialist before administering sodium chloride, IV infusion.

- Sodium chloride, IV infusion.

One litre of NaCl infusate	Total Na (mmol/l)	Indication	Fluid	Aim
5% NaCl Expect an increase of 2-3 mmol/L for every 60mL	855	» Sodium level < 120 mmol/L **or** » Severe symptoms(i.e. seizures, obtundation, coma, and respiratory arrest). **or** » Acute hyponatraemia due to water intoxication.	• Hypertonic sodium chloride, 5%, 60 mL as an IV bolus over 15 min. ○ 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 60mL	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[IX]

To calculate the infusion rate, consult a specialist. http://reference.medscape.com/calculator/hyponatraemia-correction-infusate-rate

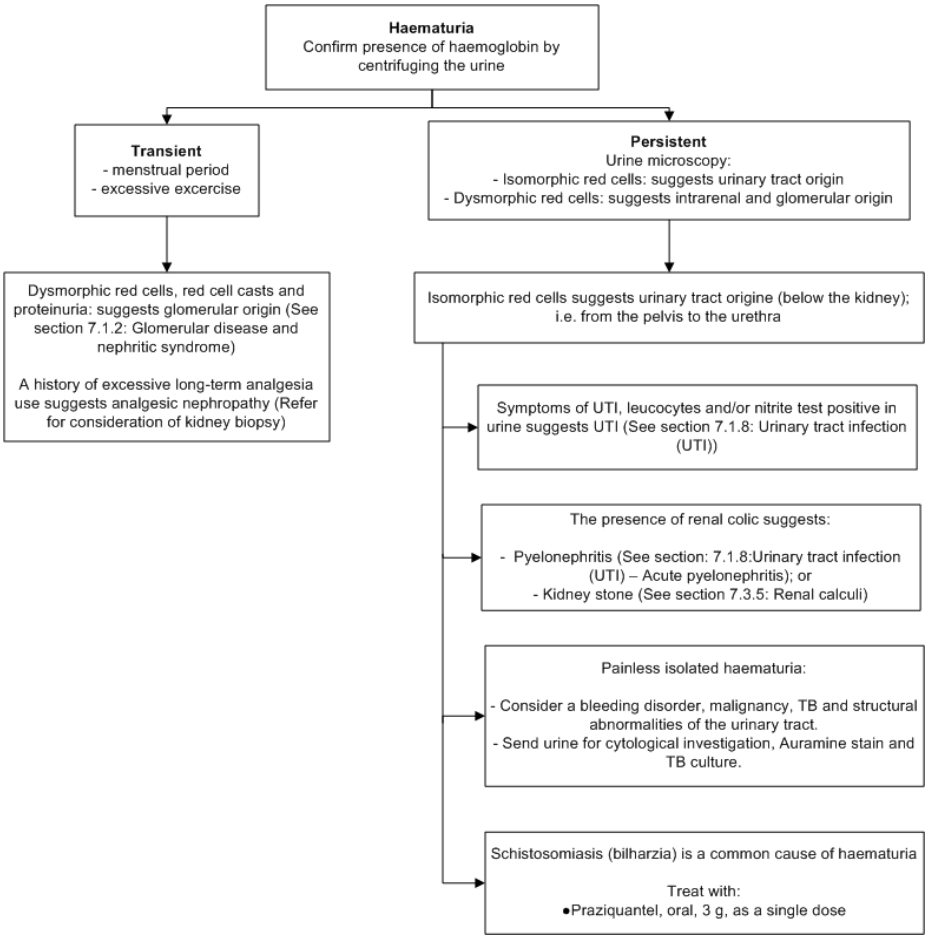
7.3 UROLOGY SECTION

7.3.1 HAEMATURIA

R31.9

DESCRIPTION

Bleeding from the urinary tract, which can be from the kidneys, collecting system, bladder, prostate and urethra.



REFERRAL

Suspected glomerular disease. *LoE:III*[x]

7.3.2 URINARY TRACT INFECTION (UTI)

N39.0

DESCRIPTION

Uncomplicated UTI involves either the lower or upper urinary in a non-pregnant woman with a normal urinary tract. UTIs in other groups of patients are complicated by definition.
Upper UTIs are more serious infections requiring longer and sometimes intravenous antibiotic treatment.

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

In complicated, recurrent or upper UTIs, 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.

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

Uncomplicated community acquired cystitis

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

Complicated community acquired cystitis

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

LoE:III[xi]

For pregnant women:

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

Severe penicillin allergy in 1st trimester:

- Fosfomycin, oral, 3 g as a single dose dissolved in a glass of water.

LoE:I[xii]

Severe penicillin allergy in 2nd and 3rd trimester:

- Nitrofurantoin, oral, 100 mg 12 hourly for 7 days.
  - Avoid near term (38 to 42 weeks) and consider fosfomycin in these cases. *LoE:III*[xiii]

Adjust antibiotics according to urine microscopy, culture and sensitivity results in complicated, recurrent or upper UTIs.

Acute pyelonephritis

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

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.

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
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.

OR

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

2–3 infections/year:

- Ciprofloxacin, oral, 500 mg as single dose for symptomatic infections (self-treatment).

UTI in relation to sexual activity:

- Ciprofloxacin, oral, 500 mg as single dose.

Treatment
Treat according to microscopy, culture and sensitivity.

REFERRAL/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

N41.0/N41.1

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

<u>If there are features of associated urethritis (STI regimen):</u>

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

LoE:III[xiv]

AND

- Azithromycin, oral, 1 g as a single dose.

LoE:I[xv]

<u>If there are **no** features of associated urethritis:</u>

- Ciprofloxacin, oral, 500 mg 12 hourly for 14 days.

LoE:III

<u>Chronic/relapse/persistent infection:</u>

- 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

N40.9

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 a urologist:
Annual follow-up.
For patients presenting with urinary retention, insert a urethral catheter.
Stop medication that may aggravate urinary retention e.g. tricyclics.

MEDICINE TREATMENT

- Alpha blocker, e.g.:
- Tamsulosin, oral, 0.4 mg daily. *LoE:I*[xvi]

7.3.6 OVERACTIVE BLADDER

N39.4

DESCRIPTION

A clinical syndrome consisting of urinary frequency (both daytime and night) and urgency, with or without urgency incontinence,

GENERAL MEASURES

Urine dipstix to exclude a 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

REFERRAL

» For confirmation of diagnosis.
» Complications.
» Not responding to medical therapy.

7.3.7 ERECTILE DYSFUNCTION

N48.4/F52.2

DESCRIPTION

The inability to attain and maintain an erect penis with sufficient rigidity for vaginal penetration.
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
Advise cessation of smoking and excessive alcohol use.

MEDICINE TREATMENT

Treat the underlying condition.

In patients with proven testosterone deficiency:

- Testosterone. Specialist initiated.

See section 8.3: Androgen deficiency.

REFERRAL

» To a urologist or appropriate specialist if surgical intervention is needed, e.g. penile prostheses, vascular surgery and pelvic fractures.

7.3.8 RENAL CALCULI

N20.2

DESCRIPTION

A kidney stone or calculus which has formed in the renal tract, i.e. pelvis, ureters or bladder, as a result of urine which is supersaturated with 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, 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.
- Ibuprofen, oral, 400 mg 8 hourly with meals. *LoE:I*[XVII]

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, 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 SYSTEM

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

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
- hyponatremia
- 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.**

Investigations

08h00 serum cortisol level (or at time of presentation in acute crisis):

- 550 nmol/L: virtually excludes the diagnosis
- < 100 nmol/L: highly suggestive of hypoadrenalism
- 100–550 nmol/L is indeterminate and may require an adrenocorticotropic hormone (ACTH) stimulation test:

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

GENERAL MEASURES

All patients should wear a notification bracelet.
Consider sepsis and investigate for other causes.

MEDICINE TREATMENT

Acute crisis

Before administering hydrocortisone, ensure blood samples are taken for serum cortisol and plasma ACTH, if feasible.

- Hydrocortisone, IV, 200 mg 6 hourly.
  - Change to oral maintenance therapy once stable. *LoE:III*

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*[1]

Monitor glucose levels closely and treat hypoglycaemia if present.

Chronic

As maintenance therapy:

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

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

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[#]

Monitor response to therapy with:

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

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

- Hydrocortisone, IV, 100 mg 6 hourly.

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

REFERRAL

All suspected cases, for full evaluation.

8.3 ANDROGEN DEFICIENCY

E29.1

DESCRIPTION

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

Investigations

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

	Serum testosterone	LH and FSH
Primary testicular failure	Below normal	Above normal
Secondary (hypothalamic/pituitary) hypogonadism	Below normal	Normal or below normal

Note: If the serum total testosterone concentration is borderline low repeat the test before replacement therapy is initiated.

» Prolactin
» Sperm count, if infertility is a consideration.
» Further investigations to determine cause to be undertaken after referral; consult a specialist.

MEDICINE TREATMENT

Screen hypogonadal men for prostate cancer before beginning testosterone replacement. 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.

LoE:III

Monitor patients for prostate cancer during treatment.

8.4 CUSHING SYNDROME

E24.9

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

Screening tests for Cushing syndrome: 24 hour urinary free cortisol.
Low dose overnight dexamethasone (or when unavailable, betamethasone 1 mg equivalent to dexamethasone 1 mg) suppression test:

- Dexamethasone, oral, 1 mg.
  - Administer close to midnight.
  - Measure plasma cortisol at 8 am, after breakfast.
  - In normal people morning cortisol will be suppressed to <50 nmol/L.
  - Refer if levels not suppressed.

LoE:III[III]

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.
In patients with type 2 diabetes mellitus, weight loss if weight exceeds ideal weight.
Correct meal/energy distribution.
Moderate or no alcohol intake.
Encourage smoking cessation.
Increased physical activity, aim for 30 minutes per day 5 times a week.
Education about foot care is essential.

Monitoring

At every visit:

» Inquire about:
  - symptoms of hypoglycaemia, symptoms of microvascular and macrovascular complications
  - changes in medication
  - changes in weight, physical activity, diet, smoking and alcohol
  - mood and symptoms of depression
  - impact of diabetes on occupation, driving
» Examination:
  - blood glucose (finger prick)
  - weight, height
  - blood pressure and cardiovascular examination
  - inspect insulin injection sites, if relevant
  - inspect feet and look for signs of peripheral neuropathy

LoE:III^{IV}

Measure HbA_{1c}:

» 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 HbA_{1c} implies that active clinical management will be implemented if the level is sub-optimal.

LoE:III^{V}

Annually:

» Examination:
  - Examine visual acuity and retinae with an ophthalmoscope or retinal camera
  - Examine the cardiovascular system for signs of macrovascular disease.
  - Examine for peripheral neuropathy.
» Laboratory tests:
  - creatinine (including eGFR)

- spot urine albumin/creatinine ratio (microalbuminuria is defined as 2.5 to 25 mg/mmol in men, and 3.5 to 35 mg/mmol in women).

TARGETS FOR CONTROL

Glycaemic targets for control:

Patient type	Target HbA_{1c}	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:

- Body mass index ≤ 25 $kg/m^{2.}$
- BP ≤ 140/80 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

E11.9

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 HbA_{1c} 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 HbA_{1c} 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.

The use of thiazolidinediones is not advised.

If the combination of two oral agents and basal insulin fails to lower HbA_{1c} 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.
  - 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. *LoE:I[VI]*
  - Dose-adjust in renal impairment as follows:
    - eGFR > 60 mL/min: Normal daily dose (see above).
    - eGFR < 60 mL/min: Half of the daily dose.
    - eGFR < 30 mL/min: Stop metformin.
  - Contra-indicated in:
    - renal impairment i.e. eGFR < 30 mL/min, *LoE:III[VII]*
    - uncontrolled congestive cardiac failure,
    - severe liver disease,
    - patients with significant respiratory compromise, or
    - peri-operative cases.

Sulphonylurea derivatives: glimepiride or glibenclamide.

- Glibenclamide, oral, 2.5 mg daily 30 minutes before breakfast.
  - Titrate dose slowly depending on HbA_{1c} and/or fasting blood glucose levels to 15 mg daily.
  - When ≥7.5 mg per day is needed, divide the total daily dose into 2, with the larger dose in the morning.
  - Avoid in the elderly and patients with renal impairment (i.e. eGFR < 60 ml/min).

OR

- Glimepiride, oral, 1 mg daily.
  - Titrate the dose to a maximum of 4 mg daily. *LoE:III*[VIII]

Oral agents should not be used in type 1 diabetes and used with caution in liver and renal impairment.
Metformin should be dose adjusted in renal impairment.

Monitor serum creatinine and estimated eGFR in patients with kidney disease. Three monthly in patients with renal impairment.

Insulin therapy in type 2 diabetes

Indications for insulin therapy:

» Inability to control blood glucose with oral drugs, i.e. combination/substitution insulin therapy.
» Temporary use for major stress, e.g. surgery, medical illness.
» Severe kidney or liver 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: • Neutral Protamine Hagedorn (NPH) / isophane insulin	8 units, (or 0.3 units per kg body weight), 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: 15 units divided as follows: • 2/3 of total daily dose, i.e. 10 units, 30 minutes before breakfast. • 1/3 of total daily dose, i.e. 5 units, 30 minutes before supper.	4 units weekly. First increment is added to dose before breakfast Second increment is added to dose before supper.	Refer if recurrent hypoglycaemia occurs and targets for control are not met.
Basal bolus insulin therapy	Start with 0.4 to 0.6 units per kg body weight 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[ix]

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

To reduce cardiovascular risk

All patients > 40 years of age:

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

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

Aspirin therapy:

Use in adult Type 1 and Type 2 diabetic patients; only with a history of cardiovascular disease i.e.

- ischaemic heart disease
- peripheral vascular disease
- previous thrombotic stroke

- Aspirin, orally, 150 mg daily.

LoE:I[x]

Renal impairment

If urine albumin:creatinine ratio is > 2.5 mg/mmoL (men) or > 3.5 mg/mmoL (women), add ACE-inhibitor, e.g.:

- Enalapril, oral, 5 mg 12 hourly, increasing to 10 mg 12 hourly depending on blood pressure and albumin: creatinine ratio

See section 7.1.1: Chronic Kidney Disease (CKD). *LoE:I*[xi]

8.5.2 TYPE 1 DIABETES MELLITUS

E10.9

Management includes:

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

Insulin protocols

- Insulin, short acting SC, three times daily, 30 minutes before meals:
  Regular human insulin.
  Onset of action: 30 minutes.
  Peak action: 2–5 hours.
  Duration of action: 5–8 hours.
- Insulin, intermediate acting, SC, once or twice daily, usually at night, not later than 10pm.
  Neutral Protamine Hagedorn (NPH) insulin.

Onset of action: 1–3 hours.
Peak action: 6–12 hours.
Duration of action: 16–24 hours.

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

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

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

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

Adjust dose on an individual basis.

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. It is a practical option for patients who cannot monitor blood glucose frequently.

Insulin delivery devices
In visually impaired patients prefilled syringes should be used.

Home glucose monitoring
Patients on basal/bolus insulin should measure glucose at least twice daily This may be individualised depending on the clinical need of the patient.

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[xii]

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

8.6.1 HYPOGLYCAEMIA

E10.64/E11.65

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.

At home:
Oral sugary drinks or paste, if able to swallow. Initially 15 g of quick-acting oral carbohydrate should be administered and the glucose response checked in 15-20 minutes; the treatment should be repeated if finger-prick glucose fails to increase. If the episode is severe, family members should administer glucagon.

In hospital:

- Dextrose 50%, rapid IV injection, 50 mL.

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

LoE:III[XIII]

Establish a large bore intravenous line and keep open with:

- Dextrose 10%, IV.

If no clinical response, give a second injection of:

- Dextrose 50%, IV, 50 mL.

To prevent recurrent hypoglycaemia, continue infusion with:

- Dextrose 10%, IV infusion, at a rate of ± 1 L 6 hourly.

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

If intravenous glucose cannot be given, for any reason, give:

- Glucagon, IM, 1 mg.
  - Blood glucose will take 10–15 minutes to rise.
  - May cause nausea and vomiting.

If the patient has not regained consciousness after 30 minutes with 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,
» 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

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 the elderly type 2 diabetic and develops over days to weeks.

» Blood glucose usually > 40 mmol/L.
» Blood ketones usually negative to moderately elevated.
» Urine ketones 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 and electrolytes and venous blood gas.
» Look for precipitating causes, e.g. infection and MI.

MEDICINE TREATMENT

Fluids

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

- Sodium chloride 0.9%, IV, 15–20 mL/kg in the first hour.
  - 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 5% in sodium chloride 0.9%, IV.

LoE:III[xiv]

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**:**

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

OR

- Low molecular weight heparin, e.g.:

Enoxaparin, SC, 40 mg daily. *LoE:I*[xv]

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

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

DESCRIPTION

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

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

MEDICINE TREATMENT

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

Pain

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

AND/OR

- Paracetamol, oral, 1 g 4–6 hourly when required to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum dose: 4 g in 24 hours.

If ineffective consider adding:

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

Gastroparesis

- Metoclopramide, oral, 10 mg 8 hourly, 30 minutes before meals.

If ineffective consult a specialist.

8.7.2 DIABETIC KIDNEY DISEASE

N18.9

See section 7.1.1: Chronic Kidney Disease (CKD).

8.7.3 DIABETIC FOOT ULCERS

L97

GENERAL MEASURES

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

Deep (limb-threatening) infection

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

Local wound care

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

MEDICINE TREATMENT

Superficial ulcer with extensive infection

Debridement with removal of all necrotic tissue.

Antibiotic therapy

For polymicrobial infection:

- Topical antibiotics are not indicated.

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

Severe infection

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

Severe penicillin allergy

- Clindamycin, oral, 150 mg 8 hourly.

AND

- Gentamicin, IV, 6 mg/kg daily

REFERRAL

Arterial revascularisation procedures.

8.8 DYSLIPIDAEMIA

E78.9

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

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

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

Patients without established vascular disease, with a risk of MI of greater than 20% in 10 years, and who have not achieved lipid goals within 3 months of dietary management – (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) that lowers LDL by at least 25%, e.g.:
- Simvastatin, oral, 10 mg daily.

OR

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

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

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

REFERRAL

» Patients with 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

E83.50/E21.0

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 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

- Pamidronic acid, IV infusion, 30 mg over 4 hours according to plasma calcium concentration (specialist initiated).
  - Dilute each 15 mg in 125 mL sodium chloride solution 0.9% and

administer over 1 hour.
  - Doses should not be repeated until after 7 days.
  - A response is noted within 48 hours and trough reached in 5–7 days.

LoE:II[xvi]

In patients with granulomatous disease and haematological malignancies:

- Prednisone, oral, 40 mg depending on response, daily.

LoE:III

REFERRAL

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

8.10 HYPOCALCAEMIA

E83.5

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:

- Calcium gluconate 10%, IV, 10 mL given over 15–30 minutes, with ECG monitoring.
  - This may be repeated.

AND/OR

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

LoE:III

For hypoparathyroidism:

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

AND

- Alfacalcidol, oral, 1–3 mcg daily.

Correct magnesium deficiency if present.

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

REFERRAL

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

8.11 HYPOTHYROIDISM

E03.9

DESCRIPTION

Causes

Common causes of primary hypothyroidism are:
» 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 (microgram) 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 >1.2) 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 reference range is trimester-specific.

LoE:II[XVII]

8.12 OSTEOPOROSIS

M81.9

DESCRIPTION

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

GENERAL MEASURES

Prevention

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

MEDICINE TREATMENT

In the 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, oral, 800 units daily.

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*[xviii]

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

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

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

This should be given with:

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

AND

- Vitamin D, oral, 800 units daily.

Hormone replacement therapy

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

REFERRAL
» To establish diagnosis (bone densitometry).
» For initial assessment.
» Initiation and monitoring response to therapy and 18–24 monthly bone mineral density (BMD).
» Fractures suspected to be due to osteoporosis for consideration for alendronate
» Patients not tolerating oral alendronate.

8.13 OSTEOMALACIA/RICKETS
M83.9

DESCRIPTION
A disorder of mineralisation of newly synthesised bone matrix.

REFERRAL
All patients

8.14 PAGET'S DISEASE
M88.9

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

GENERAL MEASURES
Most cases are mild and asymptomatic and no treatment is required. The diagnosis is supported by isolated high alkaline phosphatase and typical CXR 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:
- Ibuprofen, oral, 400 mg 8 hourly with meals.

REFERRAL
All patients.

8.15 PITUITARY DISORDERS

8.15.1 PROLACTINOMA

D35.2

DESCRIPTION

Prolactinoma is the most common functioning pituitary tumour.

Investigations

Serum prolactin, beta-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.

Urgent

» Visual disturbances suggesting compression of optic chiasm.

» Pituitary apoplexy.

8.15.2 ANTERIOR HYPOPITUITARISM

E23.0

DESCRIPTION

Absent or diminished secretion of one or more anterior pituitary hormones due to primary damage of the anterior pituitary gland or secondary to

hypothalamic dysfunction, which may result in hypothyroidism and/or hypoadrenalism and/or hypogonadism or growth retardation in children.

GENERAL MEASURES

Surgery is required for large tumours, pituitary apoplexy, and hormone secreting tumours (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, 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
Replacement therapy
- Desmopression, oral, 0.2–1.2 mg daily.
  - Optimal dose: 0.1–0.2 mg 8 hourly.

LoE:III

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

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

OR
- Desmopressin, SC, 1 mcg every 12 to 24 hours.

LoE:III

REFERRAL
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
C74.9

Description
Catecholamine-secreting tumour of the adrenal medulla.

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

There is marked inter-individual variation in symptoms.
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 patient;
» hypertensive patients with paroxysmal symptoms; and
» patients with:
- a labile BP,
- a family history of a phaeochromocytoma,
- neurofibromatosis, or
- radiologic evidence of an adrenal mass.

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.
  - Dose increase above 8 mg daily to control blood pressure may be required.

LoE:III[xix]

- Calcium channel blockers may be added, e.g.:
- Amlodipine, oral, 5–10 mg daily

Note:
» Patients should not be given diuretic therapy unless pulmonary oedema is present.
» β-blockers must be used with extreme caution in the management of phaechromocytoma.

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 **or** 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
Adrenalectomy.

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

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.

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 $T_{4/3}$

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 T_4 levels normalise.
- Atenolol, oral, 50 mg daily.
  - Titrate according to symptom control up to 100 mg daily.

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.
It is contraindicated during pregnancy and lactation and in active thyroid associated ophthalmopathy, unless corticosteroid cover is given.

Surgery
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.

Patients requiring longer than 18 months of therapy with carbimazole, require specialist input.

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, 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.

- Atenolol, oral, 50 mg daily.
    - Titrate according to symptom control up to 100 mg daily.

8.18.4 THYROIDITIS

E06

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.

- Atenolol, oral, 50 mg daily
  - Titrate according to symptom control up to 100 mg daily.

For painful subacute thyroiditis (De Quervain's):

- NSAIDs, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with meals.

AND

- Prednisone, oral, 40 mg daily. Specialist consultation.

8.18.5 THYROID CRISIS

E05.5

MEDICINE TREATMENT

IV fluids as indicated.

- Carbimazole, oral, 30 mg 6 hourly.
  - After 30 minutes follow with 10 drops of Lugol's iodine in milk and continue 8 hourly.
  - Administer second dose of carbimazole and continue 6 hourly until crisis is controlled.

AND *LoE:III*[xx]

- Atenolol, oral, 50 mg daily
  - Titrate according to symptom control up to 100 mg daily.

LoE:III

If life-threatening:

ADD

- Hydrocortisone, IV, 100 mg 8 hourly.

Treat precipitating illness and infection. ICU admission is desirable.

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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 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. Antibiotics must only be used for 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, such as for vancomycin or 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

T80–88

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, there must be no evidence that the infection was present or incubating at the time of admission. Healthcare associated infections should be considered in persons with extensive healthcare contact such as: residence in a nursing home or other long-term care facility, hospitalization in an acute care hospital for >2 days during the prior 90 days, or attendance at a hospital or hemodialysis 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

T80.2

PERIPHERAL LINE INFECTION:

Common organisms:

» coagulase negative staphylococci particularly *S. epidermis*
» *S. aureus*

The intravascular line should always be removed.
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 that 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.

Microbiologic specimen: peripheral blood culture, blood culture from central catheter prior to removal, and culture of the catheter tip.

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
» candidaemia, where treatment should be continued for 2 weeks after the 1st negative blood culture. *LoE:III[ii]*

Note: For candidaemia and *S aureues* 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**

- Empirically vancomycin, IV, 30 mg/kg as a loading dose. Follow with 20 mg/kg/dose 12 hourly. (See Appendix I for guidance on prescribing and monitoring).
    - Tailor therapy to drug-susceptibility results. *LoE:III[III]*

Candidaemia

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.

Treatment duration should be 2 weeks after 1st negative blood culture:

- Amphotericin B, IV, 0.7 mg/kg daily. *LoE:III[IV]*
    - Ensure adequate hydration to minimise nephrotoxicity. (See Appendix I for preventing, monitoring and management of toxicity). *LoE:III[V]*

Once improved, complete course with:

- Fluconazole, oral, 800 mg daily.

Intolerance to amphotericin B: *LoE:III[VI]*

- Fluconazole, oral, 800 mg daily

Renal failure:

- Fluconazole, oral, dose adjusted according to eGFR. *LoE:III[VII]*

9.1.2 SURGICAL WOUND INFECTIONS

T81

DESCRIPTION

Common organism: *S. aureus.*
Microbiologic specimen: deep wound swab or aspirate of pus, and blood culture.
Antibiotics are not usually necessary.

MEDICINE TREATMENT

Empiric antibiotic therapy
If surrounding cellulitis or systemic sepsis:
Total duration of therapy: 7 days.

Parenteral therapy:

- Cloxacillin, IV, 2 g 6 hourly.

Switch to oral therapy as soon as possible:

- Flucloxacillin, oral, 500 mg 6 hourly.

Severe penicillin allergy:

- Clindamycin, IV, 600 mg 8 hourly.

Switch to oral therapy as soon as possible:

- Clindamycin, oral, 450 mg 8 hourly. *LoE:III[VIII]*

Methicillin (cloxacillin) reistant *S. aureus* (MRSA)

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

If surgery was on female uro-genital tract or open GIT surgery:

- Ceftriaxone, IV, 2 g daily for 7 days.

AND

- Metronidazole, IV, 500 mg 8 hourly for 7 days. *LoE:III*[ix]

9.1.3 HOSPITAL-ACQUIRED PNEUMONIA (HAP)

J13/J15.9

DESCRIPTION

HAP is defined as a lower respiratory tract infection that was not present on admission, occurring >48 hours after admission to hospital. HAP has a high morbidity and mortality and early appropriate antibiotic therapy is essential.

Infection is often due to multi drug resistant organisms particularly in patients with any of the following risk factors:

» Hospitalised > 5 days,
» Hospitalised for > 2 days in the past 3 months.
» Immunocompromised with poor functional status.
» Developed pneumonia after admission to ICU.

Microbiologic specimen: blood culture and sputum/tracheal aspirate bacterial culture. Therapy should be adjusted according to culture result.

MEDICINE TREATMENT

Empiric antibiotic therapy

HAP with no risk factors for MDR infection:

- Ceftriaxone, IV, 2 g daily.

AND

- Amikacin, IV, 15 mg/kg daily.

Severe Penicillin allergy:

- Moxifloxacin, oral/IV, 400 mg daily.

AND

- Amikacin, IV, 15 mg/kg daily.

HAP with risk factors and ventilator associated pneumonia.

Choice will depend on local susceptibility patterns. One or more of the following antibiotics/classes must be available:

- Piperacillin/tazobactam, IV, 4.5 g 8 hourly.

AND

- Amikacin, IV, 15 mg/kg daily.

LoE:III[x]

OR

Instead of piperacillin/tazobactam + amikacin:

- Carbapenem with activity against Pseudomonas, e.g.:
- Imipenem, IV, 1 g 8 hourly (except CNS infections or known epileptics).

LoE:III[xi]

OR

Instead of piperacillin/tazobactam + amikacin **OR** imipenem:

- Meropenem, IV, 2 g 8 hourly (CNS infections or known epileptics).

9.1.4 URINARY TRACT INFECTIONS, CATHETER ASSOCIATED

N39.0

DESCRIPTION

Common organisms:

» resistant aerobic Gram-negative organisms.

Microbiologic specimen: blood culture and MSU/CSU for microscopy and bacterial culture.

In most patients with longterm 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:</u>

- Ciprofloxacin, oral, 500 mg 12 hourly. *LoE:III*[xii]

9.2 ADULT VACCINATION

Vaccine	Indications	Comments
• Influenza vaccine	» Elderly patients > 65 years. » HIV-infected patients. » Patients with chronic pulmonary, cardiac, and renal conditions. » healthcare workers with direct patient contact.	○ Contraindication: egg allergy. ○ Dose: IM, 0.5 mL. Repeat annually.
• Pneumococcal vaccine (23 valent polysaccharide)	» Asplenic patients. » Chronic cerebrospinal fluid (CSF) leak.	○ Contraindication: pregnancy. ○ Dose: IM, 0.5 mL. Booster: after 5 years and at 65 years of age. *LoE:III*[xiii]
• Hepatitis B vaccine*	» High risk groups, e.g. hospital personnel or sexual contacts of infected patients. » Sexual assault.	○ Dose: IM, 1 mL immediately then 1 mL after 1 month and 1 mL 6 months after 1st dose . ○ Administer deep IM in deltoid muscle.
• Tetanus toxoid vaccine	Booster when there is a high risk for tetanus e.g. contaminated wound or pregnant women to prevent neonatal tetanus. (See trauma section).	○ Dose: IM, 40 iu (0.5 mL).

* Not to be given to patients who have already been immunised.

9.2.1 RABIES VACCINATION

Z24.2

For prevention of disease in patient exposed to a suspected rabid animal, it is important to estimate risk of rabies first by assessment of the following:

» type of contact (higher risk for penetrating bites or scratches),
» incidence of rabies in the animal's district of origin,
» higher risk with abnormal animal behaviour,
» species of animal involved.
  > High risk: domestic dog, cat, cattle, black backed jackal, bat eared fox, mongoose species, amongst others.
  > Higher risk: if animal not vaccinated.
» when the biting animal cannot be found, or the brain is not available for laboratory examination, it should be assumed that the animal was infected

Note: If animal is still well with no symptoms ≥ 10 days after exposure, or if the animal's brain shows no rabies, post-exposure prophylaxis is not needed or can be discontinued.

Patient not previously immunised

Active immunisation with human diploid cell vaccine:

- Rabies inactivated whole virus vaccine, IM.
  - Administer 1 dose on 0, 3, 7 and14 days post exposure, according to the standard or essential schedule.
  - If the patient is immunocompromised: administer 5th dose on day 28.
  - Administer vaccine by deep IM injection in the deltoid region and not the thigh or buttock.

Caution: Anaphylaxis. *LoE:III*[xiv]

If patient presents after 48 hours, administer double the initial dose on day 0.

AND

Passive immunisation, for temporary prophylaxis with human rabies immunoglobulin (HRIG):

- HRIG, 20 units/kg on day 0 or within 7 days after giving the first active vaccine dose.
  - Infiltrate around the wound with the largest proportion of the dose.
  - Administer the rest of the dose IM.

It is recommended that HRIG be given simultaneously with the first vaccine dose (day 0) but into a different injection site. HRIG should not be given >7 days after exposure or in patients previously immunised.

Patient previously immunised

- Rabies inactivated whole virus vaccine, IM.
  - Administer 1 dose on day 0 and day 3.

In these cases HRIG (see above) is not given.

Caution: Anaphylaxis.

If patient presents after 48 hours, double initial dose on day zero.

Risk Category	Type of exposure	Action
1	» Touching or feeding animal. » Licking intact skin.	None if reliable history.
2	» Nibbling uncovered skin. » Superficial scratch without bleeding. » Licking broken skin.	Wound treatment. Give rabies vaccine. Do not give HRIG, except in HIV infected people. Stop vaccination if laboratory tests of animal are negative for rabies or animal remains well after 10 days observation.
3	» Bites or scratches penetrating skin and drawing blood.	Wound treatment. Give rabies vaccine. Give HRIG.

	» Licking of mucous membranes.	Give tetanus toxoid vaccine and antibiotic. Stop vaccination if laboratory tests of animal are negative for rabies or animal remains well after 10 days observation.

Rabies Vaccine
Must be given for category 2 and 3 bites.
Administer the vaccine on days 0, 3, 7 and 14.
If the patient is immunocompromised: administer 5th dose on day 28.
Ideally, the vaccine should be given as soon as possible after exposure, but should still be given if patient presents some time after the exposure.
If vaccine administration is delayed > 48 hours, give an initial double dose.
Administer rabies vaccine IM, never in the buttock. In adults, give the vaccine into the deltoid muscle.

HRIG
Must be given for category 3 bites **only**.
However, in the HIV-infected administer HRIG for category 2 bites.
Always give the vaccine first.
Immunoglobulin must be given as soon as possible after exposure, but may be administered up to 7 days after the first vaccine is given.
Do not give HRIG if the patient has previously received pre- or post-exposure prophylaxis.

- HRIG, 20 units/kg.
  - Infiltrate around wound with the largest proportion of the dose.
  - Administer remaining immunoglobulin into deltoid muscle opposite to vaccine administration site.
  - If multiple wounds, dilute in sodium chloride 0.9% to 2–3 times so that all wounds are infiltrated.
  - Do not exceed maximum dose as antibody production to the vaccine is inhibited.
  - If unavailable, do not delay active immunisation.

9.3 BRUCELLOSIS

A23.1
*This is a notifiable disease.

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. *LoE:III*[xv]
  (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 HAEMORRHAGIC FEVER SYNDROME

A98.0

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 (see above) 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.

9.5 HYDATID DISEASE

B67

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.

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), for 3–6 months according to response on imaging. *LoE:III*[xvi]
    - Monitor liver function tests and full blood counts monthly.

With medical therapy as above, cure is achieved in about half, improvement in about a quarter and no response in about a quarter of cases.
Definitive treatment with surgery or PAIR (percutaneous aspiration injection of helminthicidal agent and re-aspiration) is preferred for all accessible lesions.

<u>Before PAIR or surgery:</u>

- Albendazole, oral, 15 mg/kg/day or 200 mg 12 hourly, up to maximum of 400 mg per day with a fatty meal (e.g. a glass of full cream milk), for 14 to 28 days.

- Follow with 28 days after surgery.

LoE:I[xvii]

REFERRAL

All cases to a centre with experience in surgery and PAIR.

9.6 MALARIA

9.6.1 MALARIA, NON-SEVERE

B54

*This is a notifiable disease.

DESCRIPTION

The most important element in the diagnosis of malaria is a high index of suspicion. Test any person resident in, or returning from, a malaria area **and** who presents with fever (usually within 3 months of exposure). Malaria may also occur in people bitten by mosquitoes travelling from endemic areas in aeroplanes or vehicles, or from blood transfusion. The progression to severe falciparum malaria may be rapid, therefore early diagnosis and effective treatment is crucial.

