

**STANDARD TREATMENT GUIDELINES  
AND  
ESSENTIAL MEDICINES LIST  
FOR  
SOUTH AFRICA**

**HOSPITAL LEVEL  
ADULTS**

**2012 EDITION**

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**NOTE:**

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## FOREWORD

I am proud to present the third edition of the Standard Treatment Guidelines and Essential Medicines List for Hospital level.

Access to affordable essential medicines is a vital component of an efficient health care system. In our resource-constrained environment with the high burden of disease, the value of the Standard Treatment Guidelines and Essential Medicines List in ensuring affordable and equitable access to medicines should not be underestimated.

Practice guidelines should keep pace with changes in health care. A continuous review of the Standard Treatment Guidelines and Essential Medicines List is imperative to provide access to quality and needed health care to all South Africans. I am pleased to note that evidence based medicine principles were, once again, applied during the review of this edition. We can be confident that using these guidelines will contribute to achieving positive health outcomes for our patients.

I am grateful to the members of the National Essential Drugs List Committee and the Expert Review Committees for completing the review despite their demanding schedules. I am also pleased with the number of contributions received in the form of comments and remarks.

It is our sincere wish that doctors and pharmacists, particularly those working at District and Regional Hospitals, will continue to incorporate the Standard Treatment Guidelines and Essential Medicines List in their daily practice. This will contribute to realising our vision of a long and healthy life for all citizens.



**DR A MOTSOLEDI, MP**  
**MINISTER OF HEALTH**  
**DATE: 16/4/2012**

## INTRODUCTION

It is my pleasure to introduce the third edition of the Standard Treatment Guidelines and Essential Medicines List for Hospital Level. This edition marks the culmination of an intense and thorough review process.

The Standard Treatment Guidelines have been aligned with current developments in medicine and scientific advances. Clinical evidence was used in the selection of medicines. In addition, prevailing medicine cost, affordability, as well as practice implications were taken into consideration. Furthermore, harmonisation with priority guidelines within the Department of Health has also been attained.

An integral part of the review process is the consultation with key stakeholders. This positive interaction has substantially contributed to the improvement and usability of the Standard Treatment Guidelines. I would like to thank everyone who took the time to comment when called upon to do so.

Users are encouraged to provide feedback by following the recommended guidelines at the back of the book when submitting comments or requesting additions or deletions of medicines from the list. Once again, the Adverse Drug Reaction Report Form has been included in the book. Health care workers are requested to use the reporting form so that patient safety and medicine selection in the future is not compromised.

Implementation of the Standard Treatment Guidelines and Essential Medicines List is still a major challenge. The inefficient use of resources has a negative impact on equitable access to essential medicines, and therefore on the quality of care. Provincial Pharmaceutical and Therapeutics Committees are encouraged to use the Standard Treatment Guidelines and Essential Medicines List to attain economic efficiencies in terms of optimising available resources and the rational use of medicines.

The National Essential Drugs List Committee and the Hospital Level Expert Review Committees are to be commended for this excellent achievement. Their dedication and commitment has contributed towards realising our vision of an accessible, caring and high quality health system.



**MS MP MATSOSO**  
**DIRECTOR-GENERAL: HEALTH**  
**DATE: 20/4/2012**

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We would also like to thank the many doctors, pharmacists, professional societies and other health care professionals who contributed by way of comment, remarks and the supply of appropriate evidence. Your involvement in the consultative process is an integral part of the review and has undoubtedly contributed to the excellence of this edition.

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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 drugs.
- » 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 drug list wherever appropriate.

The criteria for the selection of essential drugs for Primary Health 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.

It should be noted that the Primary Health Care Essential Medicines List (EML) reflects only the minimum requirements for Primary Health Care level facilities. In keeping with the objectives of the National Drug Policy, provincial and local Pharmacy and Therapeutics Committees should provide additional drugs from the Hospital level EDL based on the services offered and the competency of the staff at each facility.

# HOW TO USE THIS BOOK

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## **Principles**

The National Drug Policy makes provision for an Essential Medicines Program (EMP) which is a key component in promoting rational medicines.

Each treatment guideline in the Adult Hospital Level Standard Treatment Guidelines (STGs) and Essential Medicines List (EML) has been design as a progression in care from the current Primary Health Care (PHC) STGs and EML. In addition where a referral is recommended the relevant medicines have either been reviewed and included in the tertiary level EML, or is in the process of being reviewed. Given that the PHC STGs are reviewed prior to the Adult Hospital level technical consideration may dictate that there is a period when the two STGs are not always perfectly aligned.

All reasonable steps have been taken to align the STGs with Department of Health guidelines that are available at the time of review.

A medicine is included or removed from the list using an evidence based medicine review of safety and effectiveness followed by consideration of cost and other relevant practice factors.

The EML has been developed down to generic or International Non-propriety Name (INN) level. 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 STG.
- Select the preferred member of the therapeutic class based on cost.
- Implement 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 STG which provides a class of medicines followed by example such as, HMGC<sub>o</sub>A reductase inhibitors (statins) e.g. Simvastatin, These therapeutic classes have been designated where none of the members offer a significant benefit over the other registered members of the class. It is anticipated that by limiting the listing to a class there is increased competition and hence an improved chance of obtaining the best possible price in the tender process. In circumstances where you encounter such a class always consult the local formulary to identify the example that has been approved for use in your facility.

The perspective adopted is that of a competent medical officer practicing in a public sector hospital. As such the STGs serves as a standard for practice but does not replace sound clinical judgment.

### **Navigating the book**

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.

The standard treatment guideline begins with the ICD-10 code which is an international classification system used for epidemiological and health management purposes. This is followed by a brief description which may relevant clinical information such as diagnostic criteria, radiological and laboratory tests to assist the medical officer in arriving at a diagnosis. This is followed by medicine treatment which lists the approved medicines and provides fundamental prescribing information. The dosing regimens provide the recommended doses used in usual circumstances however the final dose should take into consideration capacity to eliminate the medicine, interactions and comorbid states.

This edition of the Adult Hospital Level Standard Treatment Guidelines and Essential Medicines List provides additional information regarding Patient Adherence in Chronic Conditions, Measuring Medication Level and Prescription Writing.

In the preface of the book guidance has been provided regarding dosing modification for reduced kidney function as well as therapeutic monitoring. Finally the guidelines make provision for referral of patients with more complex and uncommon conditions to facilities with the resources for further investigation and management.

### **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 drug events, interactions and medicines quality. These systems should not only support the regulatory pharmacovigilance plan but should also provide pharmaco-epidemiology data that will be required to inform future essential medicines decisions as well as local interventions that may be required to improve safety.

In accordance with the Medicines control Council's guidance on reporting adverse drug reactions in South Africa, the medical office 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 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.

Comments from persons and institutions outside the public service should be sent to:

The Essential Drugs Programme  
Affordable Medicines  
Department of Health  
Private Bag X828  
Pretoria  
0001

## **MEASURING MEDICATION LEVELS**

Potentially toxic drugs, drugs 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.

Routine measurement is rarely warranted, but rather should be tailored to answering a specific clinical question, and is of most value in medicines with a narrow therapeutic index or where there is considerable individual variation in pharmacokinetics. Essential medicines for which there is evidence to support such monitoring include:

### **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**

When dosed based on body weight, peak levels will usually be adequate, e.g. 6 mg/kg/day in a single daily dose. Trough levels taken immediately before the next dose may be valuable in identifying potential toxicity before it manifests as deafness or renal impairment.

Aminoglycosides are contra-indicated 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 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 medicines. In certain conditions simple advice and general 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 weight of the patient in the case of children
- 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 ( $\mu$ ): 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 250 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 up.
- After writing a script, check that you have stated dose, dose units, route, frequency, and duration for each item. 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 the script is dated and that the patient’s name and folder number are on the prescription card. 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.)

## PENICILLIN DESENSITISATION

This has been included for information only.

Perform only in an ICU setting.

Discontinue all  $\beta$ -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.

<b>A: Reconstitute phenoxymethylpenicillin 250 mg/5mL</b>		
<b>Step</b>	<b>Drug mg/mL</b>	<b>Amount to administer (mL)</b>
Strictly every 15 minutes	<b>B: To make 0.5 mg/mL solution</b> Dilute 0.5 mL of reconstituted phenoxymethylpenicillin solution in 49.5 mL water.	
1	0.5 mg/mL solution	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
	<b>C: To make 5 mg/mL solution</b> Dilute 1 mL of reconstituted phenoxymethylpenicillin solution in 9 mL water	
8	5 mg/mL solution	1.2 mL
9		2.4 mL
10		4.8 mL
	<b>D: Reconstituted phenoxymethylpenicillin 250 mg/5mL = 50 mg/mL</b>	
11	50 mg/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.

## Parenteral route

Step	Drug 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
9		0.24
10		0.48
11	100 mg/mL	0.1
12		0.2
13		0.4
14		0.8
15		0.16
16		0.32
17		0.64

Interval between doses: 15 minutes.

After Step 17, observe for 30 minutes, then 1 g IV.

## COTRIMOXAZOLE DESENSITISATION

Patients with a history of cotrimoxazole hypersensitivity should be considered for desensitisation.

Desensitisation should not be considered for patients with hypersensitivity that is life threatening such as Steven–Johnsons syndrome.

This desensitisation schedule should only be done as an inpatient.

### Note:

Antihistamines should **not** be given with this regimen:

Dilute 0.1 mL (0.8/4 mg) of cotrimoxazole suspension in 200 mL sodium chloride 0.9% or dextrose 5% solution.

1 mL dilute solution = 0.004/0.02 mg cotrimoxazole

Hour	dose	cotrimoxazole, administer orally
0	0.004/0.02 mg	1 mL of dilute solution
1	0.04/0.2 mg	10 mL of dilute solution
2	0.4/2 mg	0.05 mL of syrup or 100 mL of dilute solution
3	4/20 mg	0.5 mL of syrup
4	40/200 mg	5 mL of syrup or ½ tablet
5	160/800 mg	2 single strength or 1 double strength tablet



# A GUIDE TO PATIENT ADHERENCE IN CHRONIC CONDITIONS

---

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

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

## Patient Adherence

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

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

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

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

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

Barriers that contribute toward poor adherence

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

**BARRIER****RECOMMENDED SUPPORT**

medication.

**Attitudes and beliefs**

- » The condition is misunderstood or denied.
- » Treatment may not seem to be necessary.
- » May have low expectations about treatment.

**Social and economic**

- » May lack support at home or in the community
- » May not have the economic resources to attend appointments.

**Healthcare team related**

- » Little or no time during the visit to provide information.
- » Information maybe provided in a way that is not understood.
- » Relationship with the patient may not promote understanding and self management.

**Treatment related**

- » Complex medication regimens (multiple medications and doses) can be hard to follow.
- » May be discouraged if they don't feel better right away.
- » May be concerned about adverse effects.

- » Remind patients that they have a long term illness that requires their involvement.
- » Use change techniques such as motivational interviewing.
- » Identify goals to demonstrate improvement/stabilisation.

- » Encourage participation in treatment support programs.
- » Consider down referral or reschedule appointment to fit in with other commitments.

- » Encourage patient to ask questions.
- » Use patient literacy materials in the patient's language of choice.
- » Engage active listening.

- » If possible reduce treatment complexity
- » Help the patient understand the condition and the role of their medication
- » Discuss treatment goals in relation to potential adverse effects.

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

For a patient to consistently adhere to long term pharmacotherapy requires integration of the regimen into his or her daily life style. The successful integration of the regimen is informed by the extent to which the regimen differs from his or her established daily routine. Where the pharmacological proprieties of the medication permits it, the pharmacotherapy dosing regimen should be adapted to the patient's daily routine. For example, a shift worker may need to take a sedating medicine in the morning when working night shifts, and at night,

when working day shifts. If the intrusion into life style is too great alternative agents should be considered if they are available. This would include situations such as a lunchtime dose in a school-going child who remains at school for extramural activity and is unlikely to adhere to a three times a regimen but may very well succeed with a twice daily regimen.

### **Towards concordance when prescribing**

Establish the patient's

- » occupation
- » daily routine
- » recreational activities;
- » past experiences with other medicines
- » 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 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-drug 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.
- » Involve the patient in the care plan.
- » Every patient on chronic therapy should know:
  - his/her diagnosis
  - the name of every medicine
  - the dose and interval of the regimen
  - his/her BP or other readings

**Note:** The prescriber should reinforce this only once management of the condition has been established.

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

## Patient Adherence Record

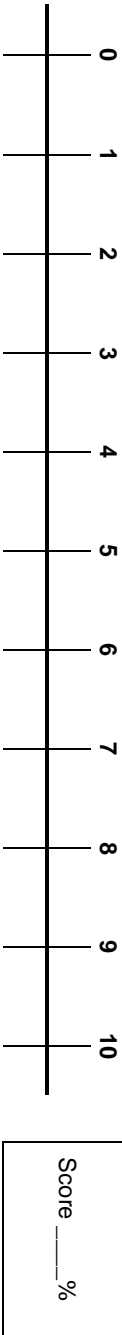
Folder No. \_\_\_\_\_

Date \_\_\_\_\_ / \_\_\_\_\_ / \_\_\_\_\_  
(dd/mm/yyyy)

### Self-Reporting

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

### Visual Analogue Scale (VAS)



### 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.

$$\text{Dispensed} \quad - \quad \text{Returned} \quad = \quad \boxed{\phantom{00}} \quad - \quad \boxed{\phantom{00}}$$

$$\% \text{ Adherence} = \frac{\phantom{0000}}{\phantom{0000}} \times 100 = \frac{\phantom{0000}}{\phantom{0000}} \times 100 = \phantom{0000} \%$$

Expected to be taken



**Adherence Assessment**

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

# CHAPTER 1

## ALIMENTARY TRACT

---

### 1.1 GASTROINTESTINAL DISORDERS

#### 1.1.1 COLITIS, ULCERATIVE (UC)

K51.9

##### DESCRIPTION

Idiopathic and chronic intestinal inflammation. Ulcerative colitis (UC) is a mucosal disease that almost always involves the rectum and may extend proximally to all or part of the colon.

##### Note:

There are more common infective causes of bloody stools e.g. amoebiasis and schistosomiasis, and dysentery e.g. shigellosis, which should be excluded.

##### GENERAL MEASURES

Surveillance colonoscopy to exclude dysplasia is required every 1–2 years in chronic ulcerative colitis of >10 years duration.

Patients with disease limited to the rectum do not require surveillance colonoscopy.

##### MEDICINE TREATMENT

Correct electrolyte, haematinic and nutritional deficiencies via the enteral or parenteral route.

Loperamide should not be used during the acute flare due to the risk of toxic megacolon.

##### Acute episode

Mild to moderate disease:

- Sulfasalazine, oral, 1–2 g, 6 hourly.
  - Monitor FBC.

If there is no response to sulfasalazine:

##### ADD

- Prednisone, oral, 1.5 mg/kg, daily.
  - Once the symptoms have resolved, taper dose by 5 mg/week over a period of three months.

Severe disease:

Admit patient.

Intravenous corticosteroids, e.g.:

- Hydrocortisone, IV, 100 mg 6 hourly.  
Failure to respond to 10 days of intravenous corticosteroids is an indication for an emergency colectomy.

**ADD**

- Azathioprine, oral, 2 mg/kg daily. Specialist initiated.  
Continue treatment until corticosteroids can be tapered.

Local disease: proctosigmoiditis

Patients with limited disease rarely require inpatient treatment. They are usually systemically well.

- Mesalazine, rectal, 1 g daily. Specialist initiated.

**AND/OR**

- Prednisone, oral, 1.5 mg/kg daily for 14 days.

**Maintenance of remission**

- Sulfasalazine oral, 500 mg 12 hourly.
  - May be titrated to 1 g 6 hourly.

Patients with recurrent severe attacks to maintain remission:

- Azathioprine, oral, 2 mg/kg daily. Specialist initiated.

**REFERRAL**

- » Confirmation of diagnosis.
- » Initiation of long-term therapy.
- » Refractory cases.
- » Fulminant colitis needs hospital admission and surgery may be required.
- » All patients with a severe flare should have abdominal X-rays. Markers of a severe flare are:
  - > Tachycardia (> 100 beats per minute).
  - > Temperature > 38°C.
  - > > 6 bloody stools per day.
  - > Dilated colon or small bowel on X-ray.
- » Toxic megacolon (transverse colon diameter > 6 cm on X-ray) requires hospital admission, parenteral fluids, corticosteroids, antibiotics and nasogastric suction. This is a medical emergency and if the colonic dilation does not resolve within 24 hours an emergency colectomy is indicated, as the risk of perforation is high.
- » Surgery.



### 1.1.2 CROHN'S DISEASE (CD)

K50.9

#### DESCRIPTION

Idiopathic and chronic intestinal inflammation. This is a transmural inflammatory condition affecting mainly the distal ileum or colon, but may affect the entire gastro-intestinal tract. Common complications are intestinal obstruction and abscess formation.

#### GENERAL MEASURES

Smoking cessation, as smoking is a strong predictor of relapse.  
Refer to dietician for dietary advice.

#### MEDICINE TREATMENT

Antidiarrhoeal medication should not be used in acute flares of inflammatory CD.

Diarrhoea will subside with appropriate care.

After terminal ileal resections, to reduce diarrhoea due to bile salt malabsorption:

- Cholestyramine, oral, 2–8 g daily.

#### Ileal disease

All patients:

- Vitamin B<sub>12</sub>, IM, 1 mg, 3 monthly.

Monitor for iron and folate deficiency.

#### Colonic disease

- Sulfasalazine, oral, 500 mg 12 hourly, up to 1.5 g 8 hourly.
  - Acute attacks: 1–2 g, 4–6 hourly.
  - Maximum dose: 3–4 g daily.

#### AND

- Prednisone, oral, 1.5 mg/kg daily. Taper dose to lowest possible maintenance dose over 3–4 weeks.

#### Severe disease

Maintenance of remission:

Sulfasalazine may be useful for maintaining remission in patients with Crohn's colitis but is of no real use in purely ileal CD.

For patients with recurrent attacks of CD or those with extensive disease, i.e. ileum and colon:

- Azathioprine, oral, 2 mg/kg daily. Specialist initiated.

#### OR

- Methotrexate, oral, 15–25 mg weekly. Specialist initiated.

**PLUS**

- Folic acid, oral, 5 mg weekly with methotrexate.

Emergency management at specialist facility will include:

- » resuscitation with parenteral fluids;
- » blood transfusions;
- » corticosteroids;
- » antibiotics; and
- » nasogastric suction as indicated.

**Peri-anal disease**

There is evidence of recurrence on withdrawal of therapy and prolonged treatment may be indicated.

- Metronidazole, oral, 400–800 mg 8 hourly.

**OR**

- Ciprofloxacin, oral, 500 mg 12 hourly.

**REFERRAL**

- » For further therapy.
- » Peri-anal abscesses/fistula if surgery is required after appropriate assessment.

**1.1.3 CONSTIPATION/ FAECAL IMPACTION**

K56.4

**DESCRIPTION**

A condition characterised by a change in usual bowel habits and dry, hard stools.

There is a decreased frequency of bowel action and patients should be assessed individually.

Constipation may have many causes:

- |  |                                     |
|--|-------------------------------------|
| » incorrect diet (fibre and fluid);    | » certain drugs;                    |
| » lack of exercise;                    | » metabolic;                        |
| » pregnancy;                           | » endocrine;                        |
| » old age;                             | » neurogenic;                       |
| » psychogenic disorders;               | » lower bowel abnormalities;        |
| » chronic use of enemas and laxatives; | » ignoring the urge;                |
| » cancer of the bowel;                 | » behavioural problems in children. |

**GENERAL MEASURES**

Dietary advice preferably by dietician.

Dietary measures i.e. balanced diet with unprocessed foods, e.g. cereals, legumes, fruit and vegetables.

Correct dehydration. Ensure adequate fluid intake.

Wheat bran: introduce slowly and take with sufficient fluid. Side-effects include: bloating, cramps and flatulence.

Manual removal of impacted stools.

Encourage regular bowel habits.

Physical exercise.

**MEDICINE TREATMENT****Osmotic laxatives**

- Lactulose, oral, 10–20 mL daily.
  - Titrate to effect i.e. up to 60 mL daily.

**Stimulant laxatives**

For short term use only, except in the elderly where long-term treatment may be indicated:

- Sennosides A and B, oral, 7.5–15 mg at night 2–3 times a week for up to 4 weeks.

**Polyethylene glycol-based purges**

For acute bowel preparation or for chronic constipation on specialist advice.

**Saline or phosphate enemas**

May occasionally be indicated in acute constipation.

**REFERRAL**

- » For investigation for organic disease.

**1.1.4 DIVERTICULOSIS**

K57.9

**GENERAL MEASURES**

Increase unprocessed foods in diet.

Supplement with bran.

**MEDICINE TREATMENT**

Localised diverticulitis:

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

Severe disease:

- Ampicillin, IV, 1 g 6 hourly.

**PLUS**

- Gentamicin, IV, 6 mg/kg daily.

**PLUS**

- Metronidazole, IV, 500 mg 8 hourly.

**REFERRAL**

- » Clinical deterioration or failure to improve.
- » Peritonitis
- » Fistulae
- » Strictures
- » Massive haemorrhage

### 1.1.5 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**

Dietary advice by dietician.

Weight reduction is recommended if overweight.

All patients with alarm symptoms, i.e. weight loss, haematemesis and melaena, dysphagia, and anaemia, should have an endoscopy at the earliest opportunity.

**MEDICINE TREATMENT**

Empiric treatment only if there are no alarm symptoms, i.e. no weight loss, no haematemesis and under 45 years of age:

- Ranitidine, oral, 150 mg 12 hourly for 4 weeks.

**OR**

**Proton pump inhibitors (PPIs)**

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

- Omeprazole, oral, 40 mg daily for 4 weeks.

**Recurrence of symptoms**

After endoscopic confirmation of disease:

- Omeprazole, oral, 20 mg daily.
  - Decrease to 10 mg daily after 4 weeks.

**Barretts' oesophagitis**

Restart PPI:

- Omeprazole, oral, 20 mg daily.

**Note:**

These patients usually need maintenance PPI therapy.

There is no convincing evidence that long-term treatment of Barrett's oesophagitis reduces dysplasia or progression to malignancy.

**REFERRAL**

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 with significant expense;
- » patients with large hiatus hernias and "volume reflux";
- » a rolling hiatus hernia with obstructive symptoms requires surgery.

**1.1.6 HIATUS HERNIA**

K44

See section 1.1.5: Gastro-Oesophageal Reflux Disease (GORD).

**1.1.7 IRRITABLE BOWEL SYNDROME (IBS)**

K58

(Synonyms: spastic colon, irritable colon)

**DESCRIPTION**

Functional bowel disorder: motility disturbance of the entire gastrointestinal tract (GIT) resulting in recurrent symptoms of pain, constipation and/or diarrhoea and bloating.

**GENERAL MEASURES**

Reassure patient, after limited investigations, that there is no serious organic disorder.

Dietary advice by dietician.

**MEDICINE TREATMENT**

Not specifically indicated.

Based on patients' predominant symptoms.

Short-term symptomatic treatment for diarrhoea and/or constipation.

Laxatives only for constipation-specific IBS, see Section 1.1.3: Constipation/Faecal impaction.

Antidiarrhoeals only for diarrhoea-specific IBS, see Section 1.3.3: Diarrhoea, Acute Non-Inflammatory.

Tricyclic anti-depressants may be used as adjuvant therapy.

- Amitriptyline, oral, 25–75 mg daily.
  - Titrate dose as appropriate.

### 1.1.8 PANCREATITIS, ACUTE

K85

#### DESCRIPTION

Acute inflammatory condition of the pancreas.

#### GENERAL MEASURES

Nil per mouth.

Nasogastric suction when persistent vomiting or ileus occurs.

Parenteral fluid replacement to correct metabolic and electrolyte disturbances.

Parenteral nutrition support may be necessary.

Drainage of abscess, pseudocyst, if required.

#### MEDICINE TREATMENT

For pain:

- Morphine, slow IV, 10–15 mg 4–6 hourly as required.

#### 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.

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 to patients with severe necrotising pancreatitis prior to the diagnosis of infection is not recommended.

For abscess of the pancreas, etc:

Broad spectrum IV antibiotics, e.g.:

- Ampicillin, IV, 1 g 6 hourly.

#### PLUS

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

#### PLUS

- Metronidazole, IV, 500 mg 8 hourly.

**REFERRAL**

- » All patients with moderate or severe pancreatitis.

**1.1.9 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 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 12.1: Chronic Pain

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

**1.1.10 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 investigation, preferably by endoscopy, as all GUs require 4-quadrant biopsy to exclude malignancy.

GUs and complicated DUs, those that have bled, perforated or are recurrent, must be rescoped 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):

- Omeprazole, oral, 40 mg daily.
  - Duodenal ulcer: for 7 days.
  - Gastric ulcer: for 28 days.

**AND**

*H. pylori* eradication:

- Amoxicillin, oral, 1 g 12 hourly.

**OR**

For penicillin allergy:

- Clarithromycin, oral, 500 mg 12 hourly.

**PLUS**

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

Failure of *H. pylori* eradication (best dealt with in a specialist setting):

- Clarithromycin, oral, 500 mg 12 hourly.

**PLUS**

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

If resistant to this, refer.



***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):

- Omeprazole, oral, 40 mg daily.
  - Duodenal ulcer: for 7–14 days.
  - Gastric ulcer: for 28 days.

**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.:

- Omeprazole, oral, 20 mg daily. Specialist initiated.

**1.2 HEPATIC DISORDERS****1.2.1 HEPATITIS, NON-VIRAL**

K70.1/K71/K75.4

\* Notifiable if caused by agricultural chemicals and 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.

**MEDICINE TREATMENT****Hepatitis due to infections**

Antibiotic therapy based on culture.

**Alcohol-induced hepatitis**

Even if no bleeding:

- Vitamin K<sub>1</sub>, IM/IV, 5–10 mg daily for 10 days
- Thiamine, oral, 100 mg daily

Other vitamins if indicated.

**Drug-induced hepatitis**

Stop all potentially hepatotoxic medication immediately.

**Auto-immune hepatitis**

Patients with hepatitis persisting with negative viral markers and no hepatotoxins. Biopsy and autoimmune markers are necessary to make the diagnosis.

- Prednisone, oral, 0.5–1 mg/kg daily
  - Taper dose to a suitable maintenance dose.

**PLUS**

- Azathioprine, oral, 0.5–1 mg/kg daily.

**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 occurs.

**1.2.2 LIVER FAILURE**

K72.9

**GENERAL MEASURES**

Patient education.

Avoid hepatotoxic drugs and alcohol.

Rest and reduced physical activity are recommended.

Normal diet. Protein restriction indicated only when encephalopathy is evident. 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. drugs, that may worsen or precipitate functional deterioration.

Avoid vigorous paracentesis.

Exclude infection as precipitant, especially spontaneous bacterial peritonitis.

**MEDICINE TREATMENT**

On admission to change pH of large bowel:

- Lactulose, oral, 10–30 mL immediately.

Thereafter, to attain 2–3 soft stools a day:

- Lactulose, oral, 10–30 mL 8 hourly.
  - Titrate dose to 2–3 soft stools a day.

Consider:

- Vitamin K<sub>1</sub>, IM/IV, 5–10 mg daily.

Other vitamins if indicated.

Multivitamin supplements should be considered and may be indicated.

## REFERRAL

- » All cases with severe acute or advanced chronic liver failure.
- » Where a liver transplant is to be considered.

## 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: salt restriction, i.e. < 2 g/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, oedema

If no response to strict bed rest after 2–3 days:

- Spironolactone, oral, 50–200 mg daily.
  - Titrate to higher dosages with caution.
  - Maximum dose: 400 mg daily.
  - May cause hyperkalemia.
  - Can be combined with furosemide.
  - Potassium supplementation is not necessary.

**AND**

If there is no response to spironolactone or if there is gross fluid retention:

- Furosemide, oral, 20–40 mg daily, initially for a few days to increase natriuresis.
  - Titrate carefully to desired effect as rapid fluid shift may precipitate liver failure.
  - Optimal dose: 160 mg daily.
  - Measure response to diuretics. Aim for weight loss of:

300–500 g/day	patients without oedema
800–1 000 g/day	patients with peripheral oedema

### **Resistant ascites**

Patients not responding to optimal diuretic therapy, sufficient salt restriction and avoiding NSAIDs.

These patients may require regular large volume paracentesis, i.e. > 5 L, as outpatients, if possible.

Protect against haemodynamic collapse.

Crystalloid replacement.

### **Large-volume ascites**

Large volume paracentesis is the method of choice as it is faster, more effective and has fewer adverse effects compared to diuretics.

Diuretics are indicated as maintenance therapy to prevent recurrence of ascites.

### **Encephalopathy**

- Lactulose, oral, 10–30 mL 8 hourly.

### **Oesophageal varices**

To reduce the risk of bleeding:

- Propranolol, oral 10–20 mg 12 hourly.

## **1.2.4 HEPATITIS, VIRAL**

B19.9

\* Notifiable disease

### **DESCRIPTION**

Hepatitis caused by one of the hepatotropic viruses, hepatitis A, B, C and E. Hepatitis A and E only cause acute hepatitis, whilst B and C cause acute and chronic hepatitis.

### **GENERAL MEASURES**

#### **Acute hepatitis**

Bed-rest until acute phase is over.

Avoid alcohol during the illness and for at least 6 months after clinical recovery.

In cases of hepatitis B serologically screen sexual contacts. If they are seronegative (Anti-HBs negative) 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 prophylaxis for hepatitis B in HCW.

HbsAg: hepatitis B surface antigen

HbsAb: hepatitis B surface antibody

HBIG: hepatitis B immune globulin

	Source patient		
Vaccination status and antibody response status of HCW	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 <sup>#</sup>	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)	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.

<sup>#</sup> If the delay in obtaining HBsAb results is more than 24 hours initiate treatment as for vaccinated AND HBsAb < 10 units/mL.

## 1.2.5 LIVER ABSCESS, PYOGENIC

K75.0

### DESCRIPTION

Focal bacterial infection of the liver with pus, usually polymicrobial.

### 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

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

#### PLUS

- Gentamicin, IV, 6 mg/kg daily.

#### PLUS

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

## 1.2.7 ACUTE CHOLECYSTITIS AND ACUTE CHOLANGITIS

### 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)
- » Co-morbidity
- » Immune compromise

#### Acute cholecystitis and acute cholangitis

- Ampicillin, IV, 1 g 6 hourly.

#### PLUS

- Gentamicin, IV, 6 mg/kg daily.

#### PLUS

- Metronidazole, IV, 500 mg 8 hourly.

### REFERRAL

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

## 1.3 DIARRHOEA, GASTROINTESTINAL

### 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 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. Causes include shigella, salmonella and campylobacter.

**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 severe cases or significant underlying disease.

- Ciprofloxacin, oral, 500 mg 12 hourly for 3–7 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 blood or mucus. Common causes include viruses and enterotoxigenic strains of *E. coli*.

**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. Severe cases present with pseudomembranous colitis. Toxins produced by *Clostridium difficile* can be demonstrated on stool samples.

**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.

If diarrhoea does not settle on antibiotic withdrawal or if pseudomembranous colitis is present:

- Vancomycin, oral, 125 mg 6 hourly.

**OR**

- Metronidazole, oral, 800 mg 8 hourly for 10 days.

**1.3.5 AMOEBIC DYSENTERY**

A06

**DESCRIPTION**

Diarrhoea with blood and/or mucus due to *E. histolytica*.

**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.

### 1.3.6 GIARDIASIS

A07.1

#### DESCRIPTION

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

#### GENERAL MEASURES

Fluid and electrolyte replacement in severe diarrhoea.

#### MEDICINE TREATMENT

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

### 1.3.7 TYPHOID

A01.0

See section 9.9: Typhoid fever.

### 1.3.8 PERITONITIS

K65

#### DESCRIPTION

Infection of the peritoneum, usually secondary to a surgical cause such as perforated bowel. In this setting polymicrobial infection with anaerobes 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  $>0.25 \times 10^9/L$  (250 cells/mm<sup>3</sup>).

#### GENERAL MEASURES

##### Secondary peritonitis

Intravenous fluids and nasogastric suction.

Prompt surgical intervention is essential.

#### MEDICINE TREATMENT

##### Empiric antibiotic therapy

For surgical causes of peritonitis:

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

##### PLUS

- Gentamicin, IV, 6 mg/kg daily.

##### PLUS

- Metronidazole, IV, 500 mg 8 hourly.

As soon as patient can tolerate oral medication:

- Metronidazole, oral, 400 mg 8 hourly.

For spontaneous bacterial peritonitis:

- Ceftriaxone, IV, 1 g daily.

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.

# CHAPTER 2

## BLOOD AND BLOOD FORMING ORGANS

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### 2.1 ANAEMIA, APLASTIC

D61.9

#### DESCRIPTION

Pancytopenia due to a hypoplastic bone marrow.

Clinical features:

- » pallor,
- » petechiae,
- » purpura, and
- » bleeding

with frequent or severe infections.

#### MEDICINE TREATMENT

If neutropenic and febrile, see section 2.7: Febrile Neutropenia.

#### REFERRAL

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

### 2.2 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,
- » acute or chronic infections, e.g. HIV and TB,
- » chronic kidney disease, and
- » chronic rejection of solid-organ transplantation, etc.

#### TREATMENT

Treat the underlying condition.

Transfusion is seldom necessary.

Do not treat with iron, folic acid or vitamin B<sub>12</sub> unless there is a documented deficiency.

## 2.3 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, medications.
- » Abnormalities of the cell membrane, e.g. hereditary spherocytosis.
- » Enzymes, e.g. G6PD deficiency.
- » Haemoglobin, e.g. sickle cell anaemia, thalassaemia.

### Investigations

Evidence of haemolysis: anaemia, reticulocytosis, decreased haptoglobin, increased lactate dehydrogenase (LDH) and unconjugated hyperbilirubinaemia.

Coombs' test (direct antiglobulin) is usually positive with autoimmune haemolysis.

### 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, 1–2 mg/kg daily, initial dose.
    - When a satisfactory response is obtained with recovery of the haemoglobin and a decrease in LDH serum concentrations, taper dose over a period of 4 weeks to 30 mg daily.
    - Thereafter further reduction should be slower to prevent disease recurrence.
- Prednisone treatment can be stopped when the Coombs' reaction becomes negative.

If inadequate response:

#### **ADD**

- Azathioprine, oral, 2.5 mg/kg daily.
  - Titrate to Hb response.
  - May be required for several months
  - Monitor for neutropenia.

Patients who fail medicine treatment should be considered for splenectomy.

### **REFERRAL/CONSULTATION**

- » No response to medicine treatment.
- » Other causes of haemolytic anaemia.

## **2.4 ANAEMIA, IRON DEFICIENCY**

D50.9

### **DESCRIPTION**

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

#### **Hypochromic microcytic anaemia**

##### **Investigations**

Assess for a haematological response to iron therapy.

### **GENERAL MEASURES**

Identify and treat the cause.

Dietary adjustment.

### **MEDICINE TREATMENT**

#### **Oral iron supplementation**

Reticulocytosis begins on the 3<sup>rd</sup> or 4<sup>th</sup> day after therapy, peaks at approximately day ten and lasts between 12 and 21 days.

The expected haemoglobin rise is approximately 2 g/dL every 3 weeks.

**Treatment**

- Iron, elemental, oral, 100–200 mg daily with a meal, e.g.:  
Ferrous sulphate compound, oral, BPC 170 mg daily with food.  
After the haemoglobin has returned to normal, treatment should be continued for 6 months in order to replenish the iron stores adequately.

**Prophylaxis**

For example during pregnancy:

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

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<sub>12</sub> deficiency.

**Parenteral iron**

Parenteral iron is seldom required.

The use of parenteral iron may be associated with anaphylaxis.

Parenteral iron is **only** indicated when oral iron is:

- » ineffective, e.g. malabsorption or patients on haemodialysis and erythropoietin therapy, or
- » not tolerated.

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

Where a once-off dose is required, give intramuscularly. Minimum required dose is 250 mg of iron per gram of Hb below normal.

Use in consultation with a specialist.

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

Ensure that the correct formulation is given as some preparations can be given IM, or IV only, or both.  
Resuscitation equipment should be ready to manage anaphylaxis.

**Blood transfusion**

Indicated in patients with:

- » anaemia leading to cardiac failure or severe dyspnoea,
- » active, ongoing bleeding, or
- » where correction of anaemia to at least 7 g/dL is required prior to performing an urgent invasive procedure or surgery.

**2.5 ANAEMIA, MEGALOBLASTIC**

D53.1

**DESCRIPTION**

Anaemia caused by a deficiency of folate and/or vitamin B<sub>12</sub>.

**Investigations**

Elevated MCV (mean corpuscular volume) and MCH (mean corpuscular haemoglobin).

Macro-ovalocytes on blood smear; polysegmentation of neutrophils, thrombocytopenia with giant platelets.

Decreased serum vitamin B<sub>12</sub> or red blood cell folate.

Pancytopenia in severe cases.

Intrinsic factor antibodies in vitamin B<sub>12</sub> deficiency, and anti-parietal cell antibodies in pernicious anaemia.

**GENERAL MEASURES**

Dietary modifications to ensure adequate intake of folate and vitamin B<sub>12</sub>.

Identify and treat the underlying cause, e.g. antibiotics for intestinal overgrowth with bacteria.

**MEDICINE TREATMENT**

After blood samples for RBC, folate and vitamin B<sub>12</sub> levels have been taken, start with folic acid and vitamin B<sub>12</sub>.

Monitor serum potassium and replace if necessary.

Give vitamin B<sub>12</sub> and folic acid together until the test results are available as giving folic acid alone in patients with a B<sub>12</sub> 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<sub>12</sub> deficiency**

- Vitamin B<sub>12</sub>, 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, except in patients with clearly modifiable nutritional deficiency.

**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 is corrected 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, short-term iron and folic acid supplementation is also recommended.

Consider the following if there is failure to respond:

- » co-existing folate and/or iron deficiency,
- » infection,
- » hypothyroidism,
- » myelodysplasia,
- » incorrect diagnosis, and
- » drug-induced, e.g. hydroxyurea, stavudine and zidovudine.

**Prophylaxis**

Vitamin B<sub>12</sub> is indicated for patients after total gastrectomy or ileal resection.

- Vitamin B<sub>12</sub>, 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.

**2.6 ANAEMIA, SICKLE CELL**

D57

**DESCRIPTION**

Homozygous sickle cell anaemia (HbSS: HbS > 50–100%). Individuals with sickle cell trait have < 50% HbS and are generally asymptomatic. The disease is characterised by various crises: vaso-occlusive, aplastic, megaloblastic and sequestration crises, and infection.

**The pain crisis/vaso-occlusive crisis**

The most common type of crisis is characterised by acute episodes of severe, agonising and relentless pain. The pain may be localised to a single long bone, typically in the juxta-articular area. It can be symmetrical in several limbs or involve the axial skeleton, i.e. lumbar spine, ribs or pelvis, abdomen, chest or organ systems.

**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**

Bed rest and/or hospitalisation.

**MEDICINE TREATMENT**

- Oxygen.

All patients:

- Folic acid, oral, 5 mg daily.

**Analgesia**

For severe pain:

- Morphine, IV, 10 mg 4 hourly.

**Fluids**

Keep well hydrated with intravenous fluids.

**REFERRAL**

- » All for chronic management in a specialised centre.

**2.7 FEBRILE NEUTROPENIA**

D70

**DESCRIPTION**

Febrile neutropenia is defined as an absolute neutrophil count of  $< 0.5 \times 10^9/L$  with a temperature of greater than  $38^\circ C$  for  $> 1$  hour.

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 drug that may cause neutropenia.

Take blood 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:

- 3<sup>rd</sup> generation cephalosporin, e.g.:
- Ceftriaxone, IV, 1 g daily.

### PLUS

- Gentamicin, IV, 6 mg/kg daily.

If IV line infection is suspected as the cause at any stage:

### ADD:

- Vancomycin, IV, 20 mg/kg/dose 12 hourly.
  - Monitor trough levels after the third dose.
  - Adjust dose to maintain a trough level of 15–20 micromol/L.

If fever develops after 48 hours of admission:

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 **or** cefepime, IV, 1 g 12 hourly.

### OR

- 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.

If no response after 5–7 days:

### ADD

- Amphotericin B, IV, 1 mg/kg daily in dextrose 5 % over 4 hours.
  - Ensure adequate hydration to minimise nephrotoxicity.
  - Regular, e.g. 3 times a week, monitoring of potassium, magnesium and renal function is essential.

Duration of therapy:

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

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

**REFERRAL/CONSULTATION**

- » All cases – consult with haematologist/oncologist.

**2.8 MYELODYSPLASTIC SYNDROMES**

D46

**DESCRIPTION**

A group of disorders characterised by refractory cytopenias due to bone marrow failure. Anaemia is very common and there is a risk of developing acute leukaemia.

**Investigations**

Evidence of cytopenia, with normal B<sub>12</sub> and folate levels and 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 2.7: Febrile Neutropenia.

**REFERRAL**

- » All patients for further investigation and management.

**2.9 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. Early consultation with a haematologist or a clinician with expertise in the handling of such patients is advisable.

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.

## 2.9.1 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.

### Subclassification (factor VIII and IX deficiency):

CLASS	CLOTTING FACTOR	% OF NORMAL	SIGNS
Mild	VIII or IX	5–25%	Occasional bleeds
Moderate	VIII or IX	2–5%	
Severe	VIII or IX	< 1–2%	Trauma/spontaneous bleeds

### Investigations

Prolonged partial thromboplastin time (PTT).

Factor VIII or factor IX concentration < 25% of normal activity.

Prolonged bleeding time (Von Willebrand's).

Patient with factor VIII deficiency should be tested annually for factor VIII inhibitor.

### GENERAL MEASURES

Haemophilia register.

