STANDARD TREATMENT GUIDELINES

AND

ESSENTIAL DRUGS LIST

FOR

SOUTH AFRICA

HOSPITAL LEVEL
ADULTS

2006 EDITION
It is the vision of the National Department of Health to ensure that every citizen has access to good quality and affordable health care, including the access to medicines.

The goal of the National Drug Policy is to ensure an adequate and reliable supply of safe and efficacious medicines of acceptable quality in the most cost-effective manner to all citizens of South Africa. Resources are not unlimited and the appropriate management and use of drugs has often been underestimated and is increasingly being identified as a critical component of an efficient health care system. Thus affordability is a key element in ensuring access.

The National Department of Health through the Cluster: Pharmaceutical Policy and Planning has reviewed the Standard Treatment Guidelines and Essential Drugs List at hospital level for adults and paediatrics. These provide a vital tool to guide prescribers, particularly doctors working in district and regional hospitals.

More attention has been given to address healthy lifestyles, mental health conditions, neonatal conditions, palliative care and to strengthen the implementation of the Department’s Comprehensive HIV and AIDS Prevention, Care, Management and Treatment Plan. More in depth emphasis has been placed on the review of the endocrine, hypertension, infections and tuberculosis chapters. Evidence-based decision-making has been strengthened in the selection of drug entities.

The National EDL Committee has endeavoured to consult widely with colleagues within the Department, Provincial Pharmacy and Therapeutic Committees, universities, experts in different specialities, relevant societies and stakeholders. I would like to take this opportunity to thank the National Essential Drugs List Committee, the Expert Review groups and all those who have contributed for their dedication and hard work. Congratulations to all role players on this achievement.

I hope this edition of the Standard Treatment Guidelines and Essential Drugs List for Hospital Level will guide you daily in treating all patients optimally.

DR MANTO TSHABALALA–MSIMANG
MINISTER OF HEALTH
INTRODUCTION

The Department of Health is committed to providing quality and affordable health care including access to medicines to all citizens in South Africa. This is a challenging task in our health care system.

One of the goals of the National Drug Policy is to develop the full potential of drugs to improve the health status of South Africans within the available resources. The second edition of the Standard Treatment Guidelines (STGs) and Essential Drugs List (EDL) at Hospital level for adults and pediatrics is a vehicle for implementation of the National Drug Policy. Legislation has been adapted to address issues of affordability and improved access to medicines.

Advocacy and training are vital elements for successful utilisation of the Hospital Level STGs and EDL. The concepts of evidence based selection of medicines and cost-effective treatment protocols need to be included in the training of doctors, pharmacists, nurses and other health care professionals. Pharmacovigilance remains an important aspect of ensuring the safety of medicine used. A reporting form in this regard is included in the book. The inclusion of the ICD-10 codes for conditions should facilitate analysis, peer review, billing, etc.

The Hospital Level STGs and EDL are aimed for use at District and Regional Hospitals. Formularies remain the responsibility of Provincial Pharmacy and Therapeutics Committees. The Hospital Level STGs and EDL should be used as guidelines to develop these formularies. Updating the STGs and EDL is an ongoing process. Suggestions for improvement will be welcomed and considered.

The intention of the STGs and EDL is to strengthen priority health interventions. The implementation of Department’s Comprehensive HIV and AIDS Care, Management and Treatment Plan is encapsulated in this edition, particularly with regard to the use of antiretrovirals and treatment of opportunistic infections.

It should not be forgotten that patients must take full responsibility for their own health, including adherence to prescribed treatment and lifestyle changes.

I wish to record a special word of appreciation to the chairpersons to the expert groups, the groups themselves and all other contributors to this edition of the STGs and EDL.

Mr. T.D. Mseleku
Director General: Health
ACKNOWLEDGEMENTS

It is impossible to name all who have played a part in producing this edition. The treatment guidelines and essential drugs list, which appear in this book, have been compiled after a lengthy consultative process. They include recommendations and advice from numerous individuals and groups, including professional societies, expert committees, medical schools and secondary and tertiary hospitals. Most of the persons acknowledged also contributed much of their free time and without their dedication to the process this publication would not have been possible.