Pregnant women and young children up to 5 years of age are at high risk of developing severe malaria.

Clinical features include:

- » severe headache,
- » fever above 38°C,
- » muscle and joint pains,
- » shivering attacks,
- » nausea and vomiting,
- » flu-like symptoms.

Progression to severe malaria may occur – see section 9.6.2: Malaria, severe.

Diagnosis

- » Microscopic examination of thick and thin blood smears. Thick films are more sensitive than thin films in the detection of malaria parasites.
- » One negative malaria test does not exclude the diagnosis of malaria. Request a 2nd test.
- » Where rapid diagnostic tests are available, e.g. plasma reagent dipsticks, these can be used to diagnose malaria within 10–15 minutes. Rapid tests may remain positive for up to 1 month after successful treatment.

Note: If neither microscopy nor rapid tests are available diagnosis should be made on the basis of clinical symptoms.

GENERAL MEASURES

Provide supportive and symptomatic relief.
Monitor for complications.

Beware of over-hydration.
All patients with *P. falciparum* malaria should be carefully observed for the first 24 hours.

MEDICINE TREATMENT

Vomiting oral treatment is one of the commonest reasons for treatment failure. If vomiting is a presenting symptom, the patient has severe malaria and needs IV therapy (see 9.6.2). Give all first doses of oral medicines under supervision and observe patients for at least an hour. Repeat the oral treatment or give IV treatment if the patient vomits within the first hour.

Malaria should be treated at primary health care level in areas of South Africa where malaria occurs seasonally. In other areas, patients should be referred to a hosptal for treatment.

Uncomplicated *P. falciparum* malaria in South Africa
(If unsure of species, treat as for *P. falciparum* malaria)

- 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.
  - Follow with second dose 8 hours later.
  - Then 12 hourly for another 2 days. (Total number of doses in 3 days = 6; i.e. 24 tablets).

REFERRAL

» Patients not responding to oral treatment within 48 hours.
» Patients with *P. vivax* and *P. ovale* malaria.

9.6.2 MALARIA, SEVERE

B50.0
*This is a notifiable disease.

See section 9.6.1: Malaria, Non-severe for uncomplicated malaria and primary care book for non-falciparum malaria.

DESCRIPTION

P. falciparum malaria with one or more of the following features:

» impaired consciousness
» convulsions
» vomiting
» severe anaemia (Hb < 6 g/dL)
» haemoglobinuria
» acidosis (plasma bicarb <15 mmol/L)
» renal dysfunction
» 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[XVIII]

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.

9.7 TETANUS

A35

*This is a notifiable disease.

GENERAL MEASURES

Maintain 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:

- 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.
  - Doses as high as 50–100 mg 2 hourly are sometimes required.

LoE:I[xix]

Muscle relaxants should be used sparingly and may exacerbate autonomic instability.

Antibiotic treatment:

- Benzylpenicillin (penicillin G), IV, 5 MU 6 hourly for 10 days.

OR

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

For passive immunisation:

- Tetanus immunoglobulin, IM, 3 000 units as a single dose.

For active immunisation of all patients: (as clinical tetanus does not always confer immunity)

- 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 fever:

- Paracetamol, oral, 1 g 4–6 hourly when required to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum dose: 4 g in 24 hours.

For shock, dehydration, maintenance of hydration:

- IV fluids.

For prophylaxis for deep vein thrombosis:

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

OR

- Enoxaparin, SC, 40 mg daily.

LoE:I[xx]

For pain:

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

REFERRAL

All cases to a facility with resources for artificial ventilation.

9.8 TICK BITE FEVER

A79.9

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, i.e. 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.

MEDICINE TREATMENT

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

In pregnancy:

- Azithromycin, oral, 500 mg 12 hourly for 3 days.
  - In severe cases, initiate therapy with 1–2 days of doxycycline.

LoE:III[xxi]

For the rare patient unable to take oral therapy:

Total duration of therapy: 7 days.

- Ciprofloxacin, IV, 400 mg 8 hourly.

LoE:III[xxii]

Note: This is inferior to doxycycline, which should be commenced as soon as possible.

9.9 ENTERIC FEVER (TYPHOID)

A01.0

*(Typhoid fever) This is a notifiable disease.

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.

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*[xxiii]

Switch to oral therapy as soon as possible and 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:

- Ciprofloxacin, oral, 500 mg 12 hourly for 6 weeks (if sensitive to ciprofloxacin).

REFERRAL

Surgical consultation for complications such as intestinal haemorrhage, threatening bowel perforation or localisation with metastatic infection with or without abscess formation, and peritonitis.

9.10 VARICELLA (CHICKENPOX), COMPLICATED

B01

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 aciclovir, oral, 800 mg five times daily.

For patients who are severely immunologically compromised and are not immune:

- Varicella-zoster immunoglobulin (VZIG), IM, 125 units/10 kg.
  - Maximum dose: 625 units.
  - Administer within 96 hours after significant exposure.

9.11 ZOSTER (SHINGLES)

B01.8

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.

- Aciclovir, oral, 800 mg five times daily for 7 days (4 hourly missing the middle of the night dose).

For zoster with secondary dissemination or neurological involvement:

- 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.

Eye involvement:
ADD

- Aciclovir opthalmic ointment 3%, applied into lower conjunctival sac, five

times daily.

Secondary infection

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 to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum dose: 4g in 24 hours.

AND/OR

If pain is not adequately controlled:

- Tramadol, oral, 50 mg 6 hourly.
  - If response not adequate, increase dose to 100 mg 6 hourly.

See section 12.13: Pain, chronic.

Post-herpetic neuralgia:

Initiate treatment with adjuvant therapy early.

- Amitriptyline, oral, 25 mg at night.
  - Titrate as necessary to a maximum of 75 mg.

See section 12.13: Pain, Chronic.

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.

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CHAPTER 10
HIV AND AIDS

Consult the most recent HIV Guidelines from the National Department of Health.

10.1 ANTIRETROVIRAL THERAPY

B20

Combination antiretroviral therapy (ART) consists of ≥ 3 antiretroviral medicines that are capable of suppressing HIV replication. The current recommended ART regimen contains 2 nucleoside reverse transcriptase inhibitors (NRTIs) together with either a non-nucleoside reverse transcriptase inhibitor (NNRTIs) or a protease inhibitor.
High levels of adherence are essential for long-term success with ART.

ELIGIBILITY FOR ART

Eligibility to start ART:
All patients with CD4 count < 500 cells/mm^3

LoE: III^{I}

OR

All patients with WHO stage 3 or 4

OR

HIV/hepatitis B co-infection

LoE: III^{II}

Immediate initiation:
All pregnant and breastfeeding women, irrespective of CD4 count.

LoE:III^{III}

Fast tracking (within 7 days):
Patients with CD4 < 200 cells/ mm^3.

OR

LoE:III^{IV}

Patients with WHO stage 4, even if CD4 is not yet available.

Timing of ART initiation:

» ART should be started as soon as the patient is ready, and generally within 2 weeks of CD4 count result availability. However, with some opportunistic diseases early ART initiation can cause harm by increasing the risk of the immune reconstitution inflammatory syndrome (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: ART initiation may be delayed up to 8 weeks after starting TB treatment.

LoE:I^V

» In patients with TB meningitis (irrespective of CD4 count), defer ART until 8 weeks after initiating TB treatment.

LoE:I^{VI}

» 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^{VII}

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/alcohol is an impediment to adherence and, if possible, should be addressed prior to initiating ART.

ART REGIMENS

1ST LINE ART	
Treatment-naïve patients	Tenofovir (TDF) + Emtricitabine (FTC) + Efavirenz (EFV)
Contraindications to EFV » psychiatric co-morbidity » intolerance to EFV (neuro-psychiatric toxicity, shift workers)	TDF + FTC + Nevirapine (NVP)* *Avoid NVP in women with a CD4 count > 250 cells/mm^3 and men with a CD4 count > 400 cells/mm^3 at ART initiation due to increased risk of rash-associated hepatitis.
Contraindications to EFV + NVP	Start protease inhibitor based regimen: TDF + FTC + Lopinavir/ritonavir (LPV/r)
Contraindication to TDF » eGFR <50 mL/min. » Use of additional nephrotoxic drug e.g. aminoglycoside.	Abacavir (ABC) + lamivudine (3TC) + EFV or (NVP) *LoE:I^{VIII}*
Contraindication to TDF and ABC intolerance » eGFR < 50 mL/min. » Use of additional nephrotoxic drug e.g. aminoglycoside. » Hypersensitivity.	Zidovudine (AZT) + 3TC + EFV or (NVP)
Note: In the unlikely scenario where there is intolerance/contraindication to all currently available NRTIs (TDF, AZT and ABC), an alternative dual-therapy regimen comprising a combination of an NNRTI (EFV) and PI (LPV/r) may be used. Consult a specialist.	

2ND LINE ART	
Management of virological failure **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 2nd line regimen.	<u>If plasma HIV RNA (VL) >1000 copies/mL:</u> » Assess adherence, tolerability, medicine interactions & psychosocial factors. » Repeat VL test 2 months later. <u>If plasma VL confirmed >1000 copies/mL, and adherence issues addressed:</u> » Change regimen to 2nd line therapy.
Failing a TDF-based 1st line regimen » Patients with anaemia and renal impairment, switch to ABC. » Check HBsAg and if positive, continue TDF with the new regimen.	AZT + 3TC + Lopinavir/Ritonavir (LPV/r) (**PLUS** TDF, if HBsAg positive).
Failing a d4T/AZT-based 1st line regimen	TDF + FTC and LPV/r
Dyslipidaemia or diarrhoea associated with LPV/r	Switch LPV/r to atazanavir (ATV/r)

3RD LINE ART	
Failing any 2nd line regimen	Refer to a specialist. Resistance to protease inhibitors 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.

Assessment of renal function in HIV-infected patients *LoE:III*[ix]

It is important to monitor the eGFR in patients on TDF.

As far as possible, avoid combining potentially nephrotoxic medicines such as TDF, aminoglycosides, amphotericin B and NSAIDs. *LoE:III*[x]

More frequent monitoring may be needed in malnourished patients as the eGFR may be overestimated in this group.

Currently available ARV FDC preparations on contract circular: *LoE:III*

- ABC 600 mg + 3TC 300 mg
- FTC 200 mg + TDF 300 mg
- AZT 300 mg + 3TC 150 mg
- TDF 300 mg + FTC 200 mg + EFV 600 mg *LoE:III*[xi]

DOSING OF ART

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	» Renal failure (weeks to months). » Reduced bone mineral density (months). » 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 <10mL/min: 300 mg daily	» Anaemia, neutropaenia (weeks to months). » Gastro-intestinal upset. » Headache. » Myopathy. » Hyperlactataemia / steatohepatitis (medium risk - months). » Lipoatrophy (months).
Lamivudine (3TC)	NRTI	300 mg daily (or 150 mg 12 hourly)	CrCl 10-50mL/min: 150 mg daily CrCl <10mL/min: 50 mg daily	» Anaemia due to pure red cell aplasia (very rare). » Hyperlactataemia / steatohepatitis (very low risk - months).
Emtricitabine (FTC)	NRTI	200 mg daily	CrCl 30-50 mL/min: 200 mg every 2 days CrCl 15-29mL/min: 200 mg every 3 days CrCl <15mL/min: 200 mg every 4 days	» Palmar hyperpigmentation. » Hyperlactataemia / steatohepatitis (very low risk - months).
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). » Rash (1 to 6 weeks). » Hepatitis (weeks to months) » Gynaecomastia.
Lopinavir/ ritonavir (LPV/r)	Boosted PI	400/100 mg 12hourly **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 as there is no associated hepatitis). » Dyslipidaemia (low risk). » Hepatitis (1 to 6 weeks). » Renal stones (not common).

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[xii]

Important drug interactions to consider in patients treated for TB with rifampicin regimens:

» Efavirenz is not affected and no dose adjustment is needed.

» Nevirapine concentrations are modestly reduced. If efavirenz is contra-indicated nevirapine can be used, but the lead-in dose of nevirapine must be omitted.

LoE:III[xiii]

» Lopinavir concentrations are markedly reduced.
The dose should be doubled slowly (increase to 3 tablets 12 hourly after a week, then 4 tablets 12 hourly after another week, with monthly ALT monitoring).

» In patients on atazanavir or darunavir requiring treatment for TB, rifampicin is contraindicated. Instead use:
- Rifabutin, oral, 150 mg 3 times a week.

LoE:III[xiv]

MONITORING FOR SAFETY

At HIV Diagnosis	» Confirm HIV positive result with antibody test. » WHO staging. » Check CD4 count. – CD4 <100 cells/mm^3: Check cryptococcus 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 TB using the WHO screening questionnaire (any one of cough, fever, night sweats, or weight loss).

Prior to initiating ART	» Check creatinine if requires TDF (avoid TDF if eGFR/CrCl <50 ml/min). » Check FBC if requires AZT (avoid AZT if Hb <8 g/dl). » Check ALT if requires NVP (avoid NVP if underlying liver disease or HBsAg positive). » Check HBsAg (If positive, TDF and FTC should form part of the regimen). » Urine dipstix for glycosuria and proteinuria.
On ART	» VL at 6 and 12 months after initiating ART and every 12 months thereafter. » CD4 at 12 months after initiating ART*. » Creatinine at 3, 6 and 12 months after initiation, and every 12 months thereafter if on TDF. » Urine dipstix at 3, 6 and 12 months after initiation, and every 12 months thereafter if on TDF. » FBC at 3 and 6 months after initiating AZT, then every 12 months. » ALT if rash or features of hepatitis develops on NVP. » 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 repeated as cotrimoxazole may need to be commenced/recommenced.

LoE:III[xv]

10.1.1 HIV IN KIDNEY DISEASE

B20/ N18

DESCRIPTION

Various forms of kidney disorders are described among patients who are HIV-infected.

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.

Screening for kidney disease should be done in all patients at time of HIV diagnosis.

Patients at high risk or susceptible for HIV renal disease includes:

» CD4 count < 200 cells/mm^3.
» History 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 dipstix for haematuria and proteinuria.
  – Serum creatinine and eGFR.

» If there is no evidence of kidney disease at the initial evaluation, and the patient is receiving TDF, screening should be repeated at months 3, 6 and 12 after initiation, and then annually.
» For patients receiving TDF, monitor creatinine on initiation and at months 3, 6, 12 and then annually.

Dose adjustment of ART in renal impairment: Refer to table: Dosing of ART for renal adjusted doses.

10.1.2 MANAGEMENT OF SELECTED ANTIRETROVIRAL ADVERSE DRUG REACTIONS

Dyslipidaemia
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 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 CVS 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 section 3.1: 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.

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 below 8.0 g/dL), or
» the neutrophil count is below 0.75×10^9/L.

Lamivudine can cause a 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.

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. Other drugs, notably co-trimoxazole, can also cause cutaneous hypersensitivity.

If any of the following features are present or develop 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.

ABC can cause a rash as part of a systemic hypersensitivity reaction, which is confined to people who are HLA-B*5701 positive.

LoE:III[xvi]

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 as follows:
stavudine > zidovudine > lamivudine or tenofovir or emtricitabine

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 e.g. TDF and ABC.
Monitor serial lactate measurements (initially weekly) until the lactate has returned to within the normal range.
Note: The resolution of hyperlactataemia may take 3 months or more.

Patients with lactate levels > 5 mmol/L:
Stop the NRTIs.
If the patient is on a 1st line regimen, continue the EFV or NVP and add LPV/r.
If the patient is on the 2nd line regimen, continue with LPV/r alone.

Note: Many patients will remain with a suppressed viral load when treated with a boosted protease inhibitor only.
» If severe acidosis was present (serum bicarbonate < 15 mmol/L) NRTIs should probably not be used again.
» In cases where acidosis was absent or not severe, TDF and 3TC (or FTC) or ABC could be introduced once symptoms have resolved with serial lactate monitoring as above. If the patient is on a first line regimen then the LPV/r can be stopped when the TDF and 3TC have been added and is tolerated.

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
All currently available antiretrovirals are potentially hepatotoxic. The NNRTIs, especially nevirapine, have 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 (glutaryl

transferase) 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 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 co-trimoxazole. Co-trimoxazole, co-amoxiclav 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 (especially stavudine and didanosine).
  - 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 the patient is on an NNRTI-based regimen, stop the NNRTI first and the NRTIs after 7 days unless the hepatitis is severe, in which case stop all medicines at once. If the patient is on a PI-based regimen, stop all medicines at once. Monitor the ALT twice weekly and restart ART once the ALT has settled to < 2.5 x ULN and the bilirubin has normalised.

Restart and substitute ART as follows:
» If the hepatitis occurred on nevirapine, substitute with efavirenz.
» If the hepatitis occurred on efavirenz, substitute with a boosted PI (efavirenz may be rechallenged in cases of mild hepatitis).
» If hepatitis occurred on PI, substitute with an alternative PI.
» NRTI fatty liver – safer NRTI combination (TDF, ABC, 3TC, FTC).

Monitor the ALT twice weekly for the first 2 weeks and then once weekly until 4 weeks.

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 (if on a NNRTI-based regimen the NRTIs should be continued for a week), co-trimoxazole 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.

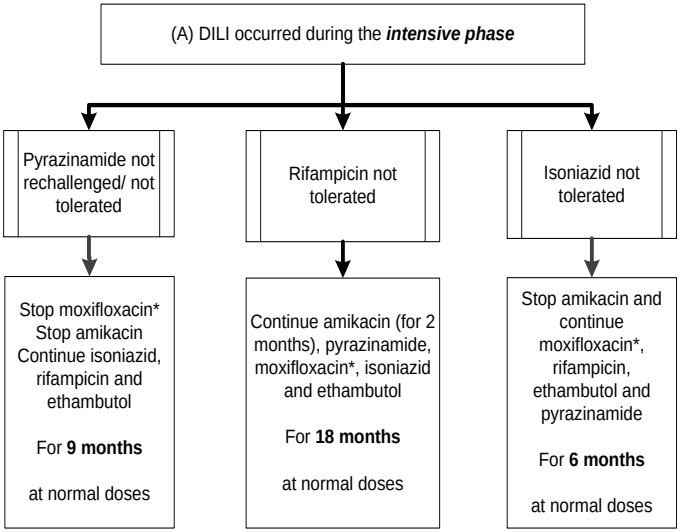
Management:
» Stop TB therapy and initiate background TB therapy and continue throughout rechallenge:
  - Amikacin, IV, 15 mg/kg daily.
  - Moxifloxacin, oral, 400 mg daily or levofloxacin 750 - 1000 mg daily.
  - Ethambutol, oral, 800 - 1200 mg daily.

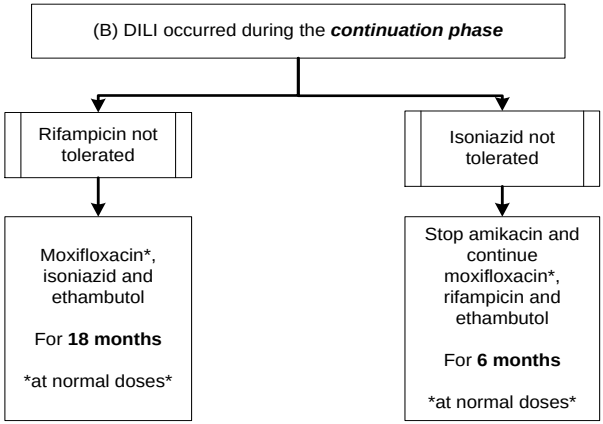
» Stop co-trimoxazole prophylaxis and do not rechallenge.
» Stop ART as described above.
» Repeat ALT and bilirubin in 2 days (inpatient) or 7 days (outpatient).
» When ALT is <100 IU/L and total bilirubin is normal, start TB medicine rechallenge as follows:

Day 1:	• Rifampicin, oral 600 mg daily. ○ 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:	» 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:
	  ○ If DILI developed on NVP, then rechallenge with EFV after TB medicine rechallenge
	  ○ If DILI developed on EFV, then start a PI-based regimen with lopinavir/ritonavir (with dose adjustment if receiving rifampicin).
	  ○ Monitor ALT every 2 weeks for 2 months after ART rechallenge.

Duration of therapy following successful rechallenge





*or levofloxacin

LoE:III[XVII]

10.1.3 IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME (IRIS)

D89.3

DESCRIPTION

IRIS occurs when improving immune function unmasks a previously occult opportunistic disease, which has an unusual inflammatory presentation (this is called "unmasking IRIS"), or causes paradoxical deterioration of an existing opportunistic disease (this is called "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. About a third of patients starting ART while on treatment for tuberculosis will experience paradoxical IRIS, presenting as recurrence of their TB symptoms/signs, or worsening, or new manifestations. The commonest presentation is with enlarging lymph nodes, often with extensive caseous necrosis. In addition, 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

For pain and fever:

- Paracetamol, oral, 1 g 4–6 hourly when required to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum dose: 4 g in 24 hours.

OR

- NSAIDs, e.g.:
  - Ibuprofen, oral, 400 mg 8 hourly with meals.

For severe IRIS manifestations (e.g. compression of major structures by enlarging lymph nodes, expanding CNS tuberculomata, worsening meningitis):

- Prednisone, oral, 1.5 mg/kg daily for 2 weeks.
  - Then 0.75 mg/kg daily for 2 weeks.

Note: Steroids should not be used in patients with Kaposi sarcoma.

10.2 OPPORTUNISTIC DISEASES

10.2.1 ISONIAZID PREVENTIVE THERAPY (IPT)

Z79.2

TB occurs more commonly in HIV-infected patients. IPT 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
» HIV-infected, Tuberculin Skin Test (TST) negative, Pre-ART
» Liver Disease
» Peripheral neuropathy
» Alcohol abusers
» Previous MDR- or XDR-TB

Note:
» TB must be excluded prior to initiating IPT by screening for the following:
  - Cough (any duration)
  - Fever
  - Weight loss
  - Night sweats
» IPT should not be initiated in patients if any of the above is present. These patients require further investigation for active TB.

Duration of IPT

	TST POSITIVE	TST NEGATIVE	TST NOT AVAILABLE
Pre-ART	**36 months** If patient becomes eligible for ART while on IPT, initiate ART and continue IPT.	**not indicated**	**6 months**
On ART	**36 months**	**12 months**	**12 months**

MEDICINE TREATMENT

- Isoniazid, oral 5 mg/kg/day (maximum 300 mg daily).

AND

- Pyridoxine, oral 25 mg daily.

LoE:I[xviii]

10.2.2 OPPURTUNISTIC INFECTION PROPHYLAXIS, WITH COTRIMOXAZOLE

Z29.2

DESCRIPTION

Primary prophylaxis reduces the probability of developing many infections, e.g.:

» Pneumocystis pneumonia
» bacteraemia
» toxoplasmosis
» isosporiasis
» bacterial pneumonia

Indications for primary prophylaxis:

» WHO Clinical stage II, III or IV.
» CD4 count < 200 cells/mm^3.

MEDICINE TREATMENT

Prophylaxis

- Cotrimoxazole, oral, 160/800 daily. *LoE:I*[xix]

Note: Once the CD4 > 200 cells/mm^3 for longer than 6 months, 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 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: Fluconazole prophylaxis for candidiasis is discouraged.

10.2.4 CRYPTOCOCCOSIS

10.2.4.1 ASYMPTOMATIC CRYPTOCOCCOSIS, CRAG POSITIVE

B45.1

DESCRIPTION

All ART-naïve patients with CD4 < 100 cells/mm^3 should have cryptococcal antigen (CrAg) test done on serum (unless they had a diagnosis of cryptococcal infection). The treatment of patients who are **CrAg positive and asymptomatic of meningitis** is outlined below.

LoE:III[xx]

MEDICINE TREATMENT

Induction phase

- Fluconazole, oral 800 mg daily for 14 days

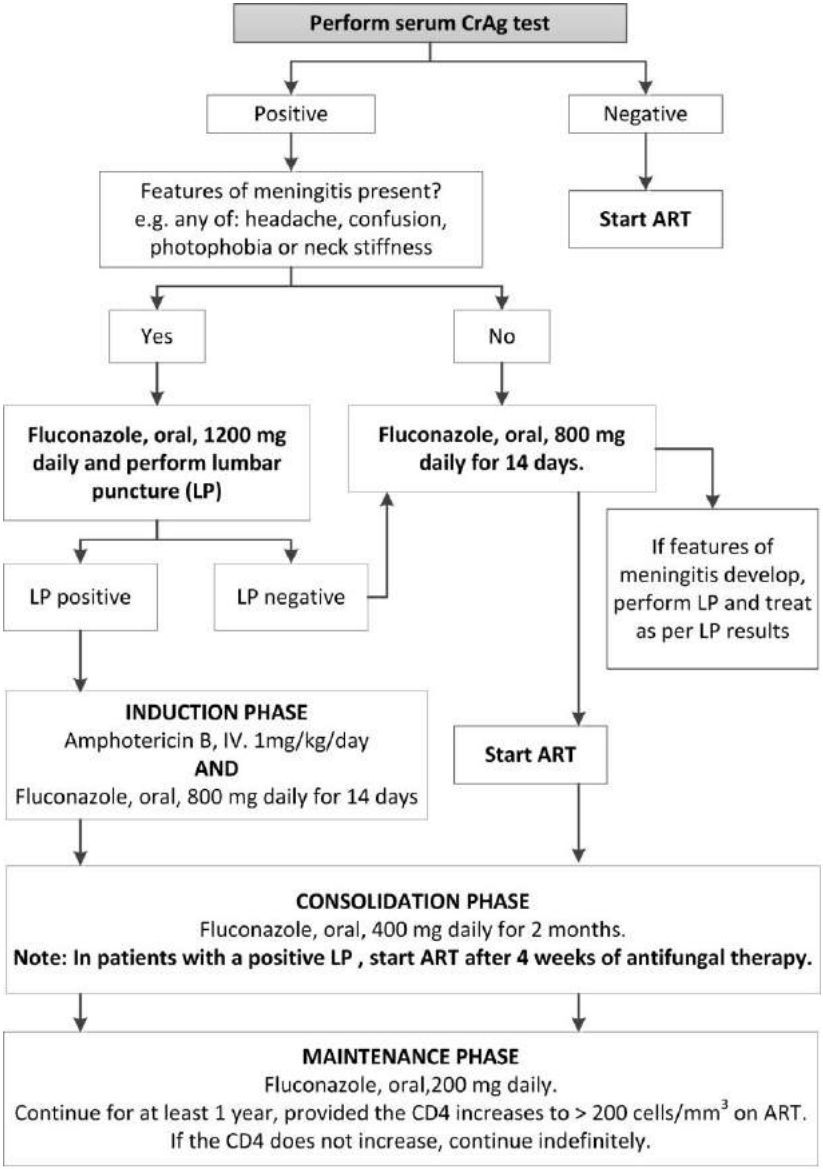
Consolidation phase

Follow with:

- Fluconazole, oral, 400 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*[xxi]
- Commence ART after completion of the induction phase i.e. at 2 weeks. *LoE:III*[xxii]



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

B45

DESCRIPTION

This refers to patients who are CrAg positive with non-meningeal cryptococcal disease. Any anatomical site may be involved, but the lungs are the commonest site.

MEDICINE TREATMENT

Induction phase

- Fluconazole, oral 800 mg daily.

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, 400 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[xxiii]

10.2.4.3. CRYPTOCOCCAL MENINGITIS

B45

DESCRIPTION

Cryptococcal meningitis is the commonest manifestation of disseminated cryptococcosis in patients with advanced HIV. Severe headache is common due to raised intracranial pressure.

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 800 mg daily.

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, 400 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[xxiv]

- Commence ART 4–6 weeks after starting antifungal therapy.

LoE:III[xxv]

REFERRAL

Specialist or tertiary

» 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

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)

B25

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,
» git ulceration,
» 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 can 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.
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 untilCD4 count rises to > 100 cells/mm^3 on ART, if available. Specialist initiated.

OR *LoE:III*[xxvi]

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 ISOSPORIASIS

A07.3

DESCRIPTION

Diarrhoea due to *Isospora belli*. Disease lasting > 4 weeks is AIDS-defining (WHO clinical stage 4).

GENERAL MEASURES

Rehydration with oral rehydration solution (ORS).

MEDICINE TREATMENT

- Cotrimoxazole 80/400 mg, oral, 4 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 80/400, oral, 2 tablets 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[xxvii]

- 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

All patients:

- Cotrimoxazole 80/400 mg, oral, 6 hourly for 21 days.
  - < 60 kg three tablets
  - > 60 kg four tablets

Monitor FBC and potassium when on high dose therapy.

OR

If vomiting:

- Cotrimoxazole, IV, 6 hourly.
  - < 60 kg 240/1200 mg
  - > 60 kg 320/ 1600 mg

For hypoxic patients:

- Oxygen by face mask or CPAP as necessary.

AND

- Prednisone, oral, 80 mg daily for 5 days, then taper over 14 days. (Refer to page xxvii 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 80/400 mg, oral, 2 tablets daily.

Alternatively, in case of intolerance:

- 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-lesional oedema.

MEDICINE TREATMENT

- Cotrimoxazole 80/400, oral, 4 tablets 12 hourly for 28 days, followed by 2 tablets 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 80/400 mg, oral, 2 tablets daily.

See cotrimoxazole desensitisation: Page 10.23.

REFERRAL/CONSULTATION

Specialist or tertiary
Intolerance to cotrimoxazole.
Note: Attempt desensitisation first.

10.3 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 intestines).
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 and cotrimoxazole prophylaxis 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 such as:
  - 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.

10.4 POST-EXPOSURE PROPHYLAXIS

Z29.2

National HIV Health Care Worker Hotline: 0800 212 506 or 021 406 6782.

10.4.1 POST-EXPOSURE PROPHYLAXIS, OCCUPATIONAL

Z29.2

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 >60 mL/min).

and

- Emtricitabine, oral, 200 mg daily for 4 weeks.

and

- Atazanavir/ritonavir 300/100 mg daily for 4 weeks.
  OR
- Lopinavir/ritonavir 200/50, 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. The highest rates of adverse effects occur with 3-drug regimens. Nevirapine must never be used for PEP as there is a high risk of severe hepatitis when given to people without HIV infection. Efavirenz is also 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 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 or stavudine, 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 Health Care 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** 4th generation ELISA	Rapid test **PLUS** 4th generation ELISA		4th generation ELISA	4th generation 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.

10.4.2 NON OCCUPATIONAL POST EXPOSURE PROPHYLAXIS, SEXUAL ASSAULT AND INADVERTENT EXPOSURE

Z29.2

PEP should be offered to rape survivors who present within 72 hours.
Rape survivors who test HIV seropositive must not be given PEP.

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 oral, 1.5 mg as a single dose as soon as possible after unprotected intercourse. *LoE:III*[xxviii]

CAUTION
Tablets must be taken as soon as possible, preferably within 72 hours of unprotected intercourse and not > 5 days later.

An anti-emetic:

- Metoclopramide oral, 10 mg 8 hourly as needed.

LoE:III[xxix]

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[xxx]

Inadvertent (non-occupational) exposure to infectious material from HIV sero-positive persons often requires clinical judgement and includes:

» human bites
» sharing of needles during recreational drug use
» consensual sexual exposure, burst condoms
» contact sports with blood exposure

LoE:III[xxxi]

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 uninfected 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).

» Prophylaxis is not recommended for most uncomplicated clean procedures.

» The antibiotic of choice should be active against the pathogens most likely to be associated with surgical site infections. Specific epidemiological considerations may alter the choice of agents.

» Give prophylaxis < 60 minutes before the first incision, usually 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]*

» Antibiotic prophylaxis should be used in conjunction with good pre- and intra-operative infection prevention strategies.

Dosage recommendations:

- Cefazolin, IV.
  - If < 80 kg: 1g
  - If ≥ 80 kg: 2 g. *LoE:III[V]*
- Metronidazole, IV, 500 mg.
- Gentamicin, IV, 6 mg/kg.
- 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.

» 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:I[VI]*

» 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[VII]*

LoE:III[VIII]

ANTIBIOTIC PROPHYLAXIS

TYPE OF SURGERY	ANTIBIOTIC RECOMMENDED	
	• Cefazolin, IV	• Cefazolin, IV **AND** • Metronidazole, IV
Orthopaedic surgery	Primary total hip or total knee replacement; internal fixation of hip; spinal procedures; open reduction and internal fixation of fractures; insertion of prostheses, screws, plates, etc.	Lower limb amputation.
Gastrointestinal surgery	Gastric/ duodenal/ oesophageal hernia repair.	Biliary, colorectal, manipulation of viscera, appendicectomy, division of adhesions, Exploratory laparotomy.
Thoracic surgery		Pneumonectomy/ lobectomy.
Cardiac surgery	Coronary artery bypass surgery/routine cardiac valve surgery (continue cefazolin, IV, 8 hourly for 24 hours); cardiac device insertion (pacemaker implantation).	
Vascular surgery (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.

TYPE OF SURGERY	ANTIBIOTIC RECOMMENDED	
	• Cefazolin, IV	• Cefazolin, IV **AND** • Metronidazole, IV
Urology	Clean procedures with entry into urinary tract.	Clean-contaminated procedures.
Plastic and reconstructive surgery (Prophylaxis is **not** recommended for clean bone or soft tissue surgery).	Craniotomy procedures.	
Otorhinolaryngology/ head and neck surgery (Prophylaxis is **not** recommended for other procedures such as tonsillectomy, sinus procedures, etc.).	No incision through the oropharyngeal mucosa.	With incision through the oropharyngeal mucosa.
Obstetrics/ gynaecology (Prophylaxis is **not** recommended for early suction termination).	Caesarean section.	Hysterectomy, laparotomy procedures, vaginal repair.
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.	

Beta lactam allergies:
Avoid beta-lactam antimicrobials in patients with a history of anaphylaxis, urticaria, or angioedema after exposure to one of these agents.

- Clindamycin, IV.

ADD

- Gentamicin, IV **for the procedures listed below:**

» 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[ix]

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 not given prior to surgery it is recommended to give it at least 14 days post-splenectomy.

LoE:II[x]

» The following vaccines should be administered:

VACCINE	SCHEDULE
• Polyvalent pneumococcal vaccine, 0.5 mL, subcutaneous.	Revaccinate every 5 years. *LoE:II*[xi]
• Haemophilus influenza type B, 0.5 mL, intramuscular.	–
• Meningococcal polysaccharide vaccine, 0.5 mL, subcutaneous.	Revaccinate every 5 years.
• Influenza vaccine, 0.5 mL, intramuscular.	Revaccinate annually.

LoE:III[xii]

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, PAIN AND INTENSIVE CARE

Anaesthetic and sedative medication may only be administered by medical practitioners trained and experienced in their use.

Medicines and equipment for resuscitation should be 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, 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 elderly.
  - Duration of action (10-20 hours).
  - Unsuitable for day case surgery.

LoE:III

- Midazolam, 7.5mg oral one hour preoperatively.
  - Use only in healthy adults < 65 years of age.
  - Duration of action 1–4 hours.
  - Suitable for day case surgery.