Ideally, patients should attend a specialised haemophilia centre with a dedicated multi-disciplinary health care team.

Medic alert bracelet.

Dental care (see below for management of tooth extraction).

Avoid contact sport.

**Acute bleeds into joints**

Apply ice packs.

Bed rest.

Rest the affected joint/limb until pain free and no further bleeding.

No weight bearing.

Splint (no circumferential casting).

**MEDICINE TREATMENT**

For mild to moderate pain:

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

If needed:

**ADD**

- Tramadol, oral, 50mg, 6 hourly.

For severe pain:

- Morphine, IV, 10 mg 4 hourly.

Exercise great caution when taking blood specimens.  
Taking blood from femoral veins is absolutely contra-indicated.

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)**

Bleeding event	Target plasma level of factor VIII	Duration of therapy
Minor nose and mouth bleeds, trauma with no bleeding, painless haematuria.	30%	At least 1 day.
Major oral bleeds (e.g. molar tooth extractions), severe throat and tongue bleeding, bleeding from calf and forearm.	40-50%	3–4 days or until the wound has healed well.
Head trauma, severe nose bleeds, any internal bleeding, major operations, any trauma with bleeding or with serious injuries.	60-100%	3–4 days or until the wound has healed well.

- Lyophilised factor VIII concentrate, slow IV infusion.  
Required units = body weight (kg) X desired factor increase (%) X **0.5**

Desired factor increase (%)	Body weight (kg)		
	50 kg	60 kg	70 kg
30%	750	900	1 050
40%	1 000	1 200	1 400
50%	1 250	1 500	1 750
60%	1 500	1 800	2 100
100%	2 500	3 000	3 500

### Factor IX deficiency (with no inhibitor present)

Bleeding event	Target plasma level of factor IX	Duration of therapy
Minor nose and mouth bleeds, trauma with no bleeding, painless haematuria	30%	At least 1 day
Major oral bleeds (e.g. molar tooth extractions), severe throat and tongue bleeding, bleeding from calf and forearm	30–50%	3–4 days or until the wound has healed well
Head trauma, severe nose bleeds, any internal bleeding, major operations, any trauma with bleeding or with serious injuries,	50–75%	3–4 days or until the wound has healed well

- Lyophilised factor IX concentrate, slow IV infusion  
Required units = body weight (kg) X desired factor increase (%) X **1.2**

Desired factor increase (%)	Body weight (kg)		
	50 kg	60 kg	70 kg
30%	1 800	2 160	2 520
50%	3 000	3 600	4 200
60%	4 500	5 400	6 300
100%	6 000	7 200	8 400

### Dental extraction

Check that inhibitors are absent.

In haemophilia A:

- Lyophilised factor VIII concentrate, IV, 40 units/kg immediately before extraction.

In haemophilia B:

- Lyophilised factor IX concentrate, IV, 40 units/kg immediately before extraction.
- Tranexamic acid, 250 mg dissolved in 10 mL of water.
  - Rinse mouth for 2 minutes 6 hourly.

### **Mucous membrane bleeds**

- Tranexamic acid, oral, 1 g 6 hourly.
  - Contraindicated in haematuria or in patients with thrombotic tendencies.

### **In mild von Willebrand's disease or established responders of mild factor VIII deficiency:**

- Desmopressin, IV, 0.3 mcg/kg in at least 30 mL sodium chloride 0.9% administered over 30 minutes.

### **Emergency treatment while awaiting transfer, if indicated**

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

- Fresh frozen plasma, IV, 10–20 mL/kg.

### **HAEMOPHILIA WITH INHIBITORS**

Refer for assessment and planning with a haematologist.

- Factor VIII inhibitor-bypassing activity (FEIBA) – under haematologist supervision only.

### **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**

For mild von Willebrand's Disease, which occurs in 80% of patients:

- Desmopressin, IV, 0.3 mcg/kg in at least 30 mL sodium chloride 0.9% administered over 30 minutes.

#### **Note:**

Desmopressin is not effective in type 3 and the majority of type 2 von Willebrand's disease.

Intermediate-purity factor VIII concentrates, which contain both von Willebrand factor and factor VIII, may be used for patients with very low von Willebrand factor levels.



During surgery or after major trauma, patients should receive:

- Cryoprecipitate, IV, 1 unit/10 kg 12 hourly.

**OR**

- Lyophilised factor VIII concentrate, IV, 30–50 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.

Antifibrinolytic agents may be used in combination with desmopressin or von Willebrand factor containing concentrates (cryoprecipitate or factor VIII) to treat bleeding episodes.

## 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 against factor VIII.
- » For further replacement, complex situations and complications in consultation with a haematologist.

## 2.10 IMMUNE THROMBOCYTOPENIC PURPURA (ITP)

D69.3

### DESCRIPTION

A common bleeding disorder due to immune destruction of platelets. To diagnose ITP, isolated thrombocytopenia is present (rest of the complete blood count, including an examination of the peripheral blood smear, is entirely normal). 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 series. Anaemia may be present due to blood loss.

Peripheral blood smear to exclude RBC fragments. Smear may show large platelets.

Do INR and aPTT, which should be normal in ITP.

If there is a poor response to treatment do a bone marrow biopsy.

## GENERAL MEASURES

Avoid:

- » medication that affects platelet function, e.g. NSAIDs and aspirin,
- » platelet transfusions unless 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.

## MEDICINE TREATMENT

### Acute ITP

- Prednisone, oral, 2 mg/kg daily.
  - Taper dose once response is achieved, usually within 10–14 days.
  - Therapy may be required for a few months before prednisone is eventually discontinued.
  - Also indicated for HIV-associated immune thrombocytopenia. Also start combination antiretroviral therapy urgently in these patients.

### Platelet transfusions

Platelet transfusions are only indicated in acute active bleeding uncontrolled by other means or before procedures. In an adult, 1 mega-unit of 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.

## REFERRAL

- » All cases not responding to steroids and, in the case of HIV patients, not responding to ART – discuss with haematologist.

## 2.11 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:

- » anaemia,
- » thrombocytopenia, often with purpura but not usually severe bleeding,
- » acute renal insufficiency that may be associated with anuria and may require acute dialysis,
- » neurologic abnormalities, and
- » fever.

TTP-HUS is associated with HIV infection and patients should be tested for HIV. TTP-HUS should be distinguished from disseminated intravascular coagulation (DIC) and severe pre-eclampsia where the coagulation profile is deranged.

### TREATMENT

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

- Fresh frozen plasma, IV infusion, 30 mL/kg in 3–4 divided doses.

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

### REFERRAL

- » All patients – discuss with a haematologist.

## 2.12 ACQUIRED COAGULATION DEFECTS

### 2.12.1 DISSEMINATED INTRAVASCULAR COAGULATION (DIC)

D65

#### MANAGEMENT

Identify and treat the underlying cause.

If the patient is bleeding, replace haemostatic factors with cryoprecipitate or fresh frozen plasma.

If the patient is not actively bleeding and platelet count > 20 000, then platelet transfusion is not necessary.

Replacement therapy for thrombocytopenia should consist of 1 apheresis single donor unit / megaunit (expected platelet count increment  $30\text{--}50 \times 10^9/\text{L}$ ) or 6 random donor units (expected increment  $50\text{--}60 \times 10^9/\text{L}$ ), ideally aiming to raise the platelet count >  $50 \times 10^9/\text{L}$ .

In chronic DIC, or in the absence of bleeding, platelet transfusions should not be given merely to correct the thrombocytopenia.

For hypofibrinogenaemia:

- Cryoprecipitate, 8–10 units.

For depletion of other coagulation factors:

- Fresh frozen plasma, 2–4 units, i.e. 15–20 mL/kg as initial dose
  - Volume:  $\pm 280$  mL/unit.

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

Perform frequent estimation of the platelet count and coagulation screening tests.

## 2.13 VENOUS THROMBO-EMBOLISM

182

### DESCRIPTION

Venous thrombosis should be seen as a spectrum from calf deep venous thrombosis to pulmonary thrombo-embolism. All patients should be seen as high risk.

Differential diagnosis include:

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

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

### GENERAL MEASURES

#### Acute management

In pulmonary embolism, cardiovascular resuscitation may be necessary and surgery may be undertaken for intractable disease.

#### Note:

Superficial thrombosis does not require anticoagulation.

Distal venous thrombosis in the lower limbs, i.e. involving tibial veins only, need not be treated with anticoagulants. Monitor patients with repeat ultrasound if anticoagulants are not used. Ultrasonography should be repeated after a week but may be omitted if D-dimer is negative.

#### Prophylaxis

Advice on prophylaxis should be emphasised.

Eliminate all predisposing factors.

Prevent deep vein thrombosis.

**MEDICINE TREATMENT****Acute treatment**

Unfractionated heparin initially, plus simultaneous warfarin. After 4–6 days, heparin is usually stopped and oral warfarin continued when a therapeutic INR level is reached.

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. However in 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.

**OR**

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

Do not use LMWH in morbid obesity and renal failure (eGFR <30 mL/minute).

Follow with:

- Warfarin, oral, 5 mg daily.
  - Adjust dose to keep INR within therapeutic range.
  - Continue warfarin for 3 months if there was a transient precipitating cause.
  - Continue life-long if there is a non-transient precipitating cause or if repeated episodes.
  - Contraindications for warfarin: first trimester and the last month of pregnancy. In these instances, replace with heparin.

Most patients can be managed successfully with therapeutic anticoagulation.

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

### **Prophylaxis**

Prophylaxis is indicated for most medical and surgical patients.

- Low molecular weight heparin, e.g.:
  - Dalteparin, SC, 5 000 units daily.

#### **OR**

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

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 epidural anaesthesia within 12 hours,
- » renal insufficiency,
- » coagulopathy, or
- » uncontrolled hypertension.

### **Heparin induced thrombocytopenia**

A severe immune-mediated drug reaction occurring in 1–5% of patients receiving heparin (unfractionated or 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 refer all patients.

### **REFERRAL/CONSULTATION**

- » Heparin-induced thrombocytopenia.

# CHAPTER 3

## CARDIOVASCULAR SYSTEM

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### 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  $\geq 102$  cm (men) and  $\geq 88$  cm (women).
- » 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 male relatives  $< 55$  years and in female relatives  $< 65$  years.
- » Age: men  $> 55$  years, women  $> 65$  years.

### GENERAL MEASURES

#### Lifestyle modification

All persons with risk factors for ischaemic heart disease should be encouraged to make the following lifestyle changes as appropriate:

- » Smoking cessation.
- » Weight reduction in the overweight patients, i.e. BMI  $> 25$  kg/m<sup>2</sup>.
- » Maintain ideal weight, i.e. BMI  $< 25$  kg/m<sup>2</sup>.
- » 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. 30 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 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.



Systolic BP (mmHg)	MEN		WOMEN	
	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 drug therapy

- » 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.
- » Chronic kidney disease (eGFR < 60 mL/minute.)
- » A risk of MI of greater than 20% in 10 years (see table above).

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

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

### Note:

When lipid-lowering drugs are used, this is always 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 blood pressure monitoring.

### 3.2.1 ST ELEVATION MYOCARDIAL INFARCTION (STEMI)

121

#### DESCRIPTION

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

#### MEDICINE TREATMENT

If clinically hypoxic:

- Oxygen.

- Aspirin, oral, 300 mg immediately as a single dose (chewed or dissolved).
  - Followed with 75–150 mg daily with food.

**PLUS**

Thrombolytic therapy:

- Streptokinase, IV 1.5 million units diluted in 100 mL sodium chloride 0.9%, infused over 30–60 minutes. **Do not use heparin if streptokinase is given.**

Indications	Contra-indications
» For acute myocardial infarction <u>with ST elevation</u> : <ul style="list-style-type: none"> <li>&gt; if history of onset is less than 6 hours. (Beyond 6 hours treat as NSTEMI (see below),</li> <li>&gt; if on-going ischaemic pain, or</li> <li>&gt; for new left bundle branch block.</li> </ul>	» Absolute: <ul style="list-style-type: none"> <li>&gt; streptokinase used within the last year,</li> <li>&gt; previous allergy,</li> <li>&gt; CVA within the last 3 months,</li> <li>&gt; history of recent major trauma,</li> <li>&gt; bleeding within the last month,</li> <li>&gt; aneurysms,</li> <li>&gt; brain or spinal surgery or head injury within the preceding month, or</li> <li>&gt; active bleeding or known bleeding disorder.</li> </ul> » Relative: <ul style="list-style-type: none"> <li>&gt; refractory hypertension,</li> <li>&gt; warfarin therapy,</li> <li>&gt; recent retinal laser treatment,</li> <li>&gt; subclavian central venous catheter,</li> <li>&gt; pregnancy,</li> <li>&gt; TIA in the preceding 6 months,</li> <li>&gt; traumatic resuscitation.</li> </ul>

**Adjunctive treatment**

For pain:

- Morphine, IV, 1–2 mg/minute.
  - Dilute 10 mg up to 10 mL with sodium chloride 0.9%.
  - Total maximum dose: 10 mg.
  - Repeat after 4 hours if necessary.

Pain not responsive to this dose may suggest ongoing unresolved ischaemia.

Nitrates, e.g.:

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

For ongoing chest pain, control of hypertension or pulmonary oedema:

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

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, bradycardias or asthma:

- $\beta$ -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.

For anterior myocardial infarction, pulmonary congestion or ejection fraction < 40%:

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

## REFERRAL

- » Refractory cardiogenic shock.
- » Refractory pulmonary oedema.
- » Haemodynamically compromising ventricular dysrhythmia.
- » 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/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 enzymes and ST segment depression or T wave inversion on ECG.

**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 enzymes.

### MEDICINE TREATMENT

If clinically hypoxic:

- Oxygen.
- Aspirin, oral, 300 mg immediately as a single dose (chewed or dissolved).
  - Followed with 75–150 mg daily.

### PLUS

Anticoagulation:

For acute myocardial infarction with no ST elevation:

- Unfractionated heparin, IV bolus, 5 000 units.
  - Follow with 1 000–1 200 units hourly monitored by aPTT.
  - Continue infusion for 3–5 days.

**OR**

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

**Note:**

Thrombolysis is not indicated except if new left bundle branch block (LBBB). See section 3.2.1: ST elevation myocardial infarction (STEMI).

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:

- Glycerol 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 drug no longer tolerated.
  - Flush the PVC tube before administering to patient.
  - Monitor blood pressure carefully.

Volume of diluent	Glycerol 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

To relieve pain:

- Morphine, IV, 1–2 mg/minute.
  - Dilute 10 mg up to 10 mL with sodium chloride 0.9%.
  - Total maximum dose: 10 mg.
  - Repeat after 4 hours if necessary.
  - Pain not responsive to this dose may suggest ongoing unresolved ischaemia.

If there is cardiac failure or LV dysfunction:

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

### 3.2.3 CHRONIC MANAGEMENT OF STEMI / NSTEMI / UA

#### 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

- » Ongoing chest pain or post-infarct angina.

### 3.2.4 ANGINA PECTORIS, STABLE

I20

#### DESCRIPTION

Characteristic chest pain due to myocardial ischaemia usually occurring on exercise and relieved by rest.

#### GENERAL MEASURES

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

#### MEDICINE TREATMENT

Long-term prophylaxis for thrombosis:

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

#### PLUS

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.

#### **PLUS**

##### **Step 1**

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

If  $\beta$ -blocker cannot be tolerated or is contraindicated, consider long acting calcium channel blocker.

##### **Step 2**

#### **ADD**

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

##### **Step 3**

#### **ADD**

- Isosorbide mononitrate, oral, 10–20 mg.
  - To provide a nitrate-free period to prevent tolerance, take at 8:00 and 14:00.
  - Modify for night shift workers.

#### **OR**

- Isosorbide dinitrate, oral, 20–40 mg.
  - To provide a nitrate-free period to prevent tolerance, take at 8:00 and 14:00.
  - Modify for night shift workers.
- 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.

### **REFERRAL**

- » When diagnosis is in doubt.
- » Failed medical therapy.

## **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, 75–150 mg daily with food.
- 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.

## 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 ( $\leq$  0.1 seconds) tachycardias.

#### REFERRAL

##### **Narrow QRS complex (supraventricular) tachydysrhythmias**

- » Poor rate control.
- » Severe symptoms.

##### **Regular narrow QRS (supraventricular) tachycardias**

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

**3.3.1.1 ATRIAL FIBRILLATION**

148

**Acute onset (<48 hours)**

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

Consider anticoagulation with heparin or warfarin.

Synchronised direct current (DC) cardioversion is occasionally necessary in emergency. Consider if first episode.

**Non-acute/chronic (> 48 hours)**

As above, but not immediate DC cardioversion, unless emergency.

**MEDICINE TREATMENT**

Patients with rheumatic heart disease require anticoagulation with warfarin.

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

Risk factors of stroke in atrial fibrillation are:

- » cardiac failure,
- » hypertension,
- » age > 65,
- » diabetes, and
- » stroke.

If patient has one of those risk factors use either aspirin or warfarin. Where more than one risk factor is present, use warfarin

**Initial therapy**

Anticoagulate with warfarin:

- Warfarin, oral, 5 mg daily adjusted according to INR.
  
- Atenolol, oral, 50–100 mg daily.
  - Contraindicated in asthmatics, heart failure.

**OR**

In CCF:

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

**PLUS**

If control not adequate add:

- Digoxin, oral 0.25 mg daily according to response.
  - Higher doses require digoxin trough level monitoring.

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

- Verapamil, oral, 80 mg 12 hourly.

If not controlled on those agents, refer to specialist for consideration of alternative therapy, e.g. amiodarone.

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 patient is stable; do 3 monthly monitoring
  - INR < 1.5 or > 3.5 do monthly monitoring

#### Caution

Use warfarin only if INR can be monitored regularly.

For rate control:

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

In CCF:

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

### PLUS

If control not adequate add:

- Digoxin, oral 0.25 mg daily according to response.
  - 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.

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

- Verapamil, oral, 80 mg 12 hourly.

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

**Prevention of recurrent paroxysmal atrial fibrillation****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:

- Halve dosage of warfarin and monitor INR closely, until 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**

148

Atrial rate >250 beats/minute with no flat baseline.

Can be difficult to recognize 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 and make the dysrhythmia more obvious.

**GENERAL MEASURES**

Synchronised DC cardioversion, 200 J, after sedation with:

- Diazepam, IV, 10–20 mg.

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.

**Long-term therapy**

Recurrent atrial flutter is an indication for referral as some may be cured by radio-frequency catheter ablation.

**3.3.1.3 AV JUNCTIONAL RE-ENTRY TACHYCARDIAS**

147.1

Usually paroxysmal.

Often young patients with normal hearts.

AV nodal re-entry or WPW syndrome.

P waves usually not visible (hidden by QRS complexes).

**GENERAL MEASURES**

Vagal manoeuvres: valsalva or carotid sinus massage. The patient should be supine and as relaxed as possible, to avoid competing sympathetic reflexes.

**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:  $\pm$  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 drug 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 drug did not reach the heart.

If none of the above is effective, or if the patient is hypotensive, consider DC shock.

**Long term therapy**

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

For infrequent, non-incapacitating symptoms:

- $\beta$ -blocker, e.g.:
- Atenolol, oral, 50–100 mg daily.

If asthmatic, but normal heart:

- Verapamil, oral, 80–120 mg 8 hourly.

Verapamil and digoxin are contraindicated in WPW syndrome.

### 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:

- Diazepam, IV, 10–20 mg.
  - If 200 J fails, use 360 J.

##### If cardiac arrest:

Defibrillate (not synchronised).

#### MEDICINE TREATMENT

##### Caution

Never give verapamil IV to patients with a wide QRS tachycardia.

DC cardioversion is first line therapy for regular wide QRS tachycardias. Drugs 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.

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.

**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  $\pm$  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.

### **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) tachydysrhythmias.

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 drugs.

Verapamil and digoxin may precipitate ventricular fibrillation by increasing the ventricular rate.

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

These tachycardias are usually ventricular. They are common in acute myocardial infarction.

In acute myocardial infarction, treat non-sustained ventricular tachycardia only if it causes significant haemodynamic compromise.

Ensure the serum potassium level >4 mmol/L.

**MEDICINE TREATMENT**

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

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.

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.

**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  $\pm$  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 drugs.

**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 drug, 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 drugs.

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.

Torsades complicating bradycardia:

- Adrenaline infusion to raise heart rate to > 100/ 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 over 60 years old and are idiopathic, with an excellent long-term prognosis, provided a permanent pacemaker is implanted. Acute, reversible AV block commonly complicates inferior myocardial infarction. The condition 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.

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 drugs are not effective.

**REFERRAL**

- » All cases with a heart rate < 40 beats/minute after resuscitation and stabilization.
- » All cases of second or third 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.

**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/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,
- » drugs, especially combination of verapamil and  $\beta$ -blocker or digoxin,
- » hypothermia,
- » hypoxia, or
- » hypothyroidism.

Treat the cause. Consider atropine if inferior 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,                   | » thiamine deficiency,     |
| » thyroid disease,           | » ischaemic heart disease, |
| » valvular heart disease,    | » haemochromatosis, and    |
| » constrictive pericarditis. |                            |

**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.

Salt restriction.

Regular exercise within limits of symptoms.

Avoid NSAIDs as these may exacerbate fluid retention.

Counsel regarding the risk of pregnancy and the use of oral contraceptives.

**MEDICINE TREATMENT**

Mortality is significantly reduced by the use of ACE inhibitors,  $\beta$ -blockers and spironolactone in heart failure.

Digoxin has been shown to reduce hospitalisation only.

**Diuretic**

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

- Hydrochlorothiazide, oral, 25–50 mg daily.
  - Caution in patients with gout.
  - Contraindicated 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 also renal failure.

**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 up to 10 mg 12 hourly.

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 in patients presenting with Class III or IV heart failure.

Do not use if GFR <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 mg once daily.

### **β-blockers**

For all stable patients with heart failure who tolerate it.

Patients should not be fluid overloaded or have low blood pressure before initiation of therapy.

- Carvedilol, oral.
  - Initial dose: 3.125 mg daily.
  - Increase after two weeks to 3.125 g 12 hourly, if tolerated.
  - Increase at two-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 can take several months.

### **Digoxin**

Symptomatic CCF owing to systolic dysfunction.

- Digoxin, oral, 0.125 mg daily. Specialist initiated.
  - Digoxin trough blood levels (before the morning dose) should be maintained between 0.65 and 1.5 nmol/L
  - Patients at high risk of digoxin toxicity are:
    - » the elderly,
    - » patients with poor renal function,
    - » hypokalaemia, and
    - » patients with low body weight.

### **Anticoagulants**

Heparin for DVT prophylaxis.

For patients admitted to hospital, unless contraindicated:

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

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

- Warfarin, oral, 5 mg daily.
  - Control with INR to therapeutic range, i.e. between 2.0 and 2.5.

### **Anti-dysrhythmic drugs**

See Section 3.3: Cardiac Dysrhythmias.

Only for potentially life-threatening ventricular dysrhythmias.

Always exclude electrolyte abnormalities and drug toxicity first.

### **Thiamine**

Consider in all unexplained heart failure.

- Thiamine, oral/IM, 100 mg daily.

**REFERRAL**

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

**3.5 ENDOCARDITIS, INFECTIVE**

I09.1

**GENERAL MEASURES**

Bed rest.

Early surgical intervention in acute fulminant and prosthetic valve endocarditis is often indicated.

**MEDICINE TREATMENT**

Treat accompanying complications, e.g. cardiac failure.

**Antibiotic therapy**

It is essential to do at least three and no more than six blood cultures taken by separate venipunctures before starting antibiotics.

In patients with subacute presentation and no haemodynamic compromise, wait for the results 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).

In **penicillin-allergic patients** vancomycin is the antibiotic of choice.

**Empiric therapy**

<b>Native valve</b>	<ul style="list-style-type: none"> <li>• Benzylpenicillin (penicillin G), IV, 5 million units 6 hourly for 4 weeks</li> </ul> <p><b>PLUS</b></p> <ul style="list-style-type: none"> <li>• Gentamicin, IV, 1.5 mg/kg 12 hourly for 2 weeks</li> </ul> <p>If staphylococcal infection is suspected (acute onset):</p> <p><b>ADD</b></p> <ul style="list-style-type: none"> <li>• Cloxacillin, IV, 3 g 6 hourly.</li> </ul>
<b>Prosthetic valve*</b>	<ul style="list-style-type: none"> <li>• Vancomycin, IV, 15 mg/kg 12 hourly for 6 weeks.</li> </ul> <p><b>PLUS</b></p> <ul style="list-style-type: none"> <li>• Rifampicin, oral, 7.5 mg/kg 12 hourly for 6 weeks.</li> </ul> <p><b>PLUS</b></p> <ul style="list-style-type: none"> <li>• Gentamicin, IV, 1.5 mg/kg 12 hourly for 2 weeks.</li> </ul>

\* All cases of prosthetic valve endocarditis should be managed in consultation with an appropriate specialist.

**Directed therapy (native valve)**

<b>Streptococcal</b>	
<b>Fully susceptible to penicillin</b> MIC: < 0.2mg/L	<ul style="list-style-type: none"> <li>• Benzylpenicillin (penicillin G), IV, 5 million units 6 hourly for 4 weeks.</li> </ul>
<b>Moderately susceptible</b> MIC: 0.12–0.5 mg/L	<ul style="list-style-type: none"> <li>• Benzylpenicillin (penicillin G), IV, 5 million units 6 hourly for 4 weeks.</li> </ul> <b>PLUS</b> <ul style="list-style-type: none"> <li>• Gentamicin, IV, 1.5 mg/kg 12 hourly for 2 weeks.</li> </ul>
<b>Moderately resistant</b> MIC: 0.5–4mg/L Enterococci and Abiotrophia spp. (nutritionally variant streptococci)	<ul style="list-style-type: none"> <li>• Benzylpenicillin (penicillin G), IV, 5 million units 6 hourly for 4 weeks.</li> </ul> <b>PLUS</b> <ul style="list-style-type: none"> <li>• Gentamicin, IV, 1.5 mg/kg 12 hourly for 4 weeks. Six weeks of therapy may be required in cases with a history of &gt; 3 months, or mitral or prosthetic valve involvement.</li> </ul>
<b>Fully resistant</b> MIC: > 4 mg/L	<ul style="list-style-type: none"> <li>• Vancomycin, IV, 15 mg/kg 12 hourly for 6 weeks.</li> </ul> <b>PLUS</b> <ul style="list-style-type: none"> <li>• Gentamicin, IV, 1.5 mg/kg 12 hourly for 6 weeks.</li> </ul>
<b>Enterococcal</b>	
<b>Fully susceptible to penicillin</b> MIC: < 4mg/L	<ul style="list-style-type: none"> <li>• Benzylpenicillin (penicillin G), IV, 5 million units 6 hourly for 4 weeks.</li> </ul>
<b>Resistant to penicillin</b> MIC $\geq$ 4mg/L or significant $\beta$ -lactam allergy <b>and</b> Sensitive to vancomycin MIC: $\leq$ 4 mg/L	Consult a specialist.

<b>Staphylococcal (cloxacillin/methicillin sensitive)</b>	
<i>S. aureus</i>	<ul style="list-style-type: none"> <li>• Cloxacillin, IV, 3 g 6 hourly for 4 weeks.</li> </ul> If necessary, add: <ul style="list-style-type: none"> <li>• Gentamicin, IV, 5 mg/kg daily for the first 3–5 days.</li> </ul> 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.
<b>Staphylococcal (cloxacillin/methicillin resistant) or methicillin sensitive with significant beta-lactam allergy</b>	
<i>S. aureus</i>	<ul style="list-style-type: none"> <li>• Vancomycin, IV, 15 mg/kg 12 hourly for 4 weeks.</li> </ul>
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 risk of developing infective endocarditis:

- » Acquired valvular heart disease with stenosis or regurgitation.
- » 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.
- » 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.

Penicillin allergy:

- Clindamycin, oral, 600 mg one hour before the procedure.

If patient cannot take oral:

- Ampicillin, IV/IM, 2 g one hour before the procedure.

Penicillin allergy:

- Clindamycin IM/IV, 600 mg 1 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.

**REFERRAL**

- » Complications such as renal failure and progressive cardiac failure.
- » For surgical intervention, e.g. emergency valve replacement.
- » Assessment for post treatment valve replacement.

**3.6 HYPERTENSION**

110

**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.

See medicine treatment choices below.

Immediate medicine treatment is needed for DBP > 110 mmHg and/or SBP >180 mmHg.



**Patient evaluation for risk stratification [target organ damage (TOD) and clinical cardiovascular disease (CCD) and co-morbidity]**

Thorough focused history and clinical examination is complemented by investigations.

Major risk factors for CVD:

- » diabetes mellitus,
- » hypertension,
- » obesity,
- » smoking,
- » dyslipidaemia, or
- » family history of primary hypertension or premature cardiovascular disease in men <55 years and in women <65 years.

Target organ damage (TOD):

- » left ventricular hypertrophy,
- » microalbuminuria, or
- » elevated creatinine level.

Associated clinical condition (ACC):

- » ischaemic heart disease (angina or prior myocardial infarction),
- » heart failure,
- » stroke or transient ischaemic attack,
- » chronic kidney disease,
- » retinopathy,
- » 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<sub>1c</sub> and fasting glucose.
- » Random total cholesterol.
- » If diabetic, do spot urine albumin creatinine ratio. Repeat yearly.
  - > normal: <3 mg/mmol
  - > microalbuminuria: 3–30 mg/mmol
  - > macroalbuminuria: >30 mg/mmol or overt nephropathy.
- » 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<sup>2</sup>. 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. 30 minutes brisk walking at least 3 times a week.

**MEDICINE TREATMENT**

Initial drug choice in patients qualifying for treatment is dependent on the presence of compelling indications.

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**

Low risk: BP <160/100 mmHg, no risk factors, Target organ damage (TOD) or Associated clinical condition (ACC).

- » Lifestyle modification for 3–6 months.
- » Start antihypertensive therapy if target BP not achieved.

Moderate risk: BP <180/110 mmHg, 1–2 risk factors, no diabetes, TOD and/or ACC.

- » Lifestyle modification for 3–6 months.
- » Start antihypertensive therapy if target BP not achieved.

High or very high risk: BP >140/90 mmHg with 3 or more risk factors, diabetes, TOD and/or ACC.

Lifestyle modification with immediate antihypertensive therapy.

Low dose thiazide diuretic e.g.:

- Hydrochlorothiazide, oral, 12.5 mg daily.

If target blood pressure is not reached after one month despite adequate adherence, 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 blood pressure is not reached after one month despite adequate adherence, add one of ACE inhibitor or calcium channel blocker, whichever has not already been used.

If target blood pressure is not reached after one month despite adequate adherence, add a  $\beta$ -blocker.

- $\beta$ -blocker, e.g.:
- Atenolol, oral, 50 mg daily.

If target blood pressure is not achieved after one month despite adequate adherence, increase the dose of drugs, one drug 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**

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

**Caution**

Lower BP over a few days.

A sudden drop in BP can be dangerous, especially in the elderly.

BP should be controlled within 1–6 months.

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

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

This therapy requires good initial evaluation, ongoing support for patients and continuous evaluation to ensure compliance.

Therapy should be initiated together with appropriate lifestyle modification and adherence monitoring.

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

## REFERRAL

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

Referrals are indicated when:

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

### 3.6.1 HYPERTENSION, SEVERE

#### DESCRIPTION

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

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

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

Follow up carefully and refer as needed.

### 3.6.2 HYPERTENSIVE URGENCY

#### DESCRIPTION

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

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

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

### MEDICINE TREATMENT

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

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

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

### 3.6.3 HYPERTENSIVE CRISIS, HYPERTENSIVE EMERGENCY

#### DESCRIPTION

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

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

Life-threatening complications include:

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

#### MEDICINE TREATMENT

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

**Intravenous therapy**

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

**OR**

If myocardial ischaemia and CCF:

- Glyceryl trinitrate, IV, 5–10 mcg/minute.
  
- Furosemide, IV, 40–80 mg.
  - Duration of action: 6 hours.
  - Potentiates all of the above drugs.

**Oral therapy**

ACE inhibitor, e.g.:

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

**3.7 RHEUMATIC HEART DISEASE**

109.9

**DESCRIPTION**

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

**GENERAL MEASURES**

Acute stage: bed rest and supportive care.

Patient education.

Intensive health education for prevention of sore throats.

**MEDICINE TREATMENT****Acute rheumatic fever**

For eradication of streptococci in throat:

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

**OR**

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

Penicillin allergy:

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

**Prevention of recurrent rheumatic fever**

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

All patients with confirmed rheumatic fever **and** rheumatic valvular disease – treat until 35 years of age.

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

**OR**

- Phoxymethylpenicillin, oral, 250 mg 12 hourly.

Penicillin allergy:

- Erythromycin, oral, 250 mg 12 hourly

**Prophylaxis for infective endocarditis**

See section 3.5: Endocarditis, infective.

**REFERRAL**

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



# CHAPTER 4

## DERMATOLOGY

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

### 4.1 ACNE

L70

#### DESCRIPTION

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

#### GENERAL MEASURES

Do not squeeze lesions.

Avoid greasy or oily topical products such as moisturisers that block the hair follicle openings.

Discourage excessive facial washing.

#### MEDICINE TREATMENT

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

#### AND/OR

For inflammatory acne:

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

#### Topical retinoids

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

The main action is to control comedone formation.

Introduce topical retinoids gradually as a night-time application to limit skin irritant effects, which are worse if used during day (UVL aggravation).

Do not use topical retinoids in pregnant women.

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

## 4.2 CELLULITIS AND ERYSIPELAS

L03.9/A46

### DESCRIPTION

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

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

### GENERAL MEASURES

Elevate the affected limb to reduce swelling.

### MEDICINE TREATMENT

For pain:

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

**OR**

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

### Antibiotic therapy

If intravenous antibiotics are given initially, patients should be switched to oral agents as soon as there is clinical improvement.

Antibiotics should usually be given for 5–10 days depending on clinical response.

- Cloxacillin, IV, 1 g 6 hourly.

When there is clinical improvement, change to:

- Flucloxacillin, oral, 500 mg 6 hourly.

### Penicillin allergy:

- Clindamycin, IV, 600 mg 8 hourly.

When there is clinical improvement, change to:

- Clindamycin, oral, 300 mg 8 hourly.

## REFERRAL

### Urgent

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

### Non-urgent

- » To surgeon for non-response.

## 4.3 IMPETIGO

L01.0

### DESCRIPTION

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

### GENERAL MEASURES

Good personal and household hygiene to avoid spreading the infection and to reduce carriage of organisms.

Wash and soak sores in soapy water to soften and remove crusts.

### MEDICINE TREATMENT

#### Antibiotic therapy

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

#### Penicillin allergy:

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

## 4.4 FURUNCLES AND ABSCESES

L02.9

### DESCRIPTION

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

The surrounding skin becomes:

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

**Note:**

Boils in diabetic or immunocompromised patients require careful management.

Check blood glucose levels if the boils are recurrent.

**GENERAL MEASURES**

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

**MEDICINE TREATMENT****Antibiotic therapy**

Systemic antibiotics are seldom necessary, except if there are:

- » tender draining lymph nodes,
- » fever,
- » extensive surrounding cellulitis, and
- » facial abscesses.

- Cloxacillin, IV, 1 g 6 hourly.

When there is clinical improvement, change to:

- Flucloxacillin, oral, 500 mg 6 hourly.

Penicillin allergy:

- Clindamycin, IV, 600 mg 8 hourly.

When there is clinical improvement, change to:

- Clindamycin, oral, 300 mg 8 hourly.

**4.5 ECZEMA**

L30.9

**DESCRIPTION**

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

**GENERAL MEASURES**

Avoid exposure to trigger or precipitating factors, where applicable.

Avoid irritants such as strong detergents, antiseptics, foam baths, perfumed soaps and rough occlusive clothing.

Good personal hygiene with regular washing to remove crusts and accretions and avoid secondary infection.

Keep fingernails short to prevent scratching.

Respect patient preference for cream or ointment topical treatment.

Wet wraps may help control eczema and pruritus but should not be used for infected eczema.

Diet modification has no role in atopic eczema treatment unless double blind challenge testing proves food sensitivity.

## MEDICINE TREATMENT

To relieve skin dryness:

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

### Mild eczema

Topical corticosteroids, e.g.:

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

### Severe eczema

Potent topical corticosteroids, e.g.:

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

### If non-responsive

Refer for dermatologist opinion.

- Prednisone, oral. Specialist initiated

### Maintenance therapy

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

Apply moisturiser as needed.

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

### Infected eczema

This is usually due to staphylococcal infection.

### Antibiotic therapy

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

### Penicillin allergy:

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

For sedation and relief of itch:

- Chlorpheniramine, oral, 4 mg at night as needed.

## REFERRAL

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

## 4.6 ERYTHEMA MULTIFORME, STEVENS JOHNSON SYNDROME, TOXIC EPIDERMAL NECROLYSIS

L51.9/L51.1/L51.2

### DESCRIPTION

#### **Erythema multiforme**

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

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

#### **Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis**

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

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

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

Systemic involvement with multi-organ dysfunction is common.

Complications include:

- » dehydration,
- » sepsis, and
- » adhesions and scarring.

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

## GENERAL MEASURES

### Principles of management

The foundation of management is supportive, good nursing and the prevention of dehydration and sepsis.

Stop all medicines.

Patients usually require care in a high or intensive care unit with dedicated nursing.

### Monitoring

Monitor vital organ function.

Examine daily for infection and swab infected lesions. Do blood cultures if septicaemic.

### Dressings

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

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

### Mucous membranes:

Regular supervised oral, genital and eye care to prevent adhesions and scarring.

Two-hourly mouth washes with bland mouth wash, e.g. glycothymol.

Examine daily for ocular lesions and treat 2-hourly with eye care and lubricants and break down adhesions.

Treat genitalia 6 hourly with Sitz baths and encourage movement of opposing eroded surfaces to prevent adhesions.

### Fluids:

Oral rehydration is preferred but intravenous fluid therapy may be required in significant dehydration.

Encourage oral fluids to prevent pharyngeal adhesions.

Provide soft, lukewarm food or nasogastric feeds if unable to eat.

### Note:

All patients should wear a notification bracelet/necklace.

## MEDICINE TREATMENT

### Corticosteroids

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

**Antibiotic therapy**

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

**Analgesia**

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

**4.7 LEG ULCERS, COMPLICATED**

L97

**DESCRIPTION**

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

**GENERAL MEASURES**

The aim of management should be to:

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

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

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

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

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

Walking and exercises are recommended.

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

Avoid excessive local heat.



Indications for surgical procedures include:

- » slough removal,
- » surgery for varicose veins,
- » arterial insufficiency, and
- » skin grafting.

## MEDICINE TREATMENT

### Antibiotic therapy

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

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

### Local wound care

#### Topical cleansing

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

For clean uninfected wounds:

- Sodium chloride 0.9% or sterile water.

For exudative, infected wounds:

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

## 4.8 PSORIASIS

L40.9

### DESCRIPTION

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

### GENERAL MEASURES

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

## MEDICINE TREATMENT

### Local plaques

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

For flares:

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

### Scalp psoriasis

For maintenance:

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

For flares

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

## REFERRAL

- » No response to treatment.
- » Severe disease.

## 4.9 URTICARIA

L50.9

### DESCRIPTION

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

### GENERAL MEASURES

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

## MEDICINE TREATMENT

### Antihistamines

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

For chronic urticaria less sedating antihistamines are preferable.

- Cetirizine, oral, 10 mg daily.

Avoid oral corticosteroids.

### 4.9.1 PAPULAR URTICARIA

L50.9

#### DESCRIPTION

Lesions due to insect bite often grouped or in a linear arrangement, show a central bite mark and are on exposed areas of the body.

Initial lesion is a red papule, which may blister, become excoriated, and then heal with hyperpigmentation.

Usually occur in crops over several months.

Chronic, severe, persistent reactions may be seen in immunocompromised patients, e.g. HIV infection, immunosuppressive therapy.

#### GENERAL MEASURES

Reduce exposure to insects by treating pets, using mosquito nets and fumigating household regularly.

Use of insect repellents may be helpful.

Examine carefully for burrows to rule out scabies.

#### MEDICINE TREATMENT

New inflamed lesions:

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

For relief of itch and sedation:

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

#### REFERRAL

- » Non-responsive and chronic cases.

### 4.10 FUNGAL INFECTIONS

B35

#### DESCRIPTION

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

Dermatophyte (tinea) infections are common and do not necessarily imply underlying systemic disease.

Deep fungal infections (mycetomas, sporotrichosis, blastomycosis) occur rarely. Systemic fungal infections (histoplasmosis, cryptococcosis) are increasingly seen in immunocompromised patients and need systemic therapy.

### **GENERAL MEASURES**

Manage predisposing factors, i.e. occlusion, maceration and underlying conditions such as diabetes, eczema, immunocompromise, etc.

Advise patient regarding spread of infection and exposure in communal, shared facilities (dermatophytes).

### **MEDICINE TREATMENT**

#### **Candida**

Imidazole, e.g.:

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

#### **Pityrosporum**

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

#### **Dermatophytes**

Imidazole, e.g.:

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

#### **Systemic antifungal therapy**

Topical treatment is generally ineffective for hair and nail infections.

Recurrent infections are not uncommon if repeat exposure is not prevented.

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

### **REFERRAL**

- » Non-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

Cryotherapy.

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

#### MEDICINE TREATMENT

##### Cutaneous warts

Treatment seldom indicated.

##### Anogenital warts

- Podophyllin 20% in Tinct. Benz. Co., topical.
    - Apply at weekly intervals to lesions by a health care professional until lesions disappear.
    - Apply petroleum jelly to surrounding skin and mucous membrane for protection.
    - Wash the solution off after 4 hours.
- Podophyllin is a cytotoxic agent.  
Avoid systemic absorption.  
Contraindicated in pregnancy. Exclude pregnancy before using podophyllin.

### 4.11.2 SHINGLES (HERPES ZOSTER)

See section 9.11: Zoster (shingles).