We offer sincere thanks to those who have contributed appropriate information and comments and to the members of the National Essential Drugs List Committee.

We are particularly grateful to members of the Adult Expert Committee for their dedication and hard work and Mr Steele, chairperson of the Committee. We are also appreciative of the technical and editorial support provided by Prof Pudifin.

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THE ESSENTIAL DRUGS 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.

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. They include the following:

- any drug included must meet the needs of the majority of the population
- sufficient proven scientific data regarding effectiveness must be available
- any drug included in the EDL should have a substantial safety and risk/benefit ratio
- all products must be of an acceptable quality, and must be tested on a continuous basis
- the aim, as a rule, is to include only products containing single pharmacologically active ingredients
- combination products, as an exception, will be included where patient compliance becomes an important factor, or two pharmacologically active ingredients are synergistically active in a product
- products will be listed according to their generic names only
where drugs are clinically equally effective, the drugs will be compared using the following:

- the best cost advantage
- the best researched
- the best pharmacokinetic properties
- the best patient compliance
- the most reliable local manufacturer

- a request for a new product to be included on the EDL must be supported by scientific data and appropriate references on its advantages and benefits over an existing product.

The implementation of the concept of essential drugs 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 Essential Drugs List (EDL) reflects only the minimum requirements for Health Care level facilities. In keeping with the objectives of the National Drug Policy, provincial and local Pharmacy and Therapeutics Committees may provide additional drugs based on the services offered and the competency of the staff at each facility.
HOW TO USE THIS BOOK

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

Where relevant this book is consistent with the Standard Treatment Guidelines for Primary Health Care, Integrated Management of Childhood Illness Strategy (IMCI) and other National Programme treatment guidelines.

The ICD-10 number, included with the conditions, refers to an international classification method used when describing certain diseases and conditions. A brief description and diagnostic clinical, radiological and laboratory tests are included to assist the medical officer to make a diagnosis. These guidelines also make provision for referral of patients with more complex and uncommon conditions to facilities with the resources for further investigation and management.

It is important to remember that the recommended treatments provided in this book are guidelines only and are based on the assumption that prescribers are competent to handle patients’ health conditions presented at their facilities.

The treatment guidelines are presented in chapters according to the organ systems of the body. In order to find the relevant sections in the book easily, use the indices at the back of the book. These have been divided into indices of disease conditions and drugs. Some of the drugs listed are only examples of a therapeutic class. In such cases the Provincial Pharmacy and Therapeutics Committees (PTCs) will decide on their drug of choice within that therapeutic class.

All suspected adverse drug reactions must be reported. In this book, only the common adverse effects have been mentioned. Information on the reporting of adverse drug reactions is provided in the section Guidelines for Adverse Drug Reaction Reporting. The purpose of ADR reporting is to reduce the risks associated with the use of drugs and ultimately improve patient care.

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

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
Pharmaceutical Programmes and Planning
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 should rather be tailored to answer a specific clinical question, and is of most value in drugs with a narrow therapeutic index or where there is considerable individual variation in pharmacokinetics.

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

Aminoglycosides
Peak levels will be adequate if dosing is adequate (5 mg/kg/day in a single daily dose); trough levels taken immediately before the next dose are 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
Drugs should be prescribed only when they are necessary for treatment following a clear diagnosis. Not all patients or conditions need a prescription for drugs. In certain conditions simple advice and non-drug treatment 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 fetus 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
• 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 drug or preparation should be written in full using the generic name and
• no abbreviations should be used due to the risk of misinterpretation. Avoid the Greek 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 which 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:
  ▪ drug 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 prescriptions 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 the 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 that the prescription is dated and that the patient’s name and folder number are on the prescription card. Only then sign the prescription, 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 ß-adrenergic antagonists. Have an IV line, ECG monitor and spirometer in place. Once desensitised, treatment must not lapse as risk of subsequent allergy increases. A history of Stevens-Johnson 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.