12.2 GENERAL ANAESTHESIA

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.
Propofol is the most widely used IV induction agent but can produce hypotension. Etomidate or ketamine is preferred in haemodynamically

unstable patients. Thiopentone has a rapid onset and may be preferred for Caesarean sections.

- 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 4%.

OR

- Sevoflurane, titrated to 8%. *LoE:III*[II]

12.2.2.2 MAINTENANCE

In spontaneously breathing patients, the dose of 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

To facilitate intubation and provide intraoperative muscle relaxation for surgery. 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 suxamthonium-induced hyperkalaemia, e.g. upper or lower motor neuron defect, prolonged chemical denervation, direct muscle trauma, tumour or inflammation, thermal trauma, disuse atrophy, severe infection.

LoE:III[III]

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.

- Cisatracurium
  - 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[IV]*
  - 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[V]*

If suxamethonium is contra-indicated, consider:

- Rocuronium, 0.9 mg/kg, IV.
  - Duration +/- 60 minutes. *LoE:III[VI]*

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[VII]*

WITH EITHER:

- Atropine, IV, 20 mcg/kg (maximum 1.2 mg).

OR *LoE:III[VIII]*

Glycopyrrolate, IV, 10 mcg/kg. *LoE:III[IX]*

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 to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum dose: 4 g in 24 hours.

AND *LoE:I*[x]

- Tramadol, oral, 50**–**100 mg, 6 hourly.
  - Avoid in head injury and epilepsy.
  - Improved effect when given with paracetamol.

AND *LoE:III*[xi]

- NSAIDs, 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*[xii]

12.4.1.2 INTRAVENOUS ANALGESICS

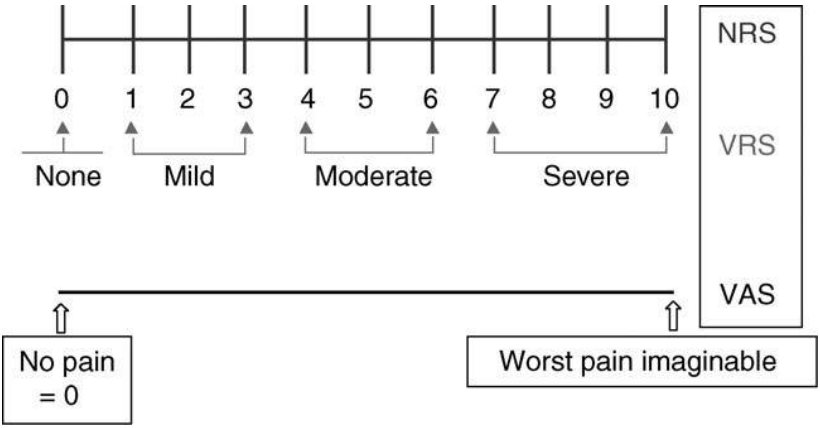
- Fentanyl, IV, 1–2 mcg/kg
  - Onset ± 3 minutes, duration of action 30–60 minutes. Higher doses last longer. *LoE:III*[xiii]
- Morphine, IV/IM, 3–5 mg as a single dose then further boluses of 1–2 mg/minute and monitor closely.
  - Dilute 10 mg up to 10 mL with sodium chloride 0.9%.
  - Total maximum 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, 0.15 mg/kg – a subanaesthetic dose given pre-incision may reduce persistent post-surgical pain. *LoE:II*[xiv]

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 (Specialist prescribed).
    - Ceiling effect i.e. higher doses do not improve pain relief. *LoE:III*[xv]

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, to upper, outer quadrant of buttock.

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.

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 to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum dose: 4 g in 24 hours.

AND

- NSAIDs, oral, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly after meals.

AND

  - Tramadol, oral, 50–100 mg, 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 to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum dose: 4 g in 24 hours.

AND

- NSAIDs, oral, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with meals.

AND

- Tramadol, oral, 50–100 mg, 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 patient controlled 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 to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum dose: 4 g in 24 hours.

AND

- NSAID, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with meals.

LoE:III[XVI]

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[XVII]

If unable to take oral medication, stop oral ibuprofen and use:

- Diclofenac, deep IM, 75 mg 12 hourly, to upper, outer quadrant of buttock.

12.5 INTRAVENOUS FLUIDS

The following IV fluids should be available for perioperative fluid replacement and maintenance therapy.

12.5.1 CRYSTALLOIDS

- Ringer Lactate, IV.

Most commonly used crystalloid for perioperative fluid maintenance:

- Sodium chloride 0.9%, IV.

Higher sodium content than Ringer lactate. Indicated if perioperative risk of hyponatraemia e.g. transurethral resection of prostate.

LoE:III[XVIII]

12.6 MEDICINES TO TREAT COMPLICATIONS OF ANAESTHESIA

12.6.1 MALIGNANT HYPERTHERMIA

T88.3

- Dantrolene IV, 2 mg/kg as a single dose.
  - Repeat doses until cardiac and respiratory symptoms stabilise.
  - Up to 10 mg/kg may be required. *LoE:III*[xix]

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*[xx]
- Lipid emulsion (20%), IV, 1.5 mL/kg over 1 min, then continuous infusion 0.25 mL/kg/min.
  - Repeat bolus 1–2 times for persistent cardiovascular collapse.
  - Double infusion rate to 0.5 mL/kg/min 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*[xxi]

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.

OR *LoE:III*[xxii]

Phenylephrine IV, 50–100 mcg as a single dose and then

infuse at 60–180 mcg/minute.
- Vasoconstrictor. *LoE:III*[xxiii]
- High doses may cause significant reflex bradycardia: treat this by discontinuing the phenylephrine only.

12.6.4 ANAESTHESIA-RELATED ACUTE HYPERTENSION

I97.3

To obtund the hypertensive response to intubation i.e. 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*[xxiv]

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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

Anti-emetic	Class	Prophylactic Dose and timing	Notes
Dexamethasone	Corticosteroid	4-8 mg, IV, on induction	Increases blood glucose in diabetics. Only used for prophylaxis, not established PONV.
Ondansetron	5-HT_3 receptor antagonist	4 mg, IV, over 2–5 minutes at end of surgery	Prolongs QTc interval
Promethazine	Phenothiazine	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.

LoE:II[xxv]

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 < 60kg: 5mg IM or IV (over 2 minutes).
  - If ≥ 60kg: 10mg IM or IV (over 2 minutes).
  - Repeat 8 hourly if required.

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, 10 mg for symptom relief.

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 section.

- Sodium citrate, 0.3M, oral, 30 mL.
  - Not more than 30 minutes pre-induction of anaesthesia.

LoE:I[xxvi]

12.7 SPINAL (INTRATHECAL) ANAESTHESIA

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.

Small amounts of fentanyl (10–25 mcg) may be added to increase duration of analgesia.

Caesarean Section
Lower doses are required due to physiologic changes of pregnancy:

- Bupivacaine, 1.8 mL (9 mg) plus dextrose.

AND

- Fentanyl, 0.2 mL (10 mcg).

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.

Timing of anticoagulants in patients receiving neuraxial anaesthesia:

Anticoagulant	Before Neuraxial Block	After Neuraxial block
Warfarin, oral	Stop warfarin and check INR normal	Restart after neuraxial block performed and epidural catheter removed.
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 hours and check PTT	Wait >1 hour before next bolus/infusion restarted
Prophylactic LMWH, SC	>12 hours after last dose	>6 hours or at least 2 hours after epidural catheter removed, whichever is later.
Therapeutic LMWH, SC	>24 hours after last dose	>24 hours or at least 2 hours after epidural catheter removed, whichever is later.

LoE:II[xxvii]

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 EPIDURAL ANAESTHESIA

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[xxviii]

- Lidocaine 2% (preservative-free).
  - Onset ±3-5 minutes.
  - Duration ±1 hour.

LoE:III[xxix]

12.9 PERIPHERAL NERVE BLOCK OR WOUND INFILTRATION

Only preservative free medicines may be used for nerve blocks.
Lignocaine 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[xxx]

12.10 TOPICAL ANAESTHESIA

- Lidocaine jelly, topical, 2 g/100mL.
  - For urethral catheterisation: female 5–7 mL, male 10–15 mL.

LoE:III[xxxi]

- Lidocaine topical spray, 4%.
  - Maximum dose 160 mg.
  - To assist with awake intubation or reduce haemodynamic response to intubation.

LoE:III[xxxii]

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[xxxiii]

12.11 SEDATION

Y47.9

Refer to chapter 23: Sedation.

12.12 PAIN, CHRONIC

R52.1

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage.

ASSESSEMENT OF CHRONIC PAIN

The aetiology of the pain needs to be ascertained, and whether treatment of the cause is possible.
Determine if the type of pain is nociceptive, neuropathic or both.

Depression and anxiety are commonly associated with chronic pain. Every patient needs a psychological assessment.

If a patient is suffering from chronic pain due to a terminal illness, ascertain the prognosis.

Response to current and previously used analgesic medication, comorbidities, and functional status should be established.

Use of a self-reporting pain scale helps to monitor treatment progress. See Numeric Rating Scale in section 12.5.2: Postoperative pain in the recovery room).

Pain at rest, on movement and during pain exacerbations should be recorded. Patients must be monitored at regular intervals so treatment can be adjusted appropriately.

GENERAL AND SUPPORTIVE MEASURES

Patients with chronic pain should be treated with a biopsychosocial approach.
A multidisciplinary team approach is required and the assistance of psychiatrists, physiotherapists, occupational therapists, social workers, dieticians and psychologists should be sought according to the patient's needs.
The goals of pain management not only include pain reduction but also improvement of function, sleep and well-being.
Family members play an important part in the patient's treatment and should be included where possible.

MEDICINE TREATMENT

Chronic pain is rarely completely cured with medication. The aim of pharmacological treatment is to reduce pain levels in order to maintain or improve function.
Medications should preferably be given orally.

12.12.1 ANALGESIA FOR CHRONIC NON-CANCER PAIN

R52.1

For chronic pain of a constant nature, analgesics should be administered on a regular basis.

MILD/MODERATE PAIN:

Paracetamol, ibuprofen and tramadol can be used alone or in combination according to the severity of the pain.

- Paracetamol, oral, 1 g 4–6 hourly when required to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum dose: 4 g in 24 hours.

- Ibuprofen, oral, 400 mg 8 hourly with meals.
  - Can be used in combination with paracetamol or opioids.

- Tramadol, oral, 50–100 mg, 6 hourly.
  - Avoid in head injury and epilepsy.
  - Improved effect when given with paracetamol.

Note:

» Tramadol blocks neuronal reuptake of noradrenaline and serotonin. If used with other medicines that also block serotonin reuptake (e.g. pethidine, fentanyl, antidepressants) the serotinergic syndrome can result (altered mental status, neuromuscular hyperactivity, autonomic hyperactivity).

» Avoid long-term use of NSAIDs as they are associated with an increased risk of arterial thrombosis, renal impairment and gastrointestinal bleeding.

SEVERE PAIN:

- 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 and 30 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.

12.12.2 ANALGESIA FOR CHRONIC CANCER PAIN

R52.1

The term “cancer pain” also includes pain due to terminal illness.
The same steps as given in section 12.12.1: 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[xxxiv]

12.12.3 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, 2 tablets at night.
  - Contraindicated in patients with potentially obstructive lesions.

In patients with potentially obstructive lesions:

- Lactulose, oral, 15 mL 12 hourly.

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.

12.12.4 ANALGESIA FOR CHRONIC NEUROPATHIC PAIN

G62.9

Neuropathic pain resulting from nerve injury or disease e.g. nerve root compression, peripheral neuropathy due to diabetes or HIV.
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.
These medications must be used regularly, as they take 2–6 weeks to work.

- Amitriptyline, oral, 10 mg, two hours before usual sleep time.
  - Titrate up to 75 mg at night. *LoE:II*[xxxv]

If no response after 2-4 weeks, (or amitriptyline contraindicated):

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.

REFERRAL

For neuropathic pain unresponsive to these medicines, refer patient to a experienced pain clinician.

12.12.5 ANALGESIA FOR ACUTE NON-SURGICAL PAIN

12.12.5.1 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 12.5.2: 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.

12.12.5.2 ACUTE PAIN DUE TO GASTROINTESTINAL COLIC

R10.84

- Hyoscine butylbromide, IV/oral, 10 mg 8 hourly.

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.

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, casuing: 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.

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 SYSTEM

13.1 ARTHRITIS, RHEUMATOID (RA)

M06.9

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 3 joint areas simultaneously.
» Pain.
» Limited movement with morning stiffness > 1 hour, which improves with activity. This distinguishes osteoarthrosis 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.
» The involved joint distribution 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 at an early stage by a specialist. Evaluate all patients with suspected RA for disease-modifying anti-rheumatic drug (DMARD):

- Methotrexate (preferred initial therapy)
- Chloroquine sulphate
- Sulfasalazine

Patients on DMARDs must be monitored regularly for toxicity, as outlined below:

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, add another DMARD.

- Methotrexate, oral, 7.5 mg once per week. Specialist consultation.
  - Increase dose gradually to a maximum of 25 mg per week.
  - 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[I]

AND/OR

- Chloroquine sulphate, oral, 150 mg (as base) daily for 5 days of each week for 2–3 months.
  - 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.
  - Gradually increase over one month from 500 mg to 1 g 12 hourly.
  - FBC and ALT monthly for first 3 months then every 3–6 months.

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.

- Prednisone, oral, 40 mg daily for 2 weeks.
  - Thereafter gradually reduce the dose to ≤ 7.5 mg daily. (Refer to page xxvii for an example of a dose reduction regimen).
  - Discontinue at 3–6 months.
  - The continued need for systemic steroids should always prompt review of treatment. *LoE:II*[II]

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 to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum 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.

> Concomitant use of more than one oral NSAID has no additional clinical benefit and only increases toxicity.
>
> Chronic use of all NSAIDs is associated with increased risks of gastrointestinal bleeding, renal failure, and cardiovascular events (stroke and myocardial infarction).

- NSAID, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with meals. *LoE:I[III]*

An extra **night-time** dose of a 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:III[IV]*

- Lansoprazole, oral, 30 mg daily whilst 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 and administered 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.

REFERRAL
» At initial diagnosis.
» Disease activity cannot be controlled with the measures as mentioned.
» Compression neuropathy.
» For joint replacement.
» Allergy to sulfasalazine.

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
M00.9/M86.1

DESCRIPTION
An acute infective condition involving one or more joints.
The joint is hot, swollen, very painful on movement, and with restricted movements.
Signs of systemic infection, including fever, are usually present. The infection is usually blood borne, but may follow trauma to the joint. The course may be acute or protracted. The commonest causative organism is Staphylococcus aureus, but a large number of other organisms may be involved, including and *N. gonorrhoeae*.
Note: Haemophiliacs with bleeding into joints may present with an acute arthritis mimicking septic arthritis.

GENERAL MEASURES
Baseline X-ray.
Rest and immobilisation.

Septic arthritis:
Drainage is important. Discuss with an appropriate 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 other fluids before administering antibiotics.

- Cloxacillin, IV, 2 g 6 hourly for 4 weeks.

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:

- 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, 450 mg 8 hourly to complete the 4 weeks' treatment.

LoE:III[V]

For gonococcal arthritis

- Ceftriaxone, IV, 1 g daily for 1 week.

Severe penicillin allergy:
Refer.

Analgesia

- NSAID until pain subsides e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with meals.

AND/OR

LoE:I[VI]

- Paracetamol, oral, 1 g 4–6 hourly when required to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum dose: 4 g in 24 hours.

REFERRAL

» Acute osteomyelitis/ septic arthritis for early drainage by specialist surgeon.
» If pyrexia persists in spite of adequate antibiotic therapy, a sub-periosteal abscess must be sought and drained by a specialist surgeon.
» Chronic osteomyelitis.
» Pathological fractures.

13.3 OSTEO-ARTHRITIS

M19.9

DESCRIPTION

A disorder typically affecting weight-bearing joints and the hand (distal and

proximal interphalangeals, and first metacarpo-phalangeal 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 to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum dose: 4 g in 24 hours.

If ineffective:

ADD

- NSAIDs e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with meals. *LoE:I[vii]*

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 ibuprofen in the morning, as taking aspirin and ibuprofen at the same time may reduce aspirin's efficacy. *LoE:III[viii]*

In high-risk patients: > 65 years of age; history of peptic ulcer disease; or on concomitant warfarin, aspirin or corticosteroids:

ADD *LoE:III[ix]*

- Lansoprazole, oral, 30 mg daily.

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.

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.

REFERRAL

» For consideration for joint replacement.
» Intractable pain.
» Neurogenic compression.

13.4 GOUT

M10.9

DESCRIPTION

A metabolic disease in which uric acid crystal deposition occurs in joints and other tissues.

Acute gout:

Joint involvement is characterized 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 metatarso-phalangeal 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 1st metatarsal phalangeal joint in most patients
» involvement of the instep, ankle, heel and knee
» involvement of bursae (such as the olecranon)
» significant periarticular inflammation
» serum uric acid over 0.5 mmol/L
» bone destruction
» prolongation of attacks, often with reduction in pain severity
» incomplete resolution between attacks

GENERAL MEASURES

Acute attack

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:

- NSAIDs e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with meals for the duration of the attack.

LoE:I[x]

If NSAIDS are contraindicated, e.g. peptic ulceration, warfarin therapy and renal dysfunction:

- 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.

Investigate for and treat secondary causes (e.g. haematological malignancies) where possible.
Assess renal function and blood urate level. The serum uric acid level may be normal during acute attacks.

Uric acid lowering therapy

Urate lowering therapy is required in the following:

» >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 urate blood levels and eGFR.
  - Titrate dose to reduce serum urate to < 0.35 mmol/L.
  - Most patients will be controlled with a dose of 300 mg daily.
  - Elderly and patients with renal impairment (eGFR between 30–60 mL/minute): start with 50 mg daily.

Allopurinol is contra-indicated in patients with eGFR < 30 mL/minute.

To prevent breakthrough gout attacks:

- Colchicine, oral, 0.5 mg 12 hourly for 3 months.

OR

LoE:III

- NSAIDs e.g.:
- Ibuprofen, oral, 400 mg 12 hourly with meals for 3 months.

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*[xi]

- Lansoprazole, oral, 30 mg daily.

Do not stop uric acid lowering drugs during an acute attack.

REFERRAL

» No response to treatment despite adequate adherence.
» Suspected secondary gout.
» Non-resolving tophaceous gout.
» Patients with eGFR < 30 mL/minute.

13.5 SERONEGATIVE SPONDYLARTHRITIS

M45–49

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 the arthritides associated with inflammatory bowel disease. Extra-articular manifestations may occur, especially uveitis, which occurs in about one third of patients.

GENERAL MEASURES

Physiotherapy to prevent back deformity.

MEDICINE TREATMENT

Initiate treatment with NSAIDs.

- NSAIDs, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with meals.

REFERRAL

» Uveitis, to an ophthalmologist.
» Refractory severe arthritis, to a rheumatologist.
» Deformity at diagnosis, to a rheumatologist.

13.5.1 ARTHRITIS, REACTIVE

M02.3

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. However, joint symptoms may persist.

MEDICINE TREATMENT

Start with a high dose and titrate downwards if not needed or if not tolerated:

- NSAIDs, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with meals.

LoE:I[xii]

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[xiii]

13.6 SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

L93

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.
Avoid sunlight exposure. Sun protective barrier creams are often indicated.
Regularly monitor urine for blood and protein.
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 to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum dose: 4 g in 24 hours.

AND/OR

- NSAIDs, e.g.:
- Ibuprofen, oral, 400 mg 8 hourly with meals. *LoE:II*[xiv]

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[xv]

Corticosteroids

Initiate therapy in patients with life threatening manifestations and organ involvement.

- Prednisone, oral, 2 mg/kg daily, initial dose.
  - Taper to the lowest maintenance dose after a response has been obtained. Refer to page xxvii for an example of a dose reduction regimen.
  - Usual maintenance dose: 10 mg daily.

Patients requiring corticosteroids for > 3 months should be educated to take in enough calcium in their diet.

Additional immunosuppressive therapy

Is often required for life-threatening disease. particularly kidney and CNS involvement. These medicines should be initiated by a specialist.

- 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).

Raynaud's phenomenon *LoE:III*

- Amlodipine, oral, 5 mg daily.

Antiphospholipid antibody syndrome *LoE:II*[xvi]

- Aspirin, oral, 150 mg daily.

Patients with previous thrombo-embolic episodes should receive lifelong warfarin (target INR 3 to 4).

Hormonal therapy in women *LoE:III*

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

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 if there are clinical features to suggest dyslipidaemia.

Although the finding of a carotid bruit in a symptomatic patient should lead to further investigation, its absence does not exclude significant carotid stenosis.

Ischaemic stroke in young adults (< 45 years of age) may be due to atherosclerosis, but also consider:

1. 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
2. Vessel wall disease: e.g. syphilis HIV infection, collagen-vascular diseases, or related to acute or chronic meningitis, and other rarer disorders such as sarcoidosis and Wegener's granulomatosis, 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. Although the finding of a carotid bruit in a symptomatic patient should lead to further investigation, its absence does not exclude significant carotid stenosis.
3. 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

Measures for secondary prevention may not be appropriate for patients with severe disability.

All patients not on anticoagulation:

- Aspirin, oral, 150 mg daily with meals. *LoE: I[i]*

Patients with a thrombotic stroke for secondary prevention, irrespective of the LDL level:

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

LoE:I[ii]

For DVT prophylaxis, low dose subcutaneous heparin:

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

OR

Enoxaparin, SC, 40 mg daily.

See section 2.13: Venous Thrombo-Embolism.

In patients with cardioembolic strokes (e.g. atrial fibrillation) start anticoagulation with warfarin 7 days after an index event provided there is no haemorrhage on CT scan.

Bridging anticoagulation with heparin, or earlier initiation of warfarin, is not recommended because, although it reduces ischaemic stroke recurrence, it causes an equivalent increase in symptomatic intracranial haemorrhage. *LoE:III[iii]*

Treat secondary pulmonary and urinary tract infections appropriately. *LoE:III*

Blood pressure management

A transient increase in BP is common after an acute stroke. Do not actively lower a BP of less than 220/120 mmHg 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 in the first 24 hours.

If BP > 220/120 mm Hg:

- Long-acting calcium channel blocker, e.g.:
- Amlodipine, oral, 5 mg daily.

OR

If adequate fluid intake can be ensured:

- Thiazide diuretic, e.g.:
- Hydrochlorothiazide, oral, 25–50 mg daily.

LoE:I[iv]

Good long term BP control is important for patients whose BP remains elevated after the first few days

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

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

Identified 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[V]

Other patients:

- Aspirin, oral, 150 mg daily.

AND *LoE:I[VI]*

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

Manage hypertension.

14.1.3 ACUTE SPINAL CORD INJURY

T09.3

There is no convincing evidence that high dose corticosteroids are beneficial in the management of traumatic cord injuries. *LoE:I[VII]*

14.1.4 SUBARACHNOID HAEMORRHAGE

I60

DESCRIPTION

Bleeding into the subarachnoid space, most commonly due to the rupture of a vascular aneurysm. Patients frequently 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, urgently by lumbar puncture, demonstrating xanthochromia.

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 to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum 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 patients with grades 1 to 3 impairment of consciousness level 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

F02*

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 treatable (reversible) systemic, neurological and psychiatric illnesses.

Common reversible causes of dementia include:
» Metabolic
  - Hypothyroidism
  - Vitamin B_{12} deficiency
  - Pellagra
  - Thiamine deficiency (Wernickes syndrome)
» Medications and drugs
  - Alcohol abuse
  - Many medications with CNS side effects
» Infections
  - Syphilis
  - HIV dementia
» Surgical
  - Chronic subdural haematoma
  - Normal pressure hydrocephalus
» Severe depression

Conditions which may worsen already existing dementia include:
» Electrolyte disturbances and dehydration.
» Infections, usually originating from the respiratory or urinary tract.
» Medication 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.

<u>For pellagra:</u>
- Nicotinamide, oral, 100 mg 8 hourly.

Wernickes syndrome

- 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):

- Thiamine, IM/oral, 100 mg 8 hourly for 14 days. *LoE:III*[VIII]

Treat other commonly associated nutritional deficiencies:

- Vitamin B complex, oral, 2 tablets 8 hourly. *LoE:III*

14.3 EPILEPSY

G40

GENERAL MEASURES

Take an adequate history to define the type of epilepsy.
Although rare, juvenile myoclonic epilepsy and absence seizures should be specifically considered and identified, as some standard medications may be less efficacious in these conditions or may even worsen seizure frequency or severity.
All patients with new onset epilepsy should have a CT scan and other investigations as clinically indicated.
A single unprovoked seizure is usually not an indication for treatment, although 40% of patients may have a subsequent seizure within 2 years.
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 hygeine,
» 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, especially valproate, can be teratogenic. Note that there are important drug-drug interactions between hormonal contraceptive (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. Physician to provide guidance.

MEDICINE TREATMENT

The aim is to use monotherapy, i.e. a single anticonvulsant, progressively increasing the dose until the seizures are controlled or clinically important side effects occur.

If the initial medication fails to achieve satisfactory control with optimal dosages, or causes unacceptable adverse effects, then a second medicine may be started. The first drug should be continued for 2 weeks and then gradually reduced over 6– 8 weeks until stopped. If the second drug fails, and alcohol and poor adherence are excluded, then combination therapy may be required. Refer patients for specialist investigation.

Patients with a history of myoclonic seizures or typical absence seizures should preferably be treated with valproate, as those seizures may be aggravated by the use of either phenytoin or carbamazepine.

Routine therapeutic drug monitoring is not useful except:

» To confirm toxicity in a symptomatic patient.
» To confirm poor adherence.
» With poor control despite good self reported adherence.

Partial seizures or generalised tonic clonic seizures

The choice between therapeutic agents must be made on the acceptability of side effects and how the number of doses influences lifestyle.

- 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*[ix]

OR

Lamotrigine, oral.

- 25 mg daily for 2 weeks, then 50 mg daily for 2 weeks.
- Thereafter, increase by 50 mg every 2 weeks according to response.
- Usual maintenance dose: 100–200 mg daily as a single dose.

OR *LoE:III*

Phenytoin, oral, 4.5–5 mg/kg (lean body mass) daily.

- Usual starting dose in an adult male: 300mg 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.

LoE:III

For patients not stabilised on or who do not tolerate the above medications:

- Valproate, oral.
  - Usual starting dose: 200–300 mg 12 hourly.
  - Increase, as required, every 2 weeks to a maximum daily dose of 1.2 g 12 hourly.

Phenytoin, phenobarbitone and carbamazepine are potent enzyme inducing agents and should be used with caution with other medicines metabolised by the liver, especially warfarin, ARVs, progestin subdermal implants and oral contraceptives.

Other epilepsy types

Manage in consultation with a specialist.

Specifically, juvenile myoclonic epilepsy is best controlled with valproate initially, and absence seizures with valproate or lamotrigine.

HIV-infected individuals on ARVs

Phenytoin, phenobarbital and carbamazepine are enzyme inducing anti-epileptic medicines. Due to potential drug interactions with antiretroviral drugs, switch patients on these anti-epileptics to lamotrigine or valproate.

- Lamotrigine, oral.
  - 25 mg daily for 2 weeks, then 50 mg daily for 2 weeks.
  - Thereafter, increase by 50 mg every 2 weeks according to response.
  - Usual maintenance dose: 100–200 mg daily, as a single dose or 12 hourly.

Note: The metabolism of lamotrigine is induced by lopinavir/ritonavir and atazanavir/ritonavir. The dose of lamotrigine may need to be increased when patients are switched to a lopinavir/ritonavir- or atazanavir/ritonavir -containing regimen.

OR

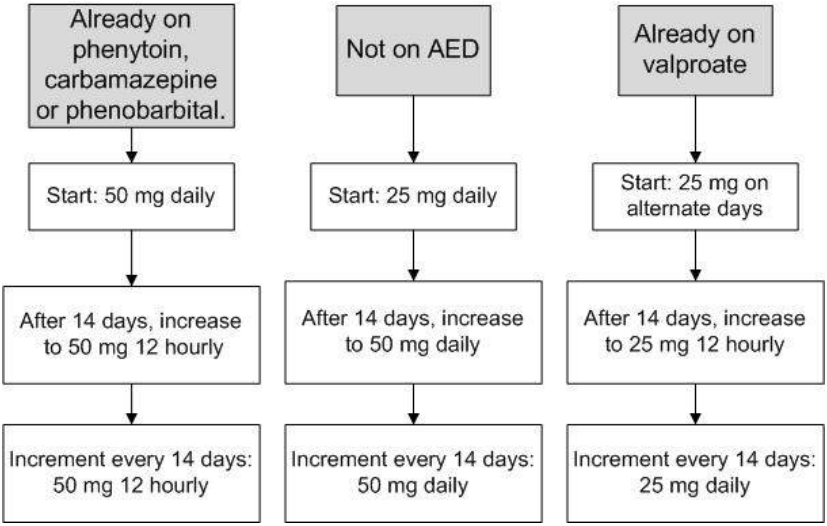
Valproate, oral.

- 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:</u>

- Lamotrigine, oral.
  - Start with 25 mg daily on alternate days for 2 weeks, increasing to 25 mg daily for 2 weeks.
  - Thereafter increase by 25–50 mg every 2 weeks according to response.

Lamotrigine dose titration



LoE:III[x]

Status epilepticus:
See section 14.3.1: Status Epilepticus.

Pregnancy
Optimal control of epilepsy on a single agent is the best management.

Do not initiate valproate during pregnancy, as it is associated with a higher teratogenic potential than the other first line agents

Before pregnancy is considered, folate supplementation:

- Folic acid, oral, 5 mg daily.
  - Pregnancy alters drug levels, adjust dose according to levels.

Prophylaxis in head trauma
Phenytoin may be of benefit during initial period following significant head trauma.

- Phenytoin, IV, 20 mg/kg diluted in sodium chloride 0.9% **(not dextrose)** administered not faster than 50 mg/minute preferably with cardiac monitoring.
  - If arrhythmias occur, interrupt the infusion temporarily and reintroduce slowly.
  - Continue with, IV, 5 mg/kg/day (300 mg daily for most adults).

LoE:II[xi]

REFERRAL

» All new onset epileptics for neuro-imaging, if unavailable locally.
» Epileptics who are poorly controlled on adequate treatment.
» For consideration of combination therapy.
» Epilepsy with unexplained neurological symptoms or signs.

14.3.1 STATUS EPILEPTICUS

G41

DESCRIPTION

A seizure lasting > 5 minutes or recurrent seizures without recovery to baseline between episodes.

GENERAL MEASURES

Start treatment immediately. Do not wait for results of special investigations.
Secure the airway.
Check serum glucose, and treat if hypoglycaemic.
Check for hyponatraemia or uraemia and measure anticonvulsant levels if the patient is on therapy.
Consider poisoning, e.g. isoniazid, theophylline, tricyclic antidepressants, cocaine.

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

- Lorazepam, IV/IM, 4 mg, repeat after 5–10 minutes if necessary.

LoE:III

OR

Diazepam, IV, 10 mg, not faster than 2 mg/minute, repeat after 5–10 minutes if necessary.

LoE:III

OR

Clonazepam, IV, 2 mg, repeat after 5–10 minutes if necessary.

LoE:III

OR

Midazolam, IM/IV 10 mg, repeat after 5–10 minutes if necessary.

LoE:I[xii]

OR

Midazolam buccal, 10 mg using the parenteral formulation.

LoE:III

AND

- Phenytoin, IV, 20 mg/kg diluted in sodium chloride 0.9% **(not dextrose)** administered not faster than 50 mg/minute preferably with cardiac monitoring.
    - If arrhythmias occur, interrupt the infusion temporarily and

reintroduce slowly.

Seizures continuing after 30 minutes
Intubate and ventilate patient.

- Thiopental, IV, 4 mg/kg, followed by 50 mg bolus every 2–3 minutes to control seizures.
  - Maintenance dose: 1–5 mg/kg/hour.
  - Beware of hypotension.
  - Once seizures controlled for 24 hours, wean off thiopental by decreasing the dose by 1 mg/kg every 12 hours.

OR *LoE:III*[xiii]

Propofol, IV, 3mg/kg/dose as a bolus
- Maintenance dose: 30–100 mcg/kg/minute.

LoE:I[xiv]

Higher initial maintenance doses of phenytoin may be needed in patients who have had thiopental. Doses should be guided by daily therapeutic drug monitoring until phenytoin levels have stabilised after thiopental has been weaned off.

MAINTENANCE THERAPY
If seizures are controlled:
- Phenytoin, IV/oral, 300 mg daily.
  - First maintenance dose should be no more than 12 hours after the loading dose.

LoE:III

Clinical signs that seizures are controlled are autonomic stability and the absence of abnormal movement.

Long term maintenance therapy: See section 14.3: Epilepsy.

14.4 HEADACHE AND FACIAL PAIN SYNDROMES

14.4.1 MIGRAINE
G43

DESCRIPTION
Episodic headache, usually focal in nature, which may occur with or without an aura. It is usually accompanied by nausea and/or vomiting. Several variants of migraine also occur.

GENERAL MEASURES
Reassure patient that this is a benign condition.
Attempt to identify any precipitating factors or food allergies from the history (although this is usually unrewarding), and try to diminish patterns of tension.

MEDICINE TREATMENT

Acute treatment

Initiate therapy during the migraine attack or at the onset of the headache.

Analgesics, e.g.:

- Paracetamol, oral, 1 g 4–6 hourly when required to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum dose: 4 g in 24 hours.

OR

- NSAIDs, e.g.:
- Ibuprofen, oral, 400 mg immediately then 8 hourly with meals, if needed.

If severe and not responding to therapy above:

- Morphine, IM, 3–5 mg as a single dose, then further boluses of 1–2 mg/minute to a total maximum dose of 10 mg and monitor closely. (See Appendix II, for individual dosing and monitoring for response and toxicity).

For nausea:

- Metoclopramide, oral/IM, 10 mg 8 hourly.

Prophylaxis

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.

Also consider for patients who tolerate therapy for acute attacks poorly.

- Amitriptyline, oral, 10–25 mg at bedtime.
  - Titrate dose up to adequate response.
  - More than 75–150 mg as a single bedtime dose is seldom required.

OR

Carbamazepine, oral.

- Start with 100 mg 12 hourly.
- Increase every two weeks up to a maximum of 400 mg 12 hourly.

Note: Only about half of patients will respond to one of these agents and this response may take 1– 2 months to occur.

14.4.2 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:
- Prednisone, oral, 40 mg daily for 5–10 days.
  - Tapering is not necessary when the above duration is used.

OR
- Verapamil, oral, 40 to 80 mg 12 hourly.

REFERRAL
Inadequate response to treatment.

14.4.3 TRIGEMINAL NEURALGIA
G50.0

DESCRIPTION
Severe, very short lived stabs of facial pain in the sensory trigeminal distribution. It is important in the diagnostic workup to exclude intracranial mass lesions, which may impinge on the trigeminal nerve.