# CHAPTER 5

## GYNAECOLOGY

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### 5.1 DYSMENORRHOEA

N94.6

#### DESCRIPTION

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

#### GENERAL MEASURES

For secondary dysmenorrhoea, investigate and treat the underlying condition.

#### MEDICINE TREATMENT

Symptomatic relief:

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

**OR**

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

For severe pain:

#### ADD

- A combined oral contraceptive and review after 3 months.

#### REFERRAL

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

### 5.2 UTERINE BLEEDING, ABNORMAL

N91–N93

#### GENERAL MEASURES

Surgical procedures as dictated by the diagnosis.

Perform a transvaginal ultrasound and endometrial sampling in all women over 45 years of age.

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

#### MEDICINE TREATMENT

Dysfunctional uterine bleeding implies that no organic cause is present.

**ARREST OF ACUTE HAEMORRHAGE**

For excessively heavy anovulatory dysfunctional bleeding:

Progestogen, e.g.:

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

**OR**

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

After bleeding has stopped, continue with:

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

**FOR RESTORING CYCLICITY**

For women in the reproductive years:

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

**OR****As alternative to combined oral contraceptives:**

Progesterone only:

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

**OR**

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

For perimenopausal women, if uterus present, HRT:

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

**ADD**

For dysmenorrhoea and abnormal bleeding:

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

### 5.3 PELVIC INFLAMMATORY DISEASE (PID)

N73.9

#### DESCRIPTION

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

Sequelae include:

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

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

#### GENERAL MEASURES

Hospitalise all patients with stage II–IV PID for parenteral antibiotic therapy. Frequent monitoring of general abdominal and pelvic signs is essential.

##### Note:

Remove IUCDs.

Test and, if necessary, treat patient for syphilis and offer HIV testing.

Perform a pregnancy test as an ectopic pregnancy forms part of the differential diagnosis.

In stage III, surgery is indicated if:

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

#### MEDICINE TREATMENT

##### STAGE I

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

##### PLUS

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

##### PLUS

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



**STAGE II–IV**

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

Followed by:

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

**PLUS**

- Gentamicin, IV, 6 mg/kg daily.

**PLUS**

- Metronidazole, IV, 500 mg 8 hourly.

Continue intravenous therapy until there is definite clinical improvement.

Thereafter, change to:

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

**PLUS**

To treat chlamydia:

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

**Note:**

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

Penicillin allergy:

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

**PLUS**

- Clindamycin, IV, 600 mg 8 hourly.

**PLUS**

- Gentamicin, IV, 6 mg/kg daily.

Continue intravenous therapy until there is definite clinical improvement.

Thereafter, change to:

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

**PLUS**

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

**REFERRAL**

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

## 5.4 ENDOMETRIOSIS

N80

### DESCRIPTION

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

### GENERAL MEASURES

For women who wish to conceive, referral for surgery.

### MEDICINE TREATMENT

- Combined oral contraceptives for 6 months.

#### OR

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

### Note:

The recurrence of symptoms is common following cessation of treatment.

### REFERRAL

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

## 5.5 AMENORRHOEA

N91.0/N91.1

### DESCRIPTION

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

### Investigations

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

FSH > 15 units/L in a young woman (< 40 years) suggests premature ovarian failure.

LH/FSH ratio of > 2:1 suggests polycystic ovarian syndrome.

### MEDICINE TREATMENT

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

If no cause for secondary amenorrhoea is found:

- Medroxyprogesterone acetate, oral, 10 mg daily for 10 days.
  - Anticipate a withdrawal bleed 5–7 days following conclusion of treatment.

### REFERRAL

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

## 5.6 HIRSUTISM AND VIRILISATION

L68.0/E25

### DESCRIPTION

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

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

### REFERRAL

- » All cases.

## 5.7 INFERTILITY

N97.9

### DESCRIPTION

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

### GENERAL MEASURES

Counselling.

Lifestyle modification, e.g. weight optimisation, smoking cessation and regular sexual intercourse.

Investigation of semen analysis and prolactin level.

Mid-luteal (day 21) progesterone assay. > 30 nmol/L suggests adequate ovulation.

Laparoscopy and/or hysterosalpingography (Specialist supervision).

### MEDICINE TREATMENT

Treat the underlying disease.

For induction of ovulation:

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

For hyperprolactinaemia after further investigation:

See section 8.15.1: Prolactinoma.

## 5.8 MISCARRIAGE

O00–O08

Both Manual Vacuum Aspiration (MVA) and medical evacuation are equally effective for miscarriage. However, in the follow settings, MVA is preferred:

- » septic miscarriage
- » anaemia
- » haemodynamic instability
- » second trimester miscarriage

### 5.8.1 SILENT MISCARRIAGE OR EARLY FETAL DEMISE

O02.0

#### GENERAL MEASURES

Counselling.

Evacuation of the uterus.

#### MEDICINE TREATMENT

Before MVA, to ripen the cervix:

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

Medical evacuation:

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

### 5.8.2 INCOMPLETE MISCARRIAGE IN THE FIRST TRIMESTER

O02.1

#### GENERAL MEASURES

Counselling.

Evacuation of the uterus after ripening the cervix.

#### MEDICINE TREATMENT

Before MVA, to ripen the cervix:

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

Medical evacuation:

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

### 5.8.3 MIDTRIMESTER MISCARRIAGE (FROM 13–22 WEEKS GESTATION)

O03.4

#### GENERAL MEASURES

Counselling.

Evacuation of the uterus after the fetus has been expelled.

#### MEDICINE TREATMENT

- Misoprostol, PV, 400 mcg immediately.

Follow with:

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

#### Warning

Uterine rupture may occur in women with previous Caesarean sections.

Caution for this group and those of high parity: use 200 mcg of misoprostol or alternative methods such as extra-amniotic saline infusion without misoprostol.

If cervical dilatation already present:

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

#### Note:

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

For analgesia:

- Morphine, IV, 10 mg 4 hourly.

If Rh-negative:

- Anti-D immunoglobulin, IM, 100 mcg as a single dose.

**REFERRAL**

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

**5.8.4 SEPTIC MISCARRIAGE**

O03.87

**GENERAL MEASURES**

Counselling.

Urgent evacuation of uterus and surgical management of complications.

**MEDICINE TREATMENT**

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

**Antibiotic therapy**

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

**PLUS**

- Gentamicin, IV, 6 mg/kg daily.

**PLUS**

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

Change to oral treatment after clinical improvement:

- Amoxicillin/clavulanic acid, oral, 875/125 mg 12 hourly for 7–10 days.

**Note:**

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

Penicillin allergy:

- Clindamycin, IV, 600 mg 8 hourly.

**PLUS**

- Gentamicin, IV, 6 mg/kg daily.

Change to oral treatment after improvement:

- Clindamycin, oral, 450 mg 8 hourly for 5 days.

**PLUS**

- Ciprofloxacin, oral, 500 mg 12 hourly.

If patient has severe sepsis, consider urgent hysterectomy.

### REFERRAL

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

## 5.8.5 TROPHOBLASTIC NEOPLASIA ('HYDATIDIFORM MOLE')

O01

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

### REFERRAL

- » All patients.

## 5.9 TERMINATION OF PREGNANCY (TOP)

O04

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

### SUMMARY OF CHOICE OF TERMINATION OF PREGNANCY ACT

#### Women eligible

Up to 13 weeks: on request.

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

More than 20 weeks: Doctor and second doctor or registered midwife are satisfied that there is danger to the mothers' life, severe fetal malformation or risk of fetal injury.

#### Venue

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

#### Practitioner

Up to 13 weeks: doctor, midwife or registered nurse with appropriate training.

More than 13 weeks: doctor responsible for decision and prescription of medication. Registered nurse/midwife may administer medication according to prescription.

Pre and post termination counselling is essential.

Consent of spouse/partner is not necessary.

Consent for TOP and related procedures e.g. laparotomy may be given by minors.

Minors are encouraged to consult parents or others but consent is not mandatory.

### **Mentally retarded/unconscious patient**

On request from spouse or guardian; doctor and second doctor or registered midwife must agree.

If indicated as for 13+ to 20 weeks (above), spouse/guardian cannot prevent TOP by withholding consent.

## **5.9.1 GESTATION UP TO 13 WEEKS**

O.04

### **GENERAL MEASURES**

Counselling.

Outpatient procedure by nursing staff with specific training.

Manual vacuum aspiration of the uterus.

### **MEDICINE TREATMENT**

Manual vacuum aspiration:

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

Routine analgesia for vacuum aspiration

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

**OR**

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

Do not give intravenous benzodiazepines and parenteral opioid analgesics concurrently.

Alternatively, consider paracervical block.

Oral analgesia as required for 48 hours.

- Paracetamol, oral, 1 g 6 hourly.

**AND**

- Ibuprofen, oral, 800 mg 8 hourly.

Women who decline MVA:

An alternative is medical TOP with:

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



Followed 24–48 hours later by:

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

**Note:**

Bleeding may persist for up to 1 week.

After administration of mifepristone, start:

- Paracetamol, oral, 1 g 6 hourly.

**ADD**

After expulsion is complete:

- Ibuprofen, oral, 800 mg 8 hourly.

## 5.9.2 GESTATION 13+ TO 20 WEEKS

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

### GENERAL MEASURES

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

### MEDICINE TREATMENT

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

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

Followed 24–48 hours later by:

- Misoprostol, PV, 400–800 mcg as a single dose.
  - Then, misoprostol, oral, 400 mcg 3 hourly for 4 doses.

If no response after 24 hours, consider adding mechanical cervical ripening.

Pass a Foley catheter with 30 mL bulb through cervix with sterile technique.

Inflate bulb with 50 mL water or sodium chloride 0.9%.

Tape catheter to thigh with light traction on catheter.

Attach sodium chloride 0.9% 1 L with giving set to catheter.

Infuse sodium chloride 0.9% at 50 mL/ hour through catheter into uterus.

**Warning**

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

**Analgesia**

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

**OR**

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

If Rh-negative:

- Anti-D immunoglobulin, IM, 100 mcg as a single dose.

**REFERRAL**

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

**5.10 SEXUAL ASSAULT**

Y05

**INVESTIGATIONS**

Urine pregnancy test

Blood for:

- » RPR,
- » HIV, and
- » Hepatitis B if no history of previous Hep B immunisation.

**GENERAL MEASURES**

Trauma counselling and completion of J88 forms

Examination under anaesthesia may be required for adequate forensic sample collection, or repair of genital tract trauma.

**MEDICINE TREATMENT**

Emergency contraception:

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

**OR**

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

**Note:**

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

**STI prophylaxis**

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

**PLUS**

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

**PLUS**

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

**HIV post-exposure prophylaxis (PEP)**

See section: 10.5 Post-exposure prophylaxis for penetrative anal or vaginal sexual assault.

**5.11 GENITAL PROLAPSE AND URINARY INCONTINENCE**

N81.9

**Note:**

All patients should be referred to a specialist for initial evaluation.

Baseline investigations can, however, be done at lower level.

**GENERAL MEASURES**

Detrusor overactivity: bladder training, fluid restriction and physiotherapy.

Stress incontinence: pelvic floor exercises.

Surgical procedures as dictated by the diagnosis at specialist care.

**MEDICINE TREATMENT**

Treat urinary tract infections and underlying conditions, as appropriate.

For detrusor overactivity as demonstrated on urodynamic studies:

- Oxybutynin, oral, 2.5 mg 12 hourly, increasing to 5 mg 6 hourly.  
Specialist initiated.

**Note:**

Dry mouth is a common side effect of treatment.

**REFERRAL**

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

**5.12 MENOPAUSE AND PERIMENOPAUSAL SYNDROME**

N95.9

**GENERAL MEASURES**

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

**MEDICINE TREATMENT****Hormone replacement therapy (HRT)**

This is not indicated in all postmenopausal women. Symptomatic menopausal women and those with osteoporosis risk factors will benefit most.

The benefits need to be weighed against evidence of potential harm, including the emergence of risks as therapy continues.

**Note:**

Contraindications to HRT:

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

**Intact uterus (no hysterectomy)**

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

Sequentially opposed therapy:

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

**OR**

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

Equivalent doses to medroxyprogesterone acetate:

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

Continuous combined therapy, e.g.:

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

**OR**

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

**Note:**

Start at the lowest possible dose to alleviate symptoms. The need to continue HRT should be reviewed annually. A mammogram should be done once a year, and abnormal vaginal bleeding requires specialist consultation/referral

Any unexpected vaginal bleeding is an indication for excluding endometrial carcinoma as with other cases of postmenopausal bleeding. The use of transvaginal ultrasound to measure endometrial thickness plus the taking of an endometrial biopsy are recommended.

**Uterus absent (post hysterectomy)**

HRT is given as estrogen only. Estrogen supplementation to prevent postmenopausal osteoporosis requires long-term treatment.

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

**OR**

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

**REFERRAL**

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

# CHAPTER 6

## OBSTETRICS

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### **Note:**

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

### **6.1 ANAEMIA IN PREGNANCY**

O99.0

#### **DESCRIPTION**

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

#### **GENERAL MEASURES**

A balanced diet to prevent nutritional deficiency.

#### **MEDICINE TREATMENT**

##### **Prophylaxis**

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

##### **PLUS**

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

##### **Folic acid deficiency**

- Folic acid, oral, 5 mg daily.

Identify and treat associated vitamin deficiencies accordingly.

##### **Iron deficiency**

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

Parenteral iron

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

Total dose = weight (kg) x [11 g/dL – actual Hb (g/dL)] x 2.4 + 200 mg.

Maximum daily dose: 200 mg.

Administer over 30 minutes in 200 mL sodium chloride 0.9%.

Repeat every second day until the total dose is given.

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

**REFERRAL/CONSULTATION**

» No response to management.

**6.2 DIABETES MELLITUS IN PREGNANCY**

O24

This condition should ideally be managed by a specialist.

**DESCRIPTION**

Established diabetes: Diabetes (type 1 or 2) predating pregnancy.

Gestational diabetes: any degree of carbohydrate intolerance first recognised during pregnancy. It does not exclude the possibility that diabetes preceded the antecedent pregnancy.

**Diagnosis of gestational diabetes mellitus**

Screen women with the following:

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

**Diagnostic criteria**

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

## GENERAL MEASURES

### Diet

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

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

Eat 3 meals and 3–4 snacks/day.

Elective delivery at about 38 weeks' gestation.

## MEDICINE TREATMENT

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

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

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

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

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

### Normal profiles (adequate control)

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

### Abnormal profiles

Start insulin.

Diabetic women should be admitted initially for good control.

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

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

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



**Preferred regimen**

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

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

- Insulin, intermediate acting, 10 units.
- Insulin, soluble, short acting, 5 units 30 minutes before main meal.

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

**Where the above recommended regimen is not feasible**

Twice-daily regimen with biphasic insulin.

Empiric starting dose if previous insulin requirements are not known:

- Insulin, biphasic.
  - Daily dose: 0.2 units/kg/day, two-thirds of the dose 30 minutes before breakfast and one-third 30 minutes before supper.
  - Titrate daily to achieve target blood glucose as above.

**During labour:**

Monitor serum glucose hourly.

Stop subcutaneous insulin.

Administer short acting insulin to maintain physiological blood glucose levels.

- Insulin, short acting, continuous IV infusion, 20 units plus 20 mmol potassium chloride in 1 L dextrose 5% at an infusion rate of 50 mL/hour, i.e. 1 unit of insulin/hour
  - If blood glucose < 4 mmol/L, discontinue insulin.
  - If > 9 mmol/L, increase infusion rate to 100 mL/hour.

Postpartum insulin requirements decrease rapidly.

During the first 48 hours give insulin 4-hourly according to blood glucose levels.

Resume prepregnancy insulin or oral hypoglycaemic regimen once eating a full diet.

The newborn is at risk of:

- » hypoglycaemia,
- » respiratory distress syndrome,
- » hyperbilirubinaemia, and
- » congenital abnormalities.

**Postpartum contraception**

Tubal ligation should be considered.

Consider:

- Low-dose combined contraceptive in well-controlled cases.
- Progestogen-only preparation or intra-uterine contraceptive device if blood glucose control is poor.

**REFERRAL/CONSULTATION**

- » Blood glucose not adequately controlled on diet alone.

**6.3 HEART DISEASE IN PREGNANCY**

O75.4

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

**GENERAL MEASURES**

Consider thyrotoxicosis, anaemia and infection, which may precipitate cardiac failure.

Spontaneous delivery is usually preferable to Caesarean section, unless there are obstetric reasons for surgery.

Nurse in semi-Fowler's position.

Avoid unnecessary intravenous fluids.

Avoid a prolonged second stage of labour by means of assisted delivery with forceps (preferably) or ventouse.

Contraception, including the option of tubal ligation should be discussed after delivery in all women with significant heart disease.

Women who had serious complications during pregnancy should be advised not to become pregnant again.

**MEDICINE TREATMENT**

Indications for full anticoagulation during pregnancy (high risk):

- » valvular disease with atrial fibrillation
- » women with prosthetic heart valves

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

**First trimester**

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

**OR**

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

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

**Second trimester**

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

**After 36 weeks until delivery**

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

**OR**

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

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

**Prophylaxis for venous thromboembolism**

- » More than one previous episode of venous thromboembolism.
  - » One previous episode without a predisposing factor, or with evidence of thrombophilia.
- Low molecular weight heparin, e.g.: dalteparin, SC, 5000 units daily.

**OR**

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

**Antibiotic therapy**

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

Procedures for which endocarditis prophylaxis is indicated include:

- » Vaginal delivery in the presence of suspected infection.
- » Caesarean section.
- » Assisted vaginal delivery.
- » Prelabour rupture of membranes.

See section 3.5: Endocarditis, Infective.

**Cardiac failure**

Refer to section 3.4: Congestive Cardiac Failure.

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

If a vasodilator is needed:

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

**PLUS**

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

**Delivery**

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

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

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

**6.4 PRE-ECLAMPSIA**

O15.9

**DESCRIPTION**

Diastolic blood pressure > 90 mmHg on two occasions measured at least 4 hours apart or > 110 mmHg on one occasion, after 20 weeks' gestation.

**PLUS**

- » proteinuria > 300 mg/24 hours, or
  - » urinary **protein-creatinine ratio** > 0.03 g/mmol
- in a woman who is not hypertensive outside pregnancy.

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

**GENERAL MEASURES****Prevention**

Advise adequate dietary calcium (at least 1 000 mg daily).

Bed rest, preferably in hospital.

Lifestyle adjustment and diet.

Monitor BP, urine output, renal and liver function tests, platelet count, proteinuria and fetal condition.

Consider delivery when risks to mother outweigh risks of prematurity to baby.

## MEDICINE TREATMENT

### Prevention

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

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

### Treatment

#### Antihypertensives

Drug treatment will be dictated by blood pressure response.

Monitor progress until a stable result is achieved.

In general, diuretics are contra-indicated for hypertension in pregnant women.

When needed, combine drugs using lower doses of the three agents before increasing the doses to a maximum.

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

#### **AND/OR**

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

#### **AND/OR**

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

### Hypertensive emergency

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

Preload with:

- Sodium chloride 0.9%, IV infusion, 200 mL.
- Nifedipine, oral, 10 mg
  - Repeat after an hour if needed until systolic blood pressure <160 mmHg and diastolic blood pressure < 110 mmHg
  - Swallow whole. Do not chew, bite or give sublingually.

#### **OR**

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

If unable to take oral or inadequate response:

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

### **Delivery**

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

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

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

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

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

## **6.5 ECLAMPSIA**

O15

### **DESCRIPTION**

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

### **GENERAL MEASURES**

Place patient in left-lateral position.

Clear airway. If necessary, insert oropharyngeal airway.

**MEDICINE TREATMENT**

If necessary:

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

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

In high-care setting:

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

Follow with:

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

Where infusion pumps are not available:

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

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

If respiratory depression occurs:

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

**Eclamptic seizure in progress despite magnesium sulphate administration**

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

**OR**

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

**OR**

If above not available:

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

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

## REFERRAL

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

## 6.6 HYPERTENSION, CHRONIC

O10.9

### GENERAL MEASURES

#### Lifestyle modification

No alcohol should be taken.

Regular moderate exercise, e.g. 30 minutes brisk walking at least 3 times a week.

Smoking cessation.

Aim to keep BP <150/100 mmHg

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

Consider labour induction if:

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

### MEDICINE TREATMENT

See prevention and treatment of pre-eclampsia.

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

## 6.7 HIV IN PREGNANCY

O98.7

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

All pregnant women should receive routine counselling and voluntary HIV testing at their very first antenatal visit.

Women who test negative should be offered repeat HIV testing from 32 weeks' gestation onwards.

HIV positive pregnant women upon diagnosis, should be clinically staged, and have a blood sample taken for CD4 cell count on the same day. The result must be obtained within a week.

Decisions about postpartum contraceptive use and method of infant feeding must be made in the antenatal period.



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

Pregnant women with CD4 counts < 350 cells/mm<sup>3</sup> must be fast-tracked for access to lifelong antiretroviral therapy (ART). Those with symptoms of tuberculosis (TB) should be investigated and started on TB treatment before ART initiation.

All women with HIV infection should be counselled about the benefits of PMTCT.

### **MEDICINE TREATMENT**

Perform a baseline ALT and creatinine concentration before starting ART.

Women with abnormal ALT should not start nevirapine.

Tenofovir is contra-indicated in women with a calculated creatinine clearance or eGFR of <60 mL/minute

In concurrent TB, use efavirenz in place of nevirapine after first trimester.

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

#### **CD4 < 250 cells/mm<sup>3</sup>:**

- Tenofovir, oral, 300 mg daily.

#### **AND**

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

#### **AND**

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

#### **CD4 ≥ 250 cells/mm<sup>3</sup>, only start after the first trimester:**

- Tenofovir, oral, 300 mg daily.

#### **AND**

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

#### **AND**

- Efavirenz, oral, 600 mg at night.

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

### **Note:**

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

**CD4  $\geq$  350 cells/ mm<sup>3</sup> and WHO stage 1 or 2 disease**

From 14 weeks' gestation onwards until the onset of labour:

- Zidovudine, oral, 300mg 12 hourly,

**AND**

At the onset of labour:

- Nevirapine, oral, 200mg immediately as a single dose

**PLUS**

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

**AND**

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

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

**Women scheduled for elective Caesarean section:**

- Antenatal zidovudine as above

**AND**

4 hours before surgery:

- Nevirapine, oral, 200 mg as a single dose.

**AND**

Within a day following Caesarean section:

- Tenofovir 300mg and emtricitabine 200 mg, oral.

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

## 6.8 SYPHILIS

A53.9

**DIAGNOSTIC CRITERIA**

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

**GENERAL MEASURES**

Inform contact(s).

**MEDICINE TREATMENT****Mother**

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

**Note:**

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

### Penicillin allergy

- Erythromycin, oral, 500mg 6 hourly for 28 days.

**Note:**

Erythromycin for syphilis is not sufficient to prevent congenital syphilis. For penicillin sensitive patients, the penicillin desensitisation regimen is an option. If penicillin is not used, the baby must be regarded as inadequately treated and given penicillin after delivery.

Retreat mother with doxycycline once she has stopped breast feeding

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

### **Asymptomatic, well baby:**

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

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

### **Symptomatic baby**

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

**OR**

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

## **6.9 JAUNDICE IN PREGNANCY**

O26.6

### **DESCRIPTION**

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

Pregnancy-specific causes include:

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

### **REFERRAL**

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

## 6.10 HYPEREMESIS GRAVIDARUM

O21.9

### DESCRIPTION

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

Exclude:

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

### GENERAL MEASURES

Counselling.

Frequent small, dry meals.

Avoid fatty and spicy foods.

Restrict oral intake for 24–48 hours, but ensure adequate intravenous hydration.

### MEDICINE TREATMENT

Correct electrolyte imbalance with IV fluids.

- Pyridoxine, oral, 25 mg 8 hourly.

#### PLUS

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

#### PLUS

- Vitamin B complex, IV, 10 mL.

In refractory cases:

Administer daily until hyperemesis is controlled:

- Dexamethasone, IM/IV, 4–8 mg daily.

#### PLUS

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

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

O60/O42

### DESCRIPTION

Preterm: <37 weeks gestation.

Most problems occur at <34 weeks' gestation.

Confirm ruptured membranes by sterile vaginal speculum.

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

**GENERAL MEASURES**

Assess fetal wellbeing.

Estimate fetal weight.

Deliver if chorio-amnionitis suspected.

**MEDICINE TREATMENT**

If gestation <34 weeks:

Pre-hydrate before administration of nifedipine:

- Sodium chloride 0.9%, IV, 200 mL.

**PLUS**

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

If gestation <30 weeks and where nifedipine contra-indicated:

- Indomethacin, oral, 50 mg immediately then 25 mg 4 hourly for up to 48 hours.

**Note:**

Indomethacin may cause oligohydramnios, and its use is associated with a risk of premature closure of the ductus arteriosus. Use only if there is intolerance to nifedipine.

To improve fetal lung maturity at 26–34 weeks:

- Betamethasone, IM, 12 mg, 2 doses 24 hours apart.

If not available:

- Dexamethasone, IM, 12 mg, 2 doses 24 hours apart.

**Note:**

Corticosteroids are maximally effective if the complete course is administered at least 24 hours before delivery. Therefore give as soon as possible following diagnosis of PTL or PPRM.

**Antibiotic therapy**

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

- Amoxicillin, oral, 500 mg 8 hourly for 10 days.

**PLUS**

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

**OR**

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

**PLUS**

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

Prepare for appropriate care of preterm infant.

**REFERRAL**

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

**6.12 SUPPRESSION OF LABOUR**

O62.9

**DESCRIPTION**

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

**MEDICINE TREATMENT**

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

**6.13 LABOUR INDUCTION**

O80

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

**GENERAL MEASURES**

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

**Cervix favourable and confirmed HIV negative mother**

Artificial rupture of the membranes.

**Cervix unfavourable**

Extra-amniotic saline infusion: recommended if attempts at ripening the cervix with prostaglandins fail.

Pass a Foley catheter with 30 mL bulb through cervix with sterile technique.

Inflate bulb with 50 mL water or sodium chloride 0.9%.

Tape catheter to thigh with light traction.

Attach sodium chloride 0.9% 1 L with giving set to catheter.

Infuse sodium chloride 0.9% at 50 mL/ hour.

Remove after 24 hours if catheter has not fallen out.

## MEDICINE TREATMENT

### Cervix favourable

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

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

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

### Note:

Avoid oxytocin in women with previous caesarean section or parity  $\geq 5$ . Oxytocin use requires continuous electronic fetal heart rate monitoring. Aim for adequate uterine contractions (3–5 contractions in 10 minutes). Most women will experience adequate contractions at a dose of 12 milliunits/minute.

If uterine hyperstimulation syndrome develops (>5 contractions in 10 minutes with fetal heart rate abnormalities), stop the oxytocin infusion and administer salbutamol as above.

### Cervix unfavourable

Prostaglandins, e.g.:

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

### OR

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

### Note:

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

**OR**

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

**6.14 LABOUR PAIN, SEVERE****GENERAL MEASURES**

Antenatal counselling.

Psychological support from family member, friend or volunteer 'doula'.

The need for analgesics may be reduced by keeping the woman informed about the progress of labour, providing reassurance and carefully explaining the procedures performed.

Anticipate the need for analgesia rather than waiting for severe distress.

**MEDICINE TREATMENT**

At the onset of a uterine contraction:

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

Follow with:

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

**AND**

- Promethazine, IM, 25 mg 4 hourly.

Titrate dose and dose frequency according to pain.

Supplement with premixed nitrous oxide 50%/ oxygen 50% in late first stage.

Absorption from intramuscular injections during labour is poor.

The preferred route is IV.



**Epidural anaesthesia**

Offer this service only at hospitals with anaesthetic staff and equipment for epidural.

- Bupivacaine 0.25%.

**OR**

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

**Perineal analgesia:**

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

**Postpartum and post-episiotomy pain**

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

**OR**

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

**OR**

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

**6.15 DEHYDRATION/KETOSIS IN LABOUR**

E86

**DESCRIPTION**

Subclinical dehydration is often missed in labour.

**GENERAL MEASURES**

Encourage adequate oral fluid intake.

**MEDICINE TREATMENT****Mild dehydration**

Give oral fluids.

**Moderate/severe dehydration**

Administer intravenous fluids, e.g.:

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

Re-evaluate hydration hourly.

**6.16 POSTPARTUM FEVER**

O75.2

**DESCRIPTION**

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

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

### GENERAL MEASURES

Prevent deep vein thrombosis.

Complete evacuation of uterine contents.

Hysterectomy may be indicated in severe uterine sepsis.

Attention to breast engorgement.

### MEDICINE TREATMENT

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

#### Empiric antibiotic therapy

- Ampicillin, IV, 1 g 6 hourly.

#### PLUS

- Metronidazole, oral, 400 mg 8 hourly.

#### PLUS

- Gentamicin, IV, 6 mg/kg daily.

## 6.17 POSTPARTUM HAEMORRHAGE

O72

### DESCRIPTION

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

### GENERAL MEASURES

Bimanual compression of the uterus.

Ensure delivery of placenta.

Check for local causes of bleeding.

Compress the abdominal aorta in situations where bleeding is not responsive to above measures when transferring or waiting for definitive treatment.

### MEDICINE TREATMENT

#### Prevention

Active management of the 3<sup>rd</sup> stage of labour:

- Oxytocin, IM, 10 units.

#### AND

Controlled cord traction.

**Treatment**

Resuscitate

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

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

If necessary:

**ADD**

- Ergometrine, IM, 0.2–0.5 mg.

**OR**

- Oxytocin, IM, 5 units.

**PLUS**

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

For non-responding cases:

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

**6.18 THE RHESUS NEGATIVE WOMAN**

O36.0

**GENERAL MEASURES****Maternal serum antibodies absent****Prevention**

Test for maternal serum antibodies at 'booking', 28 and 34 weeks' gestation.

During pregnancy, give prophylactic anti-D immunoglobulin to the mother within 72 hours of a potentially sensitising event.

**MEDICINE TREATMENT**

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

- Anti-D immunoglobulin, IM, 100 mcg.

After external cephalic version:

- Anti-D immunoglobulin, IM, 100 mcg.

At birth, determine the Rh status of the cord blood and request a Coomb's test:

Cord blood Rh negative - no treatment.

Cord blood Rh positive, Coomb's negative:

- Anti-D immunoglobulin, IM, 100 mcg.

If a large fetomaternal transfusion is suspected:

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

**PLUS**

Do a maternal blood Kleihauer test.

Rh positive, Coomb's positive:

In these cases the mother will also have antibodies.

Do not administer anti-D immunoglobulin.

**Maternal serum antibodies present**

Consult a specialist.

# CHAPTER 7

## NEPHROLOGICAL/UROLOGICAL DISORDERS

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### 7.1 NEPHROLOGY SECTION

#### 7.1.1 CHRONIC KIDNEY DISEASE (CKD)

N18.9

##### DESCRIPTION

The presence of CKD should be established, based on:

- » the presence of kidney damage e.g. proteinuria/haematuria, or small kidneys on ultrasound for at least 3 months; and/or
- » level of kidney function: GFR < 60 mL/minute for at least 3 months with or without kidney damage. GFR is calculated using the Cockcroft and Gault formula in patients with stable renal function:

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

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

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

Common causes of CKD include:

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

Chronic kidney disease can be entirely asymptomatic until over 75% of kidney function is lost.

Check all drugs for possible dose adjustment based on eGFR/CrCl.

**TREATMENT AND PREVENTION STRATEGIES ACCORDING TO STAGES**

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

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

**Staging of kidney disease**

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

**Note:**

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

**GENERAL MEASURES**

Treat underlying CVD risk factors as appropriate.

Limit salt intake and stop smoking.

Avoid nephrotoxic drugs like NSAIDs.

## MEDICINE TREATMENT

The following interventions may delay progression of renal disease.

### Proteinuria reduction

Determine the amount of proteinuria with a spot urine specimen.

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

The ideal target is: protein creatinine ratio (PCR) < 0.03 g/mmol or albumin creatinine ratio (ACR) < 2.2 mg/mmol. Most benefit is achieved by reducing PCR to < 0.1 g/mmol or ACR < 100 mg/mmol.

Achievement of these targets must be balanced against side-effects such as hypotension and hypoglycaemia.

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

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

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

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

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

### Diabetes mellitus

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

#### Note:

Insulin requirements will decrease as renal disease progresses.

Stop glibenclamide when eGFR < 60 mL/minute because of an increased risk of hypoglycaemia.

Stop metformin when eGFR < 45 mL/minute because of the risk of lactic acidosis.

In patients unable to take insulin, consider:

- Gliclazide, oral, 40 mg daily.

### **Fluid overload and oedema**

- Furosemide, oral, 40 mg 12 hourly.

When fluid overloaded and eGFR < 60 mL/minute, start:

- Furosemide, oral, 40 mg 12 hourly.
  - Titrate to a maximum of 500 mg 12 hourly.

Furosemide is ineffective when patients are on dialysis and anuric.

### **Hypocalcaemia and hyperphosphataemia**

The aim is to lower phosphate levels and maintain normal calcium levels to ensure calcium phosphate product (i.e.  $\text{Ca} \times \text{PO}_4$ ) < 4.4 mmol/L, to prevent calcium deposition in vessels and tissue which aggravates vascular disease.

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

- Calcium carbonate, oral, equivalent to 500–1500 mg daily of elemental calcium.
  - Take in divided doses with meals.
  - If serum phosphate is low, then take between meals.

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

### Patients considered suitable candidates for renal replacement therapy

Monitor  $\text{Ca}^{++}$  and  $\text{PO}_4$  and PTH levels regularly.

For hyperphosphataemia uncontrolled on calcium carbonate:

- Aluminium hydroxide BP, oral, 10 mL 8 hourly. Specialist initiated.
  - To prevent dementia-associated aluminium toxicity, do not use for longer than 3 months.

For hyperparathyroidism, initiate when PTH levels > 2–3 times normal:

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

### **Anaemia associated with CKD in patients on dialysis programmes**

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

In CKD, especially CKD stage 4–5:

- Iron, elemental, oral. Specialist initiated.
  - If no response consider parenteral iron.



**AND**

- Erythropoietin, SC/IV. Specialist initiated.

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

**Acidosis and hyperkalaemia**

See section 7.1.5: Acute Renal Failure (ARF).

**REFERRAL/CONSULTATION**

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

**7.1.2 GLOMERULAR DISEASE (GN)**

N00–N08

**REFERRAL**

All patients with:

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

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

**7.1.3 GLOMERULAR DISEASE AND NEPHRITIC SYNDROME**

N01/N03

**DESCRIPTION**

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

**GENERAL MEASURES**

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

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

See Section 7.1.1: Chronic Kidney Disease (CKD).

### MEDICINE TREATMENT

The management of glomerular disease is individualised and dependent on the type of glomerular disease.

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

Check all drugs for possible dose adjustments.

See section 7.1.1: Chronic Kidney Disease (CKD).

### CONSULTATION/REFERRAL

- » All patients.

## 7.1.4 GLOMERULAR DISEASE AND NEPHROTIC SYNDROME

N04

### DESCRIPTION

Glomerular disease characterised by:

- » severe proteinuria, i.e.: protein:creatinine ratio  $>0.25$  g/mmol

and

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

The cause cannot be determined accurately without a biopsy.

### GENERAL MEASURES

Regulate salt and fluid intake. Weigh daily.

Postural blood pressure for monitoring fluid loss and to prevent excessive diuresis.

Evaluate proteinuria with protein creatinine ratio:

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

### MEDICINE TREATMENT

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

**Note:**

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

**CONSULTATION/REFERRAL**

- » All patients.

**7.1.5 ACUTE RENAL FAILURE (ARF)**

N17

**DESCRIPTION**

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

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

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

Common causes of acute renal failure:

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

Predisposing factors for acute renal failure include:

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

Common complications of acute renal failure include:

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

**GENERAL MEASURES**

A detailed history and good clinical examination is necessary to identify potentially reversible causes.

Judicious fluid replacement for dehydrated patients.

Check all drugs for possible dose adjustments.

Early consultation with expert/experienced clinician is required.

**MEDICINE TREATMENT**

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

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

**Acute dialysis**

Discuss all cases with the referral centre.

Common indications:

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

**Note:**

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

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

**Acidosis**

If pH  $< 7.25$  and  $\text{HCO}_3^- < 15$  mmol/L and the patient is stable and not dehydrated, refer for dialysis. If dehydrated, administer fluid.

**CAUTION**

Avoid fluid overload.

If associated acidosis, see fluid preference below.

**Hyperkalaemia**

Serum  $\text{K}^+ > 6.5$  mmol/L.

Beware of spurious hyperkalaemia due to haemolysis during venipuncture.

Emergency measures

- Calcium gluconate 10%, slow IV bolus, 10 mL.
  - Maximum dose: 40 mL.
- Dextrose 50%, continuous IV infusion, 100 mL with soluble insulin, 10 units administered over 15–30 minutes.
  - Monitor blood glucose levels hourly.

**AND**

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

If there is no response, patients will require dialysis.

For long-term or chronic, non-urgent need for potassium removal:

- Sodium polystyrene sulfonate, oral, 15 g with 15 mL lactulose, 6 hourly.

**OR**

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

**Note:**

Rectal administration is less effective.

Treat acidosis to prevent cardiac instability.

Furosemide may also be of benefit.

Monitor ECG and measure serum  $K^+$  frequently.

If the above treatment fails, urgent dialysis is required.

### **Hyperphosphataemia**

To decrease absorption of phosphate in acute renal failure:

- Aluminium hydroxide 300 mg/5 mL, oral, 10 mL 8 hourly.

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

Acute renal failure may complicate chronic renal failure.

A small percentage of patients do not recover kidney function and should be treated as CKD.

## **REFERRAL/CONSULTATION**

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

### **7.1.6 END STAGE RENAL DISEASE (ESRD) - CKD STAGE 5**

N18.5

#### **DESCRIPTION**

A permanent and usually irreversible stage of kidney failure caused by a variety of diseases (See section 7.1.1: Chronic Kidney Disease), which requires dialysis or transplantation for the patient to survive.

**Note:**

These patients are best managed at a specialist centre and by specialists.

**GENERAL MEASURES**

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

Restrict salt, phosphate and potassium.

**MEDICINE TREATMENT**

Avoid magnesium and aluminium containing substances.

Manage fluid balance on an individual basis.

Review all drug doses and adjust for the level of renal function, most will be GFR < 10 mL/minute.

**REFERRAL/CONSULTATION**

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

**7.1.7 RENAL REPLACEMENT THERAPY****PATIENT SELECTION**

The final decision for selection of patients for renal replacement therapy should be made at the tertiary level hospital or by a nephrologist.

The ideal patient for renal replacement therapy is a patient with uncomplicated CKD stage 5 (ESRD), who is a suitable candidate for renal transplantation.

Referral may be most useful in identifying the conditions outlined earlier.

Individual renal units have their own criteria for acceptance and these may include:

- » considerations of presence of systemic illnesses,
- » age,
- » BMI, and
- » psychosocial factors.

Obtain these guidelines from the referral centre.

**7.1.8 URINARY TRACT INFECTION (UTI)**

N39.0

**DESCRIPTION**

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

All other UTIs are regarded as complicated.

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

Features of upper UTI include:

- » flank pain/tenderness,
- » temperature  $\geq 38^{\circ}\text{C}$  or higher,
- » other features of sepsis, i.e. tachypnoea, tachycardia, confusion and hypotension, or
- » vomiting.

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

### **MEDICINE TREATMENT**

Empirical treatment is indicated only if:

- » positive leucocytes and nitrites on urine test strips, or
- » leucocytes or nitrites with symptoms of UTI, or
- » systemic signs and symptoms.

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

#### **Uncomplicated cystitis**

- Ciprofloxacin, oral, 500 mg as single dose.

#### **Complicated cystitis**

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

For pregnant women:

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

#### **Acute pyelonephritis**

Admit all patients with vomiting, sepsis or diabetes.

Ensure adequate hydration with intravenous fluids.

If there is a poor response, perform an ultrasound on all hospitalised patients urgently as in-patients or electively as out-patients.

Adjust antibiotic according to sensitivity.

Duration of antibiotic therapy:

- » fluoroquinolones 7 days
- » other antibiotics 14 days.

Longer courses of therapy, 2–3 weeks, should be given for complicated pyelonephritis.

If normal renal function:

- Gentamicin, IV, 6 mg/kg daily.

Switch to oral therapy as soon as the patient is able to take oral fluids:

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

If impaired renal function:

- Ceftriaxone, IV, 1 g daily.

Switch to oral therapy as soon as the patient is able to take oral fluids:

- Ciprofloxacin, oral, 500 mg 12 hourly for 7 days.
  - CrCl: < 10 mL/minute      50% of normal dose

Refer to a urologist if there is failure to resolve.

### 7.1.9 RECURRENT UTI

#### DESCRIPTION

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

Two types occur:

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

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

#### GENERAL MEASURES

Women should void soon after intercourse.

Identify and treat hormone-deficient atrophic vulvo-vaginitis in the elderly.

Patients with impaired bladder emptying require careful urological examination to establish whether surgical treatment is required.

Patients with ileal conduits or long-term indwelling catheters should not receive antibiotics unless there is invasive upper UTI. In this setting, treatment with a short, intensive course of antibiotic is appropriate.

#### MEDICINE TREATMENT

##### Prophylaxis

To reduce risk of recurrence in patients with >3 infections/year requires continuous prophylaxis for at least 6 months:

- Cotrimoxazole 80/400 mg, oral, 1 tablet at night.

##### OR

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



2–3 infections/year:

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

UTI in relation to sexual activity:

- Ciprofloxacin, oral, 500 mg as single dose.

### **Treatment**

Treat according to microscopy, culture and sensitivity.

### **REFERRAL**

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

## **7.1.10 PROSTATITIS**

N41.0/N41.1

### **DESCRIPTION**

This is an infection of the prostate caused by uropathogens.