| A: Reconstitute phenoxyethylpenicillin 250 mg/5mL |
|---|---|---|
| Step | Drug mg/mL | Amount to administer (mL) |
| Strictly every 15 minutes | B: To make 0.5 mg/mL solution | |
| 1 | 0.5 mg/mL solution | 0.1 mL |
| 2 | 0.5 mg/mL solution | 0.2 mL |
| 3 | 0.5 mg/mL solution | 0.4 mL |
| 4 | 0.5 mg/mL solution | 0.8 mL |
| 5 | 0.5 mg/mL solution | 1.6 mL |
| 6 | 0.5 mg/mL solution | 3.2 mL |
| 7 | 0.5 mg/mL solution | 6.4 mL |
| C: To make 5 mg/mL solution | Dilute 1 mL of reconstituted phenoxyethylpenicillin solution in 9 mL water. | |
| 8 | 5 mg/mL solution | 1.2 mL |
| 9 | 5 mg/mL solution | 2.4 mL |
| 10 | 5 mg/mL solution | 4.8 mL |
| D: Reconstituted phenoxyethylpenicillin 250 mg/5mL = 50 mg/mL | | |
| 11 | 50 mg/mL solution | 1.0 mL |
| 12 | 50 mg/mL solution | 2.0 mL |
| 13 | 50 mg/mL solution | 4.0 mL |
| 14 | 50 mg/mL solution | 8.0 mL |

After Step 14, observe for 30 minutes, then 1 g IV benzylpenicillin (Penicillin G). Interval between doses: 15 minutes.
### Parenteral route

<table>
<thead>
<tr>
<th>Step</th>
<th>Drug mg/mL</th>
<th>Amount to administer (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.1 mg/mL</td>
<td>0.1 mL</td>
</tr>
<tr>
<td>2</td>
<td>0.1 mg/mL</td>
<td>0.2 mL</td>
</tr>
<tr>
<td>3</td>
<td>0.4 mg/mL</td>
<td>0.4 mL</td>
</tr>
<tr>
<td>4</td>
<td>0.8 mg/mL</td>
<td>0.8 mL</td>
</tr>
<tr>
<td>5</td>
<td>1 mg/mL</td>
<td>0.16 mL</td>
</tr>
<tr>
<td>6</td>
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<td>0.32 mL</td>
</tr>
<tr>
<td>7</td>
<td>1 mg/mL</td>
<td>0.64 mL</td>
</tr>
<tr>
<td>8</td>
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<td>0.12</td>
</tr>
<tr>
<td>9</td>
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<tr>
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<tr>
<td>12</td>
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</tr>
<tr>
<td>13</td>
<td>10 mg/mL</td>
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</tr>
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<tr>
<td>15</td>
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<td>0.32</td>
</tr>
<tr>
<td>17</td>
<td>100 mg/mL</td>
<td>0.64</td>
</tr>
</tbody>
</table>

Strictly every 15 minutes:

Interval between doses: 15 minutes.

After Step 17, observe for 30 minutes, then 1 g IV benzylpenicillin (Penicillin G).
A GUIDE TO PATIENT EDUCATION IN CHRONIC CONDITIONS

Poor therapeutic outcome of chronic conditions such as asthma, diabetes, epilepsy and hypertension can, in many cases, be ascribed to:
• poor or non-adherence to an otherwise sound therapeutic regimen;
• lack of communication between the various health care providers involved in the patient's management;
• lack of effective communication between health care provider and patient;
• ineffective and/or insensitive regimens;
• inconsistency of medicine supply.

Patient Compliance
A patient's compliance to his or her therapeutic regimen may be influenced by:
• medicine selection - prescribing should be the result of a process of concordance whereby the patient's needs and preferences are matched to the available therapeutic alternatives;
• patient education - this empowers the patient to make an informed decision as to whether he or she should comply or not.

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

Other influencing factors might be:
• adverse side effects of the medicines;
• lifestyle behaviour;
• level of responsibility to manage and control the disease.