MEDICINE TREATMENT
- 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.

REFERRAL
» Neuro-imaging, if not available locally.
» Poor response to single drug therapy.

14.4.4 TENSION HEADACHE
G44.2

DESCRIPTION
Headache over the back of the head, but sometimes over the entire head, described as a tight band around the head, usually worse in the afternoon.

GENERAL MEASURES
Consider use of relaxation techniques.
The importance of this diagnosis is the exclusion of other, more sinister conditions.
Exclude analgesia overuse headache.

MEDICINE TREATMENT

- Amitriptyline, oral, 10–75 mg at night.

REFERRAL

» Atypical pain, suggestive of alternate diagnosis.
» Poor response to therapy.

14.4.5 IDIOPATHIC INTRACRANIAL HYPERTENSION (PSEUDOTUMOUR CEREBRI)

G93.2

DESCRIPTION

Patients present with symptoms (chronic headache and sometimes eventual visual loss due to persistent papilloedema) and signs (papilloedema) of raised intracranial pressure in the absence of any structural intracranial abnormality or abnormal 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.
» Diagnosis is confirmed by the presence of raised CSF pressure > 20 cm H_20.

GENERAL MEASURES

Not all patients require definitive treatment.
Regular monitoring of visual fields is crucial.
Weight loss.
Repeated lumbar punctures.
Consider surgery if there is progression of visual defects, despite medical therapy, visual loss at onset or severe papilloedema.
Stop medicines known to be associated with benign intracranial hypertension (e.g. doxycycline, amiodarone, levodopa, corticosteroids).

MEDICINE TREATMENT

All patients need to be discussed with a specialist.

For visual involvement, persistent headaches, or severe papilloedema:

- Acetazolamide, oral, 1–2 g daily.

OR

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.

14.5 INFECTIOUS AND PARASITIC CONDITIONS

14.5.1 MENINGITIS

G00/G01*/G02.1*

**N. meningitidis* and *H. influenzae* Type B are notifiable diseases.

DIAGNOSIS

Lumbar puncture for chemistry and bacteriology or fungal investigation should be done in all cases, if safe.

Computed tomography needs to 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 nutritional and hydration status.
Nurse patients in a quiet, semi-dark surrounding.
In uncomplicated bacterial meningitis, repeated lumbar punctures are of no benefit.
Prompt initiation of antibiotic therapy is associated with improved outcomes.

MEDICINE TREATMENT

All patients require sufficient analgesia:

- Paracetamol, oral, 1 g 4–6 hourly when required to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum dose: 4 g in 24 hours.

AND/OR

- Ibuprofen, oral, 400 mg then 8 hourly with meals, if needed.

AND/OR

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

Antibiotic therapy

Empiric therapy for bacterial meningitis, until sensitivity results are available:

- Ceftriaxone, IV, 2 g 12 hourly for 10 days. *LoE:III*[xv]

Adjunctive corticosteroids have not been demonstrated to be of value.

Meningococcal meningitis

For confirmed meningococcal disease only:

- Benzylpenicillin (penicillin G), IV, 20–24 million units 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 (see below). This is not required if the patient was treated with ceftriaxone for ≥ 24 hours.

- Ciprofloxacin, oral, 500 mg immediately as a single dose.

Prophylaxis of contacts:

Only for close household contacts.

Only healthcare workers who resuscitate patients before they received appropriate treatment should receive prophylaxis.

- Ciprofloxacin, oral, 500 mg immediately as a single dose.

Pneumococcal meningitis

This organism may be associated with other respiratory disease or CSF leaks.

If sensitive to penicillin:

- Benzylpenicillin (penicillin G), IV, 20–24 million units daily in 4–6 divided doses for 10 days.

If resistant to penicillin:

- Ceftriaxone, IV, 2 g 12 hourly for at least 10 days.

Haemophilus influenzae

- Ceftriaxone, IV, 2 g 12 hourly for 10 days.

Severe penicillin allergy:

- 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).

AND

- Rifampicin, oral, 600 mg 12 hourly.

Note: Consult a microbiologist/infectious diseases specialist.

Tuberculous meningitis

CSF findings are extremely variable. Generally lymphocytes predominate, however, polymorphs may initially predominate 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.

- Dexamethasone, IV, 12 mg 12 hourly.

Followed with: *LoE:I*[xvi]

- Prednisone, oral, 120 mg daily.
    - After 1 week, taper dose over next 6 weeks. (Refer to page xxvii for an example of a dose reduction regimen).

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.
In HIV-uninfected patients the aim is to cure the infection.

Initial therapy:

- 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 6 weeks, provided that there are no neurological complications and follow up CSF culture at 2 weeks is negative (India ink or Cryptococcus Latex Agglutination Test (CLAT) may still be positive).
        - In patients with neurological complications or persistent positive culture: Consider lengthening the initial phase of therapy to 8 weeks in consultation with a specialist.

AND

- Fluconazole, oral, 800 mg daily.

Maintenance therapy:

- Fluconazole, oral, 200 mg daily for ≥ 6 months, in consultation with a specialist.

Follow all patients closely for relapses.

LoE:III[xvii]

Therapeutic lumbar puncture:
This should be considered as the intracranial pressure is often elevated with a communicating hydrocephalus.
See section 10.2.4: Cryptococcosis.

14.5.2 VIRAL MENINGOENCEPHALITIS

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 mildly raised cells (< 500), mainly lymphocytes (early on polymorphs may predominate). Most cases do not require specific therapy, other than analgesia.

MEDICINE TREATMENT

Analgesia, i.e.:

- Paracetamol, oral, 1 g 4–6 hourly when required to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum dose: 4 g in 24 hours.

AND

- NSAIDs, e.g.:
- Ibuprofen, oral, 400 mg immediately then 8 hourly with meals, if needed.

LoE:III[xviii]

OR

- 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, but in this condition may be additionally haemorrhagic in nature. A medial temporal focus on EEG or MRI/CT neuro-imaging is strongly supportive of the diagnosis, and positive HSV PCR test on CSF is diagnostic.

- Aciclovir, IV, 10 mg/kg 8 hourly for 21 days.
  - 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.

Treat seizures appropriately with phenytoin/carbamazepine. See section 14.3: 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.

14.5.3 MENINGOVASCULAR SYPHILIS

A52.1

DIAGNOSIS

Lumbar puncture typically shows lymphocytosis with mildly elevated protein and low/normal glucose.
Serum syphilis serology: a negative TPHA excludes the diagnosis; RPR may be negative.
CSF syphilis serology: VDRL in CSF is often of low titre, and may be negative; a negative CSF FTA-abs excludes the diagnosis of neurosyphilis.

MEDICINE TREATMENT

- Benzylpenicillin (penicillin G), IV, 20 million units daily in 4–6 divided doses for 10 days.

LoE:III

Severe penicillin allergy:

Refer for consideration of desensitisation and subsequent treatment with benzylpenicillin at a referral centre.

14.5.4 BRAIN ABSCESS

G07*

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.

14.5.5 ANTIMICROBIAL USE IN PATIENTS WITH HEAD INJURIES

S06.00

MEDICINE TREATMENT

Basal skull fractures

Antibiotic prophylaxis is not indicated.

Penetrating brain injuries

Antibiotics are given for therapy.

- 3rd generation cephalosporin, e.g.:
- Ceftriaxone, IV, 2 g 12 hourly for 7 days.

LoE:III

14.5.6 NEUROCYSTICERCOSIS

B69.0

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.
  - > 60 kg: 400 mg.
  - < 60 kg: 7.5 mg/kg to a maximum of 800 mg daily.
  - Do not use in pregnancy.

AND *LoE:II*[xix]

- Prednisone, oral, 60 mg daily for 8 days.

LoE:II[xx]

Anticonvulsants, if required.

See section 14.3: Epilepsy.

14.6 MOVEMENT DISORDERS

G25.9

DESCRIPTION

Abnormalities of movement/initiation of movement, divided into those with reduction of movement (hypokinesia or bradykinesia), or those with excessive movements (hyperkinesia).

14.6.1 PARKINSONISM

G20

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, and
» exclude secondary forms.

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.

PRIMARY PARKINSONISM

Bradykinesia, rigidity and postural disturbance:

- Carbidopa/levodopa, 25/100 mg, oral, ½ tablet 8 hourly.
  - Increase dose in consultation with a specialist.

<u>If optimal control has not been achieved, consider an alternative diagnosis or changing to a medicine containing a higher dose of levodopa:</u>

- Carbidopa/levodopa 25/250 mg. Specialist initiated.

Drug-induced parkinsonism:

Anticholinergics have a very small role in this setting and should be used with caution.

- Anticholinergic agent, e.g.:
- Orphenadrine, oral, 50 mg 8 hourly.

LoE:III[xxi]

Tremor only:

- Consider anticholinergic agent, e.g.:
- Orphenadrine, oral, 50 mg 8 hourly. Increase gradually according to clinical response or maximum dose of 400mg daily
  - Usual dose: 150–250 mg daily.

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

REFERRAL

» No improvement or poor control with treatment.
» Increasing on/off phenomenon.
» Dyskinesias.

14.6.2 ESSENTIAL TREMOR

G25.0

GENERAL MEASURES

Exclude and manage alternate causes, such as drugs, thyrotoxicosis, hyperadrenergic states and psychiatric disorders. 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[xxii]

14.6.3 CHOREA

G25.5

DESCRIPTION

Involuntary random, irregular movements.
Aetiology is classified as:

» primary – Huntington's chorea, benign hereditary chorea and others; or
» secondary – due to Sydenham's chorea, vascular pathology, metabolic, endocrine and infective conditions, amongst others.

MEDICINE TREATMENT

To be prescribed by a specialist only.

- Haloperidol, oral, 0.5–5 mg 2–3 times daily.

14.7 NEUROPATHY

G62

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 neuropathy include:

» alcohol,
» diabetes,
» HIV infection,
» thiamine deficiency, vitamin B12 deficiency, (although the latter more commonly presents as subacute combined degeneration of the cord.)
» drugs (e.g. isoniazid, stavudine, metronidazole, amiodarone)
» 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. over ≤ 7 days) 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, develop chronic bedsores and become wheel chair-bound.

MEDICINE TREATMENT

Most cases respond to management of the underlying disease process or removal of the aetiological agent.

Neuropathic pain (i.e. pain due to a disease or injury of the central or peripheral nervous system)

- Amitriptyline, oral, 25–75 mg daily.

OR

Carbamazepine, oral, 200–1200 mg daily in divided doses.

Isoniazid–induced polyneuropathy

- Pyridoxine, oral 75 mg daily for 3 weeks.
  - Follow with 25–50 mg daily.

Post-herpes zoster neuropathy
Note: Aciclovir is not beneficial in treating this condition.

- Amitriptyline, oral, 25–75 mg daily.

LoE:I[xxiii]

AND/OR

- Carbamazepine, oral 200–1200 mg daily dose in divided doses.
  - Beware of possible drug interactions in patients on ART.

Bells palsy
Prevention of corneal ulceration is important. Consider lubrication (see section 18.9; Eye Chapter), eye patch and chewing.
In patients presenting within 72 hours of onset of symptoms of a Bells palsy who are HIV uninfected and have no evidence of local herpes zoster or suppurative otitis media, corticosteroids improve the probability of facial recovery at 3 months (83% vs. 63.6%), although even without treatment over 80% will recover by 9 months. The addition of aciclovir is not of proven benefit.

- Prednisone, oral, 50 mg daily for 10 days.

LoE:I[xxiv]

REFERRAL

» Electrophysiological studies may be needed in the diagnostic assessment, although many common causes do not warrant specialist investigations, e.g. polyneuropathies due to diabetes mellitus, HIV, drugs, and alcohol. These cases may initially be managed locally, with referral of non-responding or atypical cases.
» Gullain-Barré Syndrome: referral criteria are progressive, extensive paralysis with impending respiratory failure, bulbar palsy and swallowing problems, and aspiration, as well as for diagnostic confirmation.

14.8 ACUTE MYELOPATHY

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 not perform a lumbar puncture, until obstructive lesions of the spinal cord have been excluded clinically or radiologically.

REFERRAL

All patients for urgent imaging.

14.9 MULTIPLE SCLEROSIS

G35

DESCRIPTION

A demyelinating disease of the central nervous system, characterised by 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.

14.10 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[xxv]

Corticosteroids and azathioprine should only be used in consultation with a specialist.

14.11 OEDEMA, CEREBRAL

G93.6

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.

14.11.1 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 with 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 specific 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.

14.11.2 BRAIN OEDEMA DUE TO TRAUMATIC INJURY

S06.1

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

For raised intracranial pressure, pending a definitive neurosurgical procedure only:

- 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 used in this setting have a harmful effect.

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CHAPTER 15

PSYCHIATRIC DISORDERS

15.1 AGGRESSIVE DISRUPTIVE BEHAVIOUR IN ADULTS

R45.1

DESCRIPTION

Agitated and acutely disturbed patients, with or without a known psychiatric condition.

Note: Many acute medical conditions and substance abuse can present with agitation and aggressive behaviour.

GENERAL MEASURES

» Ensure the safety of the patient and those caring for them.
» Elderly and frail patients may be vulnerable to falls and further injury if sedated.
» Physical restraint should be used only when necessary to protect the patient and others in an acute setting, and for as short a period of time as possible, at all times monitoring the safety of the patient.

MEDICINE TREATMENT

Always use non-pharmacological de-escalation techniques first:

» Calm the patient.
» Manage in a safe environment.
» Ensure the safety of all staff members.

Offer oral treatment:

- Benzodiazepines: *LoE:II*[I]
- Lorazepam, oral, 4 mg, immediately.
  OR *LoE:III*[II]
  Clonazepam, oral, 2 mg, immediately.
  OR *LoE:III*[III]
  Diazepam, oral, 10 mg, immediately.
  OR *LoE:III*[IV]
  Midazolam, oral or buccal, 15 mg, immediately. *LoE:III*[V]

If oral treatment fails after 30–60 minutes,
OR
If the patient is placing themselves and others at significant risk:

Parenteral treatment:

- Benzodiazepines: *LoE:II*[VI]
- Lorazepam, IM, 4 mg, immediately.
  OR *LoE:I*[VII]
  Midazolam, IM, 15 mg immediately.
  OR
  Clonazepam, IM, 2 mg, immediately.
  OR
  Diazepam, IV, 10 mg, immediately.
  - Repeat after 30–60 minutes if needed.

OR

Haloperidol, IM, 5 mg, immediately.
AND
Promethazine, deep IM, 25–50 mg.

LoE:II[VIII]

Repeat after 30–60 minutes if needed.
See the note regarding benzodiazepines in section 15.2: Confusional states/delirium.

If haloperidol is unavailable, use chlorpromazine without promethazine:

- Chlorpromazine, deep IM, 25–50 mg.
  - May be repeated as necessary 4 times in 24 hours. *LoE:III*[IX]

If patient is known to suffer from schizophrenia and is not neuroleptic naive:

- Zuclopenthixol acetate, IM, 50–150 mg.
  - Repeat after 2–3 days, if necessary. *LoE:III*[X]

If patient develops acute dystonia:

- Anticholinergic agent, e.g.:
- Biperiden, IM/IV, 2 mg.
  - Repeat as necessary.
  OR
  Promethazine, deep IM, 25–50 mg.
  - In the elderly 25 mg.

Repeated doses of high potency antipsychotics may lead to the development of the life-threatening neuroleptic malignant syndrome, characterized by hyperthermia, muscle rigidity, autonomic dysfunction, and alterations in consciousness. Serum CK is typically markedly elevated. If suspected, stop antipsychotic, and institute supportive care.

Always monitor vital signs of sedated patients:

» Vital signs: pulse, respiratory rate, blood pressure, temperature (If concerned about respiratory depression, monitor with oximeter).
» Monitor every 5–10 minutes for the first hour, and then every 30 minutes until the patient is ambulatory.

15.2 CONFUSIONAL STATES/DELIRIUM

F05.9

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 behavior 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

Control the acute disturbance.
Investigations need to be done to exclude or diagnose an underlying medical problem, the treatment of which is the primary management.

MEDICINE TREATMENT

Treat underlying medical condition, if present.

Acute management

For agitated and acutely disturbed patient:

- Haloperidol, IM, 5 mg.
  - This can be repeated in 60 minutes, if required.
  - Maximum dose: 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*[xi]
» 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.

15.3 BIPOLAR DISORDER

F31.9

DESCRIPTION

Bipolar disorder is a lifelong illness, which may have an episodic, variable course. The presenting episode may be manic, hypomanic, or depressive. By definition, a diagnosis of bipolar disorder requires either a current or previous episode of mania or hypomania, and a past or current major depressive episode.

An episode of mania is typically characterised by an elevated mood (e.g. extreme happiness or irritability). This mood disturbance may be associated with increased energy/goal-directed activity, talkativeness and flight of ideas, a reduction in the need for sleep, and grandiosity and/or religiose delusions. Even during periods of relative euthymia, i.e. without either clearly manic or depressive features, patients may still experience impairments in psychosocial functioning.

GENERAL MEASURES

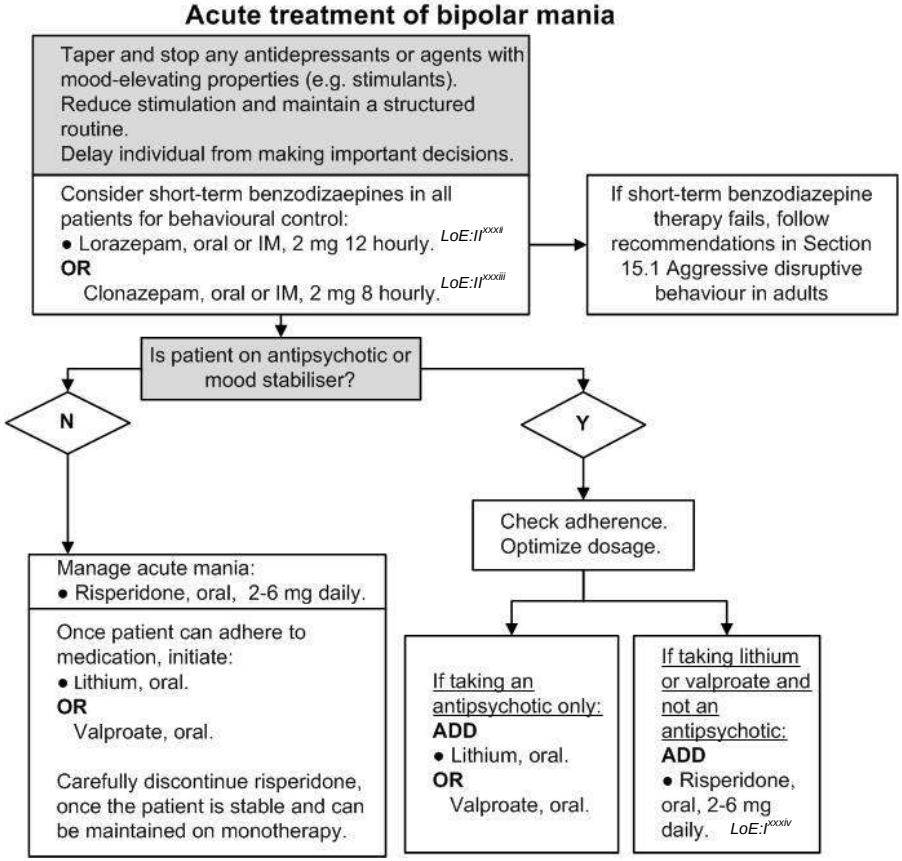
Hospitalisation may be required during acute mania.
Psychotherapy, usually after the manic episode has been controlled with medication.
Family therapy and psycho-education of patient and family to increase adherence and knowledge of the condition.
In severe cases, psychiatrist directed electroconvulsive therapy may be required.

MEDICINE TREATMENT

Manic episodes

Acute management

Manage as for any aggressively disruptive adult (see section 15.1: Aggressive disruptive behaviour in adults).



Maintenance therapy

Indicated once the patient is cooperative.

Lithium is the treatment of choice. The full therapeutic effect may require days to weeks. Check renal and thyroid function before initiating lithium therapy.

CAUTION
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.

- 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 enhance adherence.
  - Monitor trough (pre-dose) plasma levels after 5 days.
  - 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 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.
  - Monitor creatinine level, sodium and potassium 6 monthly.

LoE:III[xii]

AND/OR

- Valproate, oral, 300 mg 12 hourly.
  - Increase dose incrementally to a maximum dose of 20 mg/kg/day 12 hourly.

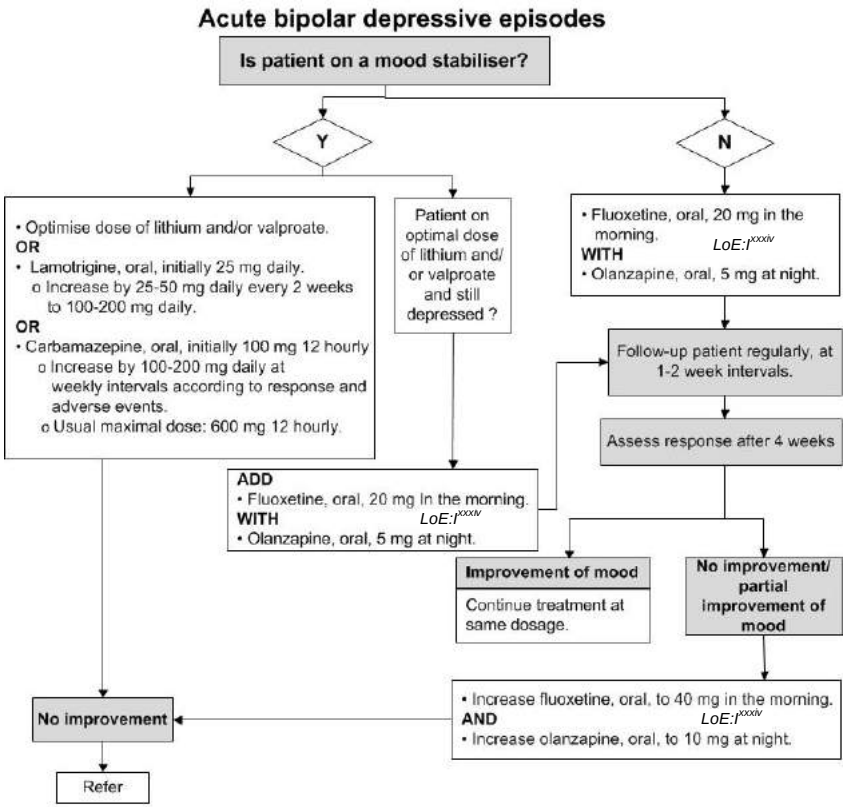
LoE:III

Acute bipolar depressive episodes

Can be difficult to manage, have a high suicide risk, and is best managed in consultation with a psychiatrist.

Note:

» Do not use antidepressants as monotherapy in bipolar patients.
» Patients on atypical antipsychotics (e.g. risperidone, amisulpiride olanzapine and clozapine) need regular monitoring for metabolic side-effects:
  - Weight, BMI and waist circumference.
  - Serum glucose and lipids.



Optimising dose of lithium and valproate:

- **Lithium**, oral, 5 mg/kg/dose 12 hourly.
  - This takes some weeks to work and during this period review the patient at least weekly, and ensure a supportive/reliable environment.
  - Target trough plasma levels 0.4-0.8 mmol/L
  - Dosing in patients with renal impairment is complex and should be done using therapeutic drug monitoring in consultation with a specialist.

- **Valproate**, oral, 600 mg daily.
  - Increase dose to 20 mg/kg/day, divided in a 12 hourly dose.
  - Valproate may be given as a daily dose, once the patient has been stabilised.

REFERRAL

To psychiatric services:

» Mixed features or rapid cycling bipolar disorder.
» Depressive episodes in bipolar patients not responding to second line treatment.
» Manic episodes not responding to treatment.

15.4 DEPRESSIVE DISORDER, MAJOR

F32.9

DESCRIPTION

Major depression is characterised by a depressed mood (sadness) accompanied by loss of interest and decreased experience of pleasure, and social withdrawal. Irritability may also occur, especially amongst adolescents. Reduction in sleep, appetite, energy, motivation, concentration and memory may occur. The patient may report feelings of worthlessness and hopelessness, and express thoughts of suicide. Symptoms are usually present for at least two weeks and impact on the person's ability to function normally.

Exclude underlying medical conditions that may present with depression, e.g. thyroid disease.

GENERAL MEASURES

Supportive psychotherapy.
Counseling of patient and family
Address social factors.
Electroconvulsive therapy is indicated under specific circumstances in consultation with a specialist.

MEDICINE TREATMENT

Antidepressant therapy

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.
The choice of therapy is guided by co-morbid states, e.g. avoid TCAs in patients with cardiac disease or a high risk of overdose or in the elderly.
Following remission continue pharmacotherapy for at least another 6 months.
Thereafter taper off slowly to avoid discontinuation symptoms. If there is a recurrence, reinstitute the medicineat the same dose.
Patients with ≥ 3 episodes may require maintenance pharmacotherapy to be reviewed every 2 years.

Adolescents with depression are at increased risk of suicidal ideation when initiated on SSRIs.

Major depressive disorder

First line

- Selective serotonin reuptake inhibitors, e.g.:
- Fluoxetine, oral.
  - Initial dose: 20 mg
  - If there is no or partial response after 4–8 weeks, increase to 40

mg, if well tolerated.

OR

Citalopram, oral.

- Initial dose: 20 mg
- If there is no or partial response after 4–8 weeks, increase to 40 mg, if well tolerated.

LoE:I[xiii]

OR

- Tricyclic antidepressants, e.g.:
- Amitriptyline, oral, at bedtime.
  - Dose range: 75 – 150 mg.
  - Start with: 25 mg, increase by 25 mg/day at 3–4 day intervals.

LoE:III[xiv]

Second line

If on an SSRI change to another SSRI (citalopram) or a TCA.
If on a TCA change to a SSRI.
If initially on fluoxetine, wait for 7 days after stopping fluoxetine before starting the other SSRI.

REFERRAL

» Inadequate response to treatment.
» High suicide risk.
» Psychotic features.

15.5 PERSISTENT DEPRESSIVE DISORDER (DYSTHYMIC DISORDER)

F34.1

DESCRIPTION

This condition presents with a depressed mood present for most of the time for at least two years and tends to be chronic. Symptomatically it is similar to major depression but does not fulfill the diagnostic criteria. In addition, the depressed mood is continuous rather than episodic. Always consider the possibility of substance abuse.

GENERAL MEASURES

As for Major Depressive Disorder.

MEDICINE TREATMENT

As for Major Depressive Disorder.

REFERRAL

No response to treatment.

15.6 GENERALISED ANXIETY DISORDER

F41.1

DESCRIPTION

Generalised anxiety disorder is characterised by excessive and inappropriate worry/concern about a range of issues. The patient may report disturbances in sleep, concentration, or mood. Physical symptoms such as muscle tension or tremulousness may also be reported.

GENERAL MEASURES

Psychotherapy.

Most patients can be treated as outpatients, but some may need to be admitted.

MEDICINE TREATMENT

Indicated where symptoms are interfering with normal functions of daily living.

Where there is concomitant drug/alcohol dependence or co-morbid major depressive episode, an antidepressant may be more appropriate.

Acute management

For an acute episode or intense prolonged anxiety:

- Benzodiazepines, e.g.:
- Diazepam, oral, 2–5 mg as a single dose.
  - Repeat if required up to 12 hourly.
  - Duration of therapy: up to 2 weeks tapering off to zero within 6 weeks.

See the note regarding benzodiazepines in section 15.2: Confusional states/delirium.

Maintenance therapy

- SSRI, e.g.:
- Citalopram, oral, 10–40 mg daily.

  OR *LoE:III*[xv]

  Fluoxetine, oral, 10–40 mg daily.
  - Duration of therapy: variable, although the condition tends to be chronic.
  - Extended medicine treatment should be monitored by a specialist.

LoE:I[xvi]

CAUTION

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.

REFERRAL

Ongoing symptoms despite treatment.

15.7 OBSESSIVE-COMPULSIVE DISORDER

F42.9

DESCRIPTION

This condition is characterised by the presence of persistent intrusive thoughts or concerns, and is usually associated with compulsions, which are mental acts or behaviours related to the obsessions, e.g. excessive hand washing. Obsessive thoughts and compulsions may interfere with daily functioning. The features are usually distressing to the patient.

MEDICINE TREATMENT

- Selective serotonin reuptake inhibitors, e.g.:
- Fluoxetine, oral.
  - Initial dose: 20 mg
  - If there is no or partial response after 4–8 weeks, increase to 40 mg, if well tolerated.

OR *LoE:III*[XVII]

Citalopram, oral.

- Initial dose: 20 mg
- If there is no or partial response after 4–8 weeks, increase to 40 mg, if well tolerated.

LoE:III[XVIII]

REFERRAL

Inadequate response to treatment.

15.8 PANIC DISORDER

F41.0

DESCRIPTION

A panic attack is characterised by an acute onset of intense anxiety accompanied by a sense of dread/impending threat, usually for no apparent reason. The patient will experience significant fear and emotional discomfort, typically peaking within 10 minutes and resolving within 30 minutes. There will usually be accompanying physical symptoms such as rapid pulse/palpitations, shortness of breath, dizziness and sweating.

Panic disorder is diagnosed if panic attacks recur, with intervening periods of comparative freedom from anxiety between attacks.

GENERAL MEASURES

Psycho-education and reassurance.
Psychotherapy, e.g. cognitive-behaviour therapy.
Exclude an underlying medical condition, e.g. thyrotoxicosis.

MEDICINE TREATMENT

Panic attack

Acute management

The initial aim is to control the panic symptoms and exclude an underlying medical cause.

- Benzodiazepines, repeated as necessary to control symptoms, e.g.:
- Lorazepam, oral, 2 mg, immediately.
  OR
  Clonazepam, oral, 1 mg, immediately.
  OR
  Diazepam, oral, 5 mg, immediately.
  OR
  Midazolam, oral or buccal, 7.5 mg, immediately.

See the note regarding benzodiazepines in section 15.2: Confusional states/delirium.

Panic disorder

- SSRI, e.g.: *LoE:III*[xix]
- Citalopram, oral, 10–40 mg daily.
  OR
  Fluoxetine, oral, 20–40 mg daily.
  - Initiate at low dose and gradually titrate to therapeutic dosages according to tolerability.
  - SSRI's onset of action in panic disorder is relatively slow, and at least 8 weeks of adequate dose treatment is required before efficacy can be assessed.
  - Duration of SSRI therapy: variable, initially 6 months–1 year.
  - Long term medicine treatment may be necessary.
  - Relapses may occur when treatment is discontinued.
  - Consider short term co-administration of a benzodiazepine, due to the slow onset of action and the potential for increased anxiety during the initial phase of treatment with antidepressants.

REFERRAL

Treatment resistant panic disorder or need for benzodiazepine treatment beyond 6 weeks.

15.9 ACUTE STRESS DISORDER AND POST-TRAUMATIC STRESS DISORDER

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 post-traumatic stress disorder last longer than 4 weeks, and may arise more than 4 weeks after the traumatic incident.

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[xx]

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*[xxi]

  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 trail of treatment is 8–12 weeks, before an alternative treatment should be considered.

REFERRAL

» Persistent symptoms.
» Inadequate response to treatment.

» Co-morbid conditions.

15.10 PSYCHOSIS, ACUTE

DESCRIPTION

Psychosis is characterised by loss of contact with reality. The patient may experience perceptual disturbances, e.g. auditory hallucinations, and delusions. There may be accompanying behavioural disturbances related to both perceptual and thought disturbances. This presentation is characteristic of psychotic disorders, such as schizophrenia. However, this presentation may occur in other psychiatric conditions (e.g. bipolar mania, major depression) or medical conditions (e.g. certain types of epilepsy). The presentation may be acute or chronic. Patients generally have no insight into their symptoms and may be resistant to intervention.

See section 15.3: Bipolar Disorder and section 15.11: Schizophrenia.

15.11 SCHIZOPHRENIA

F20-F20.9

DESCRIPTION

Schizophrenia is characterised by psychotic episodes, and is typically accompanied by deterioration in social, general and occupational functioning. Whilst the presentation may be acute, typically the illness has a chronic course.

GENERAL MEASURES

Supportive psychotherapy and psycho-educational group therapy for patients and family members.

MEDICINE TREATMENT

Psychotic episode

Acute management

For the agitated and acutely disturbed patient: see Section 15.1: Aggressive disruptive behaviour in adults.

First episode:

- Haloperidol, oral.
  - Initial dose: 1 mg daily, increasing to 5 mg daily. *LoE:III*[xxii]

OR

- Risperidone, oral.
  - Initial dose: 2–4 mg daily. *LoE:I*[xxiii]
  - 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.

OR

<u>If adherence is a problem or patients' preference:</u>

- Depot antipsychotic, e.g.:
- Flupenthixol decanoate, IM, 20–40 mg every 4 weeks.

  OR *LoE:III*[xxiv]

  Fluphenazine decanoate, IM, 12.5–50 mg every 4 weeks.

  OR *LoE:III*[xxv]

  Zuclopenthixol decanoate, IM, 200-600 mg every 4 weeks. *LoE:III*[xxvi]

<u>If extrapyramidal side-effects occur with the lowest effective dose of antipsychotic medication:</u>

Switch from haloperidol or chlorpromazine to risperidone.

<u>If this is not tolerated or if the extrapyramidal side-effects persist, add:</u>

- Anticholinergic agent, e.g.:
- Orphenadrine, oral, 50–150 mg daily according to individual response
  - Usual dose: 50 mg 12 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 akathisia (a subjective unpleasant state of inner restlessness where there is a strong desire or compulsion to move) develops:</u>

- Propranolol, oral,
  - Start at 20mg daily and titrate as needed up to 80 mg 8 hourly. *LoE:II*[xxvii]
  - Monitor pulse and blood pressure.

Maintenance therapy

» Specialist initiated.
» Psychiatrist to review patients every 6 months.

Treatment resistant cases, not responding to risperidone and/or haloperidol must be referred to tertiary level care. Psychiatrists may initiate other second generation antipsychotics; and in treatment resistant cases clozapine.

» Atypical antipsychotics need regular monitoring for metabolic side-effects.
  - Weight, BMI and waist circumference
  - Serum glucose and lipids

» Clozapine needs frequent WCC monitoring: Weekly for the first 18 weeks, then every 2 weeks for the next 6 months, then monthly.
  - If neutrophils < 1.5 x10^9/L, stop the medication.
  - If neutrophils < 0.5x10^9/L, refer to specialist medical care.

REFERRAL
» Psychotic patients with uncertain diagnosis.
» Patients who relapse and refuse treatment or become aggressive or suicidal, refer to the mental health care act in terms of involuntary treatment.
» Patients with complications due to medication.
» Poor response to therapy.

15.12 WITHDRAWAL FROM SUBSTANCES OF ABUSE

15.12.1 ALCOHOL
F10.4

GENERAL MEASURES
The following patients should be admitted for detoxification:
» past history of convulsions
» past history of psychosis
» suicidal ideation
» significant medical co-morbidity 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*[xxviii]

- 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.