Clinical features include:

- » pyrexia,
- » acute pain in the pelvis and perineum,
- » urinary retention or difficulty, and
- » acutely tender prostate on rectal examination.

### **Chronic non-bacterial prostatitis**

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

### **MEDICINE TREATMENT**

#### **Acute bacterial prostatitis**

In men < 35 years old:

- Cefixime, oral, 400 mg as single dose.

Follow with:

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

In men > 35 years old:

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

Chronic/relapse/persistent infection:

- Ciprofloxacin, oral, 500 mg 12 hourly for 28 days.

## REFERRAL

- » To a urologist if no response to treatment.

## 7.2 UROLOGY SECTION

### 7.2.1 HAEMATURIA

R31

#### DESCRIPTION

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

Proteinuria and casts on routine microscopy suggest glomerular disease.

Schistosomiasis (bilharzias) is a common cause of haematuria.

#### GENERAL MEASURES

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

**Isomorphic red cells:** suggests urinary tract below the kidney i.e. pelvis to urethra.

**Dysmorphic red cells:** suggests intrarenal and glomerular origin.

Exclude schistosomiasis.

#### Note:

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

#### MEDICINE TREATMENT

Only if evidence of associated urinary tract infection, i.e. positive leucocytes or nitrites on urine test strips.

See section 7.1.8: Urinary Tract Infection (UTI) and see section 7.1.2: Glomerular Disease.

## REFERRAL

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

**7.2.2 BENIGN PROSTATIC HYPERPLASIA**

N40

**DESCRIPTION**

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

**GENERAL MEASURES**

Annual follow-up with digital rectal examination (DRE).

For patients presenting with urinary retention, insert a urethral catheter as a temporary measure while the patient is transferred for referral.

Surgical reduction of the prostate is the preferred treatment, e.g. minimally invasive transrectal procedures or radical prostatectomy.

Remove drugs that prevent urinary outflow e.g. tricyclics and neuroleptics.

**MEDICINE TREATMENT**

When surgery is not feasible or deferred:

- Doxazosin, oral, 4 mg daily.

**REFERRAL**

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

**7.2.3 OVERACTIVE BLADDER**

N39.4

**DESCRIPTION**

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

**GENERAL MEASURES**

Health education.

Clean intermittent self-catheterisation (CISC).

Indwelling catheter, suprapubic or transurethral.

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

### **MEDICINE TREATMENT**

For detrusor hyperactivity demonstrated on urodynamic studies:

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

### **REFERRAL**

- » For confirmation of diagnosis.
- » Complications.

## **7.2.4 IMPOTENCE**

N48.4/F52.2

### **DESCRIPTION**

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

### **GENERAL MEASURES**

Thorough medical and psychosexual history

Examination should exclude gynaecomastia, testicular atrophy or penile abnormalities.

Consider the removal of drugs that may be associated with the problem. A change in lifestyle or drugs may resolve the problem.

### **MEDICINE TREATMENT**

Treat the underlying condition.

In patients with proven testosterone deficiency:

- Testosterone. Specialist initiated.

See section 8.3: Androgen deficiency.

### **REFERRAL**

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

**7.2.5 RENAL CALCULI**

N20.2

**DESCRIPTION**

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

Collect the stones and send to the laboratory for analysis.

**GENERAL MEASURES****Acute stage**

Oral fluids administered liberally.

Intravenous fluids to ensure adequate hydration and urine flow.

Surgical procedures, if required.

**Maintenance therapy, for the prevention of recurrence**

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

**MEDICINE TREATMENT**

Analgesia for pain, if needed:

- Morphine, IM/slow IV, 10–15 mg.

For hypocitraturia:

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

For uric acid stones:

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

**PLUS**

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

The treatment is long-term to prevent recurrence.

For mild metabolic hyperoxaluria:

- Pyridoxine, oral, 25–75 mg daily.

**PLUS**

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

For renal hypercalciuria (absorptive type):

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

### **REFERRAL**

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

# CHAPTER 8

## ENDOCRINE SYSTEM

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### 8.1 ACROMEGALY

E22.0

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

#### REFERRAL

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

### 8.2 ADRENAL INSUFFICIENCY (ADDISON'S DISEASE)

E27.1

#### DESCRIPTION

Primary adrenocortical insufficiency.

#### Clinical presentation

##### Acute crisis:

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

##### Chronic:

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

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

#### Investigations

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

> 550 nmol/L: virtually excludes the diagnosis

< 100 nmol/L: highly suggestive of hypoadrenalism

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

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

## GENERAL MEASURES

All patients should wear a notification bracelet.

## MEDICINE TREATMENT

### Acute crisis

Exclude sepsis.

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

To maintain adequate intravascular volume guided by blood pressure:

- Sodium chloride 0.9%, IV.

The fluid deficit is often several litres.

Monitor glucose levels closely and treat hypoglycaemia if present.

### Chronic

As maintenance therapy:

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

### OR

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

For patients who remain symptomatically hypotensive:

- Fludrocortisone, oral, 50–100 mcg daily.

Monitor response to therapy with:

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

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

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

**Note:**

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

Prolactin

Sperm count, if infertility is a consideration.

Further investigations to determine cause to be undertaken after referral.

Consult a specialist.

**MEDICINE TREATMENT**

Screen hypogonadal men for prostate cancer before beginning testosterone replacement.

Individualise dosage and review doses based on clinical response.

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

Monitor patients for prostate cancer during treatment as normal.

**8.4 CUSHING'S SYNDROME**

E24.9

**DESCRIPTION**

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

**Investigations**

Screening tests for Cushing's syndrome: 24 hour urinary free cortisol.

Low dose betamethasone (equivalent to dexamethasone) suppression test:

- Betamethasone, oral, 1 mg.
  - Administer close to midnight.
  - Measure plasma cortisol 8 hours later.
  - In normal people morning cortisol will be suppressed to <50 nmol/L.
  - Refer if levels not suppressed.

**GENERAL MEASURES**

Check for hypertension and diabetes and treat accordingly.

Check potassium.

**REFERRAL**

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

**8.5 DIABETES MELLITUS****DESCRIPTION****Types of diabetes:**

- » Type 1
- » Type 2
- » Pancreatic diabetes mellitus
- » Gestational diabetes mellitus – See Section 6.2: Diabetes Mellitus in Pregnancy.

**GENERAL MEASURES**

All patients require lifestyle modification.

In patients with type 2 diabetes mellitus, appropriate weight loss if weight exceeds ideal weight.

Correct meal/energy distribution in type 1 diabetes mellitus.

Moderate or no alcohol intake.

Discourage smoking.

Increased physical activity, aim for 30 minutes 5 times a week.

Education about foot care is essential.

**Monitoring**

At every visit:

- » blood glucose,
- » weight, and
- » blood pressure.

Measure HbA1c:

- » annually in patients who meet treatment goals, and
- » 3–6 monthly in patients whose therapy has changed until stable.

Annually:

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

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

In the elderly, the increased risk of hypoglycaemia must be weighed against the potential benefit of reducing microvascular and macrovascular complications.

In patients with severe target organ damage, therapy should be tailored on an individual patient basis and should focus on avoiding hypoglycaemia.

## REFERRAL

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

### 8.5.1 DIABETES MELLITUS TYPE 2

E11

Management includes:

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

**MEDICINE TREATMENT****Oral blood glucose lowering drugs**

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

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

For persisting HbA<sub>1c</sub> above acceptable levels and despite adequate adherence to oral hypoglycaemic agents, add insulin and withdraw sulphonylurea.

**Note:**

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

**Metformin**

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

Contra-indicated in:

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

Sulphonylurea derivatives: gliclazide or glibenclamide.

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

**OR**

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

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

Monitor serum creatinine and estimated GFR in kidney disease.

**Insulin therapy in type 2 diabetes**

Indications for insulin therapy:

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

**Note:**

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

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

Insulin type	Starting dose	Increment	Maximum daily dose
Add on therapy: <ul style="list-style-type: none"> <li>• Intermediate to long-acting insulin</li> </ul>	10 units in the evening before bedtime, but not after 22h00.	If 10 units not effective increase gradually to 20 units (2–4 units increase each week).	40units  Refer if > 40 units are needed.
Substitution therapy: <ul style="list-style-type: none"> <li>• Biphasic insulin</li> </ul>	Twice daily.  Total daily dose: 15 units divided as follows: <ul style="list-style-type: none"> <li>• 2/3 of total daily dose, i.e. 10 units, 30 minutes before breakfast.</li> <li>• 1/3 of total daily dose, i.e. 5 units, 30 minutes before supper.</li> </ul>	4 units weekly.  First increment is added to dose before breakfast  Second increment is added to dose before supper.	50 units.  Refer if > 50 units are needed.

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

**Note:**

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

**To reduce cardiovascular risk**

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

- Simvastatin, oral, 10 mg daily.

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

If urine albumin:creatinine ratio is > 2.5 mg/mmol, consider ACE inhibitor, e.g.:

- Enalapril, oral, 10 mg daily.

See section 7.1.1: Chronic Kidney Disease (CKD).

## 8.5.2 DIABETES MELLITUS TYPE 1

E10

Management includes:

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

### Insulin protocols

- Insulin, short acting, SC, three times daily, 30 minutes before meals:  
Regular human insulin.  
Onset of action: 30 minutes.  
Peak action: 2–5 hours.  
Duration of action: 5–8 hours.
- Insulin, intermediate acting, SC, once or twice daily, usually at night.  
Neutral Protamine Hagedorn (NPH) insulin.  
Onset of action: 1–3 hours.  
Peak action: 6–12 hours.  
Duration of action: 16–24 hours.
- Insulin, biphasic, SC, once or twice daily.  
Mixtures of regular human insulin and NPH insulin in different proportions, e.g. <sup>30</sup>/<sub>70</sub>.  
Onset of action: 30 minutes.  
Peak action: 2–12 hours.  
Duration of action: 16–24 hours.

### **Selection of insulin**

#### Basal bolus regimen

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

The initial total daily insulin dose:

- 0.6 units/kg body weight.

The total dose is divided into:

- 40–50% basal insulin
- the rest as bolus insulin split equally before each meal.

Adjust dose on an individual basis.

### Pre-mixed insulin

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

### Insulin delivery devices

In visually impaired patients, prefilled syringes may be used.

### Home glucose monitoring

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

### Glucagon

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

## 8.6 DIABETIC EMERGENCIES

### 8.6.1 HYPOGLYCAEMIA

E10.64/E11.65

#### **Diagnosis: Clinical**

Symptoms:

- » Anxiety
- » Palpitations
- » Headaches
- » Sweating
- » Hunger
- » Behavioural changes

Signs:

- » Sweating
- » Tachycardia
- » Tremor
- » Bizarre neurological signs
- » Confusion
- » Seizures
- » Coma

**Biochemical**

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

**TREATMENT**

Start immediately.

At home:

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

In hospital:

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

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

Establish a large bore intravenous line and keep open with:

- Dextrose 10%, IV.

If no clinical response, give a second injection of:

- Dextrose 50%, IV, 50 mL.

To prevent recurrent hypoglycaemia, continue infusion with:

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

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

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

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

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

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

If hypoglycaemia was caused by a sulphonylurea, the patient will require hospitalisation and a prolonged intravenous glucose infusion.

Observe patient for at least 12 hours after glucose infusion has stopped.



**Recurrent hypoglycaemia**

In cases of recurrent hypoglycaemia consider:

- » inappropriate management, e.g. too much insulin or too high dose of sulphonylurea,
- » poor adherence,
- » alcohol abuse,
- » factitious administration of insulin,
- » the “honeymoon” period of type 1 diabetes,
- » the advent of renal failure,
- » hypoglycaemic unawareness, or
- » pancreatic diabetes/malabsorption.

Other causes of hypoglycaemia should also be considered e.g. associated Addison’s disease or hypopituitarism.

Recurrent hypoglycaemia may be the cause of hypoglycaemic unawareness, which occurs frequently in type 1 diabetic patients. The loss of warning symptoms can lead to severe hypoglycaemia. In some cases this situation can be restored to normal with avoidance of any hypoglycaemia for at least 2–4 weeks.

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

E10.0

**Diabetic comas – recognition and clinical profiles**

DKA often occurs in younger patients and develops over hours to days. There may be vomiting, abdominal pain and acidotic breathing.

- » blood glucose usually < 40 mmol/L
- » blood ketones are positive
- » serum osmolality < 350 mOsm/L.

Hyperglycaemic hyperosmolar state is a syndrome characterised by impaired consciousness, sometimes accompanied by seizures, extreme dehydration and severe hyperglycaemia, that is not accompanied by severe ketoacidosis (pH usually >7.2). It usually occurs in the elderly type 2 diabetic and develops over days to weeks.

- » Blood glucose usually > 40 mmol/L.
- » Blood ketones usually negative to moderately elevated.
- » Urine ketones often positive.
- » Serum osmolality is > 320 mOsm/L.

Anion gap =  $\text{Na} - (\text{Cl} + \text{HCO}_3)$  (Normal =  $\pm 12$  : DKA > 20)

Calculated serum osmolality =  $2(\text{Na} + \text{K}) + \text{glucose} + \text{urea}$  (N = 275–285 mOsm/L)

## GENERAL MEASURES

All patients:

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

## MEDICINE TREATMENT

### Fluids

Average deficit 6 L, may be as much as 12 L.

If renal or cardiac disease is present, monitor with central venous pressure.

In the absence of renal or cardiac compromise:

- Sodium chloride 0.9%, IV, 15–20 mL/kg in the first hour.
  - For patients < 20 years of age, initial volume: 10–20 mL/kg in the first hour.
  - Subsequent infusion rate varies from 5–15 mL/kg/hour depending on the clinical condition.
  - Correction of estimated deficits should take place over 24 hours.
  - The volume infused in the first 4 hours should not exceed 50 mL/kg.
  - Fluid therapy thereafter is calculated to replace the estimated deficit in 48 hours,  $\pm 5$  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  $\text{Na}^+$  > 140 mmol/L:

- Sodium chloride 0.45%, IV.

If plasma  $\text{Na}^+$  < 140 mmol/L:

- Sodium chloride 0.9%, IV.

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

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

### Note:

Adjust fluid volumes according to clinical criteria.

If hypotension is still present after 2 hours, give 2 units of colloid.

Cerebral oedema may occur with over-aggressive fluid replacement or rapid sodium change.

## Potassium

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

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

- Potassium chloride, IV, added to 1 L of fluid.
  - potassium < 3.5 mmol/L: add 40 mmol (2 ampoules)
  - potassium 3.5–5.5 mmol/L: add 20 mmol (1 ampoule)
  - potassium > 5.5 mmol/L: do not add any potassiumMaximum potassium dose: 40 mmol/hour.  
Monitor potassium hourly initially, then 2 hourly when stabilised.

If serum potassium results are not readily available:

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

## Bicarbonate

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

## Insulin therapy

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

### Note:

Ketonaemia takes longer to clear than hyperglycaemia and combined insulin and glucose (and  $K^+$ ) are needed to ensure clearance of ketonaemia.

Avoid focusing on glucose control alone!

Continue insulin until ketosis and acidosis have resolved.

### Protocol 1: continuous intravenous infusion

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

Protocol 2: hourly intramuscular bolus injections

Where intravenous infusion cannot be safely administered:

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

### Progress management

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

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

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

### Heparin.

For all patients:

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

## 8.7 COMPLICATIONS OF DIABETES

### Secondary prevention

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

### Hypertension

See section 3.6: Hypertension.

### Dyslipidaemia

See section 8.8: Dyslipidaemia.

### 8.7.1 DIABETIC NEUROPATHIES

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

#### DESCRIPTION

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

There are three major categories:

- » peripheral neuropathy,
- » autonomic neuropathy, and
- » acute onset neuropathies.

#### MEDICINE TREATMENT

Ensure appropriate glycaemic control.

Exclude or treat other contributory factors e.g.:

- » alcohol excess,
- » vitamin B<sub>12</sub> deficiency, if suspected,
- » uraemia, and
- » HIV infection.

#### Pain

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

#### AND/OR

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

If ineffective consider adding:

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

#### Gastroparesis

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

If ineffective consult a specialist.

### 8.7.2 DIABETIC KIDNEY DISEASE

N18

See section 7.1.1: Chronic Kidney Disease (CKD).

### 8.7.3 DIABETIC FOOT ULCERS

L97

#### GENERAL MEASURES

Metabolic control.

Treat underlying comorbidity.

Relieve pressure: non-weight bearing is essential.

Smoking cessation is essential.

#### Deep (limb-threatening) infection

X-ray of affected limb.

Surgical drainage as soon as possible with removal of necrotic or poorly vascularised tissue, including infected bone – **refer urgently**.

Revascularisation, if necessary

#### Local wound care

Frequent wound debridement with scalpel, e.g. once a week.

Frequent wound inspection.

Absorbent, non-adhesive, non-occlusive dressings.

#### MEDICINE TREATMENT

##### Superficial ulcer with extensive infection

Debridement with removal of all necrotic tissue.

##### Antibiotic therapy

For polymicrobial infection:

- Topical antibiotics are not indicated.
- Amoxicillin/clavulanic acid, oral, 875/125 mg 12 hourly for 10 days.
  - Longer course of therapy may be necessary.

##### Severe infection

- Cloxacillin, IV, 2 g 6 hourly.

##### PLUS

- Metronidazole, oral, 400 mg 8 hourly.

##### PLUS

- Gentamicin, IV, 6 mg/kg daily.

##### Renal impairment

Replace gentamicin plus cloxacillin with 3<sup>rd</sup> generation cephalosporin, e.g.:

- Ceftriaxone, IV, 2 g daily.

##### PLUS

- Metronidazole, oral, 400 mg, 8 hourly.

Penicillin allergy

- Clindamycin, oral, 150 mg 8 hourly.

**PLUS**

- Gentamicin, IV, 6 mg/kg daily

**REFERRAL**

- » Arterial revascularisation procedures.

**8.8 DYSLIPIDAEMIA**

E78

**DESCRIPTION**

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

Accompanying modifiable risk factors for coronary artery disease (CAD) e.g. hypertension, smoking, diabetes, must be sought and treated.

Underlying causes of secondary dyslipidaemia, e.g. excess alcohol intake, hypothyroidism, should be identified and corrected.

The goal of treatment should be explained clearly to the patient and the risks of untreated dyslipidaemia should be emphasised.

**GENERAL MEASURES****Lifestyle modification**

Dietary strategies are effective.

- » Replace saturated fats with unsaturated fats (mono- and polyunsaturated fats) without increasing calories from fats.
- » Consume a diet high in fruits, vegetables, nuts and whole unrefined grains.

Smoking cessation.

Increase physical activity.

Maintain ideal body weight.

**MEDICINE TREATMENT****Indication for drug therapy**Cardiovascular

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

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

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

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

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

### **Non-cardiovascular**

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

Fibrates are the drugs of choice for severe hypertriglyceridaemia.

### Choice of drug

Depends on the type of lipid disturbance:

- » predominant hypercholesterolaemia:     statin
  - » mixed hyperlipidaemia:                 statin or fibrate
  - » predominant hypertriglyceridaemia:     fibrate
- HMGCoA reductase inhibitors (statins) that lowers LDL by at least 25%, e.g.:
  - Simvastatin, oral, 10 mg daily.

### **OR**

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

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

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

### **REFERRAL**

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



## 8.9 HYPERCALCAEMIA, INCLUDING PRIMARY HYPERPARATHYROIDISM

E83.50/E21.0

### DESCRIPTION

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

### Aetiology

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

### Investigations

Draw blood for parathyroid hormone (PTH) and simultaneous calcium and albumin concentrations.

A detectable PTH in the presence of hypercalcaemia indicates primary hyperparathyroidism.

### MEDICINE TREATMENT

#### Hypercalcaemia

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

Avoid thiazide diuretics as they increase serum calcium concentration.

The addition of furosemide has not been shown to be of benefit.

For symptomatic hypercalcaemia:

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

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

#### ADD

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

In patients with granulomatous disease and haematological malignancies:

- Prednisone, oral, 40 mg daily.

### REFERRAL

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

## 8.10 HYPOCALCAEMIA

E83.5

### DESCRIPTION

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

#### Causes

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

#### Investigations

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

### MEDICINE TREATMENT

Therapy is aimed at treating the underlying cause.

For acute hypocalcaemia with neurological problems:

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

#### AND/OR

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

For hypoparathyroidism:

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

#### AND

- Alfacalcidol, oral, 1–3 mcg daily.

Correct magnesium deficiency if present.

Renal failure:

See Section: 7.1.1 Chronic Kidney Disease (CKD).

## REFERRAL

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

## 8.11 HYPOTHYROIDISM

E03.9

### DESCRIPTION

#### Causes

Common causes of primary hypothyroidism are:

- » thyroiditis,
- » post surgery, and
- » post radio-active iodine.

Secondary hypothyroidism (less than 1% of cases) may be due to any cause of anterior hypopituitarism.

#### Investigations

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

### MEDICINE TREATMENT

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

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

Check TSH and  $T_4$  after 2–3 months and adjust dose if required.

TSH levels will take several weeks to stabilise. Once stable check  $T_4$  and TSH annually.

#### Hypothyroidism in pregnancy

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

## 8.12 OSTEOPOROSIS

M81.9

### DESCRIPTION

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

### GENERAL MEASURES

#### Prevention

Adequate energy and protein intake.

Adequate dietary calcium intake (>1 g/day) particularly in the young, in breastfeeding mothers and in the elderly.

Weight bearing exercises, e.g. brisk 30 minutes walk 3 times a week.

Smoking cessation.

Ensure alcohol intake is < 10 units /week.

Avoid falls.

### MEDICINE TREATMENT

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

In institutionalised frail elderly patients:

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

#### PLUS

- Vitamin D, oral, 800 units daily.

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

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

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

This should be given with:

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

#### PLUS

- Vitamin D, oral, 800 units daily.

### Hormone replacement therapy

See Section 5.12: Menopause and Perimenopausal Syndrome.

Only indicated early in menopause, if vasomotor symptoms are significant.

Review contra-indications before initiating therapy.

**REFERRAL**

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

**8.13 OSTEOMALACIA/RICKETS**

M83.9

**DESCRIPTION**

A disorder of mineralisation of newly synthesised bone matrix.

**REFERRAL**

- » All

**8.14 PAGET'S DISEASE**

M88.9

**DESCRIPTION**

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

**GENERAL MEASURES**

Most cases are mild and asymptomatic and no treatment is required.

Avoid high calcium diet when immobile as hypercalcaemia may occur with immobilisation.

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

**MEDICINE TREATMENT**

For pain:

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

**REFERRAL**

- » All

## 8.15 PITUITARY DISORDERS

### 8.15.1 PROLACTINOMA

D35.2

#### DESCRIPTION

Prolactinoma is the most common functioning pituitary tumour.

#### Investigations

Serum prolactin.

#### Note:

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

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

#### MEDICINE TREATMENT

Dopamine agonist therapy is the treatment of choice.

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

#### REFERRAL

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

#### Urgent

- » Compression of optic chiasm.
- » Pituitary apoplexy.

### 8.15.2 ANTERIOR HYPOPITUITARISM

E23.0

#### DESCRIPTION

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

**GENERAL MEASURES**

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

A notification bracelet is needed.

**MEDICINE TREATMENT****Acute crisis**

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

**Chronic**

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

**Hypoadrenalism**

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

**Hypothyroidism**

See section 8.11: Hypothyroidism.

**Hypogonadism**

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

Women:

As for postmenopausal HRT: See section 5.4.

Men:

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

See section 8.3: Androgen deficiency

**REFERRAL**

» All diagnosed patients for initial assessment.

**8.15.3 DIABETES INSIPIDUS (POSTERIOR HYPOPITUITARISM)**

E23.2

**DESCRIPTION**

Damage to the posterior pituitary leading to deficient production of antidiuretic hormone. Characterised by the passage of copious amounts of very dilute urine.

Causes include head trauma and neurosurgery but most cases are idiopathic.

**GENERAL MEASURES**

Rehydration with water or hypotonic fluids.

**MEDICINE TREATMENT****Replacement therapy**

- Desmopressin, oral, 0.2–1.2 mg daily.
  - Optimal dose: 0.1–0.2 mg 8 hourly.

**Acute management**

Post operatively:

- Desmopressin, nasal spray, 10–20 mcg 12–24 hourly.

**OR**

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

**REFERRAL**

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

**8.16 PHAEOCHROMOCYTOMA**

C74.9

**DESCRIPTION**

Catecholamine-secreting tumour of the adrenal medulla.

**Clinical presentation**

Always consider in hypertensive patients who have paroxysmal symptoms:

- |                 |                               |
|-----------------|-------------------------------|
| » headaches,    | » tremor,                     |
| » GIT symptoms, | » recurrent chest discomfort, |
| » palpitations, | » sweating, and               |
| » anxiety.      |                               |

There is marked inter-individual variation in symptoms.

These hypertensive patients may also have orthostatic changes in blood pressure.

**Diagnosis**

24 hour urine acidified with HCl: normetanephrine (NMA), vanillylmandelic acid (VMA), should be  $\geq$  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, or
  - > radiologic evidence of an adrenal mass.

**GENERAL MEASURES**

Surgical removal of the tumour.

**MEDICINE TREATMENT**

- Alpha blockers, e.g.:
  - Doxazosin, oral, 4 mg daily.
    - Dose increase above 8 mg daily to control blood pressure may be required.
- Calcium channel blockers may be added, e.g.:
  - Amlodipine, oral, 5–10 mg daily

Patients should not be given diuretic therapy unless pulmonary oedema is present.

**REFERRAL**

- » All patients with elevated levels of NMA and VMA for localisation studies (MIBG scanning and CT scanning).
- » When there is a suggestive clinical presentation but negative screening test.

**8.17 PRIMARY ALDOSTERONISM**

E26.0

**DESCRIPTION**

Increased aldosterone production usually due to an adrenal adenoma (Conn's syndrome) or idiopathic bilateral adrenal hyperplasia (majority).

**Clinical**

Always 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:

- Spironolactone, oral, 100–200 mg daily.

### Bilateral hyperplasia

Standard anti-hypertensive therapy.

## 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 T<sub>4</sub>.

If TSH suppressed and T<sub>4</sub> normal, request T<sub>3</sub>.

The usual biochemical abnormalities are: low TSH, elevated T<sub>4/3</sub>

Once thyrotoxicosis is confirmed, if cause is uncertain request thyroid uptake scan. If uptake is:

- » Elevated or diffuse: Graves disease.
- » Markedly decreased: Thyroiditis.
- » Patchy uptake with areas of increase: 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.

### 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.

#### $\beta$ -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.

- Propranolol, oral, 40–80 mg 6–8 hourly.
  - Titrate dose upwards as needed.

#### OR

- Atenolol, oral, 50 mg daily.
  - Titrate according to symptom control up to 50 mg 12 hourly.

#### 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 if the thyroid is very large or if there is failure of antithyroid drug therapy.

#### Monitoring

Patients with Graves' disease who are treated with antithyroid drugs should be monitored every 6–8 weeks using a serum  $T_4$ . TSH may remain suppressed for months. Once in remission, patients may be monitored less frequently to determine signs and symptoms of recrudescence of thyrotoxicosis.

Because there is a risk of neutropenia or agranulocytosis with carbimazole, therapy should be temporarily stopped and a white cell count (with differential) must be done in patients presenting with an infection or sore throat.

Post-radio-active iodine TSH and  $T_4$  should be checked at 6 weeks, 3, 6, 9 and 12 months and annually thereafter until either hypothyroidism occurs or patient remains euthyroid for  $\pm$  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.

 **$\beta$ -blockers**

Used to counteract excessive sympathetic symptoms, e.g. palpitations.

Dose is titrated according to the heart rate.

Give for 2–4 weeks.

- Propranolol, oral, 40–80 mg 8 hourly.
  - Titrate dose upwards as needed.

**OR**

- Atenolol, oral, 50 mg daily.
  - Titrate according to symptom control up to 50 mg 12 hourly.

**8.18.4 THYROIDITIS**

E06

Toxic phase lasts up to 3 months

**MEDICINE TREATMENT** **$\beta$ -blockers**

Used to counteract excessive sympathetic symptoms, e.g. palpitations.

Dose is titrated according to the heart rate.

Give for 2–4 weeks.

- Propranolol, oral, 40–80 mg 8 hourly.
  - Titrate dose upwards as needed.

**OR**

- Atenolol, oral, 50 mg daily.
  - Titrate according to symptom control up to 50 mg 12 hourly.

For painful subacute thyroiditis (De Quervain's)

- NSAIDs, e.g.:
- Ibuprofen, oral, 800 mg 8 hourly.

**PLUS**

- 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.

**PLUS**

- Propranolol, oral, 60–120 mg 6 hourly.

If life-threatening:

**ADD**

- Hydrocortisone, IV, 100 mg 8 hourly.

Treat precipitating illness and infection. ICU admission is desirable.

# CHAPTER 9

## SYSTEMIC AND NOSOCOMIAL INFECTIONS

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### 9.1 HOSPITAL-ACQUIRED INFECTIONS

T80–88

#### DEFINITION AND PRINCIPLES

Infections acquired after 48 hours of hospitalisation.

Many anatomical sites can be involved and only the four most common will be discussed.

**It is essential to obtain specimens for culture and sensitivity testing in all cases before starting antibiotics, as multi-drug resistant organisms are common causes of hospital-acquired infections.**

Infections acquired in the intensive care unit are much more likely to be due to multi-drug resistant organisms.

Empiric therapy suggestions below are only rough guidelines. Close liaison with regional microbiologists and regular review of hospital antibiotic policy are essential.

#### 9.1.1 INTRAVASCULAR LINE INFECTIONS

T80.2

#### DESCRIPTION

Common organisms:

- » coagulase negative staphylococci
- » *S. aureus*

**The intravascular line should always be removed.** In some cases of infection with coagulase negative staphylococci the infection will resolve on removal of the catheter.

#### Note:

Candida isolated from blood culture should **always** be treated, even if the fever has settled after line removal.

Microbiologic specimen: blood culture and 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: 2 weeks required. Switch to oral therapy according to antibiotic susceptibility after resolution of fever.
- » candida: 2 weeks after resolution of fever.

- Vancomycin, IV, 20 mg/kg 12 hourly.
  - Monitor trough levels after the third dose.
  - Adjust dose to maintain a trough level of 15–20 micromol/L.

### Candidaemia

Treatment duration should be at least 2 weeks.

- Amphotericin B, IV, 0.7 mg/kg daily.
  - Ensure adequate hydration to minimise nephrotoxicity.
  - Regular, e.g. 3 times a week, monitoring of potassium, magnesium and renal function is essential.

Once improved, complete course with:

- Fluconazole, oral, 400 mg daily.

### OR

If renal failure or intolerance to amphotericin B:

- Fluconazole, oral, 800 mg immediately
  - Followed by 400 mg daily.

## 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:

- Cloxacillin, IV, 2 g 6 hourly.

Follow with:

- Flucloxacillin, oral, 500 mg 6 hourly for 5–10 days.

#### Penicillin allergy:

- Clindamycin, IV, 600 mg 8 hourly.

Follow with:

- Clindamycin, oral, 450 mg 8 hourly for 5–10 days.

#### Methicillin (cloxacillin) resistant *S. aureus* (MRSA)

- Vancomycin, IV, 20 mg/kg 12 hourly.
  - Monitor trough levels after the third dose.
  - Adjust dose to maintain a trough level of 15–20 micromol/L.

### 9.1.3 HOSPITAL-ACQUIRED PNEUMONIA

J13/J15

#### DESCRIPTION

Common organisms:

- » *S. pneumoniae*, especially early in admission.
- » resistant aerobic Gram-negative organisms including *K. pneumoniae*, *P. aeruginosa* and *Acinetobacter* spp, the latter found especially in ICU.

Microbiologic specimen: blood culture and sputum/tracheal aspirate.

#### MEDICINE TREATMENT

##### Empiric antibiotic therapy

For ward cases:

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

##### PLUS

- Amikacin, IV, 15 mg/kg daily.

##### Penicillin allergy:

- Clindamycin, IV, 600 mg 8 hourly.

##### PLUS

- Amikacin, IV, 15 mg/kg daily.

##### 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.

##### OR

- Cefepime, IV, 1 g 12 hourly.

##### OR

- A carbapenem with activity against *Pseudomonas*, e.g.:
- Meropenem, IV, 1 g 8 hourly.

##### OR

- Imipenem, IV, 500 mg 8 hourly.

### 9.1.4 URINARY TRACT INFECTIONS

N39.0

#### DESCRIPTION

Common organisms:

- » resistant aerobic Gram-negative organisms.

Microbiologic specimen: blood culture and MSU/CSU.



**MEDICINE TREATMENT****Empiric antibiotic therapy**

- Amikacin, IV, 15 mg/kg daily.

**OR**

- Ciprofloxacin, oral, 500 mg 12 hourly.
  - Duration of therapy 7–14 days.

**9.2 ADULT VACCINATION**

Vaccine	Indications	Comments
<ul style="list-style-type: none"> <li>• Influenza vaccine</li> </ul>	<ul style="list-style-type: none"> <li>» elderly patients over 65 years</li> <li>» HIV infected people</li> <li>» patients with chronic pulmonary and cardiac conditions</li> <li>» healthcare workers with direct patient contact</li> </ul>	Contraindication: egg allergy. <ul style="list-style-type: none"> <li>○ Dose: IM, 0.5 mL. Repeat annually.</li> </ul>
<ul style="list-style-type: none"> <li>• Pneumococcal vaccine (23 valent polysaccharide)</li> </ul>	<ul style="list-style-type: none"> <li>» asplenic patients</li> <li>» chronic cerebrospinal fluid (CSF) leak</li> </ul>	Contraindication: pregnancy. <ul style="list-style-type: none"> <li>○ Dose: IM, 0.5 mL. Booster: every 5 years.</li> </ul>
<ul style="list-style-type: none"> <li>• Hepatitis B vaccine*</li> </ul>	<ul style="list-style-type: none"> <li>» high risk groups, e.g. hospital personnel or sexual contacts of infected patients</li> <li>» sexual assault</li> </ul>	<ul style="list-style-type: none"> <li>○ Dose: IM, 1 mL immediately then 1 mL after 1 month and 1 mL 6 months after first dose.</li> </ul>
<ul style="list-style-type: none"> <li>• Tetanus toxoid vaccine</li> </ul>	Booster when there is a high risk for tetanus e.g. contaminated wound or pregnant women to prevent neonatal tetanus. (See trauma section)	<ul style="list-style-type: none"> <li>○ Dose: IM, 40 iu (0.5 mL).</li> </ul>

\* 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.
- » negative rabies laboratory testing, where available
- » 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

### Patient not previously immunised

#### Active immunisation with Human Diploid Cell Vaccine:

- Rabies inactivated whole virus vaccine, IM.
  - Administer 1 dose on 0, 3, 7, 14 and 28 days post exposure, according to the standard or essential schedule.
  - Administer vaccine by deep IM injection in the deltoid region and not the thigh or buttock.

**Caution:** anaphylaxis.

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

#### **AND**

#### Passive immunisation, for temporary prophylaxis with HRIG:

- Human rabies immunoglobulin (HRIG), 20 units/kg on day 0 or within 7 days after exposure.
  - Infiltrate around the wound with half the dose.
  - Administer the rest of the dose IM.

It is recommended that HRIG be given simultaneously with the vaccine but into a different injection site if wound is not older than 7 days and only for patients not 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	<ul style="list-style-type: none"> <li>» touching or feeding animal</li> <li>» licking intact skin</li> </ul>	None if reliable history
2	<ul style="list-style-type: none"> <li>» nibbling uncovered skin</li> <li>» superficial scratch without bleeding</li> </ul>	Wound treatment. Give rabies vaccine. Do not give anti-rabies immunoglobulin, except in HIV infected people.

	» licking broken skin	Stop vaccination if laboratory tests of animal are negative for rabies or animal, i.e. dog or cat remains well after 10 days observation.
3	» bites or scratches penetrating skin and drawing blood » licking of mucous membranes	Wound treatment. Give rabies vaccine. Give anti-rabies immunoglobulin (RIG). Give tetanus toxoid vaccine and antibiotic. Stop vaccination if laboratory tests of animal are negative for rabies or animal, i.e. dog or cat, remains well after 10 days observation.

### Rabies Vaccine

Must be given for category 2 and 3 bites.

Vaccine is administered on days 0, 3, 7, 14, 28. Vaccine is ideally 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, a double dose should be given initially.

Rabies vaccine is given IM but never in the buttock. Give into deltoid muscle in adults.

Adverse events are uncommon and include:

- » local reactions
- » pain
- » erythema
- » swelling or itching at the injection site
- » systemic reactions
- » vomiting
- » fever
- » arthralgia
- » arthritis
- » angioedema
- » nausea
- » malaise

### Rabies Immunoglobulin (RIG)

Must be given for category 3 bites only and for category 2 bites with HIV infected people.

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 RIG if the patient has previously received pre- or post-exposure prophylaxis.

- Rabies immunoglobulin, 20 units/kg.
  - Infiltrate around wound with up to 50% of 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.

#### PLUS

- Streptomycin, IM, 1 g daily for 3 weeks.  
(Preferred regimen for osteo-articular or cardiac involvement.)

#### OR

- 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 co-agulation (DIC) and bleeding tendency. Other symptoms and organ involvement may be variable.

Some important causes other than viral haemorrhagic fevers (VHF) are:

- » bacterial septicaemia, 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 possibly 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 agent.

## 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, keeping safety precautions in mind.

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 dogs in sheep-farming areas or from inadequately cooked mutton meat. 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 for 3–6 months according to response on imaging.
  - 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 helminthocidal agent and re-aspiration) is preferred for all accessible lesions.

Before PAIR or surgery:

- Albendazole, oral, 15 mg/kg/day up to 400mg twice daily for 14 to 28 days.
  - Follow with 28 days after surgery.

### 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 in both endemic and non-endemic areas. Test any person resident in, or returning from, a malaria area **and** who presents with fever (usually within 3 months of exposure). The progression to severe falciparum malaria is rapid and early diagnosis and effective treatment is crucial.

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

Clinical features include:

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

Progression to severe malaria may occur and present with the following additional clinical features:

- » sleepiness, unconsciousness or coma, convulsions,
- » respiratory distress and/or cyanosis,
- » jaundice,
- » renal failure,
- » shock,
- » repeated vomiting,
- » hypoglycaemia, and
- » severe anaemia (Hb < 6 g/dL).

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.
- » Where rapid diagnostic tests are available, e.g. plasma reagent dipsticks, these can be used to diagnose malaria within 10–15 minutes.

### Note:

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

A blood smear should be made and sent for microscopic examination.

One negative malaria test does not exclude the diagnosis of malaria.

### GENERAL MEASURES

Provide supportive and symptomatic relief.

Monitor for complications.

Ensure adequate hydration.

All patients with *P. falciparum* malaria should be carefully observed for the first 24 hours.

### MEDICINE TREATMENT

Vomiting is common in patients with malaria. Give all first doses of drugs under supervision and observe patients for at least an hour. Repeat the treatment if the patient vomits within the first hour.

Vomiting oral treatment is one of the commonest reasons for treatment failure.

In endemic areas of South Africa where malaria occurs seasonally, it should be treated at primary health care level. In other areas, patients should be referred 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)

For fever:

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

### REFERRAL

- » All patients in non-endemic areas.
- » 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,       | » renal dysfunction,                 |
| » convulsions,                  | » heavy parasitaemia ( $\geq 5\%$ ), |
| » vomiting,                     | » ARDS,                              |
| » severe anaemia (Hb < 6 g/dL), | » shock,                             |
| » haemoglobinuria,              | » acidosis,                          |
| » clinical jaundice, or         | » hypoglycaemia.                     |

### 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 with the use of exchange transfusion.



## MEDICINE TREATMENT

- 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.
  - If there is significant renal failure increase dose interval to 12 hourly after 48 hours.

Follow with:

- 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)

Monitor treatment response with regular blood smears.

An increase in parasitaemia may occur within 24 hours due to release of sequestered parasites but a reduction should be seen after 48 hours.

### Note:

Gametocytes may appear after this stage – this does NOT mean failure of 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.

**MEDICINE TREATMENT**

For rigidity, spasms:

- Diazepam, IV, 10 mg 4 hourly, for 24 hours, then consider oral route.
  - Titrate to effect.
  - Doses as high as 50–100 mg 2 hourly are sometimes used.

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

To eradicate bacteria:

- Benzylpenicillin (penicillin G), IV, 5 million units 6 hourly for 10 days.
- OR**
- Metronidazole, oral, 400 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.

For fever combine with mechanical cooling:

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

For shock, dehydration, maintenance of hydration:

- IV fluids, plasma volume expanders.

As prophylaxis for deep vein thrombosis:

- Heparin, SC, 5 000 units 8 hourly.

For pain:

- Morphine, slow IV, 10 mg diluted up to 10 mL with sodium chloride 0.9% administered over 4–5 minutes.
  - Repeat after 4–6 hours.

**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  $\pm$  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:
- Clarithromycin, oral, 500 mg 12 hourly for 7 days.
    - In severe cases, initiate therapy with 1–2 days of doxycycline.

For the rare patient unable to take oral therapy:

- Chloramphenicol, IV, 500 mg 6 hourly.

#### Note:

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

## 9.9 TYPHOID FEVER

A01.0

\*This is a notifiable disease.

### DESCRIPTION

Systemic infection due to *S. typhi* or related organisms (e.g. *S. paratyphi*). Initial symptoms are abdominal pain, headache and fever with diarrhoea developing only late. Bacteraemia is common initially, subsequently stool culture has the highest yield.

### GENERAL MEASURES

Transfusion is indicated for severe haemorrhage.

Replace fluid and electrolytes.

### MEDICINE TREATMENT

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

#### OR

If oral therapy not possible, start with:

- Ceftriaxone, IV, 2 g daily.

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, 750 mg 12 hourly for 6 weeks.

## 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)

B01

See also Standard Treatment Guidelines for Primary Health Care.