Patients behaviour patterns contributing toward poor compliance
Patients may perceive treatment as unnecessary.
In conditions that are asymptomatic, e.g. hypertension, or those that only produce transient symptoms such as epilepsy:
• the patient often questions the validity of complying with therapy where there are no obvious results. As a result he or she decides to abandon therapy particularly where the therapy introduces new symptoms (side effects);
• the patient is compliant in a cyclical fashion - for a short period following transient symptoms (eg. seizure) or increased awareness (eg. following a BP reading at the clinic) but after a period returns to being non-compliant until the next episode of symptoms or clinic visit.

In conditions where symptoms show no improvement and where therapy merely controls the pathophysiological process.
• the patient often feels that his/her therapy has not contributed toward quality of life and in many ways has placed certain demands upon his/her lifestyle.
To be compliant on a sustained basis means that the patient must adjust his/her lifestyle in such a fashion that the regimen becomes habit. Inclusion of a regimen into the patient’s lifestyle is determined by the magnitude with which this adaption intrudes upon his/her established pattern. The greater the demand, the less likely the patient is to comply. Thus for example a lunchtime dose in a school-going child who remains at school for extramural activity is unlikely to succeed. A shift worker may need to take a sedating medicine in the morning when working night shifts, and at night, when working day shifts.

Some patients’ 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.

**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 the latter. Provide realistic expectations regarding:
- normal progression of the illness - especially important in those diseases where therapy merely controls the progression.
- 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.

**Towards concordance when prescribing**
Establish the patient’s:
- occupation
- daily routine
- recreational activities
- past experiences with other medicines
- expectations of therapeutic outcome

Balance these againsts the therapeutic alternatives identified based on clinical findings. Any clashes with the chosen therapy should be discussed with the patient in such a manner that the patient will conform to a changed lifestyle.

**Note:**
Education that focuses on these identified problems is more likely to be successful than a generic approach toward the condition/medicine.
Improving Continuity of Therapy
Clear and concise records.
Patient involvement 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.

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 compliance (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 problem ask yourself whether or not this medicine is being used to manage a side effect.
• Compliance with a once daily dose is best. Twice daily regimens show agreeable compliance. However once the interval is decreased to 3 times a day there is a sharp drop in compliance with poor compliance 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 compliance.
CHAPTER 1
ALIMENTARY TRACT

1.1 GASTROINTESTINAL DISORDERS

1.1.1 COLITIS, ULCERATIVE (UC)

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

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

NON-DRUG TREATMENT
Fully explain the condition to the patient and relatives.

Note:
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.

DRUG TREATMENT
Correct electrolyte, haematinic and nutritional deficiencies by the enteral or parenteral route.

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

ACUTE ATTACK
Mild to moderate disease
• sulfasalazine, oral, 1–2 g, 4–6 times daily
  Maximum dose: 3–4 g daily.
  Monitor FBC.
If there is no response to sulfasalazine:
ADD
• prednisone, oral, 1.5 mg/kg daily
  Minimum dose: 30–40 mg daily.
  Once the symptoms have resolved, prednisone can be tapered slowly by 5 mg/week over a 3-month period.
Severe disease
Admit patient.
Intravenous corticosteroids, e.g.:
• hydrocortisone, IV, 100 mg 6 hourly
  Failure to respond to 10 days of IV corticosteroids is an indication for an emergency
colecotomy.
ADD
• azathioprine, oral, 2 mg/kg daily. Specialist initiated.
  OR
  methotrexate, oral, 15–25 mg/week
PLUS
  folic acid, oral, 5 mg/week with methotrexate
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/day. Specialist initiated.
  These are most effective if combined with oral sulfasalazine.
AND/OR
• prednisone, oral, 1.5 mg/kg/day for 14 days

MAINTENANCE OF REMISSION
Extensive disease
• sulfasalazine, oral, 500 mg twice daily
  May be titrated to 1g 4 times daily.
Patients with recurrent severe attacks to maintain remission:
• azathioprine, oral, 2 mg/kg. Specialist initiated.