15.12.2 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 15.2: Confusional states/Delirium for management.
Cardiac monitoring and oximetry should be used when administering large doses of benzodiazepines.
Assess for infections and other co-morbid 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.

15.12.3 OPIATE WITHDRAWAL, E.G. HEROIN

F11.2

DESCRIPTION

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
» Gooseflesh
» Rhinorrhoea and lacrimation
» Myalgia
» Diarrhoea

MEDICINE TREATMENT

Mild withdrawal

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 to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose. *LoE:III*
  - Maximum dose: 4 g in 24 hours.

For muscle pains:

- 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

Hospitalise patient.

Substitution treatment

Day 1: Only if clinical signs of withdrawal are present.

- Methadone, oral, 5–10 mg. *LoE:III*[xxix]
  - If symptoms are still present after 2-4 hour, give another 5–10 mg.
  - The initial dose to suppress withdrawal symptoms may be repeated after 12 hours.
  - The total 24 hour dose should rarely be more than 30 mg. Consult a person experienced in opioid withdrawal when prescribing > 30 mg/day.

Day 2:
- Methadone, oral.
  - Repeat total dose of day 1 as a single or 2 divided doses.
  - Monitor for on-going sign and symptoms of withdrawal.
  - If the sing 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 30 mg.

Day 3 onwards:
- Methadone, oral.
  - Decrease by 5 mg/day to a total of 10 mg. Thereafter, reduce by 2 mg/day.
  - The withdrawal regimen may be shortened if the patient's withdrawal symptoms allow it.
  - Repeat total dose of day 2 if top-ups were needed and begin reductions on day 4.

If methadone is unavailable:
- Tramadol, oral, 200 mg 12 hourly for 14 days may attenuate withdrawal symptoms.

LoE:II[xxx]

15.12.4 STIMULANT WITHDRAWAL, INCLUDING COCAINE AND METHAMPHETAMINES

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.

15.12.5 METHAQUALONE 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.

15.12.6 CANNABIS WITHDRAWAL

F12.2

Withdrawal is rarely dangerous and poorly tolerated.
Assess for other accompanying psychiatric disorders e.g. mood or psychosis.

15.12.7 BENZODIAZEPINE WITHDRAWAL

F13.2

GENERAL MEASURES

The therapeutic relationship between client and doctor is extremely important in initiating dose reduction. Take time to explain concepts like tolerance and withdrawal to the patient and then convince them that stopping the benzodiazepine is the best thing to do. Encourage the patient not to seek medication from other doctors. Negotiate each reduction with the patient.

Avoid abrupt withdrawal of benzodiazepines.
Withdrawal from benzodiazepines takes time.

The patient will require regular monitoring and motivation.

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:

- chlordiazepoxide 15 mg
- lorazepam 1 mg
- alprazolam 0.5 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.

Patients are not always truthful about the amount of benzodiazepine used.

Even if the equivalent dose of diazepam is higher than 30 mg/day, start on 30 mg/day in divided doses and adjust upwards or downwards, depending on clinical response.

Decrease the dose of diazepam every 2 weeks by 2.5 mg. If symptoms reappear increase the dose a little and reduce dose over longer intervals.

Withdrawal symptoms include anxiety, nervousness, irritability, depersonalisation, delirium and seizures, increased sweating, sound

sensitivity, nausea, difficulty concentrating, myoclonus, tremor, weakness and fatigue**.**

REFERRAL

All patients treated for substance withdrawal should be referred to Social Services for rehabilitation and aftercare.

15.13 INSOMNIA

G47.0/G47.9

DESCRIPTION

Insomnia may be an independent disorder, or associated with co-morbid conditions. Insomnia may persist despite successful treatment of the co-morbidity, 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 refresh, 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[xxxi]

REFERRAL

Patients with chronic insomnia.

15.14 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 the dose.
Note: Fluoxetine seldom causes discontinuation symptoms because of its long half life.

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CHAPTER 16

RESPIRATORY SYSTEM

16.1 ASTHMA, ACUTE

J45

GENERAL MEASURES

Ensure adequate hydration.

In patients presenting with asthma for the first time, 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, PEF < 50% of predicted/personal best - see PEF charts on pg lxxvi) should ideally be closely monitored in a High Care or an Intensive Care Unit.

MEDICINE TREATMENT

If hypoxic:

- Oxygen.

Continuous nebulisation is preferable to intermittent nebulisation with $ß_2$-agonists for the 1st hour of therapy.

- Salbutamol 5 mg (1 mL 0.5% respiratory solution with 4 mL sodium chloride 0.9%). *LoE: I^{I}*
  - Nebulise continuously (refill the nebuliser reservoir every 20 minutes) at a flow rate of 6–8 L/minute until PEF > 60% of predicted/personal best.
  - If response to nebulised salbutamol is poor, add ipratropium bromide 0.5 mg with the 1st refill of the nebuliser reservoir. *LoE: II^{II}*
  - Once a patient reaches 60% of their predicted/personal best PEF, repeat salbutamol 5 mg or fenoterol 1.25–2.5 mg 4 hourly.
    Note: Fenoterol should not be used for continuous nebulisation, as a maximum safe dose in this setting has not been established. *LoE:III^{III}*

Continue nebulisations until PEF returns to 80% of predicted/ personal best, at which point the patient can be converted to:

- Salbutamol MDI, 2 puffs (200 mcg) as required.

AND

- Prednisone, oral, 40 mg immediately (within 1 hour of presentation).

Follow with:

- Prednisone, oral, 40 mg daily for 7 days. *LoE:III^{IV}*

OR

In patients who cannot use oral therapy or are vomiting:

- Hydrocortisone, IV, 100 mg 6 hourly.

Once oral medication can be taken, switch to: *LoE:II[V]*

- Prednisone, oral, 40 mg daily for 7 days

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 sulphate, IV, 2 g in 100 mL sodium chloride 0.9%, as a single dose, administered over 20 minutes. *LoE: I[VI]*

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).

Intercurrent bacterial infections *LoE: I[VII]*

Bacterial infections are seldom present in acute exacerbations of asthma and yellow sputum 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

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 >15% in PEF 10 minutes after receiving a $ß_2$-agonist.	» 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 page lxxviii).

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.

Maintenance therapy

Inhaled corticosteroids (ICS) are the mainstay of treatment in chronic asthma:

- ICS, e.g.:
- Beclometasone, inhaled, 200 mcg 12 hourly starting dose.
  - Control not optimal after 1 month: Increase dose to 400 mcg 12 hourly.
  - Well and stable after 6 months: reduce dose by 200 mcg per day every month, to determine the minimum dose to maintain control or until a dose of 200 mcg, daily is achieved.
  - Dose adjustments may be required at change of seasons.

LoE: I[VIII]

AND

As reliever/rescue therapy:

- Short acting ß$_2$-agonists, e.g.:
- Salbutamol, MDI, 200 mcg, 6 hourly as necessary.

If insufficient response to high dose ICS (800 mcg beclomethasone daily) and salbutamol, replace beclomethasone with:

- Long-acting β$_2$-agonist/corticosteroid combination inhaler, e.g.:
- Salmeterol/fluticasone 50/250, one puff 12 hourly.

AND

LoE: I[IX]

As reliever/rescue therapy:

- Short acting ß$_2$-agonists, e.g.:
- Salbutamol, MDI, 200 mcg, 6 hourly as necessary.

Failure of above therapy:

- While awaiting appointment with specialist.

ADD

- Prednisone, oral 10 mg daily. Prednisone should not be used as maintenance therapy but only as a bridging step while awaiting review by a specialist.

LoE: III

For short-term exacerbations in patients not responding to the above, while awaiting review with a specialist:

- 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 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 postural drainage is the mainstay of therapy and must be emphasised and demonstrated to the patients.

» Regular home physiotherapy, 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 sputum becomes more purulent or sputum volume is greater volume than usual. Antibiotic choices should be guided by sputum microscopy, culture and sensitivity.

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*[x]

Severe penicillin allergy:

- Moxifloxacin, oral, 400 mg daily for at least 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 2 g, IV, daily, until patient apyrexial for 24 hours.

Follow with: *LoE:I*[xi]

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

If pseudomonas infection is suspected (confirm on culture): *LoE:III*[xii]

ADD

- Ciprofloxacin, oral, 750 mg 12 hourly for 7 days.

Caution

Irrational use of quinolones contributes to the emergence of XDR-TB and potential masking of active TB.

LoE:II[xiii]

Severe penicillin allergy:

- Moxifloxacin, oral, 400 mg daily.

If penicillin allergic and unable to tolerate oral therapy:

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*[xiv]

- Moxifloxacin, oral, 400 mg 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-tuberculosis Mycobacteria which will not be detected by Xpert MTB/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

- 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/J44

DESCRIPTION

COPD is classified from stage 1 to stage 4. 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.

Spirometric classification of COPD ($FEV_1/FVC < 70\%$) severity based on % predicted post-bronchodilator FEV_1:

Stage 1	**Mild COPD** $FEV_1 \geq 80\%$ of predicted.
Stage 2	**Moderate COPD** $50\% \leq FEV_1 \leq 80\%$ predicted.
Stage 3	**Severe COPD** $30\% \leq FEV_1 \leq 50\%$ predicted.
Stage 4	**Very severe COPD** $FEV_1 < 30\%$; or $FEV_1 \leq 50\%$ with severe breathlessness at rest or minimal activity, or the presence of respiratory failure ($PaO_2 <$ 8 kPa), and/or cor pulmonale.

GENERAL MEASURES

Patients with clinical COPD should undergo spirometry to confirm and grade the severity of obstruction.
Patients should be screened for ongoing smoking and advised to stop at each visit.

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, starting with a Venturi mask that delivers not more than 24–28% (take care to avoid using oxygen flow rates above that recommended for the mask in use). If the patient's arterial $PaCO_2$ does not rise, the FiO_2 may be increased until a PaO_2 of 8kPa is reached (or oxygen saturation of 90–94%). On the other hand, the FiO_2 must be reduced to ≤ 24% if worsening hypercapnia occurs. Such 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 5 mg (1 mL 0.5% respiratory solution with 4 mL sodium chloride 0.9%).
    - 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).

Once clinically stabilised, nebulise with:

- Salbutamol 5 mg or fenoterol 1.25–2.5 mg
  - Repeat 4–6 hourly.

AND

- Prednisone, oral, 40 mg immediately.

Follow with:

- Prednisone, oral, 40 mg daily for 5 days. *LoE:I*[XV]

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:

- Prednisone, oral, 40 mg daily for 5 days.
  - Monitor response and clinical signs. *LoE:I*[XVI]

Antibiotic therapy

Patients with a moderate to severe exacerbation and who have ≥ 2 following symptoms should receive an antibiotic:

» increased dyspnoea,
» cough, or
» sputum production, especially if purulent.

- Amoxicillin, oral, 500 mg 8 hourly for 5 days. *LoE:III*[XVII]

For patients that have recently been exposed to amoxicillin, in the last 3 weeks:

- Amoxicillin/clavulanic acid, oral, 875/125 mg 12 hourly for 5 days. *LoE:III*[XVIII]

Severe penicillin allergy:

- Azithromycin, oral, 500 mg daily for 3 days. *LoE:I*[XIX]

Chronic therapy

COPD with any symptoms.

As initial therapy:

- Short acting β_2-agonist (SABA) e.g.:
- Salbutamol, MDI, 200 mcg 6 hourly as needed using a large volume spacer.

If no response in symptoms:

Replace with

- Long acting β_2-agonist (LABA), e.g.:
- Formoterol, inhaled 12 mcg 12 hourly. Specialist initiated. *LoE:I*[XX]

For frequent exacerbations (≥ 2 per year):

Replace with

- LABA/ICS combination, e.g.: (Specialist initiated)
  Salmeterol/fluticasone, inhalation, 25/125 mcg 2 puffs 12 hourly. *LoE:I*[XXI]

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[XXII]

Corticosteroids

Oral corticosteroids are not recommended for stable COPD.

For acute exacerbations:

- Prednisone, oral, 40 mg daily for 5 days. *LoE:I*[XXIII]

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.

Perioperative oral corticosteroids may be used to gain optimal control but are not advocated for routine use:

- Prednisone, oral, 40 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, 200 mcg, 30 minutes pre-intubation. *LoE:III*

Prophylaxis

- 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 of extreme importance for management.
Instruct patient to do postural drainage for at least 10 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:

- Moxifloxacin, IV, 400 mg daily, until patient apyrexial for 24 hours.

Follow with:

- Moxifloxacin, oral, 400 mg daily. *LoE:II*[xxiv]

Duration of therapy
Until no fluid level observed on repeat CXR, usually at least 4 weeks.

REFERRAL

No response to treatment after 21 days of therapy.
Complications, such as empyema or severe haemoptysis.

16.6 PNEUMONIA, COMMUNITY ACQUIRED

J18

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 usually shows a focal area of opacification or consolidation. Diffuse bilateral infiltrates in a patient with HIV infection and hypoxaemia is suspicious of *Pneumocystis jirovecii* pneumonia.
All patients should be offered HIV testing as HIV infection is associated with a markedly increased risk of bacterial pneumonia.

Even in clinically classic cases of pneumonia, exclude tuberculosis by sending sputum for Xpert MTB/RIF®.

A follow-up CXR 4–6 weeks after completion of therapy should be done in all but very mild cases or in otherwise healthy adults, to ensure complete resolution of the pneumonia. Follow-up CXRs are indicated earlier only when complications are suspected, e.g. empyema, abscess, or pneumothorax.

MEDICINE TREATMENT

- Oxygen if hypoxic.

Adequate analgesia for pleuritic chest pain if present. See chapter 21: Pain

Antimicrobial therapy
Duration of antibiotic therapy is guided by clinical response, but should usually be 5 days.

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.

Uncomplicated community-acquired pneumonia without features of severe pneumonia (see below for definition)

- Ampicillin, IV, 1 g 6 hourly, until patient apyrexial for 24 hours.

Follow with: *LoE:III*

- Amoxicillin, oral, 1 g 8 hourly.

LoE:III[xxv]

If poor response after 48 hours, consider alternative diagnosis (e.g. TB or atypical bacterial pneumonia).

Severe penicillin allergy:

- Moxifloxacin, oral, 400 mg daily for 5 days.

Patients > 65 years or co-morbid disease (including HIV infection)

- 3rd generation cephalosporin e.g.:
- Ceftriaxone, IV, 2 g daily, until patient apyrexial for 24 hours.

Follow with: *LoE:I*[xxvi]

- Amoxicillin/clavulanic acid, oral, 875/125 mg 12 hourly for 5 days.

LoE:III[xxvii]

Severe penicillin allergy:

- Moxifloxacin, oral, 400 mg daily.

Severe pneumonia (cyanosis, confusion, hypotension or respiratory rate >30 breaths/min):

- Ceftriaxone, IV, 2 g daily, until patient apyrexial and stable for 24 hours.

Follow with: *LoE:III*[xxviii]

- Amoxicillin/clavulanic acid, oral, 875/125 mg 12 hourly for 5 days.

AND

- Azithromycin, 500mg, slow IV (over 3 hours) daily for 3 days.

LoE:III[xxix]

Severe penicillin allergy:

- Moxifloxacin, IV, 400 mg daily.

Note: There is no need to add a macrolide, as moxifloxacin has adequate cover for the atypical bacteria.

HIV infected with bilateral diffuse infiltrates on CXR

Clinically may present with a dry cough of < 12 weeks duration and significant tachypnoea (CXR may be normal).

Treat as *Pneumocystis jirovecii* pneumonia (exclude TB):

- Cotrimoxazole, oral, 80/400 6 hourly for 21 days.
  - < 60 kg 240/1200 mg
  - > 60 kg 320/ 1600 mg

(See section 10.2.7 Pneumocystis pneumonia)

If Oxygen Saturation < 90% on pulse oximetry or arterial blood gas measurement:

ADD

- Prednisone, oral, 40 mg 12 hourly for 5 days.
  - Followed by Prednisone, oral, 40 mg daily for 5 days.
  - Followed by Prednisone, oral, 20 mg daily for 10 days.

LoE:I[xxx]

16.7 PNEUMONIA, ASPIRATION

J69.0

DESCRIPTION

Following aspiration a patient may develop pneumonitis or pneumonia. Aspiration pneumonitis 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 may have a more indolent onset with production of purulent sputum and low grade fever.

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 apyrexial and stable for 24 hours.

Follow with:

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

Severe penicillin allergy: *LoE:III*

- Moxifloxacin, IV, 400 mg daily, until patient apyrexial for 24 hours.

Follow with:

- Moxifloxacin, oral, 400 mg daily. *LoE:II*[xxxi]

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.

An empyema is always secondary to another process, usually pneumonia, 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.
Empyema, detected early by a low pH (< 7.2) and leucocytosis in pleural aspirate, and later by a cloudy or clearly infected pleural aspirate, should be drained completely by chest tube.
The primary management of empyemas 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 will need to be prolonged until drainage is complete).

If not a complication of pneumonia:

- 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.

Treatment duration is until drainage is complete. *LoE:III*

Severe penicillin allergy (and not a complication of pneumonia):

- Moxifloxacin, IV, 400 mg daily, until patient 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, requiring surgical decortication.

16.9 TUBERCULOSIS, PULMONARY

A15.0
* A notifiable 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 entered into a TB register.

Diagnosis

Molecular tests are now routinely available for the diagnosis of *M*. *tuberculosis* and the identification of drug resistant organisms. Two commercial molecular/PCR tests are currently available in the Public sector: Xpert MTB/RIF® and the Genotype MTBDR*plus*® The South African National TB programme uses the Xpert MTB/RIF® PCR assay as the initial diagnostic test for patients with suspected tuberculosis, and the assay also gives a result for rifampicin sensitivity. Genotype MTBDR*plus*® is a line probe assay (LPA) - it is used as a confirmatory test for rifampicin resistance detected by Xpert MTB/RIF® and gives a result for both rifampicin and isoniazid sensitivities. The LPA is not currently endorsed for use on smear negative sputum, but can be done directly on smear or culture positive sputum samples.

The diagnosis of pulmonary TB in adults is made on a positive Xpert MTB/RIF® on sputum. In patients with negative sputum smears, notably HIV infected patients, Xpert MTB/RIF® is not an adequate 'rule out' test and HIV infected TB suspects who are Xpert MTB/RIF® negative require further investigation and may need empiric anti-tuberculosis therapy while awaiting TB cultures.

All patients who are Xpert MTB/RIF® positive require further sputum to be sent for AFB to allow for monitoring of treatment. Xpert MTB/RIF® should not be used for monitoring.

All patients with Xpert MTB/RIF® rifampicin resistance require sputum to be sent for a LPA to confirm rifampicin resistance and the susceptibility to isoniazid. Send additional sputum for culture and drug susceptibility testing.

All TB patients must be screened for HIV. TB HIV co-infected patients are eligible for ART and cotrimoxazole prophylaxis regardless of CD4 count.

Sputum induction with nebulised sodium chloride 5% increases the yield of sputum smear and culture. This may be of special value in the context of HIV infected persons, as TB frequently presents without cavitation and hence there is a low sputum mycobacterial yield. Patients with HIV often have accessible peripheral lymphadenopathy, and a wide needle (e.g. 18G) aspiration smear for AFBs is often positive. The WHO has recently endorsed the use of Xpert MTB/RIF® for the diagnosis of TB from extra pulmonary specimens.

Note: Xpert MTB/RIF® may identify DNA from *M. tuberculosis* in the absence of active disease in patients who have recently completed TB treatment. In these cases, sputum for AFB and culture with sensitivities is preferred.

MEDICINE TREATMENT

All patients with active TB who are Xpert MTB/RIF® 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 (such as a 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, which cannot be detected by Xpert MTB/RIF®.

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), but routine use is not advocated.

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 is caused by *M. tuberculosis* entering the pleural cavity, leading to an inflammatory process accompanied by the formation of an exudative effusion. It usually presents with a few weeks of pleuritic pain; often associated with a dry cough, fever, night sweats, weightloss, and, with large effusions, progressive shortness of breath.

Diagnosis
It is essential to perform a diagnostic tap of pleural effusions confirmed on a 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: older than 50 years, or risk factors for malignancy, or not presenting with typical TB symptoms.

Treatment is as for pulmonary TB.

A weight gain of 2% at 1 month and 5% at 2 months of TB therapy can be expected.

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, a TB pleural empyema must be drained by intercostal under-water tube-drainage.

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
Z16.34

16.11.1 INH MONORESISTANT TB
Z16.341

MEDICINE TREATMENT
Patients with confirmed INH monoresistant TB can be successfully treated with:

- Rifampicin, oral, 10 mg/kg daily.

AND

- Ethambutol, oral, 15 mg/kg daily.

AND

- Pyrazinamide, oral, 25 mg/kg daily.

LoE:III[xxxii]

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.

Treatment should be given for at least 6 months after sputum culture conversion. In the absence of sputum culture results the duration of therapy should be 6-9 months depending on clinical response.

16.11.2 MULTIDRUG-RESISTANT TB

Z16.342

Never treat for MDR TB without laboratory confirmation, either by molecular or phenotypic (culture and sensitivity) results.

All cases should be discussed with a regional specialist centre.

Refer to the latest National Department of Health guidelines for the management of drug-resistant TB.

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. Xpert MTB/RIF® only tests for rifampicin resistance and not isoniazid resistance. However, rifampicin resistance by Xpert MTB/RIF® is sufficient to start a patient on MDR treatment pending confirmation of MDR TB by LPA.

All patients with HIV and TB (including MDR TB) qualify for ART irrespective of CD4 count. Avoid a TDF-containing regimen whilst on aminoglycoside therapy, if possible, as both medicines are nephrotoxic.

GENERAL MEASURES

Screen all close contacts for signs and symptoms of TB and by sputum Xpert MTB/RIF® to detect early disease. Contacts with positive results should be treated according to the rifampicin sensitivity, either as sensitive TB or MDR TB.

MEDICINE TREATMENT

MDR TB prophylaxis

The effectiveness of preventive therapy in adults exposed to MDR TB bacteria is not known.
In the absence of evidence, prophylaxis is not recommended in adults.

Treatment

Prolonged treatment, for at least 18 months after culture conversion, 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.

Standardised regimen for treatment of MDR tuberculosis in South Africa.

The standardised regimen consists of at least 6 months intensive phase (also known as injectable phase) with five medicines taken 6 times a week; followed by a continuation phase with four medicines taken 6 times a week and continued until 18 months after TB culture conversion.

Intensive phase: At least 6 months, guided by TB culture conversion (to be continued for 4 months after TB culture conversion).

	<33 kg	**33–50 kg**	**50–65 kg**	**>65 kg**
Kanamycin*	15 mg/kg	15 mg/kg	15 mg/kg (max:1 g)	1 g
Moxifloxacin	400 mg	400 mg	400 mg	400 mg
Ethionamide**	15–20 mg/kg	500 mg	750 mg	750 mg–1 g
Terizidone	15–20 mg/kg	750 mg	750 mg	750 mg–1 g
Pyrazinamide	30–40 mg/kg	1 g–1750 mg	1 750 mg–2 g	2 g–2 500 mg

*If kanamycin is contraindicated (e.g. deafness, renal failure) or toxicity develops, replace with bedaquiline (requires approval from a Drug Resistance TB Committee).

**If the LPA shows *katG* mutation use ethionamide. If there is the *inhA* mutation use high dose INH (15 mg/kg) in place of ethionamide. If both mutations are present use bedaquiline (requires approval from a Drug Resistance TB Committee). *LoE:III*[xxxiii]

Consult the most recent National Department of Health Policy: Introduction of new drugs and drug regimens for the management of drug-resistant tuberculosis: Policy Framework, for guidance on bedaquiline.

Pyridoxine

Both ethionamide and terizidone may cause pyridoxine deficiency.

All patients receiving terizidone should be given 50 mg of pyridoxine for every 250 mg of terizidone.

- Pyridoxine, oral, 150 mg daily. *LoE:III*

Continuation phase: at least 18 months after TB culture conversion

	< 33 kg	**33–50 kg**	**50–65 kg**	**> 65 kg**
Moxifloxacin	400 mg	400 mg	400 mg	400 mg
Ethionamide**	15–20 mg/kg	500 mg	750 mg	750 mg–1 g
Terizidone	15–20 mg/kg	750 mg	750 mg	750 mg–1 g
Pyrazinamide	30–40 mg/kg	1 g–1750 mg	1 750 mg–2 g	2 g–2 500 mg

Note:

» Patients with resistance to the above medicines should all be treated in specialised centres approved by the Department of Health.
» Do a pregnancy test at baseline.
» Birth control should be used in women of a child-bearing age, as some of the agents are teratogenic.
» In pregnant women, the benefits of MDR management outweigh the teratogenicity risks.
» Patients with renal impairment should be referred for replacement of kanamycin by bedaquiline and for dose adjustments of some other drugs.
» Conduct regular hearing tests/audiograms and renal function monitoring on patients on aminoglycosides and refer for replacement with bedaquiline if hearing loss (initially high frequency) or renal impairment is detected.
» Kanamycin can cause hypokalaemia and potassium levels must be checked monthly during the injectable phase.
» Perform TSH blood test at baseline, then 6 monthly to monitor for hypothyroidism associated with ethionamide.

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 for minimum duration of 18 months after sputum culture conversion.

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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

Intravenous therapy:
- 3rd generation cephalosporin, e.g.:
- Ceftriaxone, IV, 1 g daily.

Switch early to oral therapy to complete the 10 day course:
- Amoxicillin/clavulanic acid, oral, 875/125 mg 12 hourly.

Severe penicillin allergy to amoxicillin/clavulanic acid, oral:
- Macrolide, e.g.:
- Azithromycin, oral, 500 mg 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

J30.4

DESCRIPTION

Allergic rhinitis is an allergic inflammation of the nasal airways. Signs and symptoms include rhinorrhea, 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, e.g.
- Budesonide topical, 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.

LoE:III[IV]

If symptoms persist despite an adequate trial of topical corticosteroids administered with the correct technique:

ADD

- Cetirizine, oral, 10 mg daily.

For relief of nasal blockage**:**

- Topical nasal decongestants, e.g.:
- Oxymetazoline 0.05%, intranasal, administered 8 hourly for a maximum of 5 days.

Failure of the above:

ADD

- Prednisone, oral, 30 mg daily for 5 days whilst continuing the topical steroid.

17.3 SINUSITIS, BACTERIAL, COMPLICATED

J01.9

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 bacterial sinusitis also 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**.

URGENT REFERRAL

» Proptosis.
» Ophthalmoplegia.

REFERRAL

» 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.

17.4 OTITIS MEDIA, ACUTE

H66.9

DESCRIPTION

Inflammation of the middle ear of rapid onset.

MEDICINE TREATMENT

In previously untreated patients:

- Amoxicillin, oral, 500 mg 8 hourly for 5 days

Patients not responding to amoxicillin:

- Amoxicillin/clavulanic acid, oral, 875/125 mg 12 hourly for 5 days

Severe penicillin allergy:

- Macrolide, e.g.:
- Azithromycin, oral, 500 mg daily for 3 days.

LoE:III[v]

For patients with upper respiratory tract congestion, consider:

- Cetirizine, oral, 10 mg daily for 10 days.

For pain:
- NSAID, oral: e.g.
- Ibuprofen, oral, 400 mg 8 hourly with meals.

LoE:III

REFERRAL
» No response after 5 days treatment.
» No pain relief despite treatment.
» Bulging eardrum, not responding to treatment after 24 hours.
» Recurrent otitis media.

17.5 OTITIS MEDIA, CHRONIC, SUPPURATIVE
H66.3

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, oral, 500 mg 12 hourly for 5 days.

REFERRAL
» Focal neurological signs such as facial nerve palsy.

» Vomiting or drowsiness.
» Painful swelling behind the ear.
» 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

H70.9

DESCRIPTION

Infection of the mastoid air cells, usually complicating otitis media. Most patients have evidence of external inflammation 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 where mastoidectomy can be performed.

17.7 OTITIS EXTERNA

17.7.1 OTITIS EXTERNA, NECROTISING

H60.9

DESCRIPTION

Severe otalgia and otorrhoea which is unresponsive to medical therapy. In later stages cranial nerve palsies can occur. Most common pathogen: *P. aeruginosa*.

Necrotising otitis externa is typically associated with 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. 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.

Intravenous therapy:

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

AND

- Metronidazole, IV, 500 mg 8 hourly.

Switch to oral therapy as soon as possible:

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

Severe penicillin allergy:

- Clindamycin, IV, 600 mg 8 hourly.

Follow with:

- Clindamycin, oral, 450 mg 8 hourly.

For pain:

- NSAID, oral: e.g.
- Ibuprofen, oral, 400 mg 8 hourly with meals.

REFERRAL

Referral for ENT and/or anaesthetic review:

» Signs of airway compromise (e.g. stridor)).
» Suspicion of infective spread beyond the peritonsillar space.

17.9 VERTIGO, ACUTE

R42

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), 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

Good results may be achieved with particle relocation manoeuvres, such as the Epley manoeuvre. 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 medication 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:IV

Cerebellar stroke

See section 14.1: Cerebrovascular Disease.

REFERRAL

» Suspected 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

H13.1*/B30.1+

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

H10.1

DESCRIPTION

Inflammation of the conjunctiva with moderate to severe itching. It may be associated with hay fever, or other features of atopy. There may be acute inflammation of the conjunctiva, chronic cobblestone elevations of the tarsal conjunctiva or chronic thickening and discoloration of the perilimbal conjunctiva.

MEDICINE TREATMENT

Short-term use

Treatment should be for 5–7 days.

For relief of mild symptoms:

- Oxymetazoline 0.025%, ophthalmic drops, instill 1–2 drops 6 hourly.

Short-term use only.

Long-term use

For control of allergic response in chronic cases:

- Sodium cromoglycate 2%, ophthalmic drops, instill 1–2 drop 6 hourly.

AND

- Cetirizine, oral, 10 mg daily.

REFERRAL

No response to treatment.

18.1.3 CONJUNCTIVITIS, BACTERIAL

H13.1*

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 8 hourly for 5 days.

LoE: III[1]

OR

- Fluoroquinolone ophthalmic drops as second-line treatment, e.g.:
- Ciprofloxacin 0.3%, ophthalmic drops, instill 1 drop 4 hourly for 2 days.
  - Then reduce frequency to 1 drop 6 hourly for 5 days.

OR

Ofloxacin 0.3%, ophthalmic drops, instill 1 drop 4 hourly for 2 days.
- Then reduce frequency to 1 drop 6 hourly for 5 days.

LoE: I[II]

REFERRAL
No response to treatment.

18.2 ENDOPHTHALMITIS, BACTERIAL
H44.0

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

H40.9

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, instill 1 drop 12 hourly.

LoE:II^{V}

OR

Selective β-blocker:

- Betaxolol 0.25–0.5%, ophthalmic drops, instill 1 drop 12 hourly.

LoE:III

Poor response despite adequate adherence:

ADD

- Prostaglandin analogues, e.g.:
- Bimatoprost 0.03%, ophthalmic drops, instill 1 drop daily. *LoE:II*[VI]
  - Use as first line if patient has contra-indication to ß-blocker.
  - Use 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.
  - Use in combination with ß-blocker if there is significant reduction in IOP with ß-blocker, but patient still has progression of disease or target IOP is not reached.

Intolerance to prostaglandin analogue, or poor response:

- Alpha-agonist, e.g.:
- Brimonidine 0.15–0.2%, ophthalmic drops, instill 1 drop 12 hourly. *LoE:III*[VII]
  - Use as second line if patient has allergic reaction to prostaglandin analogue.
  - Use in place of prostaglandin analogue if there is no significant further reduction in IOP when adding prostaglandin analogue to ß-blocker.
  - Use in combination with ß-blocker and prostaglandin analogue if there is significant reduction in IOP with ß-blocker and prostaglandin analogue, but 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, instill 1 drop 6 hourly. *LoE:III*

In severe cases, as a temporary measure before ocular surgery in consultation with a specialist:

Carbonic anhydrase inhibitors:

- Acetazolamide, oral, 250 mg 6 hourly. *LoE:II*[VIII]

Angle-closure glaucoma (acute)

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, instill 1 drop 12 hourly.

Also treat patient for associated pain and nausea. See chapter 12: Anaesthesiology, pain and intensive care.

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

B02.3

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

To reduce the risk of post-herpetic neuralgic pain:

- Amitriptyline, oral, 25 mg at night for 3 months.

LoE:II[ix]

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

H16.9

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 conjuntival sac five times per day at 4 hour intervals.
  - Continue for 3 days after ulcer has healed.

Note: Topical corticosteroids are contraindicated in the treatment of dendritic ulcers.

18.5.2 KERATITIS, SUPPURATIVE

H16.0

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:

- Fluoroquinolone ophthalmic drops, e.g.:
- Ciprofloxacin 0.3%, ophthalmic drops, instill 1 drop hourly for 3 days.
  - Then reduce frequency to 1 drop 3–4 hourly.

OR

Ofloxacin 0.3%, ophthalmic drops, instill 1 drop hourly for 3 days.
  - Then reduce frequency to 1 drop 3–4 hourly.

If fungal infection:

- Natamycin 5%, ophthalmic drops, instill 1 drop 1–2 hourly for 3–4 days. (Specialist use only).
  - 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

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*[x]
  - Monitor FBC weekly during induction, then monthly as valganciclovir can cause bone marrow suppression. Avoid concomitant zidoudine use.
  - Initiate ART 2 weeks after starting induction therapy.

If valganciclovir is not available:

- Ganciclovir, intravitreal, 2 mg once a week.
  - 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, instill 1–2 drops 3–4 hourly.

OR

Atropine 1%, ophthalmic drops, instill 1 drop 12 hourly.

AND

Corticosteroids:

- Dexamethasone 0.1%, ophthalmic drops, instill 1–2 drops 4–6 hourly.

LoE:III[xi]

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 2mg/mL and phenylephrine 10 mg/mL (for fundoscopic examination)
- Carbopol gel (as coupling liquid for diagnostic contact lenses)

Local anesthetics used on the eye

- Oxybuprocaine hydrochloride 0.4%

Preparations for tear deficiency

- Hydroxypropylmethylcellulose 0.3–0.5%

18.9 DRY EYE

H04.12

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:

- Hydroxypropylmethylcellulose, ophthalmic drops, 1 drop, 6 hourly.

OR

Lanolin, anhydrous liquid, ophthalmic ointment, at night.

LoE:III[xii]

LoE:III[xiii]

18.10 MEDICAL MANAGEMENT OF EYE INJURY

18.10.1 CHEMICAL BURN

T26.50

This is a medical emergency.

DESCRIPTION

Damage to one or both eyes caused by contact with irritating chemical substances e.g. alkali or acid.

Presents with:

» pain
» inability to open eye
» blurred vision
» excessive teary and watery eye

GENERAL MEASURES

» Irrigate or wash the eye immediately and continuously with clean water or sodium chloride 0.9% for at least 20 minutes.
» In severe alkaline burn cases, irrigation should be prolonged further.