### 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 administered 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 administered over one hour 8 hourly for 7 days.
  - The course can be completed with oral aciclovir 800 mg five times daily.

Eye involvement:

#### ADD

- Aciclovir ophthalmic 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.

### 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.

### AND/OR

If pain is not adequately controlled:

- Tramadol, oral, 50 mg 6 hourly.

See Section 12.1: Chronic Pain.

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 12.1: Pain, Chronic.

## **REFERRAL**

- » to an ophthalmologist if there is ocular involvement with ophthalmic zoster (if the tip of the nose is involved then suspect ocular involvement).

See section 18.4: Herpes zoster ophthalmicus.

# CHAPTER 10

## HIV AND AIDS

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### 10.1 ANTIRETROVIRAL THERAPY

Combination antiretroviral therapy (ART) consists of three or more antiretroviral drugs that are capable of suppressing HIV replication when used together. The usual ART regimen contains two 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

##### Eligible to Start ART

CD4 count  $< 350$  cells/mm<sup>3</sup> irrespective of clinical stage

**OR**

Pregnant women WHO stage III irrespective of CD4 count

**OR**

WHO stage IV (excluding TB) irrespective of CD4 count

**OR**

MDR/XDR-TB irrespective of CD4 count

##### Require fast-track (i.e. ART initiation within 2 weeks of being eligible)

Pregnant women eligible for lifelong ART

**OR**

Patients with very low CD4 ( $< 100$  cells/mm<sup>3</sup>)

**OR**

Stage 4, CD4 count not yet available

**OR**

MDR/XDR TB

#### 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.

ART should be carefully considered if there is active substance abuse.

**ART REGIMENS****First line regimens**

Currently on stavudine: continue if stable.

- Stavudine + lamivudine + efavirenz or nevirapine.

Note:

Switch stavudine early to tenofovir:

- » in the presence of toxicity, i.e. neuropathy, lipoatrophy or hyperlactataemia, or
- » if at high risk of toxicity, i.e. BMI >28, TB treatment.

Switching a single antiretroviral for toxicity could cause resistance if the patient is failing ART. Therefore, before switching a single antiretroviral for toxicity in patients who have been on ART for longer than six months, ensure that the viral load is suppressed.  
Seek expert advice on the selection of the regimen.

New patients: all unless contra-indicated

- Tenofovir + lamivudine + efavirenz or nevirapine.
  - Only patients who have a calculated creatinine clearance or estimated glomerular filtration rate (eGFR) >50 mL/minute should receive tenofovir.
  - Nevirapine is preferred in pregnant women (see section 6.7: HIV in pregnancy) or women of child bearing age, not on reliable contraception provided the CD4 count is < 250 cells/mm<sup>3</sup>.

Contra-indications or toxicity to tenofovir:

- Zidovudine + lamivudine + efavirenz or nevirapine.

Contra-indications to both tenofovir and zidovudine:

- Stavudine + lamivudine + efavirenz or nevirapine.

**TB co-infection**

- Tenofovir + lamivudine + efavirenz

Women in the first trimester of pregnancy or efavirenz contra-indicated or not tolerated:

- Tenofovir + lamivudine + nevirapine (omit the lead-in dose of nevirapine).

Avoid tenofovir in patients whose TB regimen contains an aminoglycoside or capreomycin.



If the patient develops tuberculosis while on ART:

- ART should be continued throughout TB treatment.
- Continue efavirenz or switch nevirapine to efavirenz (unless there are contraindications to efavirenz) in patients on first line ART
- Patients on lopinavir/ritonavir should have their dose increased to 3 tablets (600/150 mg) 12 hourly after one week and then 4 tablets (800/200 mg) 12 hourly after another week.
- Monitor ALT monthly.

### Second line regimens

Failure of stavudine or zidovudine-based 1st line regimen:

- Tenofovir + lamivudine + lopinavir/ritonavir

Failure of tenofovir-based 1st line regimen:

- Zidovudine + lamivudine + lopinavir/ritonavir

### Doses of ART

#### NRTI

- Tenofovir (TDF), oral, 300 mg daily.
- Lamivudine (3TC), oral, 300 mg daily or 150 mg 12 hourly.
- Emtricitabine (FTC), oral, 200 mg daily.
  - Emtricitabine may replace lamivudine in certain fixed dose combination tablets containing tenofovir.
- Stavudine (d4T), oral, 30 mg 12 hourly.
- Zidovudine (AZT), oral, 300 mg 12 hourly.

#### NNRTI

- Efavirenz (EFV), oral, 600 mg at night.
- Nevirapine (NVP), oral, 200 mg daily for 2 weeks followed by 200 mg 12 hourly.

#### Protease inhibitor

- Lopinavir/ritonavir (LPV/r), oral, 400/100 mg (2 tablets) 12 hourly.

### MONITORING FOR SAFETY

- » ALT (to identify liver injury associated with NVP or EFV):
  - > at baseline on all patients
  - > if develop drug-associated rash or symptoms of hepatitis
- » FBC (to identify anaemia associated with AZT):
  - > at baseline, month 1, 2, 3 and 6 if on AZT
- » Fasting cholesterol and triglycerides (to identify LPV/r toxicity):
  - > at baseline and month 3 if on LPV/r.

- » Estimated creatinine clearance or eGFR (to identify TDF toxicity):
    - > at baseline, month 3 and 6 then every 12 months if on TDF.
    - > renal function can be significantly reduced with a serum creatinine in the normal range, especially in older people and those with low body weight. It is essential to calculate the creatinine clearance or obtain eGFR in all patients with:
      - > age >50 years,
      - > weight <50 kg, or
      - > serum creatinine >100 micromol/L.
- In all other patients where serum creatinine is < 100 micromol/L the calculated creatinine clearance is likely to be > 50 mL/minute and they can safely start tenofovir.

### MONITORING FOR EFFICACY

- » Viral load at month 6 and 12, then every 12 months.
  - > The viral load will indicate when resistance is developing and when regimens need to be changed.
  - > The viral load should become undetectable by 6 months. If this does not happen on the first regimen then this is nearly always due to poor adherence.
  - > If the viral load fails to suppress by six months or if the viral load rebounds having been suppressed, adherence issues should be explored and enhanced support provided. Repeat viral load three months later provided the patient is sufficiently adherent. If virological failure is confirmed (VL > 1 000 copies/mL) then switch patient to a second line regimen.
- » CD4 count at month 6 and 12, then every 12 months
  - > The CD4 response is more variable, with an average increase of around 150 cells/mm<sup>3</sup> in the first year, followed by about 75 cells/mm<sup>3</sup> per year thereafter.
  - > Some patients have a poor CD4 response even though they remain virologically suppressed. There is no advantage in changing therapy in those patients.

## 10.1.1 MANAGEMENT OF SELECTED ANTIRETROVIRAL ADVERSE DRUG REACTIONS

### HYPERLIPIDAEMIA

Certain antiretroviral medication, particularly the protease inhibitors, can cause dyslipidaemia. Fasting lipid levels should be done three months after starting lopinavir/ritonavir. Lopinavir/ritonavir is associated with a higher risk of dyslipidaemia than atazanavir/ritonavir.

Patients on lopinavir/ritonavir who develop triglycerides > 10 mmol/L or who are at high risk (>20% risk of developing a CVS event in 10 years) should

switch to atazanavir/ritonavir and repeat the fasting lipid profile in three months.

Patients with persistent dyslipidaemia despite switching, qualify for lipid lowering therapy. Criteria for initiating lipid lowering therapy are the same as for HIV seronegative patients. See section 8.8: Dyslipidaemia. 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 8.8: Dyslipidaemia), treat with a statin:

- Atorvastatin, oral, 10 mg daily.

#### **ANAEMIA AND NEUTROPENIA**

Zidovudine causes macrocytosis and can cause anaemia and neutropenia (but note that it does not cause thrombocytopenia). Zidovudine does not need to be stopped with mild anaemia and/or neutropenia, but must be stopped and replaced with an alternative drug if:

- » anaemia is symptomatic,
- » anaemia is severe (Hb below 6.5 g/dL), or
- » the neutrophil count is below  $0.5 \times 10^9/L$ .

Lamivudine can cause a red cell aplasia but this is uncommon.

#### **CUTANEOUS HYPERSENSITIVITY**

Hypersensitivity rashes, typically diffuse and maculopapular rashes, occur commonly in the 8 week period after starting nevirapine or efavirenz.

Rashes can be severe and life-threatening, especially with nevirapine. If a rash develops on nevirapine an ALT result should be checked promptly. Other drugs, notably co-trimoxazole, can also cause cutaneous hypersensitivity. Note that pre-existing dermatological conditions (especially papulopuritic eruptions and acne) may worsen after commencing ART due to immune reconstitution inflammatory syndrome (see below) – this is not a hypersensitivity reaction and ART should be continued.

If any of the following features are present or develop then nevirapine or efavirenz 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.

With mild rashes nevirapine and efavirenz can be continued with careful observation and the rash will often subside.

If mild rash occurs on nevirapine 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 efavirenz or nevirapine.

If nevirapine has been stopped due to cutaneous hypersensitivity then efavirenz 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. lopinavir/ritonavir, should be substituted.

### HYPERLACTATAEMIA

Symptomatic hyperlactataemia occurs due to mitochondrial toxicity of NRTIs. Check for acidosis in such patients.

The risk of lactate elevation differs among the NRTIs approximately as follows:

didanosine > 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.

The clinical symptoms of hyperlactataemia are non-specific and may include:

- » nausea,
- » vomiting,
- » abdominal pain,
- » weight loss,
- » malaise,
- » liver dysfunction (due to steatosis), and
- » tachycardia.

A high index of suspicion is necessary. Send blood for lactate levels (check with your local laboratory for specimen requirements for lactate). Alternatively, point of care finger prick lactate monitoring can be done. Check the serum bicarbonate level.

**Patients with mild hyperlactataemia (lactate 2.5–5 mmol/L):**

Therapy should be altered by selecting NRTIs that are less associated with hyperlactataemia. Monitor serial lactate measurements (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 first line regimen, continue the efavirenz or nevirapine and add lopinavir/ritonavir.

If the patient is on the second line regimen, continue with lopinavir/ritonavir 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, tenofovir and lamivudine (or emtricitabine) could be introduced once symptoms have resolved with serial lactate monitoring as above. If the patient is on a first line regimen then the lopinavir/ritonavir can be stopped when the tenofovir and lamivudine are started.

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.

### 10.1.2 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, or causes paradoxical deterioration of an existing opportunistic disease. IRIS is more common in patients with advanced HIV disease, particularly those with

a CD4 count  $<100$  cells/mm<sup>3</sup>. IRIS nearly always presents during the first 3 months of ART, with the median time of onset being about two weeks. The diagnosis of IRIS is often difficult as new opportunistic diseases or drug resistance of the organism causing the opportunistic disease need to be excluded.

Tuberculosis 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 IRIS, presenting as recurrence of their TB symptoms/signs, or worsening, or new manifestation. 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 to have 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.

OR

NSAIDs, e.g.:

- Ibuprofen, oral, 800 mg 8 hourly.

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's sarcoma.

## 10.2 OPPORTUNISTIC DISEASES

### 10.2.1 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 vomiting.
  - An early relapse should be treated with a 4-week course of fluconazole as above.

#### Note:

Fluconazole prophylaxis is discouraged.

### 10.2.2 CRYPTOCOCCOSIS

B45

#### DESCRIPTION

Infection due to *Cryptococcus neoformans*. Extrapulmonary disease is AIDS-defining (WHO clinical stage 4). Meningitis with or without disease elsewhere is the commonest manifestation. 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 elevated pressure but not less than 20 cm H<sub>2</sub>O.

Therapeutic lumbar puncture should be done daily until there is improvement.

**MEDICINE TREATMENT****Induction therapy**

- Amphotericin B, slow IV infusion, 1 mg/kg daily in dextrose 5 % over 4 hours for 14 days.
  - Ensure adequate hydration to minimise nephrotoxicity.
  - Regular, e.g. 3 times a week, monitoring of potassium, magnesium and renal function is essential.

This is not always feasible and an earlier switch to oral fluconazole may be considered if there has been a good clinical response, i.e. resolution of headache and normal consciousness.

**Continuation therapy**

Follow with:

- Fluconazole, oral, 400 mg daily for 8 weeks.

**Secondary prophylaxis**

Continue for at least one year provided the CD4 count increases to > 200 cells/mm<sup>3</sup> on ART. If the CD4 count does not increase continue indefinitely.

- Fluconazole, oral, 200 mg daily.

**REFERRAL/CONSULTATION****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.

**10.2.3 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.



## 10.2.4 CYTOMEGALOVIRUS (CMV)

B25

### DESCRIPTION

CMV disease outside the reticulo-endothelial system is an AIDS-defining illness (WHO clinical stage 4). The commonest manifestations are:

- » Retinitis,
- » GIT ulceration, 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 adults.

### MEDICINE TREATMENT

#### Ganciclovir

Ganciclovir 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 ganciclovir.

Consider initial therapy with systemic ganciclovir for all patients, but intra-ocular therapy is an option for limited retinitis. See Section 18.6: Retinitis, HIV CMV.

Maintenance therapy is only applicable to CNS disease and retinitis.

Monitor FBC regularly during therapy. Avoid other drugs associated with bone marrow suppression, particularly zidovudine.

#### Biopsy-proven GIT disease and other organ disease

- Ganciclovir, IV, 5 mg/kg 12 hourly for 14 days. Specialist initiated.
- Maintenance treatment is not indicated unless there has been a relapse.

#### CNS

Initial treatment:

- 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, as the cost is currently very high.

- Ganciclovir, IV, 5 mg/kg daily until CD4 count rises to  $> 100 \text{ cells/mm}^3$  on ART.

**REFERRAL/CONSULTATION****Specialist or tertiary**

- » All patients.

**10.2.5 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<sup>3</sup> on ART

- Cotrimoxazole 80/400, oral, 2 tablets daily.

**10.2.6 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 carriage only 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**

- Clarithromycin, oral, 500 mg 12 hourly.

**PLUS**

- 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<sup>3</sup> on ART.

**10.2.7 PNEUMOCYSTIS PNEUMONIA**

B20.6

**DESCRIPTION**

Interstitial pneumonitis due to *Pneumocystis jiroveci* (formerly *carinii*). AIDS-defining illness (WHO clinical stage 4).

**MEDICINE TREATMENT**

Oxygen by face mask or CPAP as necessary.

For hypoxic patients:

- Prednisone, oral, 80 mg daily for 5 days, then taper over 14 days.

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

**Cotrimoxazole intolerance**

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.

Alternative, in case of intolerance:

- Clindamycin, oral, 600 mg 8 hourly for 21 days.

**PLUS**

- Primaquine, oral, 15 mg daily for 21 days.
  - Exclude G6PD deficiency before initiating therapy.

If primaquine is not available, consider:

- Clindamycin, oral, 600 mg 8 hourly for 21 days.

**PLUS**

- 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<sup>3</sup> on ART.

- Cotrimoxazole 80/400 mg, oral, 2 tablets daily.

Alternative, in case of intolerance:

- Dapsone, oral, 100 mg daily.

**REFERRAL/CONSULTATION**

**Specialist or tertiary**

- » Intolerance to second line regimen.

## 10.2.8 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<sup>3</sup>.

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 perilesional 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<sup>3</sup> on ART.

- Cotrimoxazole 80/400 mg, oral, 2 tablets daily

See cotrimoxazole desensitisation: Page xxi.

**REFERRAL/CONSULTATION****Specialist or tertiary**

- » Intolerance to cotrimoxazole.

**Note:**

Attempt desensitisation first.

**10.3 KAPOSI'S SARCOMA (KS)**

B21.0

**DESCRIPTION**

Kaposi's 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 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, 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 positive.

### PEP REGIMENS

PEP should be commenced as soon as possible after the injury. 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, two regimens are recommended.

Standard risk, basic two-drug regimen:

- Zidovudine, oral, 300 mg 12 hourly for 4 weeks.

**AND**

- Lamivudine, oral, 150 mg 12 hourly for 4 weeks.

High-risk, expanded three-drug regimen:

**ADD**

- Lopinavir/ritonavir 200/50, oral, 2 tablets 12 hourly.

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.

Zidovudine often causes nausea and headache. If zidovudine is not tolerated, switch to tenofovir (check baseline creatinine clearance as above) or stavudine.

Lopinavir/ritonavir often causes diarrhoea. If lopinavir/ritonavir is not tolerated switch to efavirenz.

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.

Exposure	HIV status of source patient		
	Unknown	Positive Standard risk	Positive High risk*
intact skin	no PEP	no PEP	no PEP
mucosal splash/non-intact skin	consider 2-drug regimen	2-drug regimen	2-drug regimen
percutaneous (sharps)	2-drug regimen	2-drug regimen	3-drug regimen
percutaneous (needle in vessel or deep injury)	2-drug regimen	3-drug regimen	3-drug regimen

When the source patient is known to be failing ART, modify the PEP regimen:

- » If the patient is on zidovudine or stavudine then tenofovir should be used.
- » If the patient is on tenofovir then zidovudine should be used.
- » If the patient is on efavirenz or nevirapine then lopinavir/ritonavir should be used.

Patients failing second line ART almost always have no resistance to protease inhibitors, so lopinavir/ritonavir should still be effective. Consultation with a virologist or infectious diseases physician is recommended for advice on which antiretroviral drugs to use for PEP.

### **Monitoring after occupational exposure**

Laboratory monitoring is done to exclude acquisition of HIV infection and, for those given PEP, to monitor toxicity.

Test healthcare workers for HIV infection at the time of the exposure and again at 6 weeks, 3 months and 6 months. The test of choice is the HIV antibody test, usually an enzyme immuno-assay or ELISA, which should be done in a laboratory, rather than with a clinic-based rapid test in order to ensure adequate documentation. Instruct healthcare workers to practice safer sex until their HIV test is negative 6 months following exposure. The laboratory assessment of toxicity is limited to screening and monitoring for the haematological toxicity of zidovudine. Perform FBC at baseline and after 2 and 4 weeks on antiretroviral therapy.

## **10.5 POST-EXPOSURE PROPHYLAXIS FOR PENETRATIVE ANAL OR VAGINAL SEXUAL ASSAULT**

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.

Offer the basic two-drug PEP regimen:

- Zidovudine, oral, 300 mg 12 hourly for 4 weeks.

### **AND**

- Lamivudine, oral, 150 mg 12 hourly for 4 weeks.

High-risk exposure (genital lacerations or anal intercourse), expanded three-drug regimen

### **ADD**

- Lopinavir/ritonavir, oral, 400/100 mg 12 hourly.

Zidovudine often causes nausea and headache. If zidovudine is not tolerated, switch to tenofovir (check baseline creatinine clearance as above) or stavudine.

Lopinavir/ritonavir often causes diarrhoea. If lopinavir/ritonavir is not tolerated switch to efavirenz.

### **Monitoring after exposure**

See section 10.4: Post-exposure prophylaxis, occupational.



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.

National HIV Health Care Worker Hotline: 0800 212 506 or 021 406 6782.

# CHAPTER 11

## SURGICAL ANTIBIOTIC PROPHYLAXIS

### GENERAL PRINCIPLES

The need for prophylactic antibiotic therapy is based on the risk of surgical site contamination.

The antibiotic chosen should be active against the pathogens most likely to be associated with surgical site infections.

Prophylaxis must be given within 60 minutes of the first incision, usually at induction.

**The prophylactic dose is a single dose equal to the standard therapeutic dose.**

A second dose is **ONLY** given if surgery is prolonged, i.e. > 4 hours for cefazolin **OR** > 8 hours for metronidazole **OR** > 6 hours for clindamycin and gentamicin

Type of surgery	Antibiotic recommended	Severe beta lactam allergy
<b>Cardiothoracic surgery</b>	<ul style="list-style-type: none"><li>• Cefazolin, IV, 1 g</li></ul>	<ul style="list-style-type: none"><li>• Clindamycin, IV, 600 mg</li></ul>
<b>Lower limb amputation</b>	<ul style="list-style-type: none"><li>• Cefazolin, IV, 1 g</li></ul> <b>PLUS</b> <ul style="list-style-type: none"><li>• Metronidazole, IV, 500 mg</li></ul>	<ul style="list-style-type: none"><li>• Clindamycin, IV, 600 mg</li></ul>
<b>Orthopaedic surgery</b>	<ul style="list-style-type: none"><li>• Cefazolin, IV, 1 g</li></ul>	<ul style="list-style-type: none"><li>• Clindamycin, IV, 600 mg</li></ul>
<b>Head and neck surgery</b>	<ul style="list-style-type: none"><li>• Cefazolin, IV, 1 g</li></ul> <p>For procedures involving the oropharyngeal mucosa: <b>ADD</b></p> <ul style="list-style-type: none"><li>• Metronidazole, IV, 500 mg</li></ul>	<ul style="list-style-type: none"><li>• Clindamycin, IV, 600 mg</li></ul>
<b>Upper GIT</b>	<ul style="list-style-type: none"><li>• Cefazolin, IV, 1 g</li></ul>	<ul style="list-style-type: none"><li>• Clindamycin, IV, 600 mg</li></ul>
<b>Colorectal and appendix</b>	<ul style="list-style-type: none"><li>• Cefazolin, IV, 1 g</li></ul> <b>PLUS</b> <ul style="list-style-type: none"><li>• Metronidazole IV, 500 mg</li></ul> <p>If perforation has occurred, treat patient for infection with a course of appropriate antibiotics.</p>	<ul style="list-style-type: none"><li>• Clindamycin, IV, 600 mg</li></ul> <b>PLUS</b> <ul style="list-style-type: none"><li>• Gentamicin, IV, 6 mg/kg</li></ul>

Type of surgery	Antibiotic recommended	Severe beta lactam allergy
<b>Biliary</b>	Only for high risk patients: bile obstruction, jaundice, biliary stones or cholecystitis, or re-operation: <ul style="list-style-type: none"> <li>• Cefazolin, IV, 1 g</li> </ul> <b>PLUS</b> <ul style="list-style-type: none"> <li>• Metronidazole IV, 500 mg</li> </ul>	<ul style="list-style-type: none"> <li>• Clindamycin, IV, 600 mg</li> </ul> <b>PLUS</b> <ul style="list-style-type: none"> <li>• Gentamicin, IV, 6 mg/kg</li> </ul>
<b>Pelvic surgery</b>	<ul style="list-style-type: none"> <li>• Cefazolin, IV, 1 g</li> </ul> <b>PLUS</b> <ul style="list-style-type: none"> <li>• Metronidazole IV, 500 mg</li> </ul>	<ul style="list-style-type: none"> <li>• Clindamycin, IV, 600 mg</li> </ul> <b>PLUS</b> <ul style="list-style-type: none"> <li>• Gentamicin, IV, 6 mg/kg</li> </ul>
<b>ENT surgery</b>	<ul style="list-style-type: none"> <li>• Cefazolin, IV, 1 g</li> </ul> For procedures involving the oropharyngeal mucosa: <b>ADD</b> <ul style="list-style-type: none"> <li>• Metronidazole, IV, 500 mg</li> </ul>	<ul style="list-style-type: none"> <li>• Clindamycin, IV, 600 mg</li> </ul>
<b>Nephro-urological surgery</b>	<ul style="list-style-type: none"> <li>• Cefazolin, IV, 1 g</li> </ul> Treat patients with preoperative bacteriuria according to MCS.	<ul style="list-style-type: none"> <li>• Clindamycin, IV, 600 mg</li> </ul> <b>PLUS</b> <ul style="list-style-type: none"> <li>• Gentamicin, IV, 6 mg/kg</li> </ul>
<b>Ophthalmic surgery</b>	<ul style="list-style-type: none"> <li>• Chloramphenicol 0.5% ophthalmic drops, instil 1 drop 2–4 hourly for 24 hours prior to surgery</li> </ul>	
<b>Neurosurgery</b>	<ul style="list-style-type: none"> <li>• Cefazolin, IV, 1 g</li> </ul>	<ul style="list-style-type: none"> <li>• Clindamycin, IV, 600 mg</li> </ul>

**Note:**

Clindamycin has good anaerobic cover; therefore, there is no need to add metronidazole.

# CHAPTER 12

## PAIN

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### DESCRIPTION

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage. It is always a subjective experience. The perception of pain is influenced by the patient's mood, morale and the meaning the pain has for the patient.

### ASSESSMENT OF PAIN

There are a number of different classification schemes for pain. A common theme is the need to assess pain from multiple perspectives – consider describing the anatomical site, severity (a visual analogue scale may be of value), temporal features (duration of episodes, time since original onset) and suspected aetiology (nociceptive, neuropathic or psychogenic). Nociceptive pain can be superficial, deep somatic (e.g. myofascial) or visceral.

Self-report of pain is the key to pain assessment.

**The adequacy of pain control warrants regular review in each patient.**

### 12.1 PAIN, CHRONIC

R52

All patients with chronic pain require a thorough physical assessment, and associated depression or other psychological disorders should also be considered.

Also review medication use, comorbidities, and functional status.

### GENERAL AND SUPPORTIVE MEASURES

Treatment of chronic pain needs to address the physical pathology that initiated the chronic pain, as well as the important social and psychologic sequelae of chronic symptoms.

The goal of pain management should include reconditioning, reducing pain and improving function, sleep and mood.

If appropriate, include family members in the discussion.

Address all factors that may contribute to pain and associated symptoms, e.g. family stress, anxiety and sleep deprivation.

Use physical therapies, where appropriate, e.g. massage, splints, physiotherapy.

### MEDICINE TREATMENT

Although pain is rarely eliminated, treatment should reduce daily pain level, as well as the frequency, severity and duration of the pain flares.

Neuropathic pain is best treated with amitriptyline. If this fails, consider the use of antiepileptics, e.g. carbamazepine or a weak opiate, e.g. tramadol. Concerns regarding addiction should not compromise adequate pain control with opioids.

Utilise the least invasive route of medication administration, preferably oral.

### **Analgesics**

For chronic pain, analgesics must be administered regularly and not only “when required” (prn).

Additional short-acting analgesia may be required 30 minutes prior to pain-inducing activity such as physiotherapy.

Combinations of medications from different classes may have additive analgesic effects.

#### Non-opioid drugs:

- Paracetamol, oral, 1 g 6 hourly.

If no response, add non-steroidal anti-inflammatory drugs (NSAIDs).

- NSAIDs, e.g.:
  - Ibuprofen, oral, 400–800 mg 8 hourly with meals.
    - An additional night-time dose of a NSAID may be required.
    - Can be used in combination with paracetamol or opioids.

#### **Note:**

There are safety concerns with the long-term use of NSAIDs, including increased risk of CVS disease, renal impairment and GIT bleeding.

If no response, add opioid drugs.

Increase doses of opioids according to the individual need to overcome pain. Take into account the development of tolerance.

In chronic pain, the correct dose is that which relieves the patient’s symptoms and, except for **tramadol**, may exceed the recommended dose used in other pain relief settings.

- Tramadol, oral, 50 mg, 6 hourly as a starting dose.
  - May be increased to a maximum of 400 mg daily.

#### **OR**

- Morphine BP, short-acting solution, oral.
  - Starting dose: 20 mg 4 hourly.
  - Elderly, frail or patients less than 50 kg: 10 mg 4 hourly.
  - Increase dose by 50 % every dosage interval if pain control is sub-optimal.
  - Reduce the dosing interval if there is regular breakthrough pain.

#### **OR**

- Morphine, long-acting, oral, 30–60 mg 12 hourly.
  - Titrate to desired effect.

Manage nausea caused by opioids. (See adjuvant therapy below).

For constipation caused by opioids:

- Sennosides A and B, oral, 2 tablets at night.

For constipation in patients with potentially obstructive lesions:

- Lactulose, oral, 15 mL 12 hourly.

### **Adjuvant therapy**

Adjuvant agents can enhance pain control by targeting specific pain mechanisms:

- » nerve injury pain,
- » burning paraesthesia,
- » neuropathic pain,
- » nerve root compression,
- » HIV neuropathy, and
- » chemotherapeutic nerve injuries.

In addition to analgesia as above:

- Amitriptyline, oral, 10 mg at night.  
Titrate up to 75 mg at night.

### **AND/OR**

- Carbamazepine, oral, 100 mg 12 hourly for 2 weeks.
  - Then 200 mg 12 hourly.
  - Titrate dose slowly up to 600 mg every 12 hours, depending on the response.

For nausea and vomiting:

- Metoclopramide, oral, 10–20 mg 8–12 hourly.

### **OR**

- Metoclopramide, IV or IM, 10 mg 8 hourly.

For pruritus or nausea:

- Promethazine, oral/IV, 10 mg 6 hourly.

For anxiety:

- Diazepam, oral, 2–5 mg 12 hourly.

For colic:

- Hyoscine butylbromide, IV/oral, 10 mg 8 hourly.

### **REFERRAL**

- » Pain resistant to medical management.

## 12.2 PERI-OPERATIVE ANALGESIA

Effective pain management improves patient quality of life, reduces morbidity, and facilitates earlier discharge. Pain severity should be assessed frequently during the immediate post-operative period using some objective measure of severity, such as a visual analogue scale or a facial expressions pictogram.

Pain management for different types of surgery should be adjusted according to the anticipated type and severity of pain. The use of more than one analgesic type may also increase effectiveness while minimising adverse effects (targeted multimodal or 'balanced' analgesia.) Useful agents are non-opioids (paracetamol and NSAIDs), weak opioids (tramadol), strong opioids (morphine), and adjuvants (ketamine).

Poorly-controlled pain in the early post-operative period can be reduced by starting analgesia while the patient is still anaesthetised. Patient-controlled analgesia may be available in some facilities and may lead to better analgesia with reduced adverse effects.

### Mild pain

For example, after inguinal hernia repair or laparoscopy.  
Wound infiltration with local anaesthetic.

- Paracetamol, oral, 1 g 6 hourly.

If no response, add NSAIDs:

- Ibuprofen, oral, 800 mg 8 hourly with meals.

**OR**

- Tramadol, oral, 50 mg, 6 hourly as a starting dose.

**OR**

If unable to take oral:

- Morphine, IM, 0.1–0.15 mg/kg/dose, 4 hourly e.g. 10 mg 4 hourly.

### Moderate pain

For example, after hysterectomy or jaw surgery.  
Wound infiltration with local anaesthetic.

- Paracetamol, oral, 1 g 6 hourly.

**AND**

- Ibuprofen, oral, 800 mg 8 hourly with meals **or** diclofenac, IM, 50 mg 8 hourly.

**AND**

If no epidural consider:

- Morphine, IM, 0.1–0.15 mg/kg/dose 4 hourly e.g. 10 mg 4 hourly.

**Severe pain**

For example, after laparotomy or thoracotomy.

Major peripheral nerve block or epidural.

Wound infiltration with local anaesthetic.

- Paracetamol, oral, 1 g 6 hourly.

**AND**

- Ibuprofen, oral, 800 mg 8 hourly with meals **or** diclofenac, IM, 50 mg 8 hourly.

**AND**

If no epidural:

- Morphine, IM, 0.1–0.15 mg/kg/dose, 4 hourly e.g. 10 mg 4 hourly.

**Special situations**

Nil per mouth

In patients in whom oral medication is contra-indicated, parenteral options are:

- » intramuscular diclofenac, or
- » intravenous or intramuscular morphine.

Once the patient is able to take by mouth:

- » change intramuscular NSAID to an oral version (efficacy the same), and
- » consider changing morphine to tramadol, or stopping the opiate altogether if pain control using other medication is adequate.

**Contra-indication to NSAIDs**

In patients in whom NSAIDs are contraindicated because of renal dysfunction or known peptic ulcer disease, use a combination of paracetamol, morphine, and local analgesia. Parenteral NSAIDs are not contra-indicated in patients who are nil per mouth or have a history of recent alcohol abuse but should be used with caution in the elderly, those with known renal dysfunction, and patients considered to be volume depleted.

**NSAIDs in orthopaedics**

Patients with pure bone pain (e.g. dental work or orthopaedic surgery), may respond adequately to NSAIDs. Short-term use of NSAIDs is unlikely to be associated with clinically important reductions in bone healing rates.



# CHAPTER 13

## MUSCULOSKELETAL SYSTEM

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### 13.1 ARTHRITIS, RHEUMATOID (RA)

M06.9

#### 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.

#### 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

Use DMARDs only with regular monitoring for toxicity, particularly retinal toxicity caused by chloroquine and adverse effects of methotrexate i.e. bone marrow, liver toxicity, etc.

Assess response 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. Titrate the dose of sulfasalazine and methotrexate gradually to maintenance dose.

- Methotrexate, oral, 7.5 mg **once per week**. Specialist consultation.
  - Increase dose gradually to a maximum of 25 mg per week.
  - Monitor: Liver function and FBC before and 12 weekly during treatment.

#### PLUS

- Folic acid, oral, 5 mg per week with methotrexate at least 24 hours after the methotrexate dose.

#### AND/OR

- Chloroquine sulphate, oral, 150 mg (as base) daily for 5 days of each week for 2–3 months.
  - Then reduce dose if possible and administer 5 days a week with an annual drug holiday for 1 month.
  - Do ophthalmic examination annually 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.
  - Liver function and FBCs monthly for first 3 months then every 3–6 months.

**Oral corticosteroids**

Indications:

- » As bridging therapy while waiting for DMARDs to take effect.
- » The elderly if threatened by functional dependence and intolerant to NSAIDs.
- » Extra-articular manifestations, e.g. pleural effusion, scleritis.

Acute flare

- Prednisone, oral, 40 mg daily for 2 weeks.
  - Thereafter gradually reduce the dose to  $\leq 7.5$  mg daily.
  - The continued need for systemic steroids should always prompt review of treatment.

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.

**NSAIDs**

Use for active inflammation with pain. NSAIDs are used for symptomatic control only, as 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.

- NSAID, e.g.:
  - Ibuprofen, oral, 800 mg 8 hourly with meals.
    - If not tolerated: 400 mg 8 hourly.

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 induced 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 cannot occur then the use of the night-time dose must be for the shortest period possible.

In high-risk patients: i.e. patients > 65 years and those with a history of peptic ulcer disease:

- Omeprazole, oral, 20 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 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 joint replacement.

**Urgent**

- » Rupture of extensor tendons.
- » Scleritis.
- » Unstable upper cervical spine.

**13.2 ARTHRITIS, SEPTIC AND OSTEOMYELITIS, ACUTE**

M00.9/M86.1

**GENERAL MEASURES**

Rest and immobilisation.

Drainage can be done by daily needle aspiration.

Surgical drainage: (in loculated effusions or inaccessible joints like the hip).

Always consider early drainage by orthopaedic surgeon.

**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.

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 6 hourly to complete the 4 weeks' treatment.

For gonococcus:

- Ceftriaxone, IV, 1 g daily for 1 week.

Penicillin allergy

Refer.

**Analgesia**

- NSAID until pain subsides e.g.:
- Ibuprofen, oral, 800 mg 8 hourly with meals.

**AND/OR**

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

**REFERRAL**

- » For early drainage by specialist surgeon.
- » If pyrexia persists in spite of adequate antibiotic therapy, a subperiosteal abscess must be sought and drained by a specialist surgeon.
- » Growth plate involvement.
- » Chronic osteomyelitis and its complications.
- » Pathological fractures.

### 13.3 OSTEO-ARTHRITIS/OSTEO-ARTHROSIS

M19.9

#### GENERAL MEASURES

Weight reduction.

Exercise: postural and non-weight bearing. Quadriceps strengthening should be considered for OA knee.

Rest during acute painful episodes.

Support and alleviate weight bearing of affected joints, i.e. walking stick.

Consider 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

If ineffective:

#### ADD

- NSAIDs e.g.:
- Ibuprofen, oral, 400–800 mg 8 hourly.

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.

If NSAID not tolerated:

#### ADD

- Omeprazole, oral, 20 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

### 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, 1 200 mg immediately as a single dose.
  - Then 800 mg 8 hourly with meals for the duration of the attack.

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 drugs that increase uric acid, including:

- » low dose aspirin,
- » ethambutol,
- » pyrazinamide, and
- » diuretics, such as hydrochlorothiazide  $\geq 25$  mg.

Treat secondary causes where possible.

Assess renal function and blood urate level.

#### 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.
  - The elderly and patients with renal impairment (eGFR between 30–60 mL/minute), start at 50 mg daily.

Allopurinol is contra-indicated in patients with eGFR less than 30 mL/minute.

To prevent breakthrough gout attacks:

- Colchicine, oral, 0.5 mg 12 hourly for 3 months.

**OR**

- Ibuprofen, oral, 400 mg 12 hourly with meals for 3 months.

Do not stop uric acid lowering drugs during an acute attack.

## REFERRAL

- » No response to treatment despite adequate adherence.
- » Non-resolving tophaceous gout.
- » Patients with eGFR  $< 30$  mL/minute.

## 13.5 SERONEGATIVE SPONDYLARTHRTIS

M45–49

### DESCRIPTION

A group of diseases in which there is a predominant asymmetrical lower-limb seronegative arthritis, sacro-iliitis, spinal inflammation (spondylitis) and enthesitis (e.g., Achilles tendonitis). These include ankylosing spondylitis, reactive arthritis/Reiter's Syndrome, psoriatic arthropathy, the arthritides associated with inflammatory bowel disease like ulcerative colitis and Crohn's Disease. Uveitis which requires topical steroid therapy, 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.

**REFERRAL**

- » Uveitis to an ophthalmologist.
- » Refractory severe arthritis to a rheumatologist.
- » Deformity at diagnosis to a rheumatologist.

**13.5.1 ARTHRITIS, REACTIVE/REITER'S SYNDROME**

M02.3

**DESCRIPTION**

An acute non-purulent arthritis complicating an infection elsewhere in the body. A spondylarthritis often preceded by enteric or urogenital infections 1–4 weeks before the arthritis and occurring predominantly in individuals with HLA-B27 antigen. When there is associated conjunctivitis or urethritis the condition is referred to as Reiter's syndrome.

It is a clinical diagnosis with no laboratory test or radiographic findings. Test for 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, 800 mg 8 hourly with meals.
    - If not tolerated: 400 mg 8 hourly.

Prompt appropriate treatment of acute chlamydial urethritis may prevent subsequent attacks, i.e.:

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

**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.

Avoid medications implicated in triggering or causing deterioration of SLE.

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

**AND/OR**

- NSAIDs, e.g.:
  - Ibuprofen, oral, 800 mg 8 hourly with meals.
    - If not tolerated: 400 mg 8 hourly.
- Chloroquine sulphate, oral, 150 mg (base) daily for 5 days a week.
  - Regular ophthalmic examination, i.e. annually.

**Corticosteroids**

Initiate therapy in patients with life threatening manifestations and organ involvement.

- Prednisone, oral, 1–2 mg/kg daily, initial dose.
  - Taper to the lowest maintenance dose after a response has been obtained.
  - 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 patients should be managed by a specialist.

- Azathioprine, oral, 1–3 mg/kg daily.

**OR**

- Cyclophosphamide, oral, 100–200 mg daily or 1–3 mg/kg daily.

**Severe Raynaud's phenomenon**

- Amlodipine, oral, 5 mg daily.

**Antiphospholipid antibody syndrome**

- Aspirin, oral, 150 mg daily with food.

Patients with previous thrombo-embolic episodes should be adequately anticoagulated with lifelong warfarin.

**Hormonal therapy in women**

The use of oral contraceptives is controversial.

Until there is clarity it is advisable to use either progesterone-only or low dose oestrogens.

**REFERRAL**

- » All patients for initial assessment.
- » Lupus flare.
- » Nephritis.
- » Persistent haematological derangements i.e. thrombocytopenia.

# CHAPTER 14

## NEUROLOGICAL DISORDERS

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### 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.

ECG in the acute setting to rule out accompanying acute coronary ischaemic event.

RPR to exclude meningovascular syphilis.

#### MEDICINE TREATMENT

The disease requires good initial evaluation, ongoing support for patients and continuous evaluation to ensure adherence in taking medication and diet.

Measures for secondary prevention may not be appropriate for patients with severe disability

All patients not on anticoagulation:

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

Long-term anticoagulation with warfarin may be considered for thrombotic/embolic stroke, e.g. if there is a cardiac source of emboli, provided close follow-up can be anticipated. It is unclear when this should be initiated as there is a risk of haemorrhagic transformation in the immediate post stroke period.

It is advisable to use neuroimaging to exclude haemorrhage before initiating anticoagulation therapy.

Patients with a thrombotic stroke for secondary prevention, irrespective of the LDL level:

- Simvastatin, oral, 10 mg daily.

For DVT prophylaxis, initial low dose subcutaneous heparin:

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

See section 2.13: Venous Thrombo-Embolism.

Treat secondary pulmonary and urinary tract infections early and appropriately.

### **Hypertension**

In the first 72 hours following stroke, it is usual for the blood pressure to be elevated. Do not lower BP in acute stroke or use antihypertensive medication unless the systolic BP is > 220 mmHg or the diastolic BP is > 120 mmHg, as a rapid decrease may aggravate cerebral ischaemia and worsen the stroke.

If the BP is above those levels then treatment should aim to lower the BP by not more than 15–20% in the first 24 hours.

Control of hypertension following stroke reduces the risk of recurrent events. Treat according to guidelines. See section 3.6: Hypertension.

### **Dyslipidaemia**

If clinical features suggesting familial hypercholesterolaemia are present, screen for familial dyslipidaemia.

Manage cases appropriately with diet and drug treatment. See section 8.8: Dyslipidaemia.

### **REFERRAL**

- » Patients with atypical clinical presentation.
- » Patients with transient ischaemic attack who may warrant carotid endarterectomy.
- » Young patients, e.g. < 40 years, with stroke, for evaluation of aetiology.
- » 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 or infarct who may require surgical decompression.
- » All stroke patients with a history suggestive of subarachnoid haemorrhage or with neck stiffness

## **14.1.2 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.

If no response:

- Morphine, IV, 1–2 mg/minute to a maximum total dose of 10 mg.
  - Dilute 10 mg up to 10 mL in sodium chloride solution 0.9%.
  - This may be repeated 4 hourly.