MEDICINE TREATMENT

Local anaesthetic if needed:

- Tetracaine 0.5% ophthalmic drops, instil 2 drops in the affected eye.
  - Repeat irrigation of eye.
  - Evert upper eyelid and remove debris with cotton bud.

AND *LoE:III*[xiv]

- Chloramphenicol 1%, ophthalmic ointment, applied 6 hourly.

LoE:III[xv]

For pain:

- Paracetamol, oral, 1 g 4–6 hourly when required to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum dose: 4 g in 24 hours.

LoE:III[xvi]

REFERRAL

All cases within 12 hours.

18.10.2 EYE INJURY: BLUNT/PENETRATING/FOREIGN BODY

S05.90

DESCRIPTION

A foreign body may be embedded in the conjunctivae or cornea or deeper, causing:

» corneal abrasion/laceration
» disturbance of vision

» complaints of foreign body in the eye that may not be visible
» pain

GENERAL MEASURES

Establish the cause, to determine likelihood of penetrating trauma.
If no penetrating injury, irrigate eye with clean water or sodium chloride 0.9%.
Remove any foreign body if visible on sclera or conjunctivae with cotton bud.
If foreign body is not visible, check visual acuity first, before testing with fluorescein.
Stain with fluorescein to reveal corneal foreign body or complications such as abrasion.
Cover injured eye with eye pad provided there is no pressure on the eye.
Consider X-ray of orbit to exclude intra-ocular metallic foreign body.

MEDICINE TREATMENT

Corneal abrasion

- Chloramphenicol 1%, ophthalmic ointment applied 8 hourly to the injured eye.

LoE:III[xvii]

Deep corneal or scleral injuries

Cover with an eye shield and refer immediately.

<u>If immediate referral is not possible, while awaiting transfer:</u>

- Atropine, 1%, drops, instilled immediately.

AND

LoE:III[xviii]

- Chloramphenicol 1%, ophthalmic ointment applied immediately.

LoE:III[xix]

<u>For pain:</u>

- Paracetamol, oral, 1 g 4–6 hourly when required to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum dose: 4g in 24 hours.

LoE:III[xx]

REFERRAL

» Suspicion of open globe or intra-orbital penetration:
  - Decreased visual acuity.
  - Eccentric or peaked pupil.
  - Extrusion of ocular contents or foreign body.
  - Circumferential subconjunctival hemorrhage.
» Traumatic hyphema (blood in the anterior chamber).
» Conjunctival lacerations >1 cm in length that will require suturing.
» Foreign bodies that are deeply embedded.
» Chemical and thermal burns.
» Damage to other structures of the eye, including the eyelid edge.
» Limitation of movement of the eye.

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[xviii] Atropine, 1%, drops: Primary Healthcare STGs and EML. http://www.health.gov.za

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CHAPTER 19

POISONING

POISON CENTRES

POISON INFORMATION CENTRES		
Western Cape: 24 hours, every day for poisons queries	Poison Information Helpline of the Western Cape	0861 555 777
	Tygerberg Poison Information Centre Email: toxicology@sun.ac.za www.sun.ac.za/poisoncentre	0861 555 777
	Red Cross War Memorial Children's Hospital Poisons Information Service	0861 555 777
Free State: (operates until 21:00)	University of the Free State Poison Control and Medicine Information Centre	082 491 0160
Telephone numbers tested 25 February 2016		

Poison information can be accessed through: https://www.afritox.co.za/

ENVENOMATION

19.1 INSECT BITES AND STINGS

T63.4

DESCRIPTION

Insect bites and stings usually cause local effects only. Systemic effects are rare. Local inflammatory or systemic/immunological forms of toxicity are encountered occasionally, which may vary between minor local reactions and acute anaphylaxis.

Multiple bee stings may require ICU care.

GENERAL MEASURES

Severe allergic reactions may be delayed.
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 to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum dose: 4 g in 24 hours.

LoE:III

19.2 SNAKEBITES

T63.0

DESCRIPTION

As the majority of snakes are not identified in snakebite victims, the table below illustrates the syndromic management of three main envenomation syndromes namely: cytotoxic, neurotoxic and haemotoxic.

To view pictures for identification of snakes click on following hyperlink: http://www.cmej.org.za/index.php/cmej/article/view/2546/2581

Signs of systemic poisoning:

» Muscle weakness and/or difficulty in breathing.
» Difficulty in swallowing or speaking with drooling.
» Weakness.
» Double vision and drooping eyelids.
» Spreading of local tissue damage.
» Swelling of a hand or foot within 1 hour of a bite (the majority of bites occur on the hands or feet).
» Swelling extending to the elbows or knees within 4 hours of a bite.
» Swelling of the groin or chest at any time or if actively advancing.
» Significant swelling of head or neck.

Venom type	Cytotoxic	Neurotoxic	Mixed cytotoxic and neurotoxic	Haemotoxic
Snake species	Puff adder, Gaboon adder, spitting cobra (Mozambique, black-necked, zebra), stiletto snake, night adders, horned adders	Black and green mamba, non-spitting cobra (e.g. snouted, Cape, forest, Egyptian, Anchieta)	Rinkhals, Berg adder, Peringuey's adder, desert mountain adder, garter snakes, Shield-nose snake.	Boomslang, vine snakes.
Predominant clinical presentation	»Painful, progressive swelling	»Respiratory distress, »Progressive weakness »Cranial nerve palsies	»Combined painful progressive swelling and progressive weakness or respiratory failure	»Bleeding (Presents late >24 hours post bite)
Antivenom availability. See indications for antivenom treatment	Polyvalent antivenom for Puff adder, Gaboon adder and spitting cobras only	Polyvalent antivenom for all species	Polyvalent antivenom for rinkhals only	Boomslang antivenom for confirmed boomslang bites only.

GENERAL MEASURES

Supportive and symptomatic treatment is essential for survival.
Mechanical ventilation may be needed in some cases.

MEDICINE TREATMENT

Cleanse wound:

- Chlorhexidine 0.05% in water.

Antibiotics are seldom needed, except for secondary infection:

- Amoxicillin/clavulanic acid, oral, 875/125 mg 12 hourly for 5 days.

LoE:III

Immunisation, primary or booster:

- 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 to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum dose: 4g in 24 hours.

OR

For severe pain:

ADD

- Opioids, e.g.:
  - 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 an NSAID is not recommended due to the antiplatelet effect and the potential danger of renal failure in a hypotensive patient.

LoE:III[II]

Polyvalent antivenom

Obtainable from South African Vaccine Producers (tel: +2711 386-6063/2/00). See package insert for full details.

It is ineffective against the venom of:

» night and berg adder and other minor adders,
» boomslang, and
» vine and twig snakes.

Caution

Never administer antivenom without being fully prepared to manage acute anaphylaxis.

Note:

» In most cases patients do not need and should not be given antivenom.

LoE:III[III]

» Adverse reactions to antivenom are common and may be severe.
» 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.

LoE:III

Indications for polyvalent antivenom:

» Any sign of neurotoxicity.
» All patients with confirmed mamba bites should receive antivenom, even before the onset of symptoms and signs.
» Patients with confirmed puff adder or Gaboon adder bites should receive antivenom at the onset of any symptoms and signs of cytotoxicity.

» Extensive swelling or cardiovascular abnormalities despite unidentified snake.

Premedication for antivenom:

- Adrenaline (epinephrine), SC, 0.25 mL of 1:1000 solution.
  (Contraindicated in patients with IHD, stroke, uncontrolled hypertension and tachyarrhythmia).

LoE:I[IV]

- Polyvalent snake antivenom, slow IV infusion.
  - 1 ampoule contains 10 mL antivenom.
  - Dilute in sodium chloride 0.9%.
  - Administer slowly, IV, for the first 30 minutes, as most allergic reactions will occur within this period.
  - Increase the flow rate gradually to complete the infusion within 1 hour.
  - Repeat if there is no clinical improvement (e.g. improvement and recovery of muscle paralysis or improvement of neurotoxic signs) after the infusion.
  - Antivenom may be administered up to 24-48 hours or later, in serious envenomation.

Snakebite	**Dose of polyvalent snake antivenom**
Cytotoxic snakebite	○ 50mL (5 ampoules). ○ Dilute in ±100–200 mL sodium chloride 0.9%. ○ If clinically indicated, administer a second dose.
Cytotoxic snakebite of head and neck	○ 100 mL (10 ampoules) to 200 mL (20 ampoules). ○ Dilute in ±100–200 mL sodium chloride 0.9%. ○ If clinically indicated, administer a second dose.
Neurotoxic snakebite	○ 100 mL (10 ampoules) and up to 200 mL (20 ampoules). ○ Dilute in ±100–200 mL sodium chloride 0.9%. For black mamba snakebites: ○ 200 mL (20 ampoules). ○ Dilute in ±100–200 mL sodium chloride 0.9%. ○ If clinically indicated, administer a second dose.

LoE:III[V]

19.2.1 BOOMSLANG SNAKE BITE

T63.0

DESCRIPTION

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 follow these over a few days.

Other investigations include FBC, activated PTT, prothrombin time (INR), fibrinogen, D-dimer and monomers.

Management includes fluid replacement therapy with electrolyte solutions and blood components (packed cells, plasma). The haemostatic effects of boomslang envenomation are rapidly reversed on administration of the specific boomslang antivenom.

Note: Polyvalent antivenom is not effective in boomslang bite.

Boomslang antivenom

Obtainable from South African Vaccine Producers (tel: +2711 386-6063/2/00). See full details in the package insert**.**

Caution
Never administer antivenom without being fully prepared to manage acute anaphylaxis.

- Boomslang antivenom, slow IV infusion, 20 mL diluted in 50–100 mL sodium chloride 0.9% or dextrose 5%, administered over 5–10 minutes.
  - Re-evaluate at 2 hours and if evidence of ongoing coagulopathy a follow-up dose of 10 mL may be considered.

LoE:III[VI]

19.2.2 VENOM IN THE EYE

T63.094

DESCRIPTION

Direct or indirect snake venom exposure to the eye, particularly from various species of spitting cobras, can cause chemical injury with varying clinical presentations ranging from periocular swelling and mild conjunctival and corneal inflammation to frank corneal ulceration and perforation with eventual blindness.

GENERAL MEASURES

- Instil local anaesthetic and promptly perform copious irrigation to dilute or

remove the toxin with sodium chloride, 0.9%. *LoE:III*

- Apply chloramphenicol ointment and cover the affected eye with an eye patch.

REFERAL
Refer all patients to an ophthalmologist.

19.3 SCORPION ENVENOMATION
T63.2

DESCRIPTION
Poisonous 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. The venom typically causes immediate and severe local pain, followed by systemic neurotoxic symptoms and signs within 1–4 hours, but symptoms can be delayed up to 8 hours.
To view pictures for identification of scorpions click on following hyperlink:
http://www.cmej.org.za/index.php/cmej/article/view/2545/2580

Clinical features of scorpion stings include:
» Immediate and excruciating pain
» general paraesthesias and hyperaesthesia,
» tremors and involuntary movements
» muscle pain, cramps, and weakness,
» excessive sympathetic stimulation,
» dysphagia,
» dysarthria, and
» increased salivation and loss of pharyngeal reflexes with possible respiratory impairment/failure.

GENERAL MEASURES
Observe all cases for at least 12 hours.
Monitor respiratory function.
Ventilatory support may be required.

MEDICINE TREATMENT
Antivenom therapy is recommended only in cases presenting with systemic neurotoxic effects.

- Scorpion antivenom, IV infusion, 10 mL diluted in 100 mL sodium chloride 0.9% or dextrose 5%, administered over 10 minutes. *LoE:III*

Immunisation, primary or booster:
- Tetanus toxoid vaccine, IM, 0.5 mL immediately.

In unimmunised or partially immunised patients:
- Tetanus immunoglobulin, human, IM, 250 units immediately.

Analgesia
For pain:
- Paracetamol, oral, 1 g 4–6 hourly when required to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum dose: 4g in 24 hours.

LoE:III[VII]

Severe local pain:
- Lidocaine 1–2%, 2 mL: infiltrate affected area as a local anaesthetic.

LoE:III[VIII]

Opiates are not effective and increase the risk of respiratory depression.

LoE:III[IX]

Severe muscle pain and cramps:
- Calcium gluconate 10%, bolus IV infusion, 10 mL over 10 minutes.
  - Repeat if needed.

19.4 SPIDER ENVENOMATION

T63.3

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.
May present with significant bite site necrosis, which may need surgical debriding. Bites may take weeks/months to heal.
Note: Antibiotics are reserved for secondary infection.

Neurotoxic spider group
The neurotoxic group is represented by the black and brown widow (also known as button) spiders (genus *Latrodectus*). Black widow spiders are more venomous than brown widow spiders.

Features useful in the identification of the black widow 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 widow spider:
» Typical **orange coloured hourglass** shaped marking on the ventral surface of the abdomen.

Envenomation may cause:
» Local burning pain and painful, tender regional lymph nodes.
» Severe general muscle pain and cramps especially of the large girdle muscles.
» Muscle rigidity.
» Feeling of tightness of the chest.
» Board-like rigidity of a non-tender abdomen.
» Profuse sweating may be prominent.
» General muscle pain which lasts for days to a week if antivenom is not given.

GENERAL MEASURES
Observe all cases for at least 24 hours.

MEDICINE TREATMENT
- Spider antivenom, IV infusion, 5–10 mL diluted in 50–100 mL sodium chloride 0.9% or dextrose 5%, administered over 5–10 minutes.

Note: Antivenom is only indicated for systemic symptoms in patients with black widow spider bites. *LoE:III*[x]

Caution
Never administer antivenom without being fully prepared to manage acute anaphylaxis.

Severe muscle pain and cramps:
- Calcium gluconate 10%, bolus IV infusion, 10 mL over 10 minutes.
  - Repeat if needed.

Immunisation, primary or booster:
- 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 to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum dose: 4g in 24 hours.

For secondary infection:
See section 4.2: Cellulitis and Erysipelas.

EXPOSURE TO POISONOUS SUBSTANCES

GENERAL MEASURES

Limit further exposure to poison and protect healthcare workers.

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.

In case of skin exposure, wash body and remove clothes. Showering may be useful. Remove eye contaminants, especially alkalis, acids and other irritants, by continuous irrigation of the eye for 15–20 minutes.

Gastric lavage is seldom indicated.

LoE:I[xi]

Gastric lavage is ineffective unless done within an hour of ingestion (if substances are known to delay gastric emptying, consult with poisons centre). It is contra-indicated after ingestion of corrosive substances and volatile hydrocarbons such as paraffin. In patients with reduced consciousness it should be done only if the airway is protected.

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 ingestion).

LoE:III

Maintain and monitor basic clinical parameters, i.e.:
» pulse rate,
» blood pressure,
» hydration,
» ventilation,
» patent airway and oxygenation, and
» control seizures and prevent physical injury in the restless - avoid excessive sedation.

INITIATION OF TREATMENT

Reduce absorption

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 of poisonous substances. Repeated doses of activated charcoal (i.e. 50 g every 4 hours) are effective when managing carbamazepine, dapsone, phenobarbitone, quinine or theophylline overdose.

LoE:III[xii]

Activated charcoal is of no value after ingestion of the following:

» strong acids or bases,
» other corrosives substances e.g. household detergents,
» iron, lead, mercury, arsenic,
» petroleum products (e.g. paraffin or petrol), and
» ethylene glycol, methanol, ethanol.

- Charcoal, activated, oral, 50 g (equivalent to 36 level medicine measures) diluted in 300 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

Alkalinisation of urine (e.g. severe salicylate poisoning)

Caution
This is a high risk procedure and should only be performed in consultation with a specialist.

Haemodialysis

Patients with symptomatically severe poisoning due to salicylates, lithium, ethylene glycol, methanol, ethanol and theophylline may benefit from dialysis. Refer patient to a hospital with dialysis facilities.

REFERRAL

» Severely ill patient for ventilatory/circulatory support.
» Relevant diagnostic testing not available, e.g. paracetamol levels.
» Relevant medication/antidote not available.
» Dialysis/haemoperfusion required.

19.5 ANALGESIC POISONING

19.5.1 PARACETAMOL POISONING

T39.1

DESCRIPTION

Liver damage, due to the depletion of glutathione and accumulation of toxic metabolites, can occur in any individual with paracetamol overdose. High risk patients (see below) may experience toxicity at lower ingested doses.

Clinical features

Within 24 hours after overdose

Gastrointestinal symptoms (anorexia, nausea, vomiting, malaise) predominate in the first 0.5-24 hours. During the next 24-48 hours the patients may become asymptomatic. Those with normal or only slightly raised plasma paracetamol levels usually continue to full recovery. In patients with significantly raised plasma levels this "recovery" may be spurious and early hepatic toxicity (right upper quadrant abdominal pain and tenderness, elevated bilirubin, raised liver enzymes, coagulation defects) may manifest from 20-24 hours, peaking in severity at about 72-96 hours. This may be followed by full recovery by 5-7 days, or death 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:

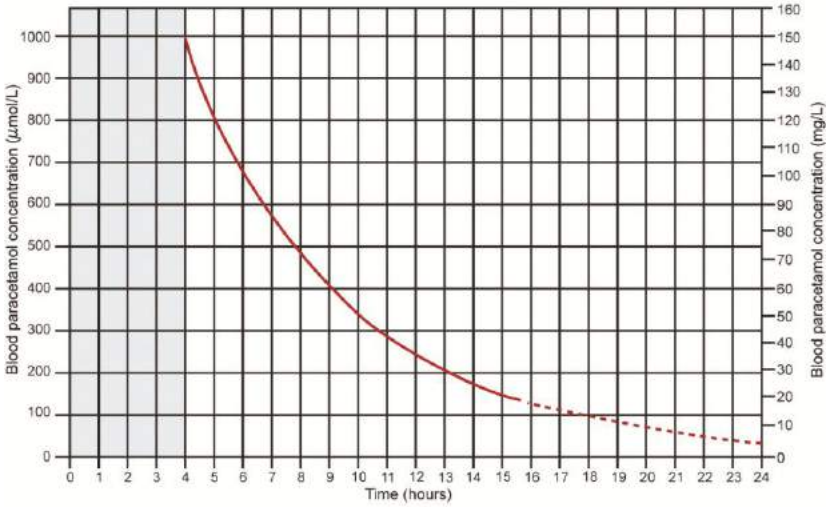
Toxic dose defined as >150 mg/kg or 7.5 g (whichever is less).
Give activated charcoal if the patient presents within 1-2 hours of ingestion
Perform a serum paracetamol level after 4 hours post-ingestion
If serum paracetamol level results will not be available before 8 hours post-ingestion, and the patient 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 use.

Acute single ingestion >8 hours post-ingestion:
Toxic dose defined as >150 mg/kg or 7.5 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 (Note the lower treatment line for high risk patients)
- » serum paracetamol level under the treatment line and abnormal ALT
- » more than 24 hours post-ingestion, measurable paracetamol level and/or ALT abnormal

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[xiii]

MEDICINE TREATMENT

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: 150 mg/kg diluted in 200 mL 5% dextrose given over 60 minutes.
  - Second infusion: 50mg/kg in 500mL 5% dextrose over 4 hours.
  - Third infusion: 100mg/kg in 1000mL 5% dextrose over 16 hours.
  - Any further N-acetylcysteine is given according to the third infusion regimen.

LoE:III

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 should be referred for further management and/or possible transplant.

Note: Avoid giving activated charcoal if giving N-acetylcysteine orally as it will reduce the systemic absorption and thus negate the effect of oral N-acetylcysteine.

19.5.2 SALICYLATE POISONING

T39.0

DESCRIPTION

Mild to moderate toxicity:
» Nausea, vomiting, tinnitus, tachypnea and respiratoric alkalosis

Severe toxicity:
» Metabolic acidosis, fever, altered mental status, seizures, coma, non-cardiogenic pulmonary oedema.

GENERAL MEASURES

Consider ICU admission for pulmonary and/or cerebral oedema.

MEDICINE TREATMENT

- Prevent absorption with activated charcoal and whole bowel irrigation of slow release or enteric coated formulations.

LoE:III[xiv]

» Assess severity with history, clinical examination and salicylate levels if possible.
Note: Wintergreen oils/ ointments contain 98 % methyl salicylate.
» Treat acidosis and enhance renal excretion (intravenous sodium bicarbonate and urinary alkalinisation, blood pH < 7.5 and urine pH 7.5–8.5) in consultation with specialist advice.

LoE:III

REFERRAL
Where acidosis does not respond rapidly to sodium bicarbonate, consider haemodialysis.

19.5.3. OPIOID POISONING
T40

DESCRIPTION
Patients present with respiratory depression and constricted pupils. Non-cardiogenic pulmonary oedema may be present.

GENERAL MEASURES
Supportive management aimed at maintaining cardiorespiratory function.

MEDICINE TREATMENT
- Naloxone, IV, 0.4 mg immediately, in patients with respiratory depression.
    - Effectiveness is limited by short half-life of ± 1 hour and repeated doses may be needed at 2 to 3 minute intervals.
    - If there is no response after 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.
    - Careful monitoring of patient where naloxone was administered is important until patient is fully awake or no longer naloxone dependant.

LoE:III[xv]

19.6 ANTIDEPRESSANTS

19.6.1. TRICYCLIC ANTIDEPRESSANT POISONING
T43.0

DESCRIPTION
Patients may have:

Mild to moderate poisoning:
- » Sedation.
- » Hallucinations.
- » Anticholinergic effects:
    - delirium,
    - dilated pupils,
    - dry mouth.
- » Tachycardia.
    - blurred vision,
    - urinary retention, or

Severe Poisoning:

» Acidaemia.
» Coma.
» Hypotension.
» Seizures.
» Pulmonary oedema.
» QRS prolongation, ventricular dysrhytmias.

GENERAL MEASURES

Do a baseline ECG in all patients.
Patients who are symptomatic 6 hours after ingestion or if there are any abnormalities on ECG:

» Admit and monitor (ECG and blood gases)
» Discharge the patient only when
  - asymptomatic, or
  - symptomatic, but ECG has normalised for 24 hours.
» ICU admission for ventilatory/circulatory support, when indicated.
» Manage gastrointestinal ileus and urinary retention appropriately by giving patients nil per mouth and inserting a urinary catheter.

MEDICINE TREATMENT

- Activated charcoal, single dose.

Serum alkalinisation for all patients with dysrhytmias or QRS widening >100 msec or hypotension:

- Sodium bicarbonate, bolus doses, to achieve a pH of 7.45–7.55. (Specialist consultation).

LoE:III

For torsades de pointes not responding to alkalinisation:
ADD

- 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

For seizures or if sedation is required for restlessness:

- Diazepam IV, 10 mg as a single dose.
  - If seizures persist refer to section 14.3.1 Status epilepticus for management to stop seizures.

Intravenous fluids
Reverse circulatory shock, if present.
In severe cases, provide inotropic support and monitor response.

Note: The use of flumazenil is not recommended in any patient with possible tricyclic antidepressant poisoning as it increases the risk of convulsions and dysrhythmias.

LoE:I[xvi]

19.7 IRON POISONING

T45.4

DESCRIPTION

Iron is a commonly prescribed drug, especially in pregnancy, and 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 side effects,
» hepatitis.
» gastrointestinal haemorrhage
» hypotension,
» renal failure, and

GENERAL MEASURES

Gastrointestinal decontamination by whole bowel irrigation is recommended, if > 40 mg/kg elemental iron has been ingested or if the amount is unknown.

Ferrous salt	Amount	Elemental iron
Ferrous sulphate	300 mg	60 mg
Ferrous gluconate	300 mg	35 mg
Ferrous fumarate	200 mg	65 mg

Activated charcoal does not bind iron and is not indicated in isolated iron overdose.

Iron concentration should be measured 4–6 hours after ingestion and repeated every 6 hours until peak.

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.

Desferrioxamine (deferoxamine) may be used for the following indications (in consultation with a poison centre):

» Severe symptoms (altered mental status, hemodynamic instability, persistent vomiting and or diarrhoea).
» Metabolic acidosis.
» Peak serum iron concentration > 90 micromol/L.

- Desferrioxamine (deferoxamine), IV infusion, 15 mg/kg/hour.
  - The infusion rate can be titrated in consultation with a specialist.
  - **Note:** Prolonged use > 24 hours of high doses is associated with acute lung injury and should be avoided.

LoE:III[XVII]

Desferrioxamine can be used in pregnant women.

LoE:III[xviii]

Consider exchange transfusion in patients who deteriorate despite supportive care and chelation therapy.

Haemodialysis may be needed to remove desferrioxamine-iron complexes in patients with renal insufficiency.

19.8 THEOPHYLLINE POISONING

T48.6

DESCRIPTION

Patients present with:

- » tachycardia and tachyarrhythmias,
- » vomiting
- » agitation
- » seizures
- » nausea
- » abdominal pain
- » restlessness
- » profound hypokalaemia

GENERAL MEASURES

Monitor ECG and treat dysrhythmias.
Monitor and correct fluid status and electrolyte abnormalities.
Monitor theophylline concentrations. Levels may continue to rise up to 24 hours after ingestion of modified release preparations.

MEDICINE TREATMENT

- Activated charcoal.
  - Give multiple doses activate charcoal (25 g every 4 hours) to increase elimination.

LoE:III[xix]

Correct hypokalaemia:

- Potassium chloride, IV, maximal dose 40 mmol/L and maximal rate 20 mmol/hour.

For seizures:

- Diazepam IV, 10 mg as a single dose.
  - Repeat after 5–10 minutes if necessary.
  - If seizure persists, consult a specialist.

REFERRAL

In patients with symptoms of severe overdose, refer for dialysis.

19.9 SEDATIVE HYPNOTIC POISONING

19.9.1 BENZODIAZEPINE POISONING

T42.4

DESCRIPTION

Patients present with depressed levels of consciousness, confusion, ataxia and dysarthria. Benzodiazepines are unlikely to cause significant respiratory suppression 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[xx]

19.9.2 LITHIUM POISONING

T43.9

DESCRIPTION

Lithium toxicity mostly occurs with chronic therapy and may be precipitated by decreased excretion of the medicine due to renal dysfunction, diuresis, dehydration or drug-drug interactions (e.g. NSAIDs, diuretics, ACE-inhibitors and ARBs).

Signs and symptoms include:

- » nausea and vomiting
- » diarrhoea
- » nystagmus
- » ataxia
- » tremors
- » dehydration
- » Other CNS symptoms: hyperreflexia, cogwheel rigidity, ataxia, agitations, confusion and lethargy

In severe toxicity:

- » decreased level of consciousness
- » restlessness,
- » confusion,
- » seizures,
- » dysrhythmias

GENERAL MEASURES

Whole bowel irrigations with polyethylene glycol considered with large ingestion or sustained-release products.

LoE:II[xxi]

Monitor:

- » Vitals signs, mental status and urine output
- » Do serial lithium levels until peaked and declined.
- » Electrolytes and renal function.

» Fluid status and administer sodium chloride 0.9 % to obtain normal urine flow but prevent hypernatremia.
» Cardiac function and treat dysrhythmias (see chapter 3: Cardiovascular system).
» Thyroid function.

MEDICINE TREATMENT

Correct hypokalaemia actively:

- Potassium chloride, IV, maximal dose 40 mmol/L and maximal rate 20 mmol/hour.

For seizures:

- Diazepam IV, 10 mg as a single dose.
  - If seizures persist refer to section 14.3.1 Status epilepticus for management to stop seizures.

Haemodialysis

Indicated in severe lithium poisoning. Discuss with a specialist.

LoE:III

19.10 ISONIAZID POISONING

T37.1

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

- Pyridoxine, oral,
  - 1 g for every gram of isoniazid ingested, or
  - 5 g for unknown amount ingested.

LoE:III[xxii]

19.11 CALCIUM CHANNEL BLOCKER POISONING

T46.1

GENERAL MEASURES

Monitor vital signs, ECG and blood glucose.
Hyperglycemia in non-diabetic patients with a history of possible CCB ingestion may assist with diagnosis.
Treat symptomatic patients in consultation with a specialist.

MEDICINE TREATMENT

Treat hypotension:

- Sodium chloride, IV, 0.9%.

LoE:III[xxiii]

Treat bradycardia:

- Atropine 0.5–1 mg every 2–3 minutes to a maximum of 3 mg.

LoE:III[xxiv]

If not effectively controlled add:

- Calcium gluconate 10%, IV, 10 mL given over 15–30 minutes, with ECG monitoring.
  - This may be repeated.

LoE:III[xxv]

Use vasopressors as needed.

In patients with resistant hypotension and bradycardia and glucose < 8 mmol/L:

- Dextrose 50%, IV, 50 mL.

Followed by:

- Short acting insulin, IV, 1 unit/kg.
  - Followed by 0.5 unit/kg/hour.
  - Titrate dose up until hypotension is corrected
  - Monitor and correct potassium and glucose.

LoE:III[xxvi]

19.12 COTRIMOXAZOLE POISONING

T37.0

DESCRIPTION

Symptoms of toxicity 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.

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

DESCRIPTION
Cocaine may be absorbed through any mucous membrane, smoked or injected intravenously.

Patients may present with one or more of the following:
- » acute myocardial infarction
- » cardiac dysrhythmias
- » tachycardia
- » pulmonary oedema
- » intestinal ischaemia
- » seizures
- » alterations in mood and confusion
- » hypertension
- » stroke
- » rhabdomyolysis with acute renal failure

GENERAL MEASURES
Supportive management aimed at preventing and managing complications.
Cool patients with hyperthermia.
Abdominal X-rays may show packages of cocaine. In these patients, conservative management is recommended.
Activated charcoal and whole bowel irrigation may decrease absorption.
Surgery is reserved for those who develop obstruction or perforation.
Raised serum creatinine kinase may indicate rhabdomyolysis or myocardial infarction.
Note: Lidocaine may precipitate seizures.

ß–blockers should not be used.

MEDICINE TREATMENT
For sedation or seizures:
- Diazepam IV, 10 mg as a single dose.
  - If seizures persist refer to section 14.3.1 Status epilepticus for management to stop seizures.

Status epilepticus:
See section 14.3.1: Status Epilepticus.

Psychosis or delirium with severe agitation:

- Benzodiazepines:
- Lorazepam, IM, 4 mg, immediately.
  OR
  Midazolam, IM, 15 mg immediately.
  OR
  Clonazepam, IM, 2 mg, immediately.
  OR
  Diazepam, IV, 10 mg.
  - Repeat after 30–60 minutes if needed.

OR

Haloperidol, IM, 5 mg, immediately.

AND

Promethazine, deep IM, 25–50 mg.

- In the elderly 25 mg.

Repeat after 30–60 minutes if needed.
If haloperidol is unavailable, use chlorpromazine without promethazine.

- Chlorpromazine, deep IM, 25–50 mg.
  - May be repeated as necessary 4 times in 24 hours.

LoE:III[xxvii]

Severe hypertension:
See section 3.6.1: Hypertension, severe.

19.14.2 POISONING WITH AMPHETAMINE DERIVATIVES

T43.6

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 in the CNS. Patients present with:

» hyperthermia, especially with MDMA,
» tachycardia,
» hypertension,
» angina pectoris and myocardial infarction,
» stroke,
» hyperactivity,
» delirium,
» tremors, and
» 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
Haemodialysis may be required for acute renal failure.

For seizures:
- Diazepam IV, 10 mg as a single dose.
  - If seizures persist refer to section 14.3.1 Status epilepticus for management to stop seizures.

Severe hypertension:
See section 3.6.1: Hypertension, severe.

19.15 HYDROCARBON POISONING
T52.0

DESCRIPTION
Poisoning due to petroleum products, including paraffin, turpentine, petrol, mineral spirits and halogenated hydrocarbons.
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.
Caustic substances cause tissue necrosis of the gut resulting in strictures later.

GENERAL MEASURES

No emesis or gastric lavage.
Rinse mouth with copious amounts of cold water.
Patients may require urgent endoscopic evaluation and possible surgical intervention. (Discuss with a specialist).

19.17 ALCOHOLS

19.17.1 ETHANOL POISONING

T51.0

DESCRIPTION

Acute poisoning usually presents with:

» nausea and vomiting,
» central nervous system depression,
» hypoglycaemia,
» hypothermia,
» hypokalaemia
» hyponatraemia, and
» 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

T52.3

DESCRIPTION

Ethylene glycol is a component of motor vehicle radiator coolant/antifreeze and 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), high anion gap metabolic acidosis (i.e. $[Na^+] - ([Cl^-] + [HCO_3^-]) > 12$), and renal failure.
Cardiovascular signs include tachycardia and hypertension. Hypocalcaemia due to calcium oxalate crystals.
One to two weeks after severe intoxication, crystals may cause cranial nerve abnormalities.

GENERAL MEASURES

Immediate consultation with a poison centre is important.
Early treatment with alcohol prevents formation of toxic metabolites.
Monitor blood gases and administer sodium bicarbonate, IV, to keep the pH above 7.2 (this decreases end organ damage by toxic metabolites).
Early haemodialysis is the treatment of choice with severe poisoning or profound acidosis.

MEDICINE TREATMENT

Ethanol

- Ethanol 95% BP, oral, diluted to 20% in any suitable liquid.
  - Loading dose: 4 mL/kg
  - Maintenance dose: non-drinker: 0.4–0.7 mL/kg/hour
    chronic drinker: 0.8 mL/kg/hour

LoE:III[xxviii]

If ethanol 95% BP is not available, administer any commercially available alcoholic beverage with an alcohol content of ± 40% e.g. whiskey (80 proof), diluted 1:2.

Note:

» If patients are not co-operative, administer ethanol via a nasogastric tube.
» Maintain plasma ethanol levels of 1–1.3 g/L (100–130 mg/dL).
» Several days of ethanol therapy may be required. Continue treatment until clinical condition improves.

Cofactor therapy:

- Thiamine, oral, 100 mg daily.
- Pyridoxine, oral, 100 mg daily.

LoE:III

Metabolic acidosis
The aim is to increase the pH to 7.2:

- Sodium bicarbonate, IV, 50–100 mmol/L administered over 30–45 minutes.

Note: The rapid infusion of large volumes of sodium bicarbonate in an already oliguric patient may precipitate pulmonary oedema and cardiac dysrhythmias.

Monitor glucose levels and correct hypoglycaemia, if necessary.
Correct severe or clinical evident hypocalcaemia.

19.17.3 METHANOL POISONING

T51.1

DESCRIPTION

Previously found in methylated spirits but methanol has recently been replaced with less toxic agents. Also found in antifreeze and windscreen washes. Methanol does not cause an ethanol-like inebriation.

Presents with:

» Initially, headache, confusion, nausea and vomiting.
» Later, high anion gap (> 12), metabolic acidosis, retinal toxicity (with visual impairment to total blindness) and renal failure due to formic acid production.

MEDICINE TREATMENT

If acidotic and there is an increased osmolar gap:
[measured osmolarity minus calculated (2 {sodium+potassium}+ urea+ glucose)], start with immediate ethanol therapy and evaluate for urgent dialysis, if available. *LoE:III*

See section 19.15.2: Ethylene glycol poisoning.