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.
- » For neurological imaging: patients in whom the diagnosis has to be confirmed radiologically and where a lumbar puncture may be considered hazardous.

## 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.

Transient worsening of condition may be due to metabolic disorders, infections and drug side effects.

**Differential diagnosis** for dementia includes:

- » Side effects of drugs, including antimuscarinic, anxiolytic and antidepressive agents.
- » Chronic subdural haematoma.
- » Depression.
- » Parkinson's Disease.
- » Huntington's Disease.

Common causes of dementia that may respond to medical therapy include:

- » Hypothyroidism. See section 8.11: Hypothyroidism.
- » Vitamin B<sub>12</sub> deficiency. See section 2.5: Anaemia, megaloblastic.
- » Wernicke's Syndrome. See below.
- » Pellagra. See below.
- » Alcohol. Cessation of alcohol abuse usually does not lead to further damage.
- » HIV-dementia. May respond to treatment with antiretrovirals. Exclude opportunistic diseases of the CNS.
- » Syphilis. Appropriate medical treatment may prevent further deterioration. See section 14.5.3: Meningovascular Syphilis.
- » Normal pressure hydrocephalus. May respond to neurosurgical intervention.
- » Multi-infarct dementia. Appropriate management may prevent further deterioration. See section 14.1: Cerebrovascular Disease.

Conditions which may worsen already existing dementia include:

- » Electrolyte disturbances and dehydration.
- » Infections, usually originating from the respiratory or urinary tract.
- » Drug 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.

To control restless patients:

- Haloperidol, oral, 0.5–1 mg 8 hourly with a higher dose at night, if required.

For pellagra:

- Nicotinamide, oral, 100 mg 8 hourly.

### WERNICKE'S SYNDROME

- Thiamine, IM, 100 mg **or** IV, 100 mg in 1 L dextrose 5% in water.

Established Wernicke's:

- 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.

Treat other commonly associated nutritional deficiencies.

## REFERRAL

- » Patients in whom a treatable underlying condition is suspected, for specialised investigations including a CT scan.

## 14.3 EPILEPSY

G40

### GENERAL MEASURES

Take an adequate history to define the type of epilepsy.

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.

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,
- » the effect of missing a dose of medication,
- » discontinuing the drug without advice of a doctor, and
- » birth control, bearing in mind adherence issues and potential drug-drug interactions.

### 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 drug 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 to 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.

Monitoring of drug levels is not useful except:

- » To confirm toxicity in a symptomatic patient.
- » To confirm poor adherence.
- » With poor control despite good self reported adherence.
- » When contemplating dose increments beyond doses exceeding 5 mg/kg daily or 300 mg daily with phenytoin.

**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.

**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/day as a single dose or 12 hourly.

**OR**

- Phenytoin, oral, 4.5–5 mg/kg (on 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.

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 1 200 mg 12 hourly.

Phenytoin, phenobarbitone and carbamazepine are potent enzyme inducing agents and should be used with caution with other drugs metabolised by the liver, especially warfarin, ARVs and oral contraceptives.

**Other epilepsy types**

Manage in consultation with a specialist.

Clonazepam may be used for certain indications.

Phenobarbitone may be considered in certain circumstances. It has a long half life and may be taken once daily. Sedation is a commonly encountered side effect.

**HIV-infected individuals on ARVs**

Phenytoin and carbamazepine are enzyme inducing anti-epileptic drugs. 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/day as a single dose or 12 hourly.

**Note:**

The metabolism of lamotrigine is induced by lopinavir/ritonavir and atazanavir. The dose of lamotrigine should be doubled every 2 weeks when patients are switched to a lopinavir/ritonavir- or atazanavir-containing regimen.

In HIV-infected women of child bearing age, lamotrigine is preferred to valproate.

**OR**

- Valproate, oral.
  - Usual starting dose: 200–300 mg 12 hourly.
  - Increase, as required, every 2 weeks to a maximum daily dose of 1200 mg 12 hourly.

Add on therapy to valproate:

- 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.

**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. For dose, see medicine treatment.

**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**

Persistent seizures, without regaining consciousness.

**GENERAL MEASURES**

Start treatment immediately. Do not wait for results of special investigations.

Maintain cardiorespiratory status.

Maintain fluid, electrolyte and blood glucose status.

Take blood sample for electrolytes and anticonvulsant levels.

**MEDICINE TREATMENT**

Seizure control should occur within 60 minutes to prevent permanent brain damage.

**INITIAL TREATMENT**

- Lorazepam, IV/IM, 4 mg.

**OR**

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

**OR**

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

**OR**

- Midazolam, buccal, 5–10 mg using the contents of an ampoule.
  - If convulsions continue repeat the dose.

**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 sodium, IV, 2–4 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 sodium by decreasing the dose by 1 mg/kg every 12 hours.

**OR**

- Propofol, IV, 3–5 mg/kg/dose as a bolus
  - Maintenance dose: 30–100 mcg/kg/minute.

Higher initial maintenance doses of phenytoin may be needed in patients who have had thiopental sodium. Doses should be guided by daily therapeutic drug monitoring until phenytoin levels have stabilised after thiopental sodium has been weaned off.

**MAINTENANCE THERAPY**

If seizures controlled:

- Phenytoin, IV, 100 mg 8 hourly or oral, 300 mg daily.
  - First maintenance dose should be no more than 12 hours after the loading dose.

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 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 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.

**OR**

NSAIDs, e.g.:

- Ibuprofen, oral, 800 mg immediately then 8 hourly, if needed.

If severe and not responding to therapy above:

- Morphine, IM, 10 mg as a single dose.

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**

- Propranolol, oral, 20–80 mg 12 hourly.

**Note:**

The evidence for using atenolol for this indication is limited.

**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 to 2 months to occur.

**REFERRAL**

- » Patients with unexplained neurological signs, additional risk factors for an alternate diagnosis, such as immune deficiency, or an atypical short history require brain imaging.
- » Sudden onset of a first severe headache, even if it resembles migraine, as this may indicate serious organic pathology, such as subarachnoid haemorrhage.
- » Acute migraine, not responding to treatment.
- » Recurrent migraine not controlled with prophylactic therapy.

**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 in this indication.

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 8 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 2–3 times daily, 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 (BENIGN) 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<sub>2</sub>O.

**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 drugs known to be associated with benign intracranial hypertension.

**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.

**OR**

- Hydrochlorothiazide, oral, 25 mg daily.

**REFERRAL**

- » For neuro-imaging, if not available locally.
- » Visual symptoms or deterioration of visual fields for ophthalmology 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 first, 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, as with an uncontrolled significant bleeding tendency, commence empirical antibiotic therapy after taking samples for blood cultures. Attempt the lumbar puncture later, once 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.

### **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.

#### **AND/OR**

- Ibuprofen, oral, 800 mg immediately.
  - Follow with 400 mg 8 hourly thereafter.

#### **AND/OR**

- Morphine, IM or slow IV infusion, 10 mg.
  - Dilute 10 mg up to 10 mL sodium chloride solution 0.9%.
  - This may be repeated 4 hourly.
  - Beware of respiratory depression in patients with reduced level of consciousness.

### **Antibiotic therapy**

Empiric therapy for bacterial meningitis until sensitivity results are available:

- Ceftriaxone, IV, 2 g 12 hourly for 10 days.

#### **OR**

- Cefotaxime, IV, 2 g 8 hourly for 10 days.

### **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  $\geq 24$  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.

### **Penicillin allergy**

Penicillin resistant strains of Pneumococcus are usually also resistant to chloramphenicol.

For meningococcus, pneumococcus or haemophilus if organism is sensitive:

- Chloramphenicol, IV, 1 g 6 hourly.

If pneumococcus is resistant to chloramphenicol:

- Vancomycin, IV, 20 mg/kg/dose 12 hourly.

### **PLUS**

- Rifampicin, oral, 600 mg 12 hourly

### **Note:**

It may be necessary to consult a microbiologist.

### **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 days later while still on ceftriaxone or cefotaxime. If aetiology is bacterial, considerable improvement in CSF findings may be expected, but with tuberculosis findings will be much the same or a little worse.

- Dexamethasone, IV, 12 mg 12 hourly.

Followed with:

- Prednisone, oral, 120 mg daily.

After 1 week taper dose gradually over next 6 weeks.

Standard combination tuberculosis therapy according to National protocol.

See section 16.9: Tuberculosis, Pulmonary.

Duration of therapy: 9 months.

### **Cryptococcal meningitis**

HIV-positive patients, see section 10.2.2: Cryptococcosis. In HIV infection the aim is to suppress the infection until immune restoration occurs with antiretroviral therapy.

In HIV-negative patients the aim is to cure the infection.

#### Initial therapy

- Amphotericin B, IV, 1 mg/kg daily.
  - Ensure adequate hydration to minimise nephrotoxicity.
  - Regular, e.g. 3 times a week, monitoring of potassium, magnesium and renal function is essential.
  - 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.

If complications arise due to amphotericin B after a minimum of 2–4 weeks in a patient responding to therapy, consider substituting with:

- Fluconazole, oral, 800 mg daily for at least 8 weeks.

#### Maintenance therapy

- Fluconazole, oral, 200 mg daily for 6 months or longer, in consultation with a specialist.

Follow all patients closely for relapses.

#### Therapeutic lumbar puncture

This should be considered as the intracranial pressure is often elevated with a communicating hydrocephalus.

See Section 10.2.2: Cryptococcosis.

**14.5.2 VIRAL MENINGOENCEPHALITIS**

A86

**DESCRIPTION**

Patients present with headache, fever and mild meningism. 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.

**AND**

- Tramadol, oral, 50 mg 6 hourly.

**OR**

- Morphine, IV, 1–2 mg/minute to a maximum total dose of 10 mg.
  - Dilute 10 mg up to 10 mL in sodium chloride solution 0.9%.
  - This may be repeated 4 hourly.
  - Beware of respiratory depression in patients with reduced level of consciousness.

**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 temporal focus on EEG or neuro-imaging is strongly supportive of the diagnosis.

A 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.
  - If PCR is negative, stop treatment.

Treat seizures appropriately with phenytoin or carbamazepine. See section 14.3: Epilepsy.

It is important to initiate therapy and then refer to centre where neuro-imaging or EEG is available.

**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 a combination of positive VDRL/FTA-absorption on CSF.

VDRL in CSF is usually of low titre, and may be negative. An elevated IgG CSF/blood index may be helpful. A negative blood FTA excludes the diagnosis of neurosyphilis.

**MEDICINE TREATMENT**

- Benzylpenicillin (penicillin G), IV, 20 million units daily in 4–6 divided doses for 10 days.

**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.

**PLUS**

- 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.

3<sup>rd</sup> generation cephalosporin, e.g.:

- Ceftriaxone, IV, 2 g 12 hourly.

**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.

**GENERAL MEASURES**

Health education.

Surgery for treatable ventricular blockage or spinal or intraocular cysts.

**DRUG TREATMENT**

For active or viable cysts only:

- Albendazole, oral, twice daily 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.

Progressive recovery may occur for a period of up to one year. The presence of viable cysts does not require repeating antihelminthic treatment.

Drug-induced damage to cysticerci may precipitate an acute inflammatory reaction, the intensity of which is related to the number of viable cysts and may cause cerebral oedema. This reaction is minimised by adding corticosteroids to the antihelminthic treatment, e.g.:

- Prednisone, oral, 60 mg daily for 8 days.

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).

### REFERRAL

- » To differentiate functional from organic disorders.
- » Tardive dyskinesia.
- » All complicated cases, i.e. patients with Parkinsonism, not responding to small doses of carbidopa/levodopa.
- » Patients with Parkinsonism developing disease-, drug- or autonomic nervous system complications.
- » Patients with myoclonus or chorea, not responding to therapy.

### 14.6.1 PARKINSON'S DISEASE

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

Educate the patient.

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.

If optimal control has not been achieved, consider an alternative diagnosis or changing to a drug containing a higher dose of levodopa:

- 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.

### **Tremor only:**

Consider anticholinergic agent, e.g.:

- Orphenadrine, oral, 50mg 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.

### **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:

β-blocker, e.g.:

- Propranolol, oral, 60–320 mg daily in divided doses.

**14.6.3 MYOCLONUS**

G25.3

**DESCRIPTION**

Irregular, involuntary movements due to muscle jerks, which may be due to myoclonic seizures, but may follow injuries to the brain and are thus not always of an ictal nature.

**REFERRAL**

- » All patients where the diagnosis is unclear.

**14.6.4 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,
- » acute inflammatory demyelinating polyradiculoneuropathy (Guillain-Barré), and
- » chronic inflammatory demyelinating polyradiculoneuropathy (CIDP).



**GENERAL MEASURES**

Observe rate of progression.

If the disease is progressing fairly rapidly, i.e. deterioration noted over  $\leq 7$  days, admit patient and monitor ventilatory status carefully with spirometry, as intubation and ventilatory support may be required.

Remove the cause where possible, i.e. drug- or alcohol-induced neuropathy, control diabetes mellitus, etc.

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 25–50mg daily.

**Post-herpes zoster neuropathy****Note:**

Aciclovir is not beneficial in treating this condition.

- Amitriptyline, oral, 25–75 mg daily.

**AND/OR**

- Carbamazepine, oral 200–1200 mg daily dose in divided doses.
  - Beware of possible drug interactions in patients on ART.

**Bells' palsy****Note:****Exclude herpes zoster**

Start within 4 days of onset of symptoms:

- Prednisone, oral, 60 mg daily for 7–10 days.

**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, isoniazid, hydralazine, dapsone, antiretrovirals (stavudine and didanosine), amiodarone 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**

G99.2\*

**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.

There are numerous causes for this condition and it is important to exclude neoplastic and infectious conditions, i.e. granulomas and abscesses, causing external compression of the spinal cord.

Lesions, such as intervertebral disk prolapse, and mass lesions below the spinal cord may present with cauda equina syndrome. These cases usually have asymmetrical weakness, but may have saddle anaesthesia and sphincter involvement alone. Incontinence is a marker of severity.

**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 degeneration in baseline is usually found.

Consult with neurologist for diagnosis and treatment.

**REFERRAL**

- » All patients.

**14.10 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.

Consider mannitol for brain oedema in traumatic brain injury causing raised intracranial pressure, pending neurosurgical intervention.

**14.10.1 BRAIN OEDEMA DUE TO TUMOURS AND INFLAMMATION****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.

**14.10.2 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 neurosurgical procedure only:

- Mannitol 15–25%, IV, 0.25–1 g/kg administered over 30–60 minutes.
  - Monitor neurological response and urine output.
  - Do not repeat more than 6–8 hourly.
  - Beware of hypovolaemia and electrolyte disturbances, especially hypokalaemia.

Currently no evidence exists to support the use of hypertonic saline infusion. Corticosteroids used in this setting have a harmful effect.

# CHAPTER 15

## PSYCHIATRIC DISORDERS

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### 15.1 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, mixed or depressive. By definition, a diagnosis of bipolar disorder requires either a current or previous episode of mania.

An episode of mania is typically characterised by an elevated mood whereby a patient may experience extreme happiness, which might also be associated with an underlying irritability. Such mood may be associated with increased energy/activity, talkativeness and a reduction in the need for sleep, and features may be accompanied by grandiose and/or religious delusions. Bipolar disorder causes substantial psychosocial morbidity, frequently affecting patients' relationships within their family as well as affecting their occupation and other aspects of their lives. 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 treatment compliance and knowledge of the condition.

In severe cases, psychiatrist directed electroconvulsive therapy may be required.

#### MEDICINE TREATMENT

##### Manic or mixed episodes

##### Acute management

For agitated and acutely disturbed patients:

- Haloperidol, IM, 2–5 mg.
  - This can be repeated in 60 minutes, if required.
  - Maximum dose: 10 mg in 24 hours.
  - Monitor vital signs and beware of acute dystonia.

To limit possibility of dystonia and to enhance sedation:

##### ADD

- Promethazine, IM, 25–50 mg.
  - In the elderly: 25 mg.

If poor response:

- Benzodiazepine, 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:**

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.

Repeated IM doses may result in toxicity owing to accumulation.

Monitor vital signs closely during and after administration.

Use haloperidol in patients with respiratory insufficiency.

In the short-term, benzodiazepines can aggravate delirium.

**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.

Therapeutic drug monitoring is essential when using lithium. Clinical toxicity may occur even within the therapeutic range.

- Lithium, oral, 5–10 mg/kg/dose 12 hourly.
  - Dose range: 200–600 mg/dose 12 hourly.
  - Monitor trough (pre-dose) plasma levels after 5 days.
  - This agent has a narrow therapeutic window: conventionally 0.4–0.8 mmol/L, but in mania targeting a range of 0.6–1 mmol/L may be appropriate.
  - If required increase the dose incrementally to 10 mg/kg/dose and repeat trough plasma levels after 5 days.
  - Maintain therapeutic blood levels of lithium for as long as the patient is on lithium. Initially, repeat lithium blood levels at least monthly.
  - Monitor lithium blood levels at 3 monthly intervals once stable levels have been achieved.
  - The toxic and therapeutic blood levels of lithium do not differ greatly; therefore, monitor patients closely.
  - Check TSH (hypothyroidism) and serum calcium (hyperparathyroidism) before starting treatment and annually thereafter.
  - Monitor renal function and electrolytes regularly.

**CAUTION**

Concomitant use of many drugs, such as ACE inhibitors, NSAIDs and diuretics may increase the risk of lithium toxicity.

Consider oral haloperidol with adjunctive benzodiazepines in patients who are difficult to manage, i.e. not settling with mood stabiliser monotherapy, and especially where there are features of psychosis.

**Depressive episodes in bipolar patients**First line

- 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.

**AND/OR**

- Valproate, oral, 600 mg daily.
  - Increase dose to 20 mg/kg/day 6–8 hourly.

Second line**ADD**

- Fluoxetine, oral, 20 mg daily. In consultation with psychiatrist.

**Note:**

Do not use antidepressants as monotherapy in bipolar patients.

Failed second line: refer.

**Mixed episode**, i.e. alternating shifts in mood within an episode, or **Rapid cycling**, i.e. at least 4 mood episodes demarcated by full remission in a 12-month period.

Stop antidepressants.

Investigate for possible medical condition that may precipitate cycling, e.g. hypothyroidism or alcohol abuse.

First line

- 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.
  - Dosing in patients with renal impairment is complex and should be done using therapeutic drug monitoring in consultation with a specialist.

- Lamotrigine, oral, initially 25 mg daily.
  - Increase by 25–50 mg daily at fortnightly intervals to 100–200 mg daily.

**AND/OR**

- Carbamazepine oral 100 mg 12 hourly starting dose.
  - Increase by 100–200 mg daily at weekly intervals according to response and adverse events.
  - Usual maximal dose: 600 mg 12 hourly.

**REFERRAL**

To psychiatric services:

- » Mixed or rapid cycling bipolar disorder.
- » Depressive episodes in bipolar patients not responding to second line treatment.
- » Manic episodes not responding to treatment.

**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. Such presentations may fluctuate and be accompanied by disturbed behaviour, e.g. agitated/stupor as well as experiences of visual, tactile or gustatory hallucinations and even paranoid ideation.

**Note:**

Many acute medical emergencies can present as delirium or apparent acute psychosis.

**GENERAL MEASURES**

Hospitalisation is mandatory for physical and environmental support.

Control the acute disturbance.

Laboratory testing/medical investigations where indicated i.e. to exclude or diagnose an underlying medical problem, the treatment of which is the primary management where delirium has been diagnosed.

**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:**

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 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 drug to take effect.

Repeated IM doses of benzodiazepines may result in toxicity owing to accumulation.

**15.3 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, as well as social withdrawal. Irritability may also occur as the presenting mood state, both in association with sadness or as the primary feature (especially amongst adolescents). Disturbances, i.e. reduction in sleep, appetite, energy, motivation, concentration and memory may occur.

The patient may report feelings of worthlessness as well as hopelessness and thoughts of suicide. Symptoms are usually present for at least two weeks and impact on the person's ability to function normally.

Consider underlying medical conditions that may present with depression, e.g. thyroid disease.

### GENERAL MEASURES

Supportive psychotherapy may be of benefit.

Counseling of patient and family

Review social factors.

Electroconvulsive therapy is indicated under specific circumstances in consultation with a specialist.

### MEDICINE TREATMENT

#### Antidepressant therapy

All antidepressants take 4–6 weeks to achieve their maximum effect. Some patients may experience an initial response within the first 1–2 weeks. There is little evidence to support combination drug treatment.

Tricyclic antidepressants (TCA) and selective serotonin reuptake inhibitors (SSRIs) are of equal efficacy.

The choice of therapy is guided by comorbid states, e.g. in patients with cardiac disease avoid TCAs and in the elderly use TCAs and SSRIs with caution.

Following remission continue the pharmacotherapy for at least another 6 months.

Thereafter review the need for ongoing pharmacotherapy. When discontinuing the medication, taper off slowly to avoid discontinuation symptoms. If there is a recurrence, reinstitute the medication at the same dose.

Patients with 3 or more episodes may require maintenance pharmacotherapy to be reviewed every 2 years.

Adolescents with depression should be treated by a specialist only, due to the increased risk of suicidal ideation when treated with SSRIs.

#### Major depressive disorder

##### First line

- 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.
  - Doses in excess of 150 mg: consult a psychiatrist.

OR

- 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, 20–40 mg daily.

If a sedating antidepressant is required and TCAs cannot be used:

- Mianserin, oral, 10 mg at night. Specialist initiated.
  - Increase incrementally by 10 mg every seven days to a maximum of 60 mg.

Second line

If on an SSRI change to the other SSRI or a TCA.

If on a TCA change to a SSRI.

If initially on fluoxetine, wait for seven days after stopping fluoxetine before starting citalopram.

**REFERRAL**

- » Inadequate response to treatment.
- » High suicide risk.
- » Psychotic features.

**15.4 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 an undiagnosed major depressive disorder as well as substance related conditions.

**GENERAL MEASURES**

As for Major Depressive Disorder.

**MEDICINE TREATMENT**

As for Major Depressive Disorder.

**REFERRAL**

- » No response to treatment.

## 15.5 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 or concentration as well as mood as a consequence of such concerns. Physical symptoms such as muscle tension or tremulousness may also be reported. Such symptoms will interfere with normal functioning.

### GENERAL MEASURES

Crisis management may be needed.

Psychotherapy.

Most patients can be treated as outpatients, but some may need to be admitted.

### MEDICINE TREATMENT

Indicated where the symptoms are interfering with normal functions of daily living.

Where there is concomitant drug/alcohol dependence or a comorbid major depressive episode, an antidepressant, e.g. an SSRI may be a more appropriate agent of choice.

#### 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.

#### Maintenance therapy

- SSRI, e.g.:
- Fluoxetine, oral, 20–40mg daily. Specialist initiated.
  - Duration of therapy: variable, although the condition tends to be chronic.
  - Extended medicine treatment should be monitored by a specialist.

#### CAUTION

Prolonged treatment with benzodiazepines often leads to tolerance and withdrawal symptoms if the drug is discontinued abruptly.  
Combination therapy with more than one benzodiazepine is not indicated.

**REFERRAL**

- » Ongoing symptoms despite treatment.

**15.6 OBSESSIVE-COMPULSIVE DISORDER**

F42

**DESCRIPTION**

This condition is characterised by the presence of obsessions, i.e. persistent intrusive thoughts or concerns e.g. related to contamination, and is usually associated with compulsions, i.e. mental acts or behaviours related to the obsessions e.g. excessive hand washing. Such thoughts and actions may take up excessive periods of the patient's day and interfere with daily functioning. Generally the features are distressing to the patient.

**REFERRAL**

- » All to psychiatrist.

**15.7 PANIC DISORDER**

F41.0

**DESCRIPTION**

A panic attack is generally 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. There will usually be accompanying physical symptoms such as rapid pulse/palpitations as well as shortness of breath, possibly dizziness and sweating. A tendency towards panic attacks, i.e. recurrent episodes, may signify the presence of a panic disorder. Such a condition does, by definition, significantly impair the patient, interfering with their ability to function normally.

**GENERAL MEASURES**

Psycho-education and reassurance.

Psychotherapy, e.g. cognitive-behaviour therapy.

Always consider the possibility of an underlying medical condition, e.g. thyrotoxicosis, etc.

## 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.:
- Diazepam, oral, 2–5 mg as a single dose.

#### OR

- Diazepam, IV, 5–10 mg as a single dose.

#### OR

- Clonazepam, IM/oral, 0.5–1 mg as a single dose.

#### OR

- Lorazepam, IM, 1–2 mg as a single dose.

### Maintenance antidepressant therapy

If panic disorder is diagnosed, long-term treatment may be required. Refer the patient.

Most patients can be treated as outpatients, but some may need to be admitted.

- SSRI, e.g.:
- Fluoxetine, oral, 20 mg daily.
  - Start with the lowest possible dose available because of increased sensitivity to side effects.
  - Duration of therapy: variable, initially 6 months–1 year.
  - Extended medicine treatment over many years and even life-long may be necessary, except where cognitive-behavioural therapy has been successful.
  - Relapses may occur when treatment is discontinued.

## REFERRAL

- » Recurrent panic attacks/panic disorder.

## 15.8 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 experienced by the patient as traumatic. In this regard, 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 between 2 days and 4 weeks whereas the symptoms posttraumatic stress disorder last longer than 4 weeks, and may arise after 4 weeks of the traumatic incident.

### **GENERAL MEASURES**

Reassurance and support of patient and family.

Appropriate medical attention.

Psychotherapy, as indicated by clinical presentation and usually of a supportive/cognitive-behavioural nature. Trauma debriefing has been questioned as a routine approach.

### **MEDICINE TREATMENT**

#### **Acute management**

For anxiety and insomnia:

- Benzodiazepines, repeated as necessary to control symptoms, e.g.:
- Diazepam, oral, 2–5 mg as a single dose.

**OR**

In more severe cases:

- Diazepam, IV, 5-10 mg as a single dose.

**OR**

- Clonazepam, IM/oral, 0.5–1 mg as a single dose.

**OR**

- Lorazepam, IM, 1–2 mg as a single dose.

#### **Maintenance antidepressant therapy**

Indicated for features of post-traumatic stress disorder as well as the possibility of an emergent, comorbid major depressive disorder.

See Section 15.3: Depressive Disorder, Major.

### **REFERRAL**

- » Persistent symptoms.
- » Inadequate response to treatment.
- » Comorbid conditions.

## 15.9 PSYCHOSIS, ACUTE

### DESCRIPTION

Psychosis is a clinical state characterised by loss of contact with reality. In such an instance the patient may experience perceptual disturbances, e.g. hallucinations that are generally auditory, as well as disturbances of thought content i.e. 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 as well as medical conditions e.g. certain types of epilepsy and HIV. The presentation may be acute or chronic. Patients generally have no insight into their symptoms and may be resistant to intervention.

See section 15.1: Bipolar Disorder and section 15.10: Schizophrenia.

## 15.10 SCHIZOPHRENIA

F20

### DESCRIPTION

Schizophrenia is characterised by psychotic episodes, and is typically accompanied by a deterioration in social and occupational functioning as well as general functioning, i.e. tasks of daily living such as hygiene and grooming. Whilst the presentation may be acute, typically the sufferer's illness tends to have a chronic course.

### GENERAL MEASURES

Supportive psychotherapy and psycho-educational group therapy for patients and family members.

### MEDICINE TREATMENT

#### Psychotic episode

#### Acute management

For agitated and acutely disturbed patient:

- Haloperidol, IM, 2–5 mg.
  - This can be repeated in 60 minutes, if required.
  - Monitor vital signs and beware of acute dystonia.
  - Exercise caution when the total dose exceeds 10 mg as the patient may be exposed to an increased risk of side effects without necessarily adding to the antipsychotic effect.



To limit possibility of dystonia and to enhance sedation:

**ADD**

- Promethazine, IM, 50 mg.
  - In the elderly: 25 mg.

If poor response:

- 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.

**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.

If patient is known to suffer from schizophrenia:

- Zuclopenthixol acetate, IM, 50–150 mg.
  - Repeat after 2–3 days, if necessary.
  - Beware of dystonia, i.e. muscle spasm which can involve any group of muscles but may also impact on respiration and are generally experienced as distressing by the patient.

If acute dystonic reactions develops:

- Biperiden, IM, 2 mg.

Benzodiazepines may be required.

Repeated doses of high potency antipsychotics may lead to the development of a neuroleptic malignant syndrome. In this regard any increase in temperature, muscle rigidity and alterations in consciousness should lead to caution and investigation. If suspected, stop antipsychotic drug use and monitor medically.

**Maintenance therapy**

Specialist initiated.

Review patients every six months by a psychiatrist.

Before progressing to long-term therapy:

- Haloperidol, oral, 1.5–10 mg daily.

**OR**

- Chlorpromazine, oral, 75–300 mg daily in divided doses.

**OR**

If adherence is a problem:

- First generation antipsychotic, e.g.:
- Flupenthixol decanoate, IM, 20–40 mg every 4 weeks.  
**OR**
- Fluphenazine decanoate, IM, 12.5–50 mg every 4 weeks.  
**OR**
- Zuclopenthixol decanoate, IM, 200 mg every 4 weeks.

If haloperidol and chlorpromazine fail and adherence problems have been excluded, refer for consideration of clozapine or other antipsychotics including “atypicals”.

- Risperidone, oral, 1–4 mg daily. Psychiatrist initiated.  
**OR**
- Clozapine, oral, 300–450 mg daily. Psychiatrist initiated.
  - Titrate up to therapeutic dose over 2–3weeks.
  - Frequent WCC monitoring is required – see package insert.

If extrapyramidal side-effects occur with the lowest effective dose of antipsychotic medication:

- 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.

In acute dystonia, parenteral therapy e.g.:

- Biperiden, IM/slow IV, 2 mg.
  - Repeat every 30 minutes if necessary up to a maximum of 4 doses daily.
  - Higher doses of up to 5 mg have been used.

**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 that cannot be managed easily.

## 15.11 WITHDRAWAL FROM SUBSTANCES OF ABUSE

### 15.11.1 ALCOHOL WITHDRAWAL

F10.4

#### GENERAL MEASURES

Admit patients with:

- » convulsions,
- » psychosis,
- » suicidal ideation,
- » significant medical comorbidity such as heart failure and liver disease,
- » inadequate support at home,
- » history of withdrawal delirium.

Assess for comorbid infections and other pathology.

Ensure adequate hydration. Overhydration is a common error made in this setting.

#### MEDICINE TREATMENT

##### Uncomplicated withdrawal

Alcohol detoxification may be managed on an outpatient basis in cases of uncomplicated withdrawal.

- Thiamine, oral, 100 mg daily for 14 days.

##### AND

- 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.

### 15.11.2 ALCOHOL WITHDRAWAL DELIRIUM (DELIRIUM TREMENS)

F10.4

#### DESCRIPTION

Although the typical delirium occurs 2–3 days following cessation of prolonged alcohol intake, reaching a peak at around 5 days, some withdrawal symptoms, such as the typical tremor, may start within 12 hours.

Typical clinical features include:

- » predominantly visual hallucinations,
- » disorientation,
- » agitation,
- » tachycardia, and
- » hypertension.

A low-grade fever may be present. Withdrawal tonic-clonic seizures may occur between 24 and 48 hours following cessation of alcohol intake.

It is important to consider alternative causes, when making the diagnosis. This is especially true for cases with an atypical presentation.

Similar symptoms may occur following withdrawal from other sedative-hypnotic agents.

Mortality figures vary from 1–5%. Subsequent episodes of withdrawal progressively worsen.

### GENERAL MEASURES

See section 15.2: Confusional states/Delirium for management. In addition: Monitor vital signs regularly. Cardiac monitoring and oximetry should be used when administering large doses of benzodiazepines.

Correct dehydration and abnormalities of electrolytes and nutrition.

Consider parenteral fluids to compensate for severe losses, i.e. in hyperthermia.

Consider meningitis as part of the differential diagnosis in febrile patients.

Consider referring appropriate patients to a formal withdrawal and rehabilitation programme.

### MEDICINE TREATMENT

Symptom-triggered regimens are associated with administering a smaller total dose of medication and a shorter total hospital stay. Administer drug doses according to severity of symptoms. See Section 15.11: Withdrawal from Substances of Abuse.

- 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, 1–2 mg as a single dose.
  - If no response, repeat dose after 60 minutes.
  - Maximum daily dose: 10 mg.

#### OR

- Lorazepam, IM, 1–4 mg every 30–60 minutes until patient is sedated.
  - Repeat doses hourly to maintain mild sedation.
  - Maximum daily dose: 6 mg.

Once patient is sedated, i.e. light somnolence, maintain mild sedation with:

- Diazepam, oral, 5–20 mg 2–6 hourly.

#### 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.

Neuroleptic medicines, i.e. medicines such as haloperidol, are associated with a reduced seizure threshold. Consider only for severe agitation and restlessness and give in combination with one of the sedative-hypnotic agents above.

- 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, 100 mg daily.

### 15.11.3 OPIATE WITHDRAWAL, E.G. HEROIN

F11.2

#### DESCRIPTION

Withdrawal is generally poorly tolerated, but not dangerous, except in very frail debilitated patients or during the first trimester of pregnancy.

#### MEDICINE TREATMENT

##### Mild withdrawal

May be done 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 up to 8 hourly as required.

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

Methadone syrup should be used in a specialist rehabilitation centre.

Day 1: Only if clinical signs of withdrawal are present:

- Methadone, oral, 10 mg.
  - If symptoms are still present after 1 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.

Day 2:

Repeat total dose of day 1 as a single or 2 divided doses.

Day 3 onwards:

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.

### **15.11.4 STIMULANT WITHDRAWAL, INCLUDING METHAMPHETAMINES AND COCAINE**

F14.2

#### **GENERAL MEASURES**

These patients usually do not require admission.

Beware of depression and assess suicide risk.

#### **MEDICINE TREATMENT**

No substitute drug available for detoxification.

For severe anxiety, irritability and insomnia:

- Benzodiazepines, short-term, e.g.:
- Diazepam, oral, 5–10 mg 8 hourly for 5–7 days.

**15.11.5 METHAQUALONE AND/OR CANNABIS WITHDRAWAL**

F12.2

Only for intolerable withdrawal symptoms:

- Diazepam, oral, 5 mg as needed.
  - Maximum dose: 20 mg daily.

**15.11.6 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. Be patient.

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:** drugs have been included for comparison only.

Decrease the dose of diazepam every 2 weeks by 2.5 mg. If symptoms reappear increase the dose a little and reduce more slowly.

# CHAPTER 16

## RESPIRATORY SYSTEM

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### 16.1 ASTHMA, ACUTE

J46

#### GENERAL MEASURES

Ensure adequate hydration.

#### MEDICINE TREATMENT

If hypoxic:

- Oxygen.

Admit to an intensive care unit in acute, severe asthma (altered mental status, paradoxical chest movement and absence of wheeze), when there is no response to treatment, as intubation and ventilatory support may be required.

- Mix salbutamol 2.5 mg with ipratropium bromide 0.5 mg and sodium chloride 0.9% 2 mL to give a solution of 5 mL (1 mL salbutamol, 2 mL ipratropium and 2 mL sodium chloride 0.9%).
  - Nebulise continuously at a flow rate of 6-8 L/minute until the peak expiratory flow rate (PEFR) is > 60%.
  - Repeat 4–6 hourly.
  - Continue nebulisations until PEFR returns to 80% of predicted, or of personal best.

#### PLUS

- Prednisone, oral, 40 mg immediately.

Follow with:

- Prednisone, oral, 40 mg daily for at least 5 days.
  - Stop when there is a response.

#### OR

In patients who cannot use oral therapy:

- Hydrocortisone, IV, 100 mg 6 hourly.

Once oral medication can be taken, follow with:

- Prednisone, oral, 40 mg daily for 7 days.

Monitor response closely by PEFR and clinical signs. Exclude upper airway obstruction, vocal cord dysfunction and anaphylaxis.



**16.2 ASTHMA, CHRONIC PERSISTENT**

J45

**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 pharmacological classification is hazardous and must be avoided.

Nocturnal symptoms of cough and wheeze and the regular need for bronchodilators are usually indicative of poor control of asthma. Consider adjustment of treatment and specialist referral.

Correct of inhaler technique should be demonstrated and checked regularly by way of placebo inhalers, as the majority of asthmatic patients do not use their inhalers correctly.

**MAINTENANCE THERAPY****▪ Inhaled corticosteroids (ICS), e.g.:**

ICS are the mainstay of treatment in chronic asthma:

- Beclomethasone, inhaled, 100 mcg 12 hourly starting dose.
  - Increase daily dose by 100 mcg 12 hourly every month, until optimum effect.
  - Maximum total daily dose: 1 200 mcg.
  - If well after 6 months reduce daily dose by 100 mcg every month until a dose of 200 mcg 12 hourly.
  - Dose adjustments may be required at change of seasons.

**PLUS**

As reliever/rescue therapy:

- $\beta_2$ -stimulants, e.g.:
- Salbutamol, MDI, 200 mcg, 6 hourly as necessary.

Poor control as evidenced by excessive use of  $\beta_2$  stimulants should warrant review.

If insufficient response to adequate steroids and salbutamol:

**ADD**

- Theophylline modified release, oral.
  - Initial dose: 150–200 mg 12 hourly.
  - Increase to 300 mg 12 hourly.
  - Further dose increases will require blood level monitoring after adherence has been considered.

If asthma is still not well controlled:

**ADD**

In patients who have followed the above regimen, a short course of long acting beta agonist therapy, e.g.:

- Formoterol, inhaled, 12 mcg 12 hourly. Specialist initiated.

Review efficacy after three months.

Failure of above therapy:

**ADD**

- Prednisone, oral, 5–10 mg daily.

Refer to specialist.

For short-term exacerbations in patients not responding to the above:

- Prednisone, oral, 30 mg daily for 10 days.

Refer to a tertiary centre.

**Exercise-induced asthma**

Recognised by symptoms appearing within 5–7 minutes after starting exercise and associated with a  $\geq 15\%$  reduction in FEV<sub>1</sub> and may require the use of an inhaled  $\beta_2$ -stimulant 15–20 minutes before exercise. These patients usually do not require steroids.

**Intercurrent bacterial infections**

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 X-ray or a fever  $>38^\circ\text{C}$ . See section 16.6: Pneumonia, community acquired.

## 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 than usual. Antibiotic choices should always 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.

### 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 culture and sensitivity determination are indicated in all cases.

- Ampicillin, IV, 1 g 6 hourly.

### **PLUS**

- Gentamicin, IV, 6 mg/kg daily.

Switch to oral treatment once there is an improvement:

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

Subsequent antibiotic therapy should be based on results of sputum investigations.

### **Inhaled bronchodilators**

Bronchodilators may be used as for asthma or COPD, if airflow obstruction is present.

There is no indication for inhaled corticosteroids.

### **Prophylaxis**

Annual influenza vaccine. See section 9.2: Adult vaccination.

## 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)

J44.9

### DESCRIPTION

COPD is classified from stage I to stage IV. However, the disease is not static; 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 severity based on % predicted post-bronchodilator FEV<sub>1</sub>:

Stage 1 (I)	<b>Mild COPD</b> Airflow limitation FEV <sub>1</sub> ≥ 80% of predicted symptoms of chronic cough and sputum production.
Stage 2 (II)	<b>Moderate COPD</b> Worsening airflow limitation 50% ≤ FEV <sub>1</sub> ≤ 80% predicted with shortness of breath on exertion with cough and sputum production.
Stage 3 (III)	<b>Severe COPD</b> Further worsening airflow limitation 30% ≤ FEV <sub>1</sub> ≤ 50% predicted with shortness of breath, decreased exercise capacity and fatigue.
Stage 4 (IV)	<b>Very severe COPD</b> Airflow limitation FEV <sub>1</sub> < 30%; or FEV <sub>1</sub> ≤ 50% in respiratory failure (PaO <sub>2</sub> < 8kPa) and/or presence of cor pulmonale.

### GENERAL MEASURES

Stop smoking.

Pulmonary rehabilitation, including exercise rehabilitation (under supervision) and cough techniques.

### MEDICINE TREATMENT

#### Note:

Correct inhaler technique should be demonstrated and checked regularly.

#### Management of acute exacerbations

If available, check blood gases looking both for the presence of hypoxaemia and hypercarbia. Some patients with long-standing lung disease may drive respiration using hypoxia rather than CO<sub>2</sub> retention. This may result in dangerous hypoventilation and drowsiness when exposed to uncontrolled high flow oxygen therapy.

Ideally, the response to face-mask oxygen therapy should be determined both clinically and using repeat blood gases, with a rise in PaCO<sub>2</sub> > 1–1.5 kPa prompting consideration of change to a face-mask delivering a lower inspired oxygen concentration (e.g. 28%).

Where blood gases are not readily available, clinical status should be reviewed regularly to check for increasing drowsiness or hypoventilation.

Where resources for 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.

- Mix salbutamol 2.5 mg with ipratropium bromide 0.5 mg and sodium chloride 0.9% 2 mL to give a solution of 5 mL (1 mL salbutamol, 2 mL ipratropium and 2 mL sodium chloride 0.9%).
  - Nebulise continuously at a flow rate of 6-8 L/minute.
  - Repeat 4–6 hourly.

#### **PLUS**

- Prednisone, oral, 40 mg immediately.

Follow with:

- Prednisone, oral, 40 mg daily for 7 days.

#### **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 14 days.
  - Monitor response closely by PEF and clinical signs.

### **Chronic therapy**

COPD with any symptoms.

As reliever therapy:

- $\beta_2$ -stimulants, e.g.:
- Salbutamol, MDI, 200 mcg 6 hourly as needed using a large volume spacer.

For stage III–IV or frequent exacerbations (2 or more per year):

#### **ADD**

- Inhaled corticosteroids, e.g.:
- Beclomethasone, inhaled, 100 mcg 12 hourly starting dose.
  - Increase daily dose by 100 mcg 12 hourly every month, until optimum effect.
  - Maximum total daily dose: 1 200 mcg.
  - If well after 6 months reduce daily dose by 100 mcg every month until a dose of 200 mcg 12 hourly.

If no response:

**ADD**

- Long acting  $\beta_2$ -agonist, e.g.:
- Formoterol, inhaled 12 mcg 12 hourly. Specialist initiated.

If inadequate control with above therapy:

- Theophylline, slow release, oral, 125 mg (or 150 mg) 12 hourly. Specialist consultation.
  - Increase the dose according to clinical response up to 600 mg.
  - Any dose adjustment above this should be done with monitoring of theophylline levels.
  - Ongoing use of theophylline should be re-evaluated periodically. If there is no benefit after 12 weeks, discontinue theophylline.
  - Interacts with many other drugs including antibiotics such as erythromycin and fluoroquinolones, e.g. ciprofloxacin.

**Corticosteroids**

A trial of corticosteroids, unless contraindicated, is recommended for all new patients. This is to exclude asthma and to evaluate whether there is significant reversibility. The only way that reversibility can be adequately assessed is with a flow volume loop pre and post steroids.

Monitor steroid usage by objective parameters such as FEV<sub>1</sub> and six minute walking test.

For acute exacerbations:

- Prednisone, oral, 40 mg daily for 7–10 days.

**Antibiotic therapy**

Exacerbations of chronic bronchitis are, in contrast to exacerbations in asthma, frequently related to bacterial infections. Only severe exacerbations i.e. increased sputum volume and purulence and increasing dyspnoea, benefit from antibiotics.

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

Penicillin allergy:

- Macrolide, e.g.:
- Erythromycin, oral, 500 mg 6 hourly for 5 days.
  
- Annual influenza vaccination.

**REFERRAL**

- » Assessment for long-term home-based oxygen therapy.
- » Symptoms that are disproportionate to level of airflow obstruction.
- » Onset in early age.
- » Lifetime history of being a non-smoker with COPD.
- » Recurrent exacerbations, i.e. > 3 per year.
- » Failure to respond to treatment.
- » Pre-operative assessment for surgical procedures.

**16.5 LUNG ABSCESS**

J85

**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 4 times a day.

Nutritional support.

**MEDICINE TREATMENT**

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

**PLUS**

- Metronidazole, IV, 500 mg 8 hourly.

In situations where gram negative organisms are suspected or cultured:

**ADD**

- Gentamicin, IV, 6 mg/kg daily.

Follow with:

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

Penicillin allergy:

- Clindamycin, IV, 600 mg 8 hourly.

Where gram negative organisms are suspected or cultured:

**ADD**

- Gentamicin, IV, 6 mg/kg daily.

Followed with:

- Clindamycin, oral, 300 mg 8 hourly.

Duration of therapy is until CRP has normalised and there is no fluid level, and is usually for several weeks.

**REFERRAL**

- » All patients for specialist opinion regarding surgical intervention once the acute infection has settled.
- » Diagnostic work-up, including bronchoscopy to exclude foreign body or tumour.
- » No response to treatment.
- » Complications, such as empyema, septicaemia, haemoptysis, etc.

**16.6 PNEUMONIA, COMMUNITY ACQUIRED**

J18

The CURB-65 score is used to determine the severity, prognosis and necessity for hospital admission for intravenous antibiotic administration for patients with pneumonia.

**CURB-65:**

C – Confusion	score = 1
U – Urea > 7 mmol/L	score = 1
R – Respiratory rate $\geq$ 30/minute	score = 1
B – BP < 90 mmHg systolic or 60mmHg diastolic	score = 1 for either
65– Age $\geq$ 65 years	score = 1
Score 0 – 1	Home treatment possible (if social circumstances permit)
Score 2	Hospital therapy indicated
Score $\geq$ 3:	Severe pneumonia

**GENERAL MEASURES**

Ensure hydration and nutritional status.

Even in clinically classic cases of pneumonia, exclude tuberculosis. An initial chest X-ray should routinely be followed by a follow-up X-ray after completion of therapy in all but very mild cases in otherwise healthy adults, to ensure complete resolution of the pneumonia. With an uncomplicated clinical course this should be done only after 4–6 weeks, as radiological resolution may be delayed. Follow-up X-rays are indicated earlier only when complications are suspected, e.g. empyema, abscess or pneumothorax.

At the onset of pneumonia X-ray changes may be unimpressive, and may develop fully only after a few days.

A control chest X-ray is always indicated after attempted pleural fluid aspiration to exclude pneumothorax, as this may need drainage.

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.



**MEDICINE TREATMENT**

- Oxygen via nasal prongs or facial mask.

Adequate analgesia for pleuritic chest pain. See chapter 9: Pain.

**Antimicrobial therapy**

Duration of antibiotic therapy is guided by clinical response, but should be at least 5 days.

Prolonged fever and clinical signs may be due to unrecognised TB or any of the complications (such as empyema), the incorrect choice of antibiotic, or to an underlying bronchus obstruction (foreign body or carcinoma). These patients should be further investigated.

**Uncomplicated community-acquired pneumonia**

CURB-65 score 0–2, without co-morbidity:

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

**OR**

- Ampicillin, IV, 1 g 6 hourly.

When temperature has settled follow with:

- Amoxicillin, oral, 1 g 8 hourly.

If poor response after 48–72 hours:

**ADD**

- Erythromycin, oral, 500 mg 6 hourly.

Penicillin allergy:

- Moxifloxacin, oral, 400 mg daily.

Moxifloxacin has adequate cover for *Pneumococcus*, *Haemophilus*, *Klebsiella* and the atypical bacteria.

**Patients > 65 years or comorbid disease**

CURB-65 score 0–2:

- 3<sup>rd</sup> generation cephalosporin e.g.:
- Ceftriaxone, IV, 1 g daily.

Penicillin allergy:

- Moxifloxacin, oral, 400 mg daily.

If poor response after 48–72 hours:

**ADD**

- Doxycycline, oral, 200 mg immediately.
  - Followed by 100 mg 12 hourly.

**OR**

- Erythromycin, oral, 500 mg 6 hourly.

**Severe pneumonia (CURB-65 score  $\geq$  3)**

- Ceftriaxone, IV, 1 g daily.

**PLUS**

- Clarithromycin, IV, 500 mg 12 hourly.

In severe penicillin allergy:

- Moxifloxacin, IV, 400 mg daily.

## 16.7 PNEUMONIA, ASPIRATION

J69.0

### DESCRIPTION

Pneumonia following aspiration of gastric content and/or commensal organisms from the oropharynx.

There may be solid (food) particles or other foreign bodies aspirated. The organisms involved are polymicrobial, i.e. gram-positive and anaerobes. The manifestations are as those of community-acquired pneumonia.

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.

Aspiration of gastric acid causes an acute fulminating chemical pneumonia with rapidly developing severe hypoxia and has a high mortality, requiring admission to an ICU for ventilatory support in all cases.

### MEDICINE TREATMENT

**Antimicrobial therapy**

Continue therapy until there are no features of sepsis.

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

**PLUS**

- Metronidazole, oral, 400 mg 8 hourly.

If nosocomial infection or nursing home resident:

**ADD**

- Amikacin 15 mg/kg daily for 5 days.

Follow with:

- Amoxicillin, oral, 500 mg 8 hourly.

**PLUS**

- Metronidazole, oral, 400 mg 8 hourly.

Penicillin allergy:

- Clindamycin, IV, 600 mg 8 hourly.

**REFERRAL**

- » Hypoxaemia non-responsive to facemask oxygen.
- » Suspected foreign body aspiration.
- » Suspected chemical aspiration pneumonia.
- » Non-resolving pneumonia.

## 16.8 EMPYEMA

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.

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 above.

If not a complication of pneumonia:

- Ampicillin, IV, 1g 6 hourly.

**PLUS**

- Metronidazole, IV, 500 mg 8 hourly.

Follow with:

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

Treatment duration is until drainage is complete.

**Penetrating chest wall injury**

- Cloxacillin, IV, 2 g 6 hourly.

**REFERRAL**

- » Loculated empyema or inadequate drainage.
- » Chronic empyema with pleural thickening and restrictive lung disease, requiring surgical decortications.

**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 consulted.

**DESCRIPTION**

A chronic, granulomatous infection of the lungs caused by *M. tuberculosis*. Pulmonary tuberculosis is a serious and growing health problem in South Africa, which is exacerbated by HIV/AIDS and multidrug resistant tuberculosis (MDR-TB).

**Note:**

All patients on TB treatment must be entered into a TB register to enable the completion of quarterly reports for case finding and case holding. This is essential for TB control at local, provincial and national level.

**Diagnosis**

The diagnosis in adults is made on positive sputum smears for acid-fast bacilli (AFB). If two sputum smears are negative then a culture should be done to confirm diagnosis. If the patient has had prior TB, culture and sensitivity should be done.

Sputum induction with ultrasonic nebulised sodium chloride 5% has been shown to increase the yield of positive smear or culture. This may be of special value in the context of HIV and AIDS, as in those patients TB frequently presents without cavitation and hence there is a low sputum smear yield. Patients with HIV often have lymphadenopathy, and a fine needle aspiration smear for AFBs is often positive. In exceptional cases bronchial washings may have to be done to confirm the diagnosis.

**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	H – Isoniazid (INH)
Z – Pyrazinamide	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

**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' history, starting with pleuritic pain, and often associated with a dry cough, fever, malaise and, sometimes, progressive shortness of breath.

**DIAGNOSIS**

The diagnosis is suspected on clinical manifestations and on the demonstration of a pleural effusion on a chest X-ray. Although a definite diagnosis can only be made by demonstrating the organisms on smear or culture, or on histology of a (needle) pleural biopsy, the presence of a pleural exudate with a high adenosine de-aminase (ADA) level on biochemistry and a predominantly lymphocytic cells profile on cytology of the pleural fluid, is usually adequate to diagnose TB pleurisy. A pleural biopsy is recommended in people older than 50 years unless there is strong suspicion of TB.

Treatment is as for pulmonary TB.

**Note:**

Total drainage by aspiration or under-water tube-drainage is not needed. For large effusions that cause dyspnoea drain a maximum of 1 litre at a time. 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 chest X-ray 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.
- » Persistent bronchopleural fistula.

## 16.11 MULTIDRUG-RESISTANT (MDR) TB

U50.0

**Never treat for MDR TB without culture and sensitivity results.**

**All cases should be discussed with a regional specialist centre.**

## 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.

All patients with HIV and MDR TB qualify for ART irrespective of CD4 count.

## GENERAL MEASURES

Screen all close contacts for signs and symptoms of MDR TB and by sputum sampling to detect early disease.

## MEDICINE TREATMENT

### MDR TB prophylaxis

Treat all new cases of sputum positive tuberculosis with a regimen containing 4 agents for the full duration of the 2-month initial intensive phase followed by 2 agents for the full duration of the 4-month consolidation phase (see below).

Never add a single agent to a TB treatment regimen that has, apparently, failed. Rather wait until sensitivity results become available before starting a MDR treatment regimen.

The effectiveness of preventive therapy in persons exposed to MDR TB bacteria is not known.

**MDR TB Treatment**

Prolonged treatment, usually for at least 18 months, is required in patients diagnosed with MDR TB.

The treatment of MDR TB should be co-ordinated and monitored by the dedicated provincial MDR TB treatment centres. All patients should be hospitalised in a dedicated MDR TB hospital for at least the initial 4 months of treatment, but preferably until sputum conversion has occurred.

After discharge from hospital, patients should be followed up at dedicated clinics until the end of their treatment.

Initial MDR TB treatment may occasionally have to be initiated before admission to a TB hospital, and MDR patients may be seen at health care facilities for treatment complications or for unrelated conditions.

**Standardised regimen for treatment of MDR tuberculosis in South Africa.**

Specialist initiated.

For MDR-TB patients previously treated with TB regimen 1 or 2:

Intensive phase: at least 6 months, guided by TB culture conversion

	<b>&lt;50 kg</b>	<b>50–65 kg</b>	<b>&gt;65 kg</b>
Kanamycin*	500–750 mg	1 000 mg	1 000 mg
Moxifloxacin	400 mg	400 mg	400 mg
Ethionamide	500 mg	750 mg	750–1 000 mg
Terizidone	750 mg	750 mg	750–1 000 mg
Pyrazinamide	1 000–1750 mg	1 750–2 000 mg	2 000–2 500 mg

\*Consider capreomycin in patients with renal insufficiency, hearing loss, or peripheral neuropathy.

Continuation phase: at least 18 months after TB culture conversion

	<b>&lt; 50 kg</b>	<b>50–65 kg</b>	<b>&gt; 65 kg</b>
Moxifloxacin	400 mg	400 mg	400 mg
Ethionamide	500 mg	750 mg	750–1 000 mg
Terizidone	750 mg	750 mg	750–1 000 mg
Pyrazinamide	1 000–1750 mg	1 750–2 000 mg	2 000–2 500 mg

**Notes:**

Patients with resistance to the above drugs should all be treated exclusively in specialised centres.

Birth control should be used in women of a child-bearing age, as the agents are teratogenic. In pregnant women, the benefits of MDR management outweigh the teratogenicity risks.

Amend the doses of the medication used in patients with impaired renal function.

Conduct regular hearing tests/audiograms on patients on aminoglycosides.

**XDR TB**

Represents a progression from MDR TB to further include resistance to second line anti-TB drugs, including any fluoroquinolone and at least one of three second line injectables, namely. kanamycin, amikacin or capreomycin. Confirmation of infection with XDR-TB requires drug susceptibility testing.

Isolate patients suspected of having XDR-TB in an acute infectious disease setting, and then triage for further management based on laboratory results. Individualised regimens are more specific as standardised regimens poorly identify resistant drug patterns.

Treatment of XDR TB should include any susceptible first line agent and any appropriate second line drug to achieve a regimen with minimum 4–5 effective drugs for duration of 18–24 months.



# CHAPTER 17

## EAR, NOSE AND THROAT DISORDERS

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### 17.1 EPIGLOTTITIS

J05.1

#### DESCRIPTION

A special form of acute laryngitis, in which the inflammatory changes affect mainly the loosely attached mucosa of the epiglottis and the whole supraglottis.

#### GENERAL MEASURES

Secure the airway.  
Adequate hydration.

#### MEDICINE TREATMENT

Humidified oxygen.

3<sup>rd</sup> generation cephalosporin, e.g.:

- Ceftriaxone, IV, 1 g daily for 5–10 days.

Switch to oral therapy as soon as possible:

- Amoxicillin/clavulanic acid, oral, 875/125 mg 12 hourly for 10 days.

#### ACUTE STAGE

For significant swelling:

- Hydrocortisone, IV, 100 mg immediately as a single dose.

Follow with:

- Prednisone, oral, 40 mg daily.

Can be stopped abruptly after a few days, once the swelling has subsided.

#### AND

- Adrenaline (epinephrine)1:1 000, 1 mL nebulised.
  - Dilute to 5 mL with sodium chloride 0.9% and administer 4–6 hourly.

### 17.2 EPISTAXIS

R04.0

#### GENERAL MEASURES

Control bleeding by applying digital pressure over the cartilaginous part of the nose.

Tilt head forward, not backwards to avoid pooling of blood in the posterior pharynx. Resuscitate, including blood transfusion, if necessary.

If the bleeding site can be identified, cauterise under local anaesthetic.

**Anterior bleeding:** insert an anterior nasal pack, using ribbon-gauze coated with BIPP (bismuth iodoform paraffin paste).

**Posterior bleeding:** insert a posterior nasal pack, using a Foley's catheter. An anterior nasal pack should then be inserted. Deflate after 24 hours. A posterior nasal pack should not be left in place for more than 48 hours.

## REFERRAL

- » Persistent bleeding.
- » Systemic disease.

## 17.3 RHINITIS, ALLERGIC, PERSISTENT

J30.4

### GENERAL MEASURES

Avoid allergens and irritants.

Provide education on the correct technique of administering topical medicines and monitor from time to time. Incorrect technique is a common cause of treatment failure.

### MEDICINE TREATMENT

- Corticosteroids, e.g. beclomethasone, topical, aqueous nasal solution, 1 spray of 50 mcg in each nostril 12 hourly.

If symptoms persist despite adequate technique

#### ADD

- Cetirizine, oral, 10 mg daily.

#### OR

If the predominant symptom is 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.

## 17.4 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 present with visual disturbances (often irreversible), ophthalmoplegia and proptosis. 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.

### GENERAL MEASURES

Radiography of the paranasal sinuses, preferably by CT scan, should be done in all cases.

Sodium chloride 0.9% spray or irrigation of the nasal cavity may provide symptomatic relief.

### MEDICINE TREATMENT

- Ceftriaxone, IV, 2 g 12 hourly and **refer**.

Topical nasal decongestants, e.g.:

- Oxymetazoline 0.05%, intranasal, administered 8 hourly.

### URGENT REFERRAL

- » Proptosis.
- » Ophthalmoplegia.

### REFERRAL

- » After initiating antimicrobial therapy, refer to a centre where an appropriate surgical specialist, i.e. ophthalmologist, ENT specialist or neurosurgeon, is available.
- » Suspected fungal sinusitis.

## 17.5 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

### Penicillin allergy

- Macrolide, e.g.:
- Erythromycin, oral, 500 mg 6 hourly.

For patients with upper respiratory tract congestion, consider:

- Cetirizine, oral, 10 mg daily for 10 days.

For pain:

- Ibuprofen, oral, 400 mg 8 hourly.

## REFERRAL

- » No response after 5 days' treatment.
- » No pain relief despite treatment.
- » Bulging eardrum, not responding to treatment after 24 hours.
- » Recurrent otitis media.

## 17.6 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 a further 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.

### 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.

Do not instil anything else 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.

## **17.7 MASTOIDITIS**

H70.9

### **DESCRIPTION**

Infection of the mastoid air cells, usually complicating otitis media. Evidence of external inflammation is present 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.

## 17.8 OTITIS EXTERNA

### 17.8.1 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, 500 mg 12 hourly for 4–6 weeks.

#### 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.

## 17.9 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 ("hot potato") voice, and
- » fever.

#### GENERAL MEASURES

There are 3 main methods:

- » needle aspiration of pus;
- » incision and drainage; or
- » abscess tonsillectomy, either unilateral or bilateral.

## MEDICINE TREATMENT

### Antibiotic therapy

Total duration of therapy: 10 days

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

### PLUS

- Metronidazole, IV, 500 mg 8 hourly.

Follow with:

- Phenoxymethylpenicillin, oral, 500 mg 12 hourly.

### PLUS

- Metronidazole, oral, 400 mg 8 hourly.

### Penicillin allergy

- Clindamycin, IV, 600 mg 8 hourly.

Follow with:

- Clindamycin, oral, 300 mg 8 hourly.

## 17.10 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 cause

Patients frequently present with motion-induced vertigo, which is most often rotational, with nystagmus and thus a positive Dix-Hallpike test. The onset is usually sudden and symptoms intermittent. Associated abnormalities of hearing may be present and associated with nausea and vomiting worse than with central causes. Aetiology includes benign paroxysmal positional vertigo and vestibular neuritis, amongst others.

#### Central cause

Patients may have additional signs of brainstem or cerebellar dysfunction with subtle onset of symptoms, which are constantly present or progressively worsening in severity. 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. Consider patients with possible cerebellar stroke or intracranial space occupying lesion 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 a second session 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.  
This is sedating and patients should not drive or operate heavy machinery

If vomiting continues:

- Metoclopramide, oral, 10 mg 6–8 hourly.

**Cerebellar stroke**

See Section 14.1: Cerebrovascular Disease.

**REFERRAL**

- » Suspected intracranial mass lesions or cerebellar stroke.
- » Suspected vestibular neuritis.
- » Patients not responding to therapy for exclusion of alternative aetiology.



# CHAPTER 18

## EYE DISORDERS

---

### 18.1 CONJUNCTIVITIS

H10

#### 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

Supportive therapy with cold compresses.

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. It may be associated with an upper respiratory tract infection and preauricular lymphadenopathy.

#### MEDICINE TREATMENT

- Sodium chloride 0.9%, eye washes or irrigation.  
If sodium chloride 0.9% is not available use cooled boiled water or 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 allergy. 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.

**PLUS**

- Cetirizine, oral, 10 mg daily.

**REFERRAL**

- » No response to treatment.

**18.1.3 CONJUNCTIVITIS, BACTERIAL**

H13.1\*

**DESCRIPTION**

It is usually bilateral. There is a mucopurulent discharge and there may be matting of lashes in the morning with the eyelids stuck shut. The eyelids may be swollen.

**MEDICINE TREATMENT**

During the day:

- Gentamicin, ophthalmic drops, instill 1 drop 4–6 hourly.

**OR**

- Chloramphenicol 0.5%, ophthalmic drops, instill 1 drop 4–6 hourly.

**AND**

Apply at night:

- Chloramphenicol 1%, ophthalmic ointment.

## 18.2 ENDOPHTHALMITIS, BACTERIAL

H44.0

### DESCRIPTION

Infection of the ocular cavity, which is an emergency as it can cause blindness. This may occur spontaneously (endogenous infection) or after penetrating ocular injury.

Blood should be sent for microscopy, culture and sensitivities. The source of infection should be identified and treated.

### MEDICINE TREATMENT

#### Spontaneous endophthalmitis

Specialist initiated.

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

#### 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.

## 18.3 GLAUCOMA

H40.9

### DESCRIPTION

Glaucoma is characterised by damage to the optic nerve (in the form of cupping) with associated visual field loss, for which raised intra-ocular pressure (IOP) is a primary risk factor. Glaucoma may occur as a primary condition or secondary to other ocular conditions.

Glaucoma can be further classified as acute or chronic and open- versus closed-angle. The condition is usually bilateral, but may be unilateral or asymmetrical (especially with secondary causes).

**Clinical features**

## Chronic 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.

## Acute closed-angle glaucoma:

- » 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.
- » Severely elevated intra-ocular pressure. When measured with finger palpation, the affected eye feels hard, compared to the other eye.

**MEDICINE TREATMENT****Open angle glaucoma chronic**

Refer to an ophthalmology unit for treatment.

**First line****β-blocker**

- Non-selective β-blocker, e.g.:
  - Timolol 0.25%, ophthalmic drops, instill 1 drop 12 hourly.

**OR**

- Selective β-blocker, e.g.:
  - Betaxolol 0.25–0.5%, ophthalmic drops, instill 1 drop 12 hourly.

No response despite adequate adherence:

**ADD**

- Prostaglandin analogues, e.g.:
  - Bimatoprost 0.03%, ophthalmic drops, instill 1 drop daily
    - Use as first line if patient has contra-indication to β-blocker.
    - Use in place of β-blocker if patient has intolerable side effects with β-blocker or if there is no significant reduction in IOP with other drugs.
    - Use in combination with β-blocker if there is significant reduction in IOP with β-blocker, but patient still has progression of disease or target IOP is not reached.

Intolerance to prostaglandin analogue, or no response:

- $\alpha$ -agonist:
- Brimonidine 0.15–0.2%, ophthalmic drops, instill 1 drop 12 hourly.
  - 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  $\beta$ -blocker.
  - Use in combination with  $\beta$ -blocker and prostaglandin analogue if there is significant reduction in IOP with  $\beta$ -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.

In severe cases, as a temporary measure before ocular surgery in consultation with a specialist:

- Carbonic anhydrase inhibitors, e.g.:
- Acetazolamide, oral, 250 mg 6 hourly.

### **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: Pain.

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 vesicular rash on the forehead, upper lid and side of the nose. A minority of patients may develop conjunctivitis, keratitis, uveitis, retinitis and cranial-nerve palsies. Permanent sequelae of ophthalmic zoster infection may include chronic ocular inflammation, loss of vision, and debilitating pain. All patients should be offered HIV testing.

### MEDICINE TREATMENT

- Aciclovir, oral, 800 mg 4 hourly for 7–10 days.

For neuralgic pain:

- Amitriptyline, oral, 25 mg at night for 3 months.

Best results are obtained if treatment is initiated within the first three days of onset of symptoms.

### REFERRAL

- » Positive Hutchinson sign, i.e. vesicle at the tip/side of the nose.
- » Fluorescein staining of cornea (keratitis/ulceration).
- » Decreased vision, i.e. a 2 line fall off in Snellen acuity in affected eye compared to healthy eye or afferent pupil defect.
- » Red eye (uveitis or keratitis).
- » Cranial nerve palsies.

## 18.5 KERATITIS

H16

### 18.5.1 KERATITIS, HERPES SIMPLEX

H16.9

### DESCRIPTION

Associated features: previous history of herpes labialis/keratitis and decreased corneal sensation.

Morphology: dendritic ulcer seen on staining with fluorescein.

### MEDICINE TREATMENT

- Aciclovir 3%, ophthalmic ointment inserted in the lower conjunctival sac five times per day at four hour intervals.
  - Continue for 3 days after ulcer has healed.

**Note:**

Topical corticosteroids are contraindicated in the treatment of dendritic ulcers.

In other settings topical corticosteroids may be used only by personnel with experience in ophthalmology and with access to both a tonometer and a slit lamp.

**18.5.2 KERATITIS, SUPPURATIVE**

H16.0

**DESCRIPTION**

Painful red eye with corneal lesion that stains with fluorescein and has creamy white appearance. If HIV positive or history of injury to eye with plant matter, need high index of suspicion for fungal infection.

**MEDICINE TREATMENT**

Treat only if access to slit lamp, otherwise refer.

Scrape ulcer for microscopy, culture and sensitivity and modify treatment accordingly.

Empiric therapy until culture results become available:

- 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 Gram positive infection:

- Vancomycin, 25 mg/mL, topical.
  - Dilute with sodium chloride 0.9%.

If Gram negative infection:

- Ceftazidime, 50 mg/mL, topical.
  - Dilute with sterile water and preservative-free artificial tears.

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**

- » No access to slit lamp.
- » 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<sup>3</sup>. The characteristic appearance is necrosis, i.e. white exudates, and hemorrhages at the edges of the exudates. Irreversible blindness may occur.

**MEDICINE TREATMENT**

- Ganciclovir, intravitreal, 2 mg once a week.
  - Once immune function has been restored with antiretroviral therapy (CD4  $> 100$  cells/mm<sup>3</sup>) and the features of active retinitis has cleared, maintenance ganciclovir can be stopped but monitor for recurrence.

**REFERRAL**

- » To ophthalmologist.

**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, brow ache, 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, e.g.:
- Dexamethasone 0.1%, ophthalmic drops, instill 1–2 drops 4–6 hourly.



**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)
- Balanced salt 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%

# CHAPTER 19

## POISONING

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### 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.

#### 19.2 SNAKEBITES

T63.0

Snakebites present with minor trauma and, rarely allergy to venom or envenomation syndrome. As the majority of snakes are not identified, the table below illustrates the syndromic management of three main envenomation syndromes namely: cytotoxic, neurotoxic and haemostatic snake bite.

Signs of systemic poisoning:

- » Muscle weakness and/or difficulty in breathing.
- » Difficulty in swallowing or speaking.
- » 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	Haemostatic
Snake species	Puff adder, Gaboon adder, spitting cobra (Mozambique, black-necked, zebra), stiletto snake, night adders, home adders	Black and green mamba, non-spitting cobra (e.g. snouted, Cape, forest, Egyptian, Anchieta)	Rinkhal, 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)
Supportive and symptomatic treatment	Applicable to all	Applicable to all	Applicable to all	Applicable to all
Antivenom for severe or limb or life-threatening bites. See indications for antivenom treatment	Polyvalent antivenom for Puff adder, Gaboon adder and spitting cobras	Polyvalent antivenom for all species	Polyvalent antivenom for rinkhals only	Boomslang antivenom for confirmed boomslang bites only. Not effective in vine snake bite.

## 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.

Secondary infection:

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

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.

### OR

For severe pain:

### ADD

- Opioids, e.g.:
  - Morphine, IV, 10 mg 4 hourly.
    - Dilute morphine up to 10 mL with water for injection or sodium chloride 0.9%.
    - Beware of respiratory suppression and hypotension when administering morphine intravenously.
    - Opioids should be used cautiously in neurotoxic snakebite.

The use of an NSAID is not recommended due to the potential danger of renal failure in a hypotensive patient.

### Polyvalent antivenom

Obtainable from SA Vaccine Producers. 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. The dose of antivenom is the same for adults and children. Serum sickness is a relatively common adverse event. Even after the administration of antivenom, patients with neurotoxic snakebites may need ventilation; monitor for any deterioration in respiratory function.

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.
- Polyvalent snake antivenom, slow IV infusion.
    - Dilute 100 mL in 300 mL sodium chloride 0.9%.
    - Administer slowly for the first 15 minutes, as most allergic reactions will occur within this period.
    - Increase the flow rate gradually to complete the infusion within one hour.
    - Repeat if there is no clinical improvement after the infusion.

Black mamba bites to reverse respiratory paralysis:

- Polyvalent snake antivenom, slow IV infusion, 200 mL or more may be required.

To prevent airway obstruction in swelling of head or neck (cytotoxic bites):

- Polyvalent snake antivenom, slow IV infusion, 500 mL.

Difficulty in breathing with muscle weakness:

- Polyvalent snake antivenom, slow IV infusion, 100 mL.
  - Repeat if necessary. See package insert.

## 19.2.1 BOOMSLANG SNAKE BITE

### 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 SA Vaccine Producers. 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.

## 19.2.2 VENOM IN THE EYE

### 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. Apply chloramphenicol ointment and cover the affected eye with an eye patch.

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 tall and small pinchers. The venom typically causes immediate and severe local pain, followed by systemic neurotoxic symptoms and signs within 1–4 hours.

These include:

- » general paraesthesias,
- » muscle pain and cramps,
- » 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, slow IV, 10 mL administered over 3–5 minutes.

#### OR

- Scorpion antivenom, IV infusion, 10 mL diluted in 50–100 mL sodium chloride 0.9% or dextrose 5%, administered over 5–10 minutes.

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

- Morphine, IM, 10 mg as a single dose.

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 neurotoxic and cytotoxic groups.

#### 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.



**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.

Antihistamines, e.g.:

- Chlorpheniramine, oral, 4–8 mg as a single dose.

**OR**

- Promethazine, IM, 25–50 mg as a single dose.

For secondary infection:

See section 4.2: Cellulitis and Erysipelas.

**EXPOSURE TO POISONOUS SUBSTANCES****GENERAL MEASURES**

Limit further exposure to poison.

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 ineffective unless done within an hour of ingestion. 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.

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.

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 diluted in 400–800 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.

### Alkalinisation of urine

**This is a high risk procedure and should only be performed in consultation with a specialist.**

Urinary alkalinisation may be of benefit in salicylate, lithium and, less clearly, tricyclic antidepressant poisoning.

**Note:**

Salicylate poisoning may cause a respiratory alkalosis, which may aggravate the metabolic acidotic state. The infusion of large volumes of sodium and water may precipitate hypernatraemia and fluid overload.

The increase in pH may also be associated with hypokalaemia, which may cause dysrhythmias in a patient with a tricyclic antidepressant overdose. In this setting consider only in the presence of cardiac involvement, i.e. prolonged QRS duration or QRS axis abnormality on ECG.

- Sodium bicarbonate, IV, 50–100 mEq in 1 L sodium chloride 0.45%.
  - Administer 250–500 mL over 1–2 hours.
  - Attempt to achieve urine pH of  $\geq 7.5$ .

**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.
- » For psychiatric evaluation.

**19.5 ANALGESIC POISONING****19.5.1 PARACETAMOL POISONING**

T39.1

**DESCRIPTION**

The liver is the main organ acutely damaged in paracetamol poisoning. An acute single paracetamol overdose that may be associated with hepatic injury in adults is  $\geq 200$  mg/kg or 10 g (whichever is less) over a period  $< 8$  hours. In patients taking enzyme inducers, particularly in those who abuse alcohol, lower doses of paracetamol may be hepatotoxic. Renal tubular necrosis may also develop. Hepatic and renal failure typically manifest after 2–5 days.

**Clinical features**Within 24 hours after overdose

The patient may experience symptoms of gastrointestinal irritability with anorexia, nausea, vomiting, abdominal pain, as well as pallor, malaise and sweating.

During this phase the patient may, however, appear normal or asymptomatic.

24–48 hours after overdose

Although the patient may be asymptomatic, the ALT may become abnormal. In severe intoxication progressive liver failure develops within 2–5 days.

For reliable hepatotoxicity risk assessment, blood for plasma paracetamol levels should be drawn 4 hours post ingestion or as soon as possible thereafter.

Blood taken before 4 hours after ingestion does not represent a peak level.

Liver damage is likely to occur in patients with paracetamol levels >300 mcg/mL at 4 hours or > 45 mcg/mL at 15 hours post ingestion of an immediate release formulation.

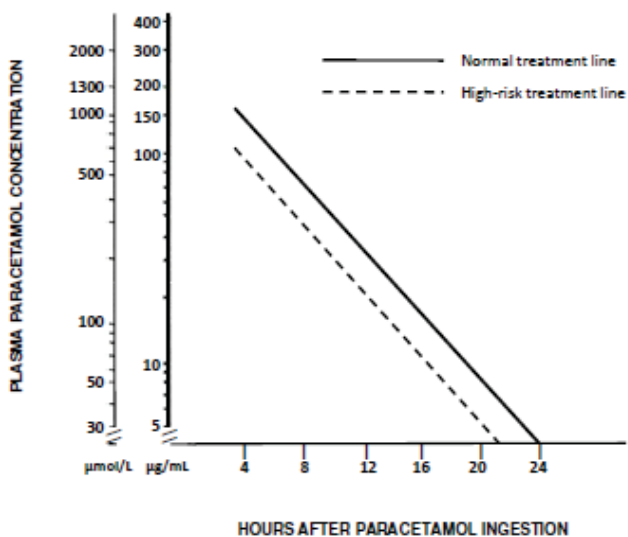
Levels < 120 mcg/mL at 4 hours are unlikely to be associated with hepatotoxicity.

If paracetamol levels are in the toxic range, defined as above the predictive graph line joining 150 mcg/mL at 4 hours and >45 mcg/mL at 15 hours after ingestion on the nomogram (see below), liver function tests (ALT, INR) should be performed daily. With significant liver damage refer patient for further management. Renal function should also be regularly monitored. Patients with initial paracetamol levels in the toxic range, who have been managed appropriately and are asymptomatic with normal liver functions after 48–72 hours, may be discharged.

Note that this nomogram is not suitable for use for modified or extended release formulation.

The decision to provide acetylcysteine should be guided by the above considerations.

## Paracetamol treatment nomogram



*Nomogram reproduced from the Guidelines of Acute Paracetamol Overdose produced by the Medicines Information Centre, UCT. Published with kind permission.*

## MEDICINE TREATMENT

Give activated charcoal within 1–2 hours after overdose.

### Acetylcysteine

Acetylcysteine is the antidote of choice and should be given intravenously, if possible. Although it is more effective when given within 8 hours of ingestion of paracetamol, there may be benefit even if liver failure has developed.

Indications for acetylcysteine:

- » In substantial overdose, defined as  $\geq 10$  g (20 tablets) or  $\geq 200$  mg/kg, whichever is smaller, administer without waiting for plasma paracetamol levels. Discontinue if plasma levels are in the non-toxic range.
- » Patients presenting  $\geq 24$  hours after an overdose, who have detectable plasma paracetamol levels or biochemical evidence of hepatotoxicity.
- » The initial paracetamol level is in the toxic range.

- » Paracetamol toxicity may occur at lower plasma concentrations in:
  - > Patients taking drugs that induce hepatic enzymes, e.g. barbiturates, phenytoin, carbamazepine, rifampicin and meprobamate.
  - > Alcohol abusers.
  - > Patients with conditions causing glutathione depletion, e.g. malnutrition and HIV infection.In these patients a lower threshold (i.e. the high-risk line) for instituting antidote therapy should be used.
- Acetylcysteine, IV, 150 mg/kg in 200 mL dextrose 5% over 1 hour as a loading dose.
  - Follow with 50 mg/kg in 500 mL dextrose 5% over next 4 hours by continuous infusion.
  - Then 100 mg/kg in 1 L dextrose 5% over 16 hours.
  - Beware of allergic reactions.
  - In mild cases of allergy administer the loading dose over 1–2 hours under antihistamine cover and continue at a lower infusion rate.

**OR**

- Acetylcysteine, oral or nasogastric, 140mg/kg immediately as a single dose.
  - Follow with 70 mg/kg 4 hourly for 17 doses.
  - Dilute solution to 5% in water.
  - Tablets/powder should be taken with enough fluid (250 mL).

**Note:**

Avoid giving activated charcoal if giving acetylcysteine orally as it will reduce the systemic absorption and thus negate the effect of oral acetylcysteine.

**19.5.2 SALICYLATE POISONING**

T39.0

**DESCRIPTION**

Patients present with:

- » nausea,
- » vomiting,
- » CNS depression,
- » tinnitus,
- » convulsions,
- » hypoglycaemia,
- » non-cardiogenic pulmonary oedema, and
- » respiratory alkalosis followed by metabolic acidosis or one or both disorders.

**GENERAL MEASURES**

Consider ICU admission for pulmonary and/or cerebral oedema.

**MEDICINE TREATMENT**

Alkalinisation of urine.

Do not give if patient has respiratory alkalosis.

Monitor closely with laboratory data, where available.

Urinary alkalinisation increases poison elimination by the administration of intravenous sodium bicarbonate to produce urine with a pH > 7.5.

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.  
Effectiveness is limited by short half-life and repeated doses may be needed.

**19.6 ANTIDEPRESSANT POISONING****19.6.1. TRICYCLIC ANTIDEPRESSANT (TCA) POISONING**

T43.0

**DESCRIPTION**

Patients may have:

- » Signs of anticholinergic effects:
  - > delirium,
  - > dilated pupils,
  - > dry mouth.
  - > blurred vision,
  - > urinary retention, or
- » Hypotension.
- » Both tachy- and bradyarrhythmias.
- » Agitation progressing to coma.
- » Pulmonary oedema.
- » Seizures.

The antimuscarinic effects of these agents may cause transient gastrointestinal ileus and urinary retention.

### GENERAL MEASURES

Monitor with ECG and blood gases.

ICU admission for ventilatory/circulatory support, when indicated.

Manage gastrointestinal ileus and urinary retention appropriately by keeping patients nil per mouth and inserting a urinary catheter.

### MEDICINE TREATMENT

- Activated charcoal, single dose.

For torsades de pointes:

#### ADD

- Magnesium sulphate, IV 2 g administered over 30 minutes.
  - Then 1 g hourly.

Manage broad QRS complexes with:

- Sodium bicarbonate to a pH of 7.55.

For seizures or if sedation is required for restlessness

- Diazepam, IV, 10 mg.

### Intravenous fluids

Reverse circulatory shock, if present.

In severe cases, provide inotropic support and monitor response.

## 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 patient may subsequently deteriorate.

Significant exposure may be associated with:

- » metabolic acidosis,
- » CNS side effects,
- » hepatitis.
- » hypotension,
- » renal failure, and



## 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, IV infusion, 15 mg/kg/hour.
  - Reduce dose after 4–6 hours.
  - Maximum total dose: 80 mg/kg in the first 24 hours.

For levels > 180 micromol/L, consider exchange transfusion.

If serum iron levels are not available and the probability of iron poisoning is high:

- Desferrioxamine, IV infusion, 1 g.
  - Observe for “vin rosé” discoloration of urine, which indicates high blood iron levels. If present, continue with chelation therapy, as above.

Give intravenous fluids for hypotension.

## 19.8 THEOPHYLLINE POISONING

T48.6

### DESCRIPTION

Patients present with:

- |  |                          |
|--|--------------------------|
| » tachycardia and<br>tachyarrhythmias, | » nausea,                |
| » vomiting,                            | » abdominal pain,        |
| » agitation,                           | » restlessness,          |
| » seizures, and                        | » profound hypokalaemia. |

### GENERAL MEASURES

Monitor cardiac function and treat dysrhythmias.

Monitor and correct fluid status and other electrolyte abnormalities.

Monitor theophylline concentrations. Levels may continue to rise up to 24 hours after ingestion of modified release preparations.

### MEDICINE TREATMENT

Give a dose of activated charcoal even if the patient presents after 2 hours.

Correct hypokalaemia:

- Potassium chloride, IV, not more than 40 mmol/L and rate not more than 20 mmol/hour.

For seizures:

- Diazepam IV, 10 mg.

In severe cases, i.e. blood levels > 80 mcg/mL, 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.  
Ventilatory support may be required

### 19.9.2 LITHIUM POISONING

T43.9

#### DESCRIPTION

Lithium toxicity mostly occurs with chronic therapy and may be precipitated by decreased excretion of the drug due to renal dysfunction, diuresis or dehydration. Blood levels provide a guide to the severity of lithium overdose. Toxicity occurs with blood concentrations > 1.5 mmol/L.

Signs and symptoms include:

- |                                     |                |
|-------------------------------------|----------------|
| » decreased level of consciousness, | » nausea,      |
| » restlessness,                     | » diarrhoea,   |
| » confusion,                        | » dehydration, |
| » seizures,                         | » ataxia, and  |
| » dysrhythmias                      |                |

#### GENERAL MEASURES

Gastric lavage if presented within 1 hour after ingestion.

Monitor:

- » cardiac function and treat dysrhythmias,
- » and correct fluid status,
- » electrolyte abnormalities and treat accordingly, and
- » lithium levels.

**MEDICINE TREATMENT**

Correct hypokalaemia actively:

- Potassium chloride, IV, not more than 40 mmol/L and rate not more than 20 mmol/hour.

For seizures:

- Diazepam IV, 10 mg

**Haemodialysis**

Consider dialysis where levels > 2.5 mmol/L.

**19.10 ISONIAZID POISONING**

T37.1

**DESCRIPTION**

Isoniazid poisoning is common and mainly presents with nausea, vomiting and dizziness. Severe poisoning can present with seizures and metabolic acidosis.