19.18 PESTICIDES AND RODENTICIDES

19.18.1 AMITRAZ POISONING

T60.9
* 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.

Patients with acute poisoning present with:

» impaired consciousness
» drowsiness
» vomiting
» hypotension
» bradycardia
» tachypnoea
» hypothermia
» generalized seizures
» constricted pupils or rarely, dilated pupils

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; however, organophosphate toxicity presents with reduced serum pseudocholinesterase.

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

For severe bradycardia:

- Atropine (See section 3.3.3 Heart block (second or third degree)). *LoE:III*

For seizures:

- Diazepam IV, 10 mg as a single dose.
  - If seizures persist refer to section 14.3.1 Status epilepticus for management to stop seizures.

19.18.2 ORGANOPHOSPHATE POISONING

T60.0
* 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.
Muscarinic overstimulation: salivation, lacrimation, vomiting, diarrhoea and increased bronchial secretions, with bronchospasm and miosis (pin point pupils).
Nicotinic overstimulation: muscle fasciculations and paresis or paralysis and often hypertension. Patients may present with either bradycardia or tachycardia.
Diagnosis is supported by low serum pseudocholinesterase levels.

GENERAL MEASURES

Decontamination of skin and clothes, where applicable.
Maintain adequate ventilation and circulation.
Ventilatory support in ICU may be required due to excess of nicotinic effects.

MEDICINE TREATMENT

- Atropine, IV, 2–5 mg, as a single dose, while monitoring patient for pulmonary muscarinic symptoms and signs.
  - Double the dose every five minutes until symptoms are alleviated. A continuous IV infusion of 0.05 mg/kg/hour may be required for continuous atropinisation.
  - Do not stop atropine therapy abruptly. Wean at a rate of no more than 1–2 mL/hour. During this phase it is important to monitor the patient as a worsening in condition commonly occurs a few days following ingestion.

LoE:II[xxix]

19.18.3 PARAQUAT POISONING

T60.3
* Notifiable condition.

DESCRIPTION

Paraquat poisoning causes multi-organ failure and can be fatal. Following oral ingestion, patients present with oral, oesophageal and gastric erosions with severe gastroenteritis. Multi-organ failure develops 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.
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 TRETAMENT

- Activated charcoal if patient presents within 1–2 hours after ingestion.

19.19 ANTICOAGULANT POISONING

T45.5

DESCRIPTION

Poisoning due to warfarin ingestion and ingestion of superwarfarins, e.g. rat poison and other vermin poisons. Warfarin poisoning can occur following an intentional ingestion of a large amount of warfarin.

It can also occur unintentionally, during chronic ingestions of prescribed amounts, whereby drug interactions increase the bioavailability of warfarin (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 very potent, therefore even a small amount can lead to serious complications, and have a very long duration of effect. Measure INR at baseline and 48 hours post ingestion, as the anticoagulant effect may be delayed by 1–2 days.

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 can be given orally. *LoE:I*[xxx]

Elevated INR with significant bleeding:

» Stop warfarin.
- Vitamin K_1, IV,10 mg diluted in 100 mL sodium chloride 0.9% over 20 minutes and monitor for anaphylaxis. *LoE:III*[xxxi]
- Give FFP 15 mL/kg

OR *LoE:III*[xxxii]

Lyophilised plasma, IV, 15 mL/kg. *LoE:II*[xxxiii]

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 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.

Super warfarins
» Treatment with vitamin K_1 needs to be prolonged for several months as these substances are very long acting.
» Monitor INR according to clinical response.
- Vitamin K_1 oral, 10–25 mg, daily may be required.

Vitamin K_1 is available in the public sector as a parenteral preparation only, but this can be given orally.

19.20 CARBON MONOXIDE POISONING

T58

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
» seizures and other CNS symptoms
» nausea and vomiting
» headache
» retinal haemorrhages
» high arterial carboxyhaemoglobin - test not commonly available
» impaired level of consciousness
» cherry red skin and lips
» tachycardia
»
» normal arterial PaO_2 but low oxygen saturation

GENERAL MEASURES

Remove patient from toxic environment.
Ventilation may be needed in deeply comatose patients.
In a Cochrane review, hyperbaric oxygen therapy has not been shown to be of benefit.

MEDICINE TREATMENT

Give 100% oxygen via facemask.

For seizures:
- Diazepam IV, 10 mg as a single dose.
  - If seizures persist refer to section 14.3.1 Status epilepticus for management to stop seizures.

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 etc. Acute toxicity of organ-systems may be summarised as follows:
Discuss all potential patients with poison centre for further investigation, treatment and possible referral.

	Respira-tory	GIT	Haema-tological	CVS	Kidneys	Hepato-toxicity	CNS
Mercury	x	x	x	x	x		x
Arsenic	x	x	x	x	x		x
Gold		x	x		X	x	
Thallium		x	x	x	x		x
Copper		x	x	x	x	x	
Lead		x	x		x		x
Cadmium		x		x	x	x	

19.22 POISONING WITH SUBSTANCES THAT CAUSE METHAEMOGLOBINAEMIA

D74.8/D74.9

DESCRIPTION

Nitrites are used to cure meat in the formal and informal butchery sector.
Patients present with:

» normal oxygen levels and deep central cyanosis, due to methaemoglobinaemia,
» CNS depression, and
» arrhythmias.

Note: Mild methaemoglobinaemia causes patients to appear cyanosed with falsely low pulse oximetry readings. An arterial blood gas analysis should be done.

MEDICINE TREATMENT

Oxygen via facemask.

In symptomatic cases or patients with high methaemoglobin values > 30%:

- Methylene blue (methylthioninium 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 praecordial 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. There are isolated case reports of use with N-acetylcysteine or high doses of ascorbic acid (vitamin C). Consult with poison information centre for management.

LoE:III[xxxiv]

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CHAPTER 20

EMERGENCIES AND INJURIES

20.1 EMERGENCIES

20.1.1 ANGIOEDEMA

T78.3

DESCRIPTION

Angioedema is well demarcated, localised oedema involving deeper layers of skin and subcutaneous tissue.
ACE-inhibitors are the most common cause, mediated by reduced bradykinin. Hereditary or acquired deficiencies of C1 esterase inhibitor, resulting in reduced bradykinin, are uncommon causes of angioedema. Treatment of these causes of angioedema is to increase bradykinin, e.g. by giving fresh frozen plasma, which contains C1 esterase inhibitor and ACE.

The other mechanism of angioedema is type 1 hypersensitivity reactions to medicines and other exogenous substances (e.g. food). Other manifestations of allergy (e.g. urticaria, bronchospasm, anaphylaxis) may be present.

Symptoms

Swelling usually occurs around eyes and lips but may occur elsewhere.
Life-threatening airway obstruction can occur with angioedema of the 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

In severe cases of hypersensitivity where airway obstruction may be imminent:
Note: A surgical airway may be required before patient responds to medical treatment.

- Adrenaline (epinephrine) 1:1000, 0.5 mL, IM, immediately into anterolateral thigh.
    - Repeat dose every 5 minutes, as required. *LoE:III*

In cases where angioedema is part of anaphylaxis, treat as anaphylaxis. See section 20.1.2: Anaphylaxis/Anaphylactic shock.

- Hydrocortisone, IV, 100 mg as a single dose.

If urticaria and/or itch present:

- Antihistamine, e.g.:
- Cetirizine, oral, 10 mg daily. *LoE:III*

Observe all cases until resolution.

Severe ACE-inhibitor induced angioedema with threatened airway:
Note: A surgical airway may be required before patient responds to medical treatment.

- FFP, IV, 2 units.

OR *LoE:II[ii]*

Lyophilised plasma, IV, at an equivalent dose. *LoE:III*

20.1.2 ANAPHYLAXIS/ANAPHYLACTIC SHOCK

T78.2

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.

Intravenous fluids

Establish an intravenous line:

- Sodium chloride 0.9%, IV.

AND *LoE:II[iii]*

- Hydrocortisone, IV, 200 mg, immediately as a single dose.

If bronchospasm:

- Oxygen.

AND

- Salbutamol 5 mg (1 mL 0.5% respiratory solution with 4 mL sodium chloride 0.9%).
  - Nebulise continuously (refill the nebuliser reservoir every 20 minutes) at a flow rate of 6–8 L/minute. *LoE:III[iv]*

If urticaria and/or itch present:

- Antihistamine, e.g.:
- Cetirizine, oral, 10 mg as a single dose.

LoE:III

20.1.3 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. **Do not use tourniquets.**
Insert one or two large bore IV catheters; peripheral lines are adequate.

MEDICINE TREATMENT

Initial volume resuscitation

- Sodium chloride 0.9%, IV, 1–2 L.

Monitor blood pressure, pulse and clinical response.

LoE:I[v]

Trauma-related haemorrhage

May be given **within 3 hours** of injury:

- Tranexamic acid, IV, 1 g, infused over 10 minutes.
  - Followed with IV infusion, 1 g, over 8 hours. *LoE:I[vi]*

Benefit is greatest, if initiated, in the 1st hour. Initiation beyond 3 hours of tranexamic acid may be harmful.

Blood transfusion, if indicated.
If patient responds initially and subsequently deteriorates, 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.

20.1.4 DISTRIBUTIVE SHOCK

R65.1/R57.9

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: 20.1.2 Anaphylaxis/anaphylactic shock).

20.1.4.1 NEUROGENIC SHOCK

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

If hypoxic:

- Oxygen.

- 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

20.1.4.2 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

If hypoxic:

- Oxygen.

Take blood culture, then administer appropriate parenteral broad spectrum antibiotics urgently, e.g.:

- Ceftriaxone, IV, 2 g daily.

LoE:II[vii]

Perform a fluid challenge for hypotension:

- Sodium chloride 0.9%, IV, 500 mL over 30 minutes.
  - 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.

LoE:III

If there is a positive response, continue with intravenous fluid.
Avoid over-hydrating as this could exacerbate hypoxia associated with adult respiratory distress syndrome.

If no haemodynamic response to fluid challenge:

- Adrenaline (epinephrine), IV infusion, 0.05 mcg/kg/minute titrated according to the response.
  - Dilute 10 mg i.e. 10 ampoules of adrenaline 1:1000 in 1 L sodium chloride 0.9%.
  - Infuse according to weight and clinical response.
  - See section 20.1.4.1: Neurogenic shock, for the infusion rate.

20.1.5 CARDIOGENIC SHOCK

R57.0

DESCRIPTION

Patients are hypotensive, cold and clammy and their pulse rate may be variable. Causes include an acute myocardial infarction (MI), myocardial contusion, myocarditis, dysrhythmias, valvular heart disease, etc.

GENERAL MEASURES

Check circulation, airway and breathing.
ECG.

MEDICINE TREATMENT

If hypoxic:

- Oxygen.

Treat the underlying cause, e.g.: MI, dysrhythmia, etc.
A right ventricular myocardial infarction may respond to a fluid challenge.

- 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*[viii]

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

20.1.6 OBSTRUCTIVE SHOCK

R57.9

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 and cold peripheries.
Causes include:

- » cardiac tamponade,
- » acute pulmonary embolism, and
- » tension pneumothorax,
- » severe bronchospasm.

TREATMENT

Treat the cause.

20.1.7 PULMONARY OEDEMA, ACUTE

J81

DESCRIPTION

A life-threatening condition with abnormal accumulation of fluid in the lungs. Acute heart failure is a common cause.

GENERAL MEASURES

Maintain open airway.
Position in Fowler's position, unless hypotensive or comatose.
Correct electrolyte disturbances.

Determine and correct any dysrhythmias.

MEDICINE TREATMENT

- Administer oxygen.
- Furosemide, slow IV, 20–80 mg, initial dose.
  - May be repeated 15 minutes later if symptoms persist.
- Isosorbide dinitrate, SL, 5 mg repeat after 1–2 hours, if necessary.

OR

- 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*[ix]
  - 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

<u>If distressed, consider adding morphine:</u>

- Morphine, IV, to a total maximum dose of 10 mg (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 20.1.5: Cardiogenic shock.

20.2 INJURIES

T14

For trauma-related haemorrhage, presenting within 3 hours of injury, see section 20.1.3 Hypovolaemic shock.

20.2.1 BURNS

T30.0

DESCRIPTION

Skin and tissue damage caused by:

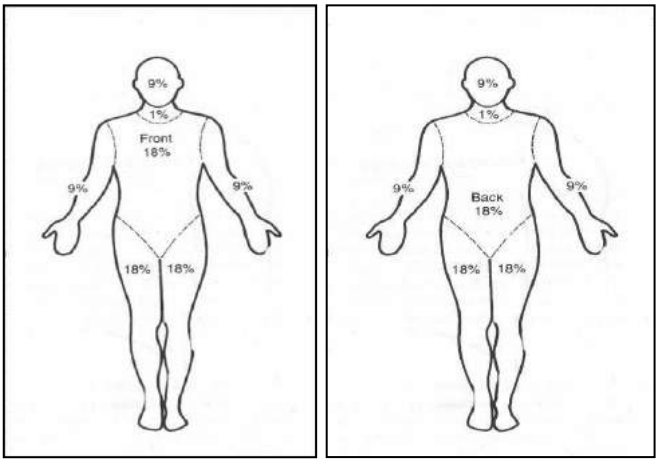
» exposure to extremes of temperature,
» contact with an electrical current,
» exposure to a chemical agent, and
» radiation.

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 and circulation.
» 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.
» Support vital organ function.
» Obtain early IV access to administer intravenous fluids
» Look for aggravating comorbidities, e.g. seizures, hyperkalaemia, renal failure.
» 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.

MEDICINE TREATMENT

Fluid replacement

Burns ≤ 10% Total Body Surface Area (TBSA):

- Oral fluids.

Burns >10% of TBSA:

- IV fluid for resuscitation.

Calculation of fluid replacement

Replacement fluids for burns

» First 24 hours:

- Sodium chloride 0.9%, IV.
  - Calculate total fluid requirement in 24 hours: *LoE:I*[x]

    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.

LoE:III[xi]

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 to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum dose: 4 g in 24 hours.

Tetanus prophylaxis

- Tetanus toxoid vaccine, IM, 0.5 mL immediately.

Burn dressing

- Silver sulfadiazine 1% cream, topical.

LoE:III

For ocular burns

- Sodium chloride 0.9% eye washes or irrigations as soon as possible.

Stress ulcer prophylaxis

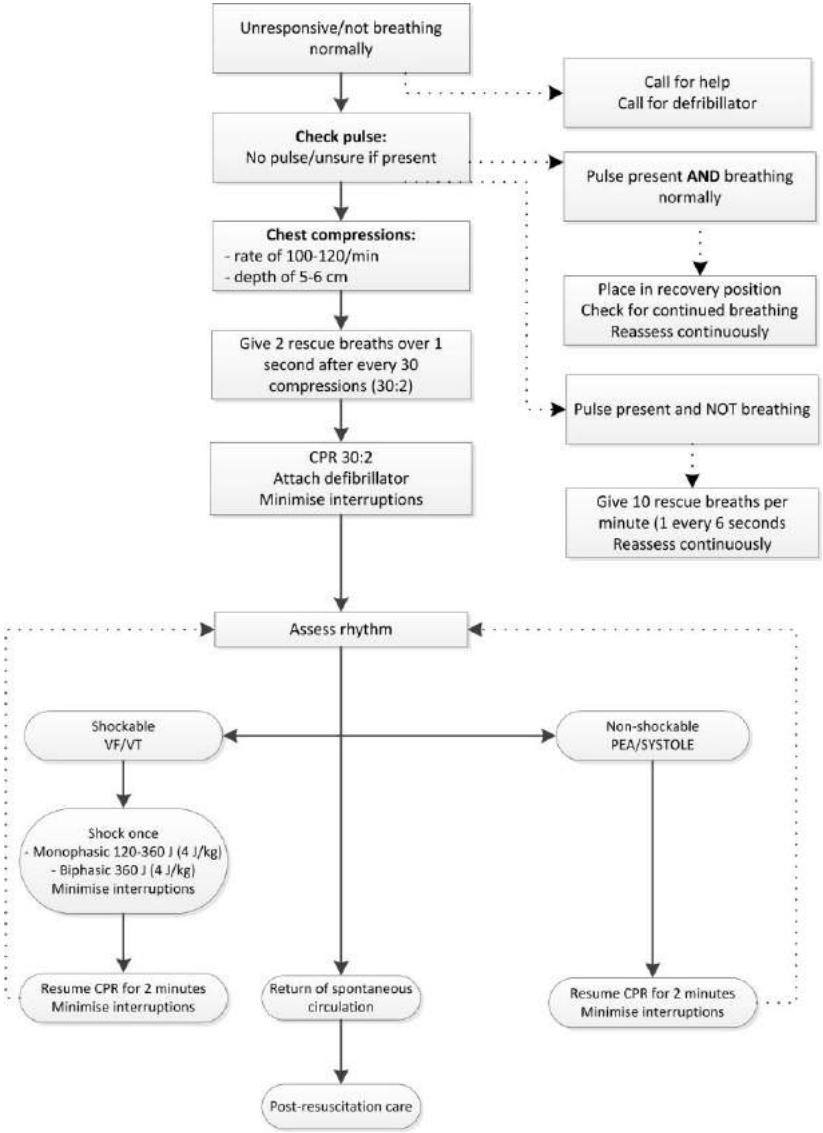
Feeding patients provides protection against gastric ulcer developing and prophylaxis is not necessary in patients who are tolerating feeds.

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 if over 50 years.
» 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.

20.3 CARDIAC ARREST – CARDIOPULMONARY RESUSCITATION



Abbreviations: CPR = Cardiopulmonary Resuscitation; PEA = Pulseless Electrical Activity; VF = Ventricular Fibrillation; VT = Ventricular Tachycardia.
Adapted with permission from the Resuscitation Council of Southern Africa. www.resuscitationcouncil.co.za

20.3.1 CARDIAC ARREST ADULTS

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 and all other pulses
» loss of spontaneous respiration

EMERGENCY TREATMENT

» Diagnose rapidly.
» 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 Airways Breathing) sequence of CPR (cardiopulmonary resuscitation).
» A single powerful precordial thump is recommended for witnessed cardiac arrest where a defibrillator is not immediately available.
» Document medication and progress after the resuscitation.

Cardiopulmonary resuscitation

Circulation

» Check for carotid pulse.
» If there is no pulse or you are not sure, start with chest compressions at a rate of 100-120 compressions per minute.

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. Do not do this where a neck injury is suspected.
» Insert correctly-sized oropharyngeal airway, if available.

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.
» If there is no normal breathing, give 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.
» Repeat the cycle of 30 compressions followed by 2 respirations for 5 cycles and then re-assess for a pulse.

- Oxygenate with 100% oxygen.

Initiate IV fluids, if able.

- Sodium chloride 0.9%, IV.

LoE:I[xii]

In pulseless tachydysrhythmias:

» Defibrillate, as indicated.
» Call a doctor, if available, without stopping CPR.
» Continue 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 endotracheal, when there is no response to initial resuscitation or defibrillation.

- Adrenaline (epinephrine), 1:1 000, 1 mL, IV immediately, as a single dose.
  - Flush with 5–10 mL IV of sterile water or sodium chloride, 0.9%.
  - Repeat every 3–5 minutes during resuscitation.

LoE:I[xiii]

If no IV line is available:

- Adrenaline (epinephrine), endotracheal, 1:1 000, 2 mL through endotracheal tube.
  - 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, or
» no success after all the above procedures have been carried out for 30 minutes or longer.

Consider carrying on for longer especially when:

» hypothermia and drowning
» poisoning or drug overdose or carbon monoxide poisoning

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CHAPTER 21
ONCOLOGY

21.1 MALIGNANCIES

D49.0-D49.9

Certain oncological conditions (e.g. Kaposi sarcoma) may be suitable for management at secondary level of care, in consultation with a specialist. In order to facilitate this process at least the following medications should be available:

- Bleomycin
- Hydroxyurea
- Tamoxifen
- Vincristine

This does not preclude procurement of down referred oncology agents (according to Provincial guidelines) for continuation of care of patients who have been stabilised.

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.
- Ioversol 300 and 350.

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]

Note: Patients allergic to iodine are at an increased risk of adverse drug reactions when exposed to iodine-containing contrast media.

Contrast induced nephrotoxicity (CIN)

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[iv, v] .

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[vi, vii].

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 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
Y47.9

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
Y47.9

Procedural sedation uses medications to allow patients to tolerate unpleasant medical 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.

GENERAL MEASURES
Procedural sedation is a continuum ranging from minimal sedation (anxiolysis), moderate sedation, deep sedation, to general anaesthesia. Deep sedation 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. They should have a detailed understanding of the risks and benefits of the medicines used, and should be competent in resuscitation, airway management and assisted ventilation.

Procedural sedation should be performed only in an area with adequate light and space, and fully functional and adequate observation and resuscitation equipment.

Besides the clinician performing the procedure, there should at least be one other trained person present responsible for observing the patient, assisting with resuscitation if necessary and monitoring the patient. The trained person 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, and 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	Often needed
Breathing	Normal	Usually normal	May need assistance	Often needs assistance
BP/Pulse	Normal	Usually normal		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

LoE:III[I]

Ketamine

Ketamine administration leads to a dissociative state 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 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):

- 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 *LoE:II[III]*

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

Nitrous oxide, inhaled 20 to 50%, in oxygen (will also provide some analgesia).

Moderate sedation and analgesia

If analgesia is required, one of the above is usually combined with an opiate. However, ketamine has analgesic activity and can be used on its own, or combined with a benzodiazepine.

Initial doses:

- Fentanyl, IV, 0.25 mcg/kg.

OR

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 emergence 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.

OR

Nitrous oxide, 20-50% inhaled, in oxygen.

LoE:III[IV]

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. *LoE:III[V]*

Etomidate is a short acting agent like propofol, but is more likely to cause myoclonus. It has no analgesic effect and is more commonly used for emergency unit procedures, rather than endoscopies.

- Etomidate, IV, 0.1 mg/kg.
  - Repeat doses of 0.05 mg/kg every 5 minutes, as required.

LoE:III[VI]

Deep sedation and analgesia

This is usually achieved with either higher doses of medications used for moderate sedation, or by combining an opiate, a benzodiazepine, and either propofol or etomidate.

When agents are combined, lower doses may be adequate.

Supplemental analgesia
Simple analgesics can be given before or after the procedure as appropriate:

- Paracetamol, oral, 1 g 4–6 hourly when required to a maximum of 4 doses per 24 hours.
  - Maximum dose: 15 mg/kg/dose.
  - Maximum dose: 4 g in 24 hours.

AND/OR

- 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.

23.1.2 SEDATION IN INTENSIVE CARE

Y47.9

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[VII]

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.

LoE:II[VIII]

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 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[ix]

23.1.3 SEDATION IN PALLIATIVE CARE

Y47.9

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. The aim is to ameliorate refractory suffering, 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.

Dosing in frail, often elderly patients should be titrated to effect.

- Lorazepam, oral, 0.5 mg 4 hourly.

OR

Haloperidol, oral, 0.5 mg 4 hourly.

LoE:III

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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.**

9.10: Varicella (chickenpox), complicated, 9.11: Zoster (Shingles – with secondary dissemination or neurological involvement), 14.5.2: Viral meningoencephalitis:

- **Aciclovir, IV, 10 mg/kg 8 hourly.**

9.11: Zoster (Shingles), 18.5.1: Keratitis, herpes simplex:

- **Aciclovir, ophthalmic ointment 3%, applied into lower conjunctival sac, five times daily.**

9.10: Varicella (chickenpox), complicated, 9.11: 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:

- **Aciclovir, oral, 400 mg 8 hourly for 7 days.**

AMIKACIN

9.1.3: Hospital-Acquired Pneumonia (HAP), 9.1.4: Urinary tract infections, catheter associated, 10.1.2: Management of selected antiretroviral ADRs - drug-induced liver injury:

- **Amikacin, IV, 15 mg/kg daily**.

AMOXICILLIN

6.11: Preterm Labour (PTL) AND Preterm Prelabour Rupture of Membranes (PPROM), 16.4: Chronic obstructive pulmonary disease (COPD), 17.4: Otitis media, acute:

- **Amoxicillin, oral, 500 mg 8 hourly for 5 days.**

16.6: Pneumonia, community acquired (uncomplicated):

- **Amoxicillin, oral, 1 g 8 hourly.**

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.**

AMOXICILLIN/CLAVULANIC ACID

1.3.8: Bacterial peritonitis, 16.3: Bronchiectasis, 16.4: Chronic obstructive pulmonary disease (COPD): exposure to amoxicillin last 3 weeks, 8.7.3: Diabetic foot ulcers, 1.1.2: Diverticulosis, 16.8: Empyema, 17.1: Epiglottitis, 4.7: Leg ulcers, complicated, 1.2.5: Liver Abscess, pyogenic , 16.5: Lung abscess, 17.4: Otitis media, acute: not responding to amoxicillin, 5.3: Pelvic Inflammatory Disease (PID): stage II-IV, 16.7: Pneumonia, aspiration, 16.6: Pneumonia, community acquired, 6.16: Postpartum Fever, 5.8.4: Septic miscarriage , 19.2: Snakebites: secondary infection, 7.3.2: Urinary tract infection (UTI): pregnant women , 6.19.1: Urinary tract infection in pregnancy, 6.19.2: Urinary tract infection in pregnancy: acute pyelonephritis:

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

1.2.7: Acute cholecystitis and acute cholangitis, 1.3.8: Bacterial peritonitis, 8.7.3: Diabetic foot ulcers: severe infection, 1.1.2: Diverticulosis: cannot take oral medicines, 16.8: Empyema, 1.2.5: Liver Abscess, pyogenic , 16.5: Lung abscess, 16.7: Pneumonia, aspiration, 6.16: Postpartum Fever, 5.8.4: Septic miscarriage , 1.1.6: Pancreatitis acute: abscess of the pancreas:

- **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.**

2.8: Febrile neutropenia, 10.2.4.2: Symptomatic, non-meningeal Cryptococcosis 10.2.4.3: Cryptococcal meningitis: , 14.5.1: Meningitis (cryptococcal meningitis):

- **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.**

AZITHROMYCIN

3.7: Rheumatic heart disease, prophylaxis of recurrent disease, severe penicillin allergy:

- **Azithromycin, oral, 250 mg daily.**

16.6: Pneumonia, community acquired (severe pneumonia):

- **Azithromycin, 500 mg, slow IV (over 3 hours) daily for 3 days.**

1.1.8: Peptic ulcer, severe penicillin allergy, 3.7: Rheumatic heart disease, acute rheumatic fever - severe penicillin allergy, 4.3: Impetigo, 6.11: Preterm Labour

(PTL) AND Preterm Prelabour Rupture of Membranes (PPROM), severe penicillin allergy, 10.2.8: Mycobacteriosis - disseminated non tuberculous, 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.**

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), 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:

- **Azithromycin, oral, 2 g as a single dose.**

9.8: Tick bite fever, in pregnancy:

- **Azithromycin, oral, 500 mg 12 hourly for 3 days.**

BENZATHINE BENZYLPENICILLIN

3.7: Rheumatic heart disease, prophylaxis,

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

3.7: Rheumatic heart disease, acute rheumatic fever:

- **Benzathine benzylpenicillin (depot formulation), IM, 1.2 million units 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.**

6.8: Syphilis, mother:

- **Benzathine benzylpenicillin (depot formulation), IM, 2.4 million units 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.**

9.7: Tetanus:

- **Benzylpenicillin (penicillin G), IV, 5 MU 6 hourly for 10 days.**

3.5: Endocarditis, infective (native valve):

- **Benzylpenicillin (penicillin G), IV, 5 MU 6 hourly for 4 weeks.**

14.5.1: Meningitis (meningococcal meningitis – confirmed meningococcal disease only), 14.5.1: Meningitis (pneumococcal meningitis):

- **Benzylpenicillin (penicillin G), IV, 20 - 24 million units daily in 4–6 divided doses for 10 days.**

14.5.3: Meningovascular Syphillis:

- **Benzylpenicillin (penicillin G), IV, 20 million units daily in 4–6 divided doses for 10 days.**

CEFAZOLIN

11: Cardiac surgery, 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, as a single dose.**
  - If < 80 kg: 1g.
  - If ≥ 80 kg: 2 g.

CEFEPIME

2.8: Febrile neutropenia:

- **Cefepime, IV, 1 g 12 hourly.**

CEFTAZIDIME

18.2: Endophthalmitis, bacterial (endogenous endophthalmitis and post-surgical endophthalmitis):

- **Ceftazidime, intravitreal, 2.25 mg.**

CEFTRIAXONE

10.4.2: Non occupational post exposure prophylaxis, sexual assault and inadvertent exposure, 5.3: Pelvic Inflammatory Disease (PID), stage I, 7.3.4: Prostatitis, associated urethritis:5.10: Sexual assault:

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

1.3.2: Acute inflammatory diarrhoea (dysentery) , 13.2: Arthritis, septic and osteomyelitis, acute , 1.3.8: Bacterial peritonitis, 17.1: Epiglottitis, 2.8: Febrile neutropenia, 5.3: Pelvic Inflammatory Disease (PID), stage II-IV, 7.3.2: Urinary tract infection (UTI), acute pyelonephritis: impaired renal function,6.19.2: Pyelonephritis, acute, in pregnancy:

- **Ceftriaxone, IV, 1 g, daily.**

14.5.5: Antimicrobial use in patients with head injuries, penetrating brain injuries, 14.5.4: Brain abscess , 9.9: Enteric fever (typhoid), 17.6: Mastoiditis, 14.5.1: Meningitis, 17.3: Sinusitis, bacterial, complicated:

- **Ceftriaxone, IV, 2 g 12 hourly.**

16.3: Bronchiectasis, 18.2: Endophthalmitis, bacterial, 9.4: Haemorrhagic fever syndrome , 16.6: Pneumonia, community acquired, patients >65 years, comorbid disease, 16.6: Pneumonia, community acquired, severe pneumonia,20.1.4.2: 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

18.10.2: Eye injury (deep corneal or scleral injuries):

- **Chloramphenicol 1%, ophthalmic ointment, applied immediately.**

18.10.1: Chemical burn, 19.2.2: Venom in the eye:

- **Chloramphenicol 1%, ophthalmic ointment, applied 6 hourly.**

18.1.3: Conjunctivitis, bacterial, 18.10.2: Eye injury (corneal abrasion):

- **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

18.1.3: Conjunctivitis, bacterial, 18.5.2: Keratitis, suppurative:

- **Ciprofloxacin 0.3%, ophthalmic drops.**

14.5.1: Meningitis, nasopharyngeal carriage eradication, 14.5.1: Meningitis, prophylaxis of contacts, 7.3.3: Recurrent UTI (2-3 infections/year) :

- **Ciprofloxacin, oral, 500 mg as a single dose.**

1.3.1: Cholera:

- **Ciprofloxacin, oral, 1 g immediately as a single dose.**

1.3.2: Acute inflammatory diarrhoea (dysentery) , 1.3.8: Bacterial peritonitis, 9.9: Enteric fever (typhoid), chronic carriers, 9.9: Enteric fever (typhoid), following ceftriaxone IV, based on culture sensitivity results,10.2.7: Isosporiasis, cotrimoxazole allergy, 17.5: Otitis media, chronic, suppurative, 5.3: Pelvic Inflammatory Disease (PID), stage II-IV: severe penicillin allergy, 7.3.4: Prostatitis, 5.8.4: Septic miscarriage, severe penicillin allergy, following clindamycin IV + gentamicin IV, 7.3.2: Urinary tract infection (UTI) , 7.3.2: Urinary tract infection (UTI), acute pyelonephritis: impaired renal function, CrCl <10ml/min, following ceftriaxone IV, 7.3.2: Urinary tract infection (UTI), acute pyelonephritis: normal renal function - following gentamicin IV, 9.1.4: Urinary tract infections, catheter associated:

- **Ciprofloxacin, oral, 500 mg 12 hourly.**

16.3: Bronchiectasis, pseudomonas infection, 18.2: Endophthalmitis, bacterial, prophylaxis/soft tissue injury, 17.7.1: Otitis externa, necrostising:

- **Ciprofloxacin, oral, 750 mg 12 hourly for 7 days.**

9.8: 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 mg 8 hourly.**

4.5: Atopic eczema/dermatitis: severe penicillin allergy,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, following gentamicin, IV + clindamycin, IV, 5.8.4: Septic miscarriage, severe penicillin allergy: following clindamycin IV + gentamicin IV, 9.1.2: Surgical wound infections, severe penicillin allergy, following clindamycin IV, 9.1.1: Intravascular catheter infections, erythema beyond catheter site, 17.8: Abscess, peritonsillar, 13.2: Arthritis, septic and osteomyelitis, acute: severe penicillin allergy:

- **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).**

CLOXACILLIN

4.2: Cellulitis and erysipelas, 4.4: Furuncles and abscesses:

- **Cloxacillin, IV, 1 g 6 hourly.**

13.2: Arthritis, septic and osteomyelitis, acute , 9.1.2: Surgical wound infections:

- **Cloxacillin, IV, 2 g 6 hourly.**

3.5: Endocarditis, infective (native valve):

- **Cloxacillin, IV, 3 g 6 hourly.**

COTRIMOXAZOLE

7.3.3: Recurrent UTI, prophylaxis:

- **Cotrimoxazole 80/400 mg, oral, 1 tablet at night.**

10.2.2: Oppurtunistic infection prophylaxis, with cotrimoxazole, 10.2.7: Isosporiasis, 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, 16.6: Pneumonia,community acquired,:HIV infected with bilateral diffuse infiltrates on CXR: <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: Isosporiasis:

- **Cotrimoxazole 320/1600, oral, 12 hourly for 10 days.**

10.2.9: Pneumocystis pneumonia, >60kg, 16.6: Pneumonia,community acquired,:HIV infected with bilateral diffuse infiltrates on CXR, >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.**

9.8: Tick bite fever:

- **Doxycycline, oral, 100 mg 12 hourly for 7 days.**

9.3: Brucellosis:

- **Doxycycline, oral, 100 mg 12 hourly for 6 weeks.**

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.**

10.1.2: Management of selected antiretroviral ADRs: drug-induced liver injury:

- **Ethambutol, oral, 800 - 1200 mg daily.**

ETHIONAMIDE

16.11.2: Multidrug-resistant (MDR) TB, intensive phase: <33kg,16.11.2: Multidrug-resistant (MDR) TB, continuation phase: <33kg:

- **Ethionamide, oral, 15–20 mg/kg daily.**

16.11.2: Multidrug-resistant (MDR) TB, intensive phase: 33-50kg,16.11.2: Multidrug-resistant (MDR) TB, continuation phase: 33-50kg:

- **Ethionamide, oral, 500 mg daily.**

16.11.2: Multidrug-resistant (MDR) TB, intensive phase: 50-65kg,16.11.2: Multidrug-resistant (MDR) TB, continuation phase: 50-65kg:

- **Ethionamide, oral, 750 mg daily.**

16.11.2: Multidrug-resistant (MDR) TB, intensive phase: >65kg,16.11.2: Multidrug-resistant (MDR) TB, continuation phase: >65kg:

- **Ethionamide, oral, 750-1000 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 , 9.11: 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, 14.5.1: Meningitis, cryptococcal meningitis, maintenance therapy:

- **Fluconazole, oral, 200 mg daily.**

10.2.3: Candidiasis of oesophagus/trachea/bronchi, if vomiting or unable to swallow:

- **Fluconazole, IV, 200 mg daily.**

9.1.1: Intravascular catheter infections, candidaemia,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 , 14.5.1: Meningitis, cryptococcal:

- **Fluconazole, oral, 800 mg daily**

10.2.4.1: Asymptomatic cryptococcosis, CrAg positive, consolidation therapy, 10.2.4.2: Symptomatic, Non-Meningeal Cryptococcosis, consolidation therapy, 10.2.4.3: Cryptococcal meningitis, consolidation therapy:

- **Fluconazole, oral, 400 mg daily for 8 weeks.**

FOSFOMYCIN

6.19.1: Urinary tract infection in pregnancy, severe penicillin allergy, 7.3.2: Urinary tract infection (UTI) – complicated community acquired cystitis, severe penicillin allergy, 1st trimester:

- **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.**

2.8: 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), 6.19.2: Pyelonephritis, acute, in pregnancy, 7.3.2: Urinary tract infection (UTI), acute pyelonephritis: normal renal function, 11: Gastrointestinal surgery: severe pencillin allergy, 11: Obstetrics/ gynaecology surgery: severe penicillin allergy, 11: Urology procedures: severe penicillin allergy:

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

IMIPENEM

2.8: Febrile neutropenia (if fever develops after 48 hours of admission – also consider local susceptibility patterns):

- **Imipenem, IV, 500 mg 6 hourly.**

9.1.3: Hospital-Acquired Pneumonia (HAP), with risk factors, Ventilator Associated Pneumonia (VAP):

- **Imipenem, IV, 1 g 8 hourly (except CNS infections or known epileptics).**

ISONIAZID

10.1.2: Management of selected antiretroviral ADRs, drug-induced liver injury, 10.2.1: Isoniazid preventive therapy (IPT):

- **Isoniazid, oral 300 mg daily.**

KANAMYCIN

16.11.2: Multidrug-resistant (MDR) TB, intensive phase, intensive phase: <33-65kg:

- **Kanamycin, IV, 15 mg/kg daily (max: 1 g daily).**

16.11.2: Multidrug-resistant (MDR) TB, intensive phase, intensive phase: >65kg:

- **Kanamycin, IV, 1 g daily.**

LEVOFLOXACIN

10.1.2: Management of selected antiretroviral ADRs, drug-induced liver injury:

- **Levofloxacin 750 - 1000 mg daily.**

MEROPENEM

2.8: Febrile neutropenia:

- **Meropenem, IV, 1 g 8 hourly.**

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, 6.11: Preterm labour (PTL) and preterm prelabour rupture of membranes (PPROM) , 14.5.4: Brain abscess:

- **Metronidazole, oral, 400 mg 8 hourly**

5.3: Pelvic Inflammatory Disease (PID), stage I, 1.1.8: Peptic ulcer, H. pylori +ve:

- **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 , 10.4.2: Non occupational post exposure prophylaxis, sexual assault and inadvertent exposure:

- **Metronidazole, oral, 2 g.**

11: Gastrointestinal surgery, 11: Obstetrics/ gynaecology surgery, 11: Orthopaedic surgery , 11: Otorhinolaryngology/ Head and neck surgery, 11: Urology, 11: Vascular surgery:

- **Metronidazole, IV, 500 mg, as a single dose.**

5.3: Pelvic Inflammatory Disease (PID), stage II-IV, 9.1.2: Surgical wound infections, female uro-genital tract, open GIT surgery, 9.7: Tetanus , 14.5.4: Brain abscess , 17.8: Abscess, peritonsillar:

- **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, 10.1.2: 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, 16.11.2: Multidrug-resistant (MDR) TB:

- **Moxifloxacin, oral, 400 mg daily.**

NATAMYCIN

18.5.2: Keratitis, suppurative, fungal infection:

- **Natamycin 5%, ophthalmic drops.**

NITROFURANTOIN

7.3.2: Urinary tract infection (UTI) , severe penicillin allergy, 2nd and 3rd trimester:

- **Nitrofurantoin, oral, 100 mg 12 hourly for 7 days.**

7.3.3: Recurrent UTI , prophylaxis

- **Nitrofurantoin, oral, 100 mg at night for 6 months.**

OFLOXACIN

18.1.3: Conjunctivitis, bacterial, 18.5.2: Keratitis, suppurative:

- **Ofloxacin 0.3%, ophthalmic drops.**

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

2.8: Febrile neutropenia, 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

10.1.2: Management of selected antiretroviral ADRs, drug-induced liver injury, 16.11.1: INH monoresistant TB:

- **Pyrazinamide, oral, 25 mg/kg daily.**

16.11.2: Multidrug-resistant (MDR) TB, intensive phase: <33kg, 16.11.2: Multidrug-resistant (MDR) TB, continuation phase: <33kg:

- **Pyrazinamide, oral, 30–40 mg/kg daily.**

16.11.2: Multidrug-resistant (MDR) TB, intensive phase: 33-50kg, 16.11.2: Multidrug-resistant (MDR) TB, continuation phase: 33-50kg:

- **Pyrazinamide, oral, 1 g–1750 mg, daily.**

16.11.2: Multidrug-resistant (MDR) TB, intensive phase: 50-65kg, 16.11.2: Multidrug-resistant (MDR) TB, continuation phase: 50-65kg:

- **Pyrazinamide, oral, 1750 mg–2 g, daily.**

16.11.2: Multidrug-resistant (MDR) TB, intensive phase: >65kg, 16.11.2: Multidrug-resistant (MDR) TB, continuation phase: >65kg:

- **Pyrazinamide, oral, 2 g–2 500 mg daily.**

RIFABUTIN

10.1: Antiretroviral therapy, TB treatment for patients on ATV/r or darunavir when rifampicin is contraindicated:

- **Rifabutin, oral, 150 mg 3 times a week.**

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.**

10.1.2: Management of selected antiretroviral ADRs, drug-induced liver injury; <60kg:

- **Rifampicin, oral 450 mg daily.**

10.1.2: Management of selected antiretroviral ADRs, drug-induced liver injury:

- **Rifampicin, oral 600 mg daily.**

14.5.1: Meningitis, severe penicillin allergy:

- **Rifampicin, oral, 600 mg 12 hourly.**

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: >55kg16.10: 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:

- **Rifampicin/isoniazid/pyrazinamide/ethambutol, oral, 300/150/800/500 mg, daily for 2 months.**

16.9: Tuberculosis, pulmonary, initial phase: 38-54kg:16.10: Tuberculosis, Pleural, initial phase: 38-54kg:

- **Rifampicin/isoniazid/pyrazinamide/ethambutol, oral, 450/225/1200/825 mg, daily for 2 months.**

16.9: Tuberculosis, pulmonary, initial phase:55-70kg, 16.10: Tuberculosis, Pleural, initial phase:55-70kg:

- **Rifampicin/isoniazid/pyrazinamide/ethambutol, oral, 600/300/1600/1100 mg, daily for 2 months.**

16.9: Tuberculosis, pulmonary, initial phase:71kg and over, 16.10: Tuberculosis, Pleural, initial phase:71kg and over,

- **Rifampicin/isoniazid/pyrazinamide/ethambutol, oral, 750/3755/2000/1375 mg, daily for 2 months.**

TENOFOVIR

1.2.4.2: Hepatitis B, chronic (non-HIV co-infection):

- **Tenofovir, oral, 300 mg daily.**

TERIZIDONE

16.11.2: Multidrug-resistant (MDR) TB, intensive phase: <33kg, 16.11.2: Multidrug-resistant (MDR) TB, continuation phase: <33kg:

- **Terizidone, oral, 15–20 mg/kg, daily.**

16.11.2: Multidrug-resistant (MDR) TB, intensive phase: 33-65kg, 16.11.2: Multidrug-resistant (MDR) TB, continuation phase: 33-65kg:

- **Terizidone, oral, 750 mg, daily.**

16.11.2: Multidrug-resistant (MDR) TB, intensive phase: >65kg, 16.11.2: Multidrug-resistant (MDR) TB, continuation phase: >65kg:

- **Terizidone, oral, 750 mg – 1000 mg, daily.**

VALGANCICLOVIR

10.2.6 Cytomegalovirus (CMV) - Biopsy-proven GIT disease and pneumonitis:

- **Valganciclovir, oral, 900 mg 12 hourly for the first 3 weeks, if available. Maintenance treatment is not indicated unless there has been a relapse.**

10.2.6 Cytomegalovirus (CMV) – CNS disease:

- **Initial treatment: Valganciclovir, oral, 900 mg 12 hourly for the first 3 weeks, if available.**
- **Maintenance treatment: Valganciclovir, oral, 900 mg daily until CD4 count rises to > 100 on ART.**

18.6 Retinitis, HIV CMV (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).**

VANCOMYCIN

1.3.4: Diarrhoea, antibiotic-associated (failure to respond to metronidazole after 5 days):

- **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.**

2.8: Febrile neutropenia, IV, skin infection, 9.1.1: Intravascular catheter infections, S. aureus infection, 9.1.2: Surgical wound infections, MRSA, 14.5.1: Meningitis, severe penicillin allergy:

- **Vancomycin, IV, 30 mg/kg as a loading dose. Follow with 20 mg/kg/dose 12 hourly.**

AMIKACIN, IV

- Amikacin, IV, 15 mg/kg (if BMI is > 40 use ideal body weight + 40% of the difference between ideal and actual body weight), daily. 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/min, 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 for a maximum of 10 days.
  - Amikacin is potentially nephrotoxic and ototoxic – monitor creatinine three times per week, as well as pre-dose amikacin trough levels; and discontinue if vestibular or cochlear symptoms develop.
  - Therapeutic drug monitoring: pre-dose amikacin trough levels. 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 also measure peak concentrations (immediately after infusion).

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

- 875/125 mg tablets containing 875mg amoxicillin trihydrate and 125mg clavulanic acid.
- **Dosage recommendation:** amoxicillin/clavulanic acid, 875**/**125 mg oral, 12 hourly.
  - When treating pneumonia in areas where there is a confirmed high level of penicillin intermediate resistant *Streptococcus pneumoniae* (>/= 5%):
  - **ADD:** Amoxicillin 1 000 mg, oral, daily between the amoxicillin/clavulanic acid doses (i.e. 8 hours after the morning dose of amoxicillin/clavulanic acid).

AMOXICILLIN/CLAVULANICACID,IV

- **Amoxicillin/clavulanic acid IV is not suitable for intramuscular or subcutaneous administration.**

- Amoxicillin/claculanic 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.
    - 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).
    - Reconstituted vials can be administered intravenously by injection over 2 minutes or slow intravenous infusion over 30 minutes.
    - The contents of the vials must be used within 20 minutes and thereafter any unused material discarded.
  - **Precautions:**
    - Allergy to penicillins.
    - Drug-induced cholestatic hepatitis may occur, typically a few weeks after starting therapy. Used with caution in patients with evidence of hepatic dysfunction.
    - Dosage adjustments required in renal impairment:
      - » Creatinine clearance > 70 ml/min = no dose adjustment required.
      - » Creatinine clearance 10–30 ml/min = 1.2 g as a single dose followed by 600 mg 12 hourly.
      - » Creatinine clearance < 10 ml/min = 1.2 g as a single dose followed by 600 mg **daily.**

AMPHOTERICN B, IV

- Amphotericin B, IV, 1 mg/kg daily.
  - Ensure adequate hydration to minimise the risk of nephrotoxicity.
  - **Monitoring**
    - Serum potassium 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, and daily weight.

AMPHOTERICN B, IV (continued)

- **Management**
  - If significant hypokalaemia (K < 3.3 mmol/L):
  - Increase potassium supplementation i.e. potassium chloride (KCL) 40 mmoL diluted in sodium chloride 0.9%, 1000 mL, at a rate of 125 mL/hour, IV, and repeat serum potassium in 24 hours.

  OR

  - Potassium chloride, oral, 600–1200 mg 8 hourly.
    - Monitor potassium daily.

  - If hypokalaemia remains uncorrected, check serum magnesium and correct as required.

  - If creatinine increases by ≥ 2 fold from baseline value, either temporary 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

CLINDAMYCIN, IV

- Clindamycin IV, 600 mg.
  - » 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.

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).
  - Follow with an oral antihypertensive regimen.

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.
  - Monitor trough (pre-dose) plasma levels after 5 days.
  - 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.

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/min: Normal daily dose (see above).
  - eGFR < 60 mL/min: Half of the daily dose.
  - eGFR < 30 mL/min: Stop metformin.
- Contra-indicated in:
  - renal impairment i.e. eGFR < 30 mL/min,
  - uncontrolled congestive cardiac failure,
  - severe liver disease,
  - patients with significant respiratory compromise, or
  - peri-operative cases.

MORPHINE, IV

- Morphine, IV, to a total maximum dose of 10 mg.
  - Morphine, IV, 3–5 mg as a single dose then further boluses of 1–2 mg/minute and monitor closely.
  - 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 blood pressure.

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 40 mmol KCl (two 10 ml ampoules of the 15% solution containing 20mmol KCl/ampoule) 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)'.

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 1g/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/min.

Dosing intervals and when to measure trough concentrations of vancomycin:

eGFR (mL/min)	**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.
  - 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, cimetidine, phenytoin, carbamazepine, etc.
    - Grapefruit juice.

Unless INR is widely 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.

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	$\frac{1}{[b/(b+d)] - [a/(a+c)]}$
Relative risk	$[a/(a+c)] \div [b/(b+d)]$
Odds ratio	$\frac{[a/(a+c)] \div [c/(a+c)]}{[b/(b+d)] \div [d/(b+d)]} = (a/c) \div (b/d)$

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 Nonproprietary 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	
PTC Title:	**Date submitted:**

GUIDELINES FOR ADVERSE DRUG REACTION REPORTING

National Pharmacovigilance Programme

The Medicines Control Council (MCC) 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 MCC 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)?

The Medicines Control Council (MCC) 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 drugs added to the EDL
- 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: *http://www.mccza.com*

1. The Registrar of Medicines

Medicines Control Council, Department of Health, Private Bag X828
Pretoria, 0001
Tel: (021) 395 8003/8176; Fax: (012) 395 8468

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

ADVERSE DRUG REACTION AND PRODUCT QUALITY PROBLEM REPORT FORM

(*Identities of reporter and patient will remain strictly confidential)*

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

NATIONAL ADVERSE DRUG EVENT MONITORING CENTRE
NADEMC
The Registrar of Medicines
Private Bag X 828
Pretoria 0001
In collaboration with the WHO International Drug Monitoring Programme

PATIENT INFORMATION

Name (or initials): .....
Patient Reference Number: ……..

Sex:	**M**	**F**	**Age:**	**DOB:**	**Weight (kg)**	**Height (cm)**
			.....	..... / ...../	.....	.....

ADVERSE REACTION/PRODUCT QUALITY PROBLEM (tick appropriate box)

Adverse reaction ☐ **and/or Product Quality problem** ☐

Date of onset of reaction:
...../...../.....
Time of onset of reaction:

….....hour.....min

Description of reaction or problem (Include relevant tests/lab data, including dates):

1. MEDICINES / VACCINES / DEVICES (include all concomitant medicines)					
Trade Name and Batch No. (Asterisk Suspected Product)	**Daily Dosage**	**Route**	**Date Started**	**Date Stopped**	**Reasons for use**

ADVERSE REACTION OUTCOME (Check all that apply)

	death		life-threatening
	disability		hospitalisation
	congenital anomaly		Other.....
	required intervention to prevent permanent impairment/damage		

Reaction abated after stopping medicine:

	Y		**N**

Event reappeared on rechallenge:

	Y		**N**		**Rechallenge not done**

Recovered:

	Y		**N**

Sequelae:

	Y		**N**

Describe Sequelae:.....

COMMENTS: (e.g. Relevant history, Allergies, Previous exposure, Baseline test results/lab data)

2. PRODUCT QUALITY PROBLEM:

Trade Name	Batch No	Registration No	Dosage form & strength	Expiry Date	Size/Type of container

Product available for evaluation?: **Y** **N**

REPORTING HEALTHCARE PROFESSIONAL:

NAME: .....

QUALIFICATIONS:.....

ADDRESS: .....

.....Postal Code: ……

TEL: (.....).....

…….. ……..
Signature Date

This report does not constitute an admission that medical personnel or the product caused or contributed to the event.

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:

- fax: (012) 395-9201
- phone: (012) 395-9341

Adverse Events Following Immunisation:

- fax: (012) 395 8905
- phone: (012) 395 8914/5

Confidentiality: Identities of the reporter and patient will remain strictly confidential.

Your support of the Medicine Control Council'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.

PLEASE USE ADDRESS PROVIDED BELOW - JUST FOLD IN THIRDS, TAPE and MAIL

Postage will be paid by the Addressee
Posgeld sal deur die geadresseerde betaal word

No Postage stamp necessary if posted in the Republic of South Africa
Geen posseël nodig nie indien in die Republiek van Suid-Afrika gepos

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BESIGHEIDSANTWOORDDIENS
Free Mail Number: **BNT 178**
Vryposnommer:

DEPARTMENT OF HEALTH
DEPARTEMENT VAN GESONDHEID
REGISTRAR OF MEDICINES
REGISTRATEUR VAN MEDISYNE
PRIVATE BAG / *PRIVAATSAK* X828
PRETORIA
0001

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 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:

a) **Category A:** these are medical conditions that require immediate notification to the regional/provincial or national Department of Health by telephone or fax upon initial diagnosis (presumptive or confirmed) with written notification form (GW17/5) to follow within five days.

Any health care professional identifying even a single case of a disease (presumptive or laboratory confirmed) contained in the Category A 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.

b) **Category B**: these are medical conditions that require written notification (GW17/5 form) only, within seven days of diagnosis.

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.

National Department of Health
Cluster: Health Information, Evaluation & Research (HIER)
Directorate: Epidemiology & Surveillance
Private Bag X828
PRETORIA
0001
Tel: 012 395 8150/1

List of Notifiable Medical Conditions

Category A: *Immediate notification (within 24 hours) of diagnosis by the health care professional (telephone or fax) to the designated district or provincial health officer*.

Acute flaccid paralysis
Anthrax
Cholera
Crimean-Congo haemorrhagic fever
Other haemorrhagic fevers of Africa
Food poisoning
Measles
Meningococcal infection
Plague
Rabies, human
Yellow fever

Category B

Brucellosis
Congenital syphilis
Diphtheria
Haemophilus Influenza type B
Lead poisoning
Legionellosis
Leprosy
Malaria
Paratyphoid fever
Poisoning agricultural stock remedies
Poliomyelitis
Rheumatic fever
Tetanus
Tetanus neonatorum
Trachoma
Tuberculosis primary
Tuberculosis pulmonary
Tuberculosis of other respiratory organs
Tuberculosis of meninges
Tuberculosis of intestines, peritoneum
Tuberculosis of bones and joints
Tuberculosis of genito-urinary system
Tuberculosis of other organs
Tuberculosis miliary
Typhoid fever
Typhus fever (lice-borne)
Typhus fever (ratflea-borne)
Viral hepatitis type A (acute)
Viral hepatitis type B (acute)
Viral hepatitis non-A non-B (acute)
Viral hepatitis unspecified
Whooping cough

INDEX OF DISEASE CONDITIONS

INDEX OF MEDICINES

ABBREVIATIONS

3TC	lamivudine
ab	antibody
ABC	abacavir
ACE-inhibitor	angiotensin-converting-enzyme inhibitor
ABG analysis	arterial blood gas analysis
ACR	albumin/creatinine ratio
ACTH	adrenocorticotropic hormone
ADR	adverse drug reaction
AED	automated external defribillator
AIDP	acute inflammatory demyelinating polyradiculoneuropathy
AIDS	Acquired Immune Deficiency Syndrome
AKI	acute kidney injury
ALP	alkaline phosphatase
ALT	alanine transaminase
ANCA	antineutrophil cytoplasmic antibodies
ANF	antinuclear factor
anti-HBs	antibody to the hepatitis B surface antigen
anti-Hbe	hepatitis B e-antibody
aPTT	activated partial thromboplastin time
ARB	angiotensin II receptor blocker
ARDS	acute respiratory distress syndrome
ART	antiretroviral therapy
ARV	antiretroviral medicine
AST	aspartate aminotransferase
ATV/r	atazanavir/ritonavir
AV	atrioventricular
AZT	zidovudine
BCG vaccine	Bacillus Calmette–Guérin vaccine
Beta-HCG test	beta-human chorionic gonadotropin test
BMI	body mass index
BMD	bone mineral density
BP	blood pressure
^{0}C	(degrees) Celcius
Ca	calcium
CAB	circulation airways breathing
CAD	coronary artery disease
CCF	congestive cardiac failure
CD	Crohn's disease
CD4	cluster of differentiation 4
CIDP	chronic inflammatory demyelinating polyradiculoneuropathy
CIN	contrast induced nephrotoxicity
CK	creatinine kinase
CKD	chronic kidney disease
Cl	chloride
CLAT	cryptococcus latex agglutination test
cm	centimetre
cmv	cytomegalovirus
CNS	central nervous system
CO_2	carbon dioxide
COPD	chronic obstructive pulmonary disease
CPAP	continuous positive airway pressure
CPR	cardiopulmonary resuscitation
CrAg	cryptococcal antigen
CrCl	creatinine clearance
CRP	C-reactive protein
CSF	cerobrospinal fluid
CSU	catheter specimen urine
CT	computerized tomography

CVA	cerebral vascular accident
CVD	cardiovascular disease
CVS	cardiovascular system
CXR	chest X-ray
d4T	stavudine
DBP	diastolic blood pressure
DC	direct current
DIC	disseminated intravascular coagulation
DILI	drug-induced liver injury
DKA	hyperglycaemia diabetic ketoacidosis
dL	decilitre
DMARD	disease-modifying antirheumatic drug
DMPA	depot medroxyprogesterone acetate
DNA	deoxyribonucleic acid
DRESS	drug reaction with eosinophilia and systemic symptoms
DR-TB	drug resistant tuberculosis
DU	duodenal ulcer
DVT	deep venous thrombosis
E or EMB	ethambutol
ECG	electrocardiogram
EEG	electroencephalogram
EFV	efavirenz
eGFR	estimated glomerular filtration rate
ELISA	enzyme-linked immunosorbent assay
EML	essential medicine list
EPI	expanded programme on immunisation
ESR	erythrocyte sedimentation rate
ESRD	end stage renal disease
FBC	full blood count
FDC	fixed dose combination
FEV_1	forced expiratory volume in 1 second
FFP	fresh frozen plasma
FH	familial hypercholesterolaemia
FiO_2	fraction of inspired oxygen
FPG	fasting plasma glucose
FSH	follicle-stimulating hormone
FTA-abs	fluorescent treponemal antibody absorption
FTC	emtricitabine
FVC	forced vital capacity
G6PD	glucose-6-phosphate dehydrogenase
g	gram
GDM	gestational diabetes
GGT	gamma-glutamyl transferase
GH	growth hormone
GI(T)	gastrointestinal (tract)
GORD	gastro-oesophageal reflux disease
GU	gastrointestinal ulcer
H or INH	isoniazid
HAP	hospital-acquired pneumonia
Hb	haemoglobin
HbA1c	glycosylated haemoglobin
HbeAg	hepatitis B e-antigen
HBIG	hepatitis B immune globulin
HbS	sickle haemoglobin
HBsAb	hepatitis B surface antibody
HBsAg	hepatitis B surface antigen
HbSS	sickle cell haemoglobin
HBV	hepatitis B virus
HCl	hydrochloric acid

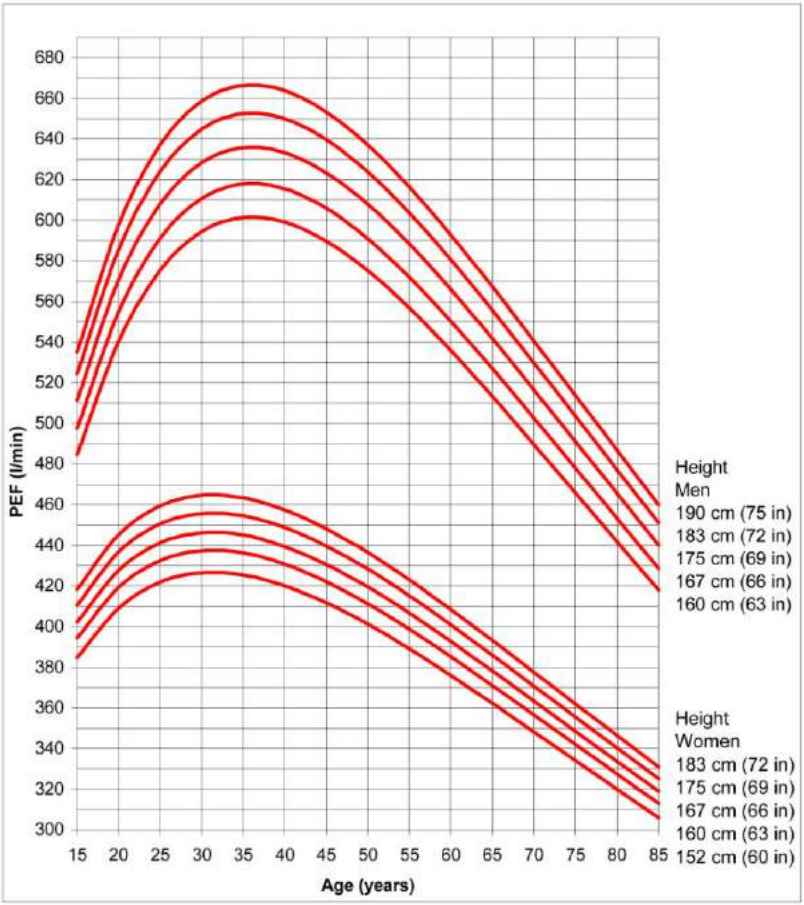
HCO_3	bicarbonate
HCW	healthcare workers
HCV	hepatitis C virus
HDL	high-density lipoprotein
Hep B	hepatitis B
HHS	hyperosmolar hyperglycaemic state
HIV	human immunodeficiency virus
HMGCoA	3-hydroxy-3-methylglutaryl–coenzyme A
H_2O	water
HR	heart rate
HRIG	human rabies immunoglobulin
HSV	herpex simplex virus
HT	hormone therapy
ICS	Inhaled corticosteroid
ICU	Intensive care unit
IgG	immunoglobulin G
IgM	immunoglobulin M
IM	intramuscular
INR	international normalized ratio
IOP	intraocular pressure
IPT	isoniazid preventive therapy
IRIS	immune reconstitution inflammatory syndrome
ITP	immune thrombocytopenia
IU	international unit
IUD	intrauterine contraceptive device
IV	intravenous
J	Joule
K^+	potassium
kg	kilogram
KS	Kaposi Sarcoma
L	litre
LABA	long-acting $beta_2$ agonist
LBBB	left bundle branch block
LDH	lactate dehydrogenase
LDL (-C)	low-density lipoprotein (-cholesterol)
LH	luteinizing hormone
LoE	level of evidence
LMWH	low molecular weight heparin
LP	lumbar puncture
LPA	line probe assay
LPV/r	lopinavir/ritonavir
LV	left ventricular
MAC	minimum alveolar concentration
mcg	microgram
MCH	mean corpuscular haemoglobin
MCV	mean corpuscular volume
MDEA	3,4-methylenedioxy-N-ethylamphetamine (“Ice”, “Eve”)
MDI	metered dose inhaler
MDR-TB	multi-drug resistant tuberculosis
MDMA	3,4-methylenedioxymethamphetamine (“Ecstacy”)
mg	milligram
MI	myocardial infarction
min	minute
mL	millilitre
mm^3	Cubic millimetre
mmHg	Millimeters mercury
mmoL	millimole
mOsm	milliosmole
MRI	magnetic resonance imaging

MRSA	Methicillin (cloxacillin) resistant *S. aureus*
MSU	midstream specimen of urine
MTB	*Mycobacterium tuberculosis*
MU	million units
MVA	manual vacuum aspiration
Na	sodium
NaCl	sodium chloride
NEMLC	National Essential Medicines List Committee
NAC	N-acetylcysteine
NERD	non-erosive reflux disease
NICD	National Institute for Communicable Diseases
NICE	National Institute for Health and Care Excellence
NMA	normetanephrine
nmol	nanomole
NNRTI	non-nucleoside reverse transcriptase inhibitor
NPH insulin	Neutral Protamine Hagedorn insulin
NRS	numeric rating scale
NRTI	nucleoside reverse transcriptase inhibitor
NSAID	non steroidal anti-inflammatory drug
NSTEMI	non ST elevation myocardial infarction
NVP	nevirapine
NYHA	New York Heart Association (functional classification)
ORS	oral rehydration solution
$PaCO_2$	partial pressure of carbon dioxide in arterial blood
PaO_2	partial pressure of oxygen in arterial blood
PAIR	percutaneous aspiration injection of helminthicidal agent and re-aspiration
PCA device	patient controlled analgesia device
PCR	polymerase chain reaction
PEF	peak expiratory flow
PEG	polyethylene glycol
PEP	post exposure prophylaxis
pH	acidity (partial pressure of hydrogen)
PHC	primary healthcare
PI	protease inhibitor
PID	pelvic inflammatory disease
PMTCT	prevention of mother to child transmission
PO_4	phosphate
PONV	post operative nausea and vomiting
PPG	post prandial plasma glucose
PPH	post-partum haemorrhage
PPI	proton pump inhibitor
PPROM	preterm prelabour rupture of membranes
PROM	prelabour rupture of membranes at term
PT	prothrombin time
PTH	parathyroid hormone
PTL	preterm labour
PTT	partial thromboplastin time
PV	per vagina (vaginal route)
PZA or Z	pyrazinamide
RA	rheumatoid arthritis
R or RIF	rifampicin
RBC	red blood cell
Rh	Rhesus
RH	rifampicin/isoniazid combination
RHZE	rifampicin/isoniazid/pyrazinamide/ethambutol combination
RNA	ribonucleic acid
RF	rheumatoid factor
RPR	rapid plasma reagin
RRT	renal replacement therapy

RUT	rapid urine test
SABA	short-acting $beta_2$ agonist
SBGM	self-blood glucose monitoring
SBP	systolic blood pressure
SC	subcutaneously
SJS	Stevens-Johnson syndrome
SIADH	syndrome of inappropriate antidiuretic hormone
SL	sublingual
SLE	systemic lupus erythematosus
SSRI	selective serotonin re-uptake inhibitor
STEMI	ST elevation myocardial infarction
STG	standard treatment guideline
STI	sexually transmitted infection
T_3	triiodothyronine
T_4	thyroxine
TB	tuberculosis
TB-IRIS	TB immune reconstitution inflammatory syndrome
TBSA	total body surface area
TCA	tricyclic antidepressants
TDD	total daily dose
TDF	tenofovir
TEN	toxic epidermal necrolysis
TIA	transient ischaemic attack
TOP	termination of pregnancy
TP	*Treponema pallidum*
TPHA	*Treponema pallidum* haemagglutination assay
TPN	total parenteral nutrition
TSH	thyroid-stimulating hormone
TST	tuberculin skin test
TTP HUS	thrombotic thrombocytopenic purpura/haemolytic uraemic syndrome
UA	unstable angina
UDV	unit dose vial
UE	ung. emulsificans BP (emulsifying ointment)
UEA	ung. emulisificans aqueosum BP (aqueous cream)
ULN	upper limit of normal
UTI	urinary tract infection
VDRL test	venereal disease research laboratory test
VF	ventricular fibrillation
VHF	viral haemorrhagic fever
VL	viral load
VMA	vanillylmandelic acid
VSD	ventricular septal defect
VT	ventricular tachycardia
VTE	venous thromboembolism
VZIG	varicella-zoster immunoglobulin
VWF	von Willebrand factor
WCC	white cell count
WHO	World Health Organisation
WPW syndrome	Wolff-Parkinson-White syndrome
XDR-TB	extensively drug-resistant tuberculosis

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.

					SCORE
1. During the past 4 weeks, how often have you had shortness of breath?					
1: Not at all	**2**: Once or twice a week	**3**: 3 to 6 times a week	**4**: Once a day	**5**: More than once a day	
2. Rate your asthma control during the past 4 weeks?					
1:Not controlled at all	**2**: Poorly controlled	**3**: Somewhat controlled	**4**: Well controlled	**5**: Completely controlled	
3. During the past 4 weeks, how often have you used your rescue inhaler or nebulizer medication?					
1: None of the time	**2**: A little of the time	**3**: Some of the time	**4**: Most of the time	**5**: All the time	
4. During the past 4 weeks, has asthma keep you from getting as much done at work or home?					
1: Not at all	**2**: Once a week or less	**3**: A few times a week	**4**: 1 or 2 times per day	**5**: 3 or more times a day	
5. During the past 4 weeks, has asthma symptoms woken you up at night or earlier than usual?					
1: Not at all	**2**: Once or twice	**3**: Once a week	**4**: 2 to 3 nights a week	**5**: 4 or more nights a week	

A total score of ≥19 suggests adequate asthma control.

Sourced from: 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

USEFUL NUMBERS AND URL LINKS

POISONS INFORMATION CENTRES	
Poison Information Helpine of the Western Cape	0861555 777
Red Cross War Memorial Children's Hospital Poisons Information Service	0861555 777
Tygerberg Poison Information Centre	0861555 777 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	
Rabies hotline (NICD)	082883 9920
Viral Haemmorhagic Fever outbreak hotline (NICD)	082883 9920
South African Vaccine Producers	0113866063/2/00
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 SAEDP@health.gov.za
Third line ART applications	TLART@health.gov.za
Medicine stock availability reporting	stockalert@health.gov.za
The National Adverse Drug Event Monitoring Centre (NADEMC)	021 4471618 Fax: 021448 6181
MISCELLANEOUS	
Ideal weight calculator	http://www.calculator.net/ideal-weight-calculator.html#
List of local haemophilia centres	http://www.haemophilia.org.za/centres.html
Medicines causing QT prolongation	www.sads.org.uk/**drugs**_to_avoid.htm
eGFR calculator	https://www.kidney.org/professionals/KDOQI/gfr_calculator
Medicines requiring dose adjustment in renal impairment	http://www.globalrph.com/index_renal.htm
Dietary phosphate restriction	https://unckidneycenter.org/files/kidney-health-library-files/renaldiet_phosphorus.pdf
Water deficit calculator	http://www.nephromatic.com/water_deficit.php
Risk stratification calculators in NSTEMI	TIMI: http://www.mdcalc.com/timi-risk-score-for-uanstemi/ Grace Risk Scores: http://www.mdcalc.com/grace-acs-risk-and-mortality-calculator/