**GENERAL MEASURES**

Supportive management aimed at preventing and managing complications. Treat hyperthermia.

**MEDICINE TREATMENT**

- Pyridoxine, oral, 1 g for every gram of isoniazid ingested.

**19.11 ILLICIT DRUG POISONING****19.11.1 COCAINE POISONING**

T40.5

**DESCRIPTION**

Cocaine may be absorbed through any mucous membrane, smoked or injected intravenously. People who smuggle cocaine, may ingest packets of it.

Patients may present with one or more of the following:

- » acute myocardial infarction,
- » cardiac dysrhythmias,
- » tachycardia and hypertension,
- » stroke, and
- » seizures,
- » alterations in mood and confusion,
- » pulmonary oedema,
- » rhabdomyolysis with acute renal failure and intestinal ischaemia.

**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. Surgery is reserved for those who develop obstruction or perforation.

Raised serum creatine kinase may indicate rhabdomyolysis or myocardial infarction.

**Note:**

Lignocaine may precipitate seizures.

**$\beta$ -blockers should not be used.**

**MEDICINE TREATMENT****For sedation or seizures:**

- Diazepam, IV, 10mg.

**Status epilepticus**

See section 14.3.1: Status Epilepticus.

Psychosis or delirium with severe agitation:

- Haloperidol, IM, 2–5 mg.

**OR**

- Lorazepam, IM, 2 mg.

Severe hypertension:

See section 3.6.1: Hypertension, severe.

**19.12 POISONING WITH AMPHETAMINE DERIVATIVES**

T43.6

**DESCRIPTION**

These include:

- » “Ecstasy”: 3,4-methylenedioxymethamphetamine (MDMA).
- » “Ice” and “Eve”: 3,4-methylenedioxy-N-ethylamphetamine (MDEA).
- » “Tic tic”: 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.

Further complications include:

- » rhabdomyolysis, which presents with elevated serum creatine kinase,
- » hyperkalaemia,
- » later acute tubular necrosis,
- » potentially fatal hyponatraemia,
- » dehydration.

## GENERAL MEASURES

Supportive management aims to maintain stable cardiorespiratory function. Manage hyperthermia, hypoglycaemia and fluid and electrolyte status.

## MEDICINE TREATMENT

**Haemodialysis may be required for acute renal failure.**

For seizures:

- Diazepam, IV, 10 mg.

Severe hypertension:

- Labetalol, IV, 2 mg/minute to a maximum of 1–2 mg/kg.

## 19.13 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.

**19.14 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.

**19.15 ALCOHOL POISONING****19.15.1 ETHANOL POISONING**

T51.0

**DESCRIPTION**

Acute poisoning usually presents with:

- » central nervous system depression,
- » hypoglycaemia,
- » hypothermia, and
- » changes in fluid and electrolyte status such as hypokalaemia and hyponatraemia.

Consider other causes for the patient's condition, including hypoglycaemia and head trauma.

## GENERAL MEASURES

Supportive management aimed at maintaining stable cardiorespiratory function. Manage hypothermia.

## MEDICINE TREATMENT

- Thiamine, IV, 100 mg in 1 L dextrose 5%.

### 19.15.2 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.

Clinical signs include:

- » resembles alcohol intoxication,
- » vomiting,
- » later hypotension,
- » cardiac failure,
- » oliguric renal failure,
- » significant metabolic acidosis with a high anion gap, i.e.:  $([Na^+] - [Cl^-] - [HCO_3^-]) > 12$ ,
- » hypocalcaemia,
- » a higher measured serum osmolality when compared to the calculated equivalent, and
- » oxalate crystals in urine.

#### MEDICINE TREATMENT

Haemodialysis is the treatment of choice in severe poisoning with profound acidosis.

#### Ethanol

In other patients and where access to dialysis facilities is not readily available:

- Ethanol 95% BP, IV, diluted to 10% in dextrose 5%.
  - Administer 10 mL/kg of dilute solution over 30–45 minutes (0.6–0.7 g/kg ethanol).
  - Follow with the dilute solution at:  
1 mL/kg/hour for non-drinkers.  
2 mL/kg/hour for patients with hepatic enzyme induction, such as chronic alcohol users.

If intravenous ethanol cannot be given:

- Ethanol 95% BP, oral, diluted to 20% in any suitable liquid.
  - Administer 1 mL/kg of dilute solution.
  - Follow with the dilute solution at:
    - 0.1 mL/kg/hour for non-drinkers.
    - 0.2 mL/kg/hour for patients with hepatic enzyme induction, such as chronic alcohol users.

If ethanol 95% BP is not available, orally administer any commercially available alcoholic beverage with an alcohol content of  $\pm$  40% e.g. vodka (80 proof), at the above oral dose.

**Note:**

The patient needs to be co-operative or administration via nasogastric tube may be required.

The aim is to maintain plasma ethanol levels of 1–1.3 g/L (0.1–0.13 g/dL). Several days of ethanol therapy may be required. Continue treatment until clinical condition improves.

- Thiamine, oral, 100 mg daily.

**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.

### 19.15.3 METHANOL POISONING

T51.1

**DESCRIPTION**

Previously found in methylated spirits but has recently been replaced with less toxic agents.

Presents with:

- » Initially, CNS and GIT effects.
- » Later, high anion gap ( $>$  12), metabolic acidosis, retinal toxicity 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 dialysis urgently, if available.

If dialysis not available, use ethanol as an antidote

See section 19.15.2: Ethylene glycol poisoning.

## 19.16 PESTICIDES AND RODENTICIDES

### 19.16.1 AMITRAZ POISONING

T60.9

#### DESCRIPTION

Amitraz is a pesticide/insecticide which is an  $\alpha_2$ -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 and potentially by inhalation.

Patients with acute poisoning present with

- » impaired consciousness,
- » drowsiness,
- » vomiting,
- » constricted pupils or rarely, dilated pupils,
- » hypotension,
- » bradycardia,
- » tachypnoea,
- » hypothermia, and
- » generalized seizures.

Other complications include:

- » hyperglycaemia,
- » glycosuria, and
- » mild increase in transaminases.

Patients usually regain consciousness within 24 hours.

#### 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 seizures:

- Diazepam, IV, 10mg.

### 19.16.2 ORGANOPHOSPHATE POISONING

T60.0

\* Notifiable condition.

#### DESCRIPTION

Poisoning due to parathion, malathion and other organophosphates

Absorption occurs through the skin or the agent is taken orally.

Patients present with muscarinic and nicotinic manifestations of intoxication.

Muscarinic overstimulation causes salivation, lacrimation, vomiting,

diarrhoea and increased bronchial secretions. Nicotinic overstimulation

causes muscle fasciculations and paresis or paralysis. 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 infusion, 2 mg/hour starting dose.
  - 10 mg in 200 mL sodium chloride 0.9% administered as a controlled infusion over 5 hours.
  - Assess degree of atropinisation by increase in pupil size (do not monitor continuous atropinisation on pupil size), pulse rate, bronchial secretions and salivation.
  - A continuous IV infusion of 0.05 mg/kg/hour may be required.
  - 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.

### 19.16.3 PARAQUAT POISONING

T60.3

#### 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

Gastric lavage if patient presents within 1 hour after ingestion. 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.

## MEDICINE TRETAMENT

- Activated charcoal if patient presents within 1–2 hours after ingestion.

## 19.17 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. Measure INR at baseline and 48 hours post ingestion, as the anticoagulant effect maybe delayed by 1-2 days.

### GENERAL MEASURES

Resuscitation.

Stop warfarin in patients on therapy.

### MEDICINE TREATMENT

#### For patients on warfarin therapy

- Vitamin  $K_1$ , IV/IM, 10 mg.
  - May be repeated depending on the INR response.
  - Note the delay in effect.

Patients who are bleeding require additional fresh frozen plasma and the first dose of intravenous vitamin K. Follow-up doses by any route may be required if INR continues to rise, as vitamin K has a shorter half-life than warfarin.

Administration of vitamin K<sub>1</sub> may induce resistance to warfarin.

Patients on chronic warfarin therapy and at high risk for thrombo-embolic complications, but who are not actively bleeding with INR between 5–9: Admit patient to hospital and monitor. If bleeding occurs, give fresh frozen plasma (FFP). If FFP is not available:

- Vitamin K<sub>1</sub>, IV, 0.5–1 mg low dose.

Resume warfarin therapy once the INR is < 4.0.

For INR > 9:

- Vitamin K<sub>1</sub>, IV, 2.5 mg.

**OR**

- Vitamin K<sub>1</sub>, oral, 5 mg.
  - For oral administration of low doses, the parenteral formulation may be used.

In all cases repeat INR in 24 hours.

### Super warfarins

Treatment with vitamin K<sub>1</sub> needs to be prolonged for several months as these substances are very long acting. Monitor INR according to clinical response.

## 19.18 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,                       | » impaired level of consciousness.        |
| » seizures and other CNS symptoms, | » cherry red skin and lips.               |
| » nausea,                          | » tachycardia.                            |
| » vomiting,                        | » ECG changes.                            |
| » retinal haemorrhages,            | » normal arterial PO <sub>2</sub> but low |
| » high arterial                    | oxygen saturation, and                    |
| carboxyhaemoglobin - test not      |   |
| commonly available.                |   |

### 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, slow IV, 10 mg.

**19.19 HEAVY METAL POISONING**

T56.1/T57.0/T56.8/T56.4/T56.0/T56.3

**DESCRIPTION**

This includes mercury, arsenic, gold, copper, lead poisoning et cetera. Acute toxicity of organ-systems may be summarised as follows:

	<b>Pneu monitis</b>	<b>GIT</b>	<b>Blood cells</b>	<b>CVS collapse</b>	<b>Kidneys</b>	<b>Hepato toxicity</b>	<b>CNS</b>
Mercury	x	x		x	x		x
Arsenic	x	x	x	x	x		x
Gold		x		?		x	
Thallium		x					x
Copper		x	x		x	x	x
Lead		x	x		x		x
Cadmium	x	x					

**MEDICINE TREATMENT****Dimercaprol**

Dimercaprol chelates metals, enabling excretion of the less toxic complexes. It is the agent of choice for mercury, gold and arsenic poisoning.

Its role is less established in cases of lead, copper and thallium poisoning.

Do not use for iron poisoning.

- Dimercaprol 10%, deep IM, 400–800 mg in divided doses on the first day.
  - Then 200–400 mg/day in divided doses for 2 days.
  - Then 100–200 mg/day in divided doses for 4–7 days.
  - These injections are painful and sterile abscesses may form.
  - In severe cases, consider a loading dose of 5 mg/kg

**Penicillamine**

Penicillamine also chelates metals.

Indicated in copper, mercury, arsenic, zinc and lead poisoning.

- Penicillamine, oral, 0.5–1.5 g daily in 4 divided doses.

## 19.20 POISONING WITH NITRITES, NITROPRUSSIDE, NITROGLYCERINE CHLORATES, SULPHONAMIDES AND OTHERS

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. After administration of methylene blue, oxygen saturation may drop initially.

### 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 precordial pain, restlessness and dyspnoea.

In life-threatening cases, not responding to methylene blue or if methylene blue is not available, exchange transfusion may be considered.

Administration of ascorbic acid (vitamin C) has not been shown to be effective, mainly due to slow onset of effect.

### POISON CENTRES

Western Cape	Tygerberg Poison Information Centre	021 931 6084 021 931 6129
	Red Cross	021 689 5227
Free State	Bloemfontein	082 491 0160
Telephone numbers tested 20 April 2012.		

# CHAPTER 20

## EMERGENCIES AND INJURIES

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### 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.

Other causes include other medicines and allergies.

##### Symptoms

Swelling usually occurs around eyes and lips but may occur elsewhere.

Life-threatening airway obstruction can occur with angioedema of the upper airways. Angioedema can be part of an anaphylactic reaction.

##### GENERAL MEASURES

Stop all the suspected agents, e.g. ACE inhibitor.

In case of angioedema with airway obstruction, early airway management is essential. A definitive airway must be established if oedema is extensive or progressing. The most skilled person available must handle airway interventions.

##### MEDICINE TREATMENT

In severe cases where airway obstruction is present:

- Adrenaline (epinephrine) 1:10 000, slow IV, 0.5 mg immediately.

In cases where angioedema is part of anaphylaxis, treat as anaphylaxis. See section 20.1.2: Anaphylaxis/Anaphylactic shock.

Antihistamines, e.g. cetirizine and H<sub>2</sub> antagonists, e.g. ranitidine may have a role when angioedema is due to allergies or medicines other than ACE inhibitors.

- Hydrocortisone, IV, 100 mg as a single dose.

Observe all cases until resolution.

## 20.1.2 ANAPHYLAXIS/ANAPHYLACTIC SHOCK

T78.2

### DESCRIPTION

An acute, potentially life-threatening hypersensitivity reaction starting 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

Cardiopulmonary resuscitation.

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

Administer the first dose of adrenaline IM, if there is no IV access

#### Intravenous fluids

Establish an intravenous line:

- Sodium chloride 0.9%, IV.
- Adrenaline (epinephrine), slow IV, 1:10 000, 0.5 mg immediately.

#### OR

- Adrenaline (epinephrine) 1:1 000, **IM**, 0.5 mL into the lateral thigh. **Not subcutaneously.**

#### PLUS

- Hydrocortisone, IV, 200 mg, immediately as a single dose.

#### PLUS

If bronchospasm:

- Oxygen.
- Salbutamol, nebulised, 5 mg diluted with sodium chloride 0.9% to a total volume of 5 mL.
  - Nebulise at a flow rate of 6–8 L/minute.



If patient has an itch:

- Cetirizine, oral, 10 mg as a single dose.

### 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.

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

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:

- » septic shock,
- » neurogenic shock, and
- » 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, IV infusion, 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
<b>0.05</b>	15	18	21	24	27	30	33
<b>0.1</b>	30	36	42	48	54	60	66
<b>0.2</b>	60	72	84	96	108	120	132
<b>0.3</b>	90	108	126	144	162	180	198
<b>0.4</b>	120	144	168	192	216	240	264
<b>0.5</b>	150	180	210	240	270	300	330
<b>0.6</b>	180	216	252	288	324	360	396
<b>0.7</b>	210	252	294	336	378	420	462
<b>0.8</b>	240	288	336	384	432	480	528
<b>0.9</b>	270	324	378	432	486	540	594
<b>1</b>	300	360	420	480	540	600	660

**20.1.4.2 SEPTIC SHOCK**

R57.2

**DESCRIPTION**

Shock caused by an infection, with vasodilatation, increased capillary permeability, and decreased contractility of the heart.

**GENERAL MEASURES**

Check breathing, airway and circulation

**MEDICINE TREATMENT**

If hypoxic:

- Oxygen.

All patients will require urgent intravenous antibiotics.

Before administering adrenaline, perform a fluid challenge:

- Sodium chloride 0.9%, IV infusion, 200 mL over 15 minutes.
  - Assess blood pressure and pulse rate response. Response is defined by a good urine output and adequate cerebral perfusion rather than an absolute blood pressure value.

If there is a positive response, then 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, IV infusion, 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
<b>0.05</b>	15	18	21	24	27	30	33
<b>0.1</b>	30	36	42	48	54	60	66
<b>0.2</b>	60	72	84	96	108	120	132
<b>0.3</b>	90	108	126	144	162	180	198
<b>0.4</b>	120	144	168	192	216	240	264
<b>0.5</b>	150	180	210	240	270	300	330
<b>0.6</b>	180	216	252	288	324	360	396
<b>0.7</b>	210	252	294	336	378	420	462
<b>0.8</b>	240	288	336	384	432	480	528
<b>0.9</b>	270	324	378	432	486	540	594
<b>1</b>	300	360	420	480	540	600	660

### PLUS

Take blood culture, then administer appropriate parenteral broad spectrum antibiotics urgently, e.g.:

- Ceftriaxone, IV, 2 g initially.
  - Then 1 g daily (for community acquired sepsis).

**20.1.4.3 CARDIOGENIC SHOCK**

R57.0

**DESCRIPTION**

Occurs when the heart does not contract adequately. Patients are hypotensive, cold and clammy and their pulse rate may be variable. Causes include an acute myocardial infarction (MI), myocardial contusion, myocarditis, arrhythmias, 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, 2–10 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:

Dose mcg/kg/min	Weight (kg)									
	30	40	50	60	70	80	90	100	110	120
2.5	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

**20.1.4.4 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,	» tension pneumothorax,
» acute pulmonary embolism, and	» severe bronchospasm.

**TREATMENT**

Treat the cause.

**20.1.5 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.

Bed rest in Fowler's position, unless hypotensive or comatose.

Correct electrolyte disturbances.

Determine and correct any arrhythmias.

**MEDICINE TREATMENT**

Administer oxygen.

- Furosemide, slow IV, 20–80 mg, initial dose.
  - May be repeated 15 minutes later if symptoms persist.
- Morphine, IV, 1–2 mg/minute to a maximum total dose of 10 mg.
  - Dilute 10 mg up to 10 mL in sodium chloride solution 0.9%.
  - This may be repeated 4 hourly.
  - Beware of respiratory depression.
- 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.
  - 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

If hypotensive consider inotropic support, e.g.:

- Dobutamine, IV infusion, 2–20 mcg/kg/minute.
  - Dilute 1 vial (250 mg/20 mL) up to 50 mL with sodium chloride 0.9% or dextrose 5%. d(Solution = 5 mg/mL or 5 000 mcg/mL.)
  - Administer under constant ECG monitoring.
  - Rate of infusion in mL/hour:
  -

Dose mcg/kg/min	Weight (kg)									
	30	40	50	60	70	80	90	100	110	120
2.5	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
12.5	4.5	6	7.5	9	10.5	12	13.5	15	16.5	18
15	5.4	7.2	9	10.8	12.6	14.4	16.2	18	19.8	21.6
20	7.2	9.6	12	14.4	16.8	19.2	21.6	24	26.4	28.8

## 20.2 INJURIES

T14

### 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	Degree	Surface/colour	Pain sensation
Superficial (Partial loss of skin)	1 <sup>st</sup>	Dry, minor blisters, erythema	Painful
Partial A (Superficial dermal)	2 <sup>nd</sup> A	Blisters	Painful
Partial B (Deep dermal)	2 <sup>nd</sup> B	Moist white slough, red mottled	Painful
Full thickness (Deep/complete loss of skin)	3 <sup>rd</sup>	Dry, charred whitish	Painless

#### GENERAL MEASURES

Remove smouldering or hot clothing.

Place the burnt area in cold running tap water to limit the extent of the burn.

Clean and dress wounds appropriately.

Intubate early if patient is hypoxic, or if soft tissue swelling, as these patients frequently tend to develop respiratory failure.

Support vital organ function.

Obtain IV access to administer intravenous fluids in as these patients lose lots of fluids.

Look for aggravating comorbidities, e.g. seizures, hyperkalaemia and renal failure.

Clean superficial burns can be managed by occlusive dressings.

Deeper wounds may have to be excised and grafted.

Rehabilitation.

Burn injuries put patients into a hypermetabolic state which requires early and adequate nutritional support.

**MEDICINE TREATMENT****Intravenous fluids**

If required, as soon as possible:

- Sodium chloride 0.9%, IV.

Ensure adequate urine output and monitor blood pressure.

**Analgesia**

Ensure adequate analgesia particularly at change of dressing, i.e.:

- Morphine, IV/IM, 10 mg 4 hourly.
  - Administer a dose at least one half hour before dressing change if possible.

**AND**

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

Immunisation, primary or booster:

- Tetanus toxoid vaccine, IM, 0.5 mL immediately.

**Burn dressing**

Topical agents, e.g.:

- Povidone iodine 5% cream, topical.

**OR**

- Silver sulfadiazine 1% cream, topical.

**Note:**

There is no evidence that silver sulfadiazine 1% is superior to other dressings.

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:**

The pharmacokinetic profile of certain drugs may be altered and will require appropriate dose adjustments, e.g. aminoglycoside doses may need to be increased.

**REFERRAL**

- » 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.



## 20.3 CARDIAC ARREST – CARDIOPULMONARY RESUSCITATION

### 20.3.1 CARDIAC ARREST ADULTS

146.9

#### DESCRIPTION

Cardiac arrest is the sudden cessation of effective cardiac output. Irreversible brain damage can occur within 2–4 minutes.

Clinical features include:

- » sudden loss of consciousness,
- » absent carotid and all other pulses, and
- » loss of spontaneous respiration.

#### EMERGENCY TREATMENT

##### Cardiopulmonary resuscitation

- » Place the patient on a firm flat surface and commence resuscitation immediately.
- » Call for skilled help and a defibrillator or AED (Automated External Defibrillator), if available.
- » Check for a carotid pulse.

##### Circulation

- » If absent or uncertain after 10 seconds, commence chest compressions at a rate of **100 compressions per minute**.
- » Alternate chest compressions with breaths in a ratio of 30 chest compressions: 2 breaths.
- » Repeat for 5 cycles and re-evaluate.
- » If no response, continue.
- » Attach defibrillator as soon as possible to check for a shockable rhythm (ventricular fibrillation or pulseless ventricular tachycardia).
- » Document medication administered and clinical progress.

Initiate IV fluids, if possible:

- Ringer's-lactate, IV.

##### Airway

- » Remove vomitus or foreign body and dentures from the mouth, if present.
- » 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.
- » Perform a jaw thrust.
- » Insert 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).

#### Breathing

- » Give 2 breaths over 1 second each.
- » Preferably with a bag-mask device. If not available, then use a mouthpiece.
- » Oxygenate with 100% oxygen.
- » Intubation must be deferred until the patient is stabilised and only if it does not interfere or interrupt chest compressions.

#### Defibrillation

- » Apply the pads for the AED or paddles for the defibrillator as soon as possible to check for and treat a shockable rhythm.

#### **Immediate emergency medicine treatment**

Adrenaline should be given when there is no response to initial resuscitation or defibrillation.

- Adrenaline, 1:1 000, 1 mL, IV immediately.
  - Follow by a flush of 20 mL IV fluid after 5 cycles of compressions and ventilation.
  - Repeat every 3–5 minutes during resuscitation.

#### **For bradycardia**

- Atropine, IV, 1 mg.
  - Repeat after 2–5 minutes if no response.
  - Maximum dose: 3 mg.

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,
- » shockable rhythm, or
- » anaphylaxis.

## 20.4 GENERAL ASPECTS APPLICABLE TO ALL TRAUMA PATIENTS

### PRIMARY SURVEY

#### Primary ABCs

Ensure that the airway is patent and that the patient is breathing and has a pulse.

Get a **rapid handover** from EMS/relatives:

- » demographics, if known,
- » mechanism of injury,
- » injuries sustained,
- » signs and symptoms: pulse, BP, level of consciousness, obvious wounds, and
- » treatment already provided/administered.

If possible assess for:

A = Allergies

M = Medications used

P = Previous medical or surgical history

L = Time of the Last Meal before the time of the trauma

E = Events surrounding the current admission

#### Airway and C-spinal control:

- » At all times the patient should be kept flat. Use a 5 cm thick padded surface – not a hard spine board.
- » The C-spine is best maintained with manual in-line support. Remove the spinal collar during any airway instrumentation (such as intubation).
- » Once airway is secure a rigid cervical collar and supporting head rolls/ head blocks/ sandbags are essential, as are body restraints. Immobilise any potential fracture.
- » Provide supplemental oxygen, preferably through a non-rebreather mask.
- » Ensure an open airway
- » **Do not** use head-tilt chin-lift: **Jaw thrust** is the first step if that patient is not able to maintain and protect their own airway.

Look for life-threatening chest injuries that might affect ventilation: e.g. tension pneumothorax.

Definitive airway: a cuffed endotracheal tube.

Alternate airway:

- » Oro-pharyngeal airway.
- » Laryngeal mask airway – the device of choice **if** unable to intubate the patient.
- » Needle cricothyroidotomy may be required. Consult an expert.

Rapid Sequence Intubation (RSI) with a muscle relaxant such as suxamethonium chloride should be instituted.

Once the airway is secured, cervical spine protective devices may be replaced and the manual in-line support can be released.

### **Breathing and ventilation:**

Assess breathing. Assist breathing if patient effort is laboured or inadequate. Give supplementary oxygen.

Treat life-threatening chest injuries that might impair ventilation: e.g. tension pneumothorax.

### **Circulation**

Control bleeding.

### **Assessment of neurological status**

#### **Note:**

- » Pupil reaction to light.
- » Any obvious neurological deficit i.e. whether the patient is moving all limbs.
- » Level of consciousness.

### **Expose the patient**

Undress the patient completely.

Keep warm with blanket, warm fluids and warm room.

### **Laboratory investigations**

- » Blood gas with lactate level.
- » Cross-match.
- » Urinalysis for blood and pH.
- » FBC, urine and electrolytes, INR and PTT.

### **Radiological investigations will be governed by trauma history and clinical assessment**

- » Chest X-ray.
- » C-spine X-ray.
- » Pelvis X-ray.
- » X-ray of relevant injured area, if required.

**SECONDARY SURVEY**

This is a head-to-toe survey of the patient. It is done to pick up the less life-threatening injuries or conditions. Examine both front and back of the patient.

**Cervical spine injury**

C-spine immobilisation may be removed without X rays if:

- » GCS =15,
- » no drugs or alcohol or a history thereof detected
- » no distracting injury (*any painful injury*),
- » no neurological signs, and
- » no midline tenderness of the neck.

If the above are not met, a minimum of 3 cervical X-rays are required, lateral, AP and open mouth. Normal X-rays are not a guarantee of a cleared C-spine.

# CHAPTER 21

## MEDICINES USED FOR ANAESTHESIOLOGY, NUTRITIONAL SUPPORT AND MISCELLANEOUS CONDITIONS

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### 21.1 ANAESTHESIOLOGY FOR ADULTS

The list is provided to give an indication of agents that should be available to provide safe anaesthesia at a regional hospital. It is assumed that medicines such as adrenaline are also available.

#### FOR INDUCTION

- Etomidate
- Ketamine
- Midazolam
- Propofol
- Thiopental sodium

#### INHALANTS

- Halothane
- Isoflurane

#### ANALGESICS

- Fentanyl
- Morphine
- Diclofenac, IM

#### MUSCLE RELAXANTS AND RELATED DRUGS

- Cisatracurium
- Suxamethonium chloride
- Vecuronium bromide
- Neostigmine
- Atropine or glycopyrronium bromide

#### LOCAL ANAESTHETICS

- Bupivacaine 0.5%
- Bupivacaine 5 mg/mL plus dextrose
- Lidocaine 1%
- Lidocaine 2%
- Lidocaine 2% plus adrenaline
- Lidocaine jelly
- Lidocaine topical spray

## OTHER DRUGS

- Dantrolene
- Ephedrine
- Ondansetron (post-operative nausea and vomiting)
- Phenylephrine

## 21.2 NUTRITIONAL SUPPORT

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 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: respiratory failure, cardiac failure, cardiac arrhythmias, rhabdomyolysis, seizures, coma, red cell and leucocyte dysfunction. The most effective way to prevent re-feeding syndrome is to be aware of it. 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 (PEG) feeding should be used in patients likely to need long-term ( $\geq 4$  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 stepwise with a daily review of the patient's progress.

### 21.3 DIAGNOSTIC CONTRAST AGENTS AND RELATED SUBSTANCES

- Bowel preparation, e.g. sodium phosphate
- Barium sulphate suspension enema
- Barium sulphate powder
- Non-ionic contrast media, e.g.:
  - iohexol, or
  - iopamidol, or
  - iopromide
- Ioversol 300 and 350

### 21.4 MALIGNANCIES

The following medicines must be available at certain facilities to continue care of patients who have been stabilised.

- Bleomycin
- Hydroxyurea
- Tamoxifen
- Vincristine



# GUIDELINES FOR THE MOTIVATION OF A NEW MEDICINE ON THE NATIONAL ESSENTIAL MEDICINES LIST

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## Section 1: Medication details

- » Generic name  
A fundamental principle of the Essential Drug Programme is that of generic prescribing. Most clinical trials 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<sub>1</sub>, CD<sub>4</sub>, VL etc.
  - Risk benefit: this should be 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 reciprocal of the absolute risk or can be calculated using the formula below.

### Calculations

	Bad outcome	Good outcome	Total patients
Intervention group	<i>a</i>	<i>c</i>	<i>a + c</i>
Control group	<i>b</i>	<i>d</i>	<i>b + d</i>

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 Drug List Committee has endorsed the adoption of the SORT system for categorising levels of evidence. This system<sup>1</sup> 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 maybe 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:
    - o 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.
    - o 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.

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<sup>1</sup> 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-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.



## 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)		
<b>A. Newer product:</b> High quality systematic reviews or peer-reviewed high quality randomised controlled trials (Level I)		
Author	Title	Journal ref
<b>B. Older product with weaker evidence base:</b> 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

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## **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) reaction 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
- 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)*

 <p><b>health</b> Department: Health REPUBLIC OF SOUTH AFRICA</p>	<p><b>NATIONAL ADVERSE DRUG EVENT MONITORING CENTRE NADEMC</b></p> <p>The Registrar of Medicines Private Bag X 828 Pretoria 0001</p> <p>In collaboration with the WHO International Drug Monitoring Programme</p>
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**PATIENT INFORMATION**

Name (or initials): .....

Patient Reference Number: .....

Sex:	<input type="checkbox"/> M	<input type="checkbox"/> F	Age:	DOB:	Weight	Height (cm)
			.....	..... / ..... / .....	(kg)	.....
					.....	

**ADVERSE REACTION/PRODUCT QUALITY PROBLEM (tick appropriate box)**

Adverse reaction	<input type="checkbox"/>	and/or Product Quality problem	<input type="checkbox"/>	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 & Batch No. (Asterisk Suspected Product)	Daily Dosage	Route	Date Started	Date Stopped	Reasons for use

**ADVERSE REACTION OUTCOME (Check all that apply)**

<input type="checkbox"/>	death	<input type="checkbox"/>	life-threatening
<input type="checkbox"/>	disability	<input type="checkbox"/>	hospitalisation
<input type="checkbox"/>	congenital anomaly	<input type="checkbox"/>	Other.....
<input type="checkbox"/>	required intervention to prevent permanent impairment/damage	<input type="checkbox"/>	

<b>Reaction abated after stopping medicine:</b>					
<input type="checkbox"/>	Y	<input type="checkbox"/>	N	<input type="checkbox"/>	
<b>Event reappeared on rechallenge:</b>					
<input type="checkbox"/>	Y	<input type="checkbox"/>	N	<input type="checkbox"/>	Rechallenge not done
<b>Recovered:</b>					
<input type="checkbox"/>	Y	<input type="checkbox"/>	N	<input type="checkbox"/>	
<b>Sequelae:</b>					
<input type="checkbox"/>	Y	<input type="checkbox"/>	N	<input type="checkbox"/>	
<b>Describe Sequelae:.....</b>					

**COMMENTS:** (e.g. Relevant history, Allergies, Previous exposure, Baseline test results/lab data)

<b>2. PRODUCT QUALITY PROBLEM:</b>					
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, 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*

**BUSINESS REPLY SERVICE  
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**

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## DISEASE NOTIFICATION PROCEDURES

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The disease reporting system in South Africa is based on government law (Health Act, Act 63 of 1977) and regulations where specific infectious diseases (see list of notifiable medical conditions below) must be reported to the Provincial Health Departments, who then report to the National Department of Health (see flow chart of data below). Disease surveillance comprises mainly four types: Notifiable disease-reporting system, Laboratory-based surveillance, Hospital-based surveillance and Population based surveillance.

### **Notifiable Disease reporting**

A notification serves as the first step in a surveillance cycle, namely for data-capturing or data collection. Notification can be done via the mail, fax or telephone to the local authority concerned. Any person (not necessarily a health worker) can notify a notifiable medical condition (see the Health Act regulations - legal obligations). The list of notifiable medical conditions at the moment determines that 40 different diseases are notifiable (see list below).

### **Process**

Forms involved

GW17/5:	initial diagnosis (complete immediately)
GW17/3:	line list of cases (complete weekly)
GW17/4:	line list of deaths (complete weekly)

The initial diagnosis of a notifiable medical condition are done on a case-based form with the relevant address and fine details on it, to make tracing of the case as easy as possible, since a disease notification demands action (follow-up) at the lowest level (GW17/5 - for cases and deaths).

In South Africa it is required by law that completed weekly disease notification forms are submitted for all notifiable diseases from each local authority or district office to the Provincial office. These should be completed and sent by all reporting units e.g.hospitals, health centres, health posts, clinics, private practitioners, private nurses, to the district public health office. The initial diagnosis forms are summarised weekly on separate line list forms for cases (GW17/3) and for deaths (GW17/4).

**To ensure complete reporting of all EPI diseases, a zero report should be sent if no cases of a notifiable disease were seen for the reporting period.**

## **Reporting**

from reporting units to district office within 9 days  
reporting week is Sunday to Saturday

All the reporting units should submit their disease notifications to reach the district no later than 9 days after the end of the reporting week. A reporting week is normally taken from Sunday to Saturday. Thus, the weekly notifications are normally expected by the following Monday.

All reports received within that period are considered to be **on time**. After that period has passed, any reports received is considered **late**.

Some diseases can be monitored more accurately through the laboratory because of the nonspecificity of the clinical syndrome e.g. most types of food poisoning. For other diseases, laboratory data acts only as a confirmation of the clinical diagnosis.

These include Rabies, Cholera and Crimean Congo Haemorrhagic fever

### **Hospital-based surveillance**

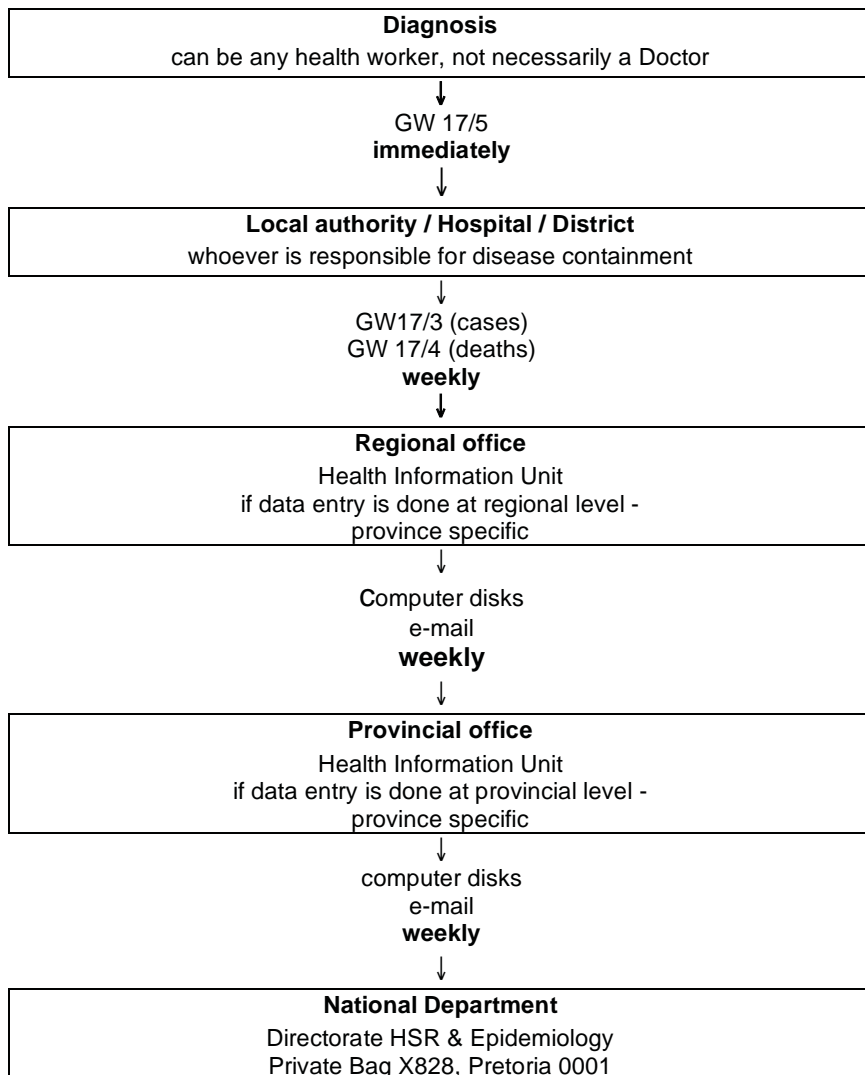
Hospital discharge information as well as mortality data can be used to monitor disease trends and disease burden in a particular area served by the hospital.

### **Population-based surveillance**

A population-based surveillance system collects and analyses medical information in a well-defined population.

Complete reporting is needed when doing surveillance on rarely occurring diseases as well as for the elimination of diseases (e.g. polio eradication in SA by 2000 - surveillance of Acute Flaccid Paralysis).

**FLOW CHART**  
**Procedure to follow with notifiable medical conditions**



## Notifiable Medical Conditions

Acute flaccid paralysis  
Anthrax  
Brucellosis  
Cholera  
Congenital syphilis  
Crimean-Congo haemorrhagic fever  
Other haemorrhagic fevers of Africa  
Diphtheria  
Food poisoning  
Haemophilus Influenza type B  
Lead poisoning  
Legionellosis  
Leprosy  
Malaria  
Measles  
Meningococcal infection  
Paratyphoid fever  
Plague  
Poisoning agricultural stock remedies  
Poliomyelitis  
Rabies  
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  
Tuberculosis total  
Typhoid fever  
Typhus fever (lice-borne)  
Typhus fever (rat flea-borne)  
Viral hepatitis type A  
Viral hepatitis type B  
Viral hepatitis non-A non-B  
Viral hepatitis unspecified  
Viral hepatitis total  
Whooping cough  
Yellow fever

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## ABBREVIATIONS

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ACE inhibitor	angiotensin-converting enzyme inhibitor
ACTH	adrenocorticotrophic hormone
AIDS	acquired immunodeficiency syndrome
ALT	alanine transaminase
aPTT	activated partial thromboplastin time
ARDS	acute respiratory distress syndrome
ART	antiretroviral therapy
ARVs	antiretrovirals
AST	aspartate amino transferase
ATG	antithymocyte immunoglobulin
BMD	bone mass density
BMI	body mass index
BP	blood pressure
BSA	body surface area
oC	degrees Celsius
Ca	calcium
CAD	coronary artery disease
CD4	cluster designation 4
Cl	chloride
cm	centimetre
CNS	central nervous system
CO <sub>2</sub>	carbon dioxide
Cr	creatinine
CrCl	creatinine clearance
CRP	C-reactive protein
CSF	cerebrospinal fluid
CSU	catheter specimen of urine
CT	computerised tomography
CVA	cerebrovascular accident
CVS	cardiovascular system
DBP	diastolic blood pressure
dL	decilitre
DOH	Department of Health
DVT	deep vein thrombosis
E	ethambutol
ECG	electrocardiogram
EEG	electroencephalogram
ELISA	enzyme-linked immunosorbent assay
ERCP	endoscopic retrograde cholangiopancreatography
FBC	full blood count
FEV <sub>1</sub>	forced expiratory volume in 1 second
FH	familial hypercholesterolaemia
FSH	follicle-stimulating hormone
FTA	fluorescent treponema antibody

g	gram
G6PD	glucose-6-phosphate dehydrogenase
GFR	glomerular filtration rate
GIT	gastro-intestinal tract
H	isoniazid
H <sub>2</sub> O	water
Hb	haemoglobin
HbA1C	glycosylated haemoglobin
HBIG	hepatitis B immune globulin
HbS	sickle haemoglobin
HbsAb	hepatitis B surface antibody
HbsAg	hepatitis B surface antigen
HbSS	sickle cell haemoglobin
HCl	hydrochloric acid
HCO <sub>3</sub>	bicarbonate
HDCV	human diploid cell
HGT	haemogluco-test
HIV	human immunodeficiency virus
HMGCoA	3-hydroxy-3-methylglutaryl coenzyme
HRT	hormone replacement therapy
HSV	herpes simplex virus
IgE	immunoglobulin E
IgG	immunoglobulin Gamma
IM	intramuscular
INR	international normalised ratio
IUCD	intrauterine contraceptive device
IV	intravenous
JVP	jugular venous pressure
K	potassium
kg	kilogram
L	litre
LBBB	left bundle branch block
LDH	lactate dehydrogenase
LDL	low-density lipoprotein
LH	luteinising hormone
LV	left ventricular
mcg	microgram
MCS	microscopy culture and sensitivity
MDI	metered dose inhaler
MEq	milliequivalent
mg	milligram
MI	myocardial infarction
MIBG	meta-iodobenzylguanidine
MI	myocardial infarction
mL	millilitre
mm <sup>3</sup>	cubic millimetre

mmHg	millimetres mercury
mmol	millimole
mOsm	milliosmole
MSU	midstream urine specimen
Na	sodium
ng	nanograms
nmol	nanomoles
NSAID	non-steroidal anti-inflammatory drug
NYHA	New York Heart Association
ORS	oral rehydration solution
PaO2	partial pressure of oxygen in arterial blood
PCR	polymerase chain reaction
pH	acidity (partial pressure of hydrogen)
PID	pelvic inflammatory disease
PO2	oxygen partial pressure
PO4	phosphate
PPI	proton pump inhibitors
PSA	prostate specific antigen
PTH	parathyroid hormone
PTT	prolonged partial thromboplastin time
PV	vaginally
R	rifampicin
RBC	red blood cell
RDA	recommended dietary allowance
RH	rifampicin/isoniazid combination
RHZE	rifampicin/isoniazid/pyrazinamide/ethambutol combination
RPR	rapid plasma reagent test
SBP	systolic blood pressure
SC	subcutaneous
SL	sublingual
SLE	systemic lupus erythematosus
T3	triiodothyronine
T4	thyroxine
TB	tuberculosis
TCO2	total carbon dioxide
TIA	transient ischemic attack
TOD	target organ damage
TSH	thyroid stimulating hormone
VSD	ventricular septal defect
WBC	white blood cell
WHO	World Health Organisation
Z	pyrazinamide