Limited disease
• sulfasalazine, oral, 500 mg twice daily
  May be titrated to 1 g 4 times daily.

REFERRAL
  o confirmation of diagnosis
  o initiation of long-term therapy
  o refractory cases
  o 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)
    • temperature > 38ºC
    • > 6 bloody stools per day
    • dilated colon or small bowel on X-ray
  o toxic megacolon (transverse colon diameter > 6 cm) 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.

1.1.2 CROHN’S DISEASE (CD)

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

NON-DRUG TREATMENT
Patients must stop smoking as this is a strong predictor of relapse.
Patient education and general support.
Parenteral nutrition support may be necessary.
Dietary advice.
Long-term specialist follow up is required.
Vitamin deficiencies are very common in small bowel Crohn’s disease.

DRUG TREATMENT
The aim is to induce and maintain remission.
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 B₁₂, IM, 1 000 mcg, 3 monthly
Monitor for iron and folate deficiency.

COLONIC DISEASE
• sulfasalazine, oral, 500 mg twice daily, up to 1.5 g 3 times daily
  For acute attacks, 1–2 g, 4–6 times daily may be given.
  Maximum dose: 3–4 g daily.
Monitor FBC.

AND
• prednisone, oral, 1.5 mg/kg/day tapered 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.
Immunomodulators
For patients with recurrent attacks of CD or those with extensive disease, i.e. ileum and colon:
• azathioprine, oral, 2 mg/kg/day. Specialist initiated.
  OR
  methotrexate, oral, 15–25 mg/week. Specialist initiated.
  PLUS
  folic acid, oral, 5 mg/week with methotrexate

Emergency management at specialist facility will include:
  o resuscitation with parenteral fluids
  o blood transfusions
  o corticosteroids,
  o antibiotics, and
  o nasogastric suction as indicated

PERI-ANAL DISEASE
There is evidence of recurrence on withdrawal of therapy prolonged treatment may be indicated.
• metronidazole, oral, 400–800 mg 8 hourly
  OR
  ciprofloxacin, oral, 500 mg 8 hourly

REFERRAL
  o for further therapy
  o peri-anal absceses/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:
  o incorrect diet (fibre and fluid)
  o lack of exercise
  o pregnancy
  o old age
  o psychogenic disorders
  o chronic use of enemas and laxatives
  o cancer of the bowel
  o certain drugs
  o metabolic
  o endocrine
  o neurogenic
  o lower bowel abnormalities
  o ignoring the urge
  o behavioural problems in children

NON-DRUG TREATMENT
Treat underlying disease if possible.
Dietary advice 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.
Encourage regular bowel habits.
Physical exercise to be encouraged.

**DRUG TREATMENT**

**Osmotic laxatives**
- lactulose, oral, 10–20 mL daily
  - Titrate to effect i.e. up to 60 mL/day.

**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**
- investigation for organic disease

**1.1.4 DIVERTICULOSIS**

**K57.9**

**NON-DRUG TREATMENT**
Increase unprocessed foods in diet.
Supplement with bran.

**DRUG TREATMENT**

**LOCALISED DIVERTICULITIS**
- ciprofloxacin, oral, 500 mg 12 hourly
  **PLUS**
  - metronidazole, oral, 400 mg 8 hourly

**REFERRAL**
- clinical deterioration or failure to improve
- peritonitis
- fistulae
- strictures
- massive haemorrhage
1.1.5 GASTRO-ÖESOPHAGEAL REFLUX DISEASE (GORD)

DESCRIPTION
GORD is 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 and are termed non-erosive reflux disease (NERD).

LOS ANGELES CLASSIFICATION OF ENDOSCOPIC GRADING
A One or more mucosal breaks no longer than 5 mm, none of which extends between the tops of the mucosal folds.
B One or more mucosal breaks more than 5 mm long, none of which extends between the tops of two mucosal folds.
C Mucosal breaks that extend between the tops of two or more mucosal folds, but which involve less than 75% of oesophageal circumference.
D Mucosal breaks which involve at least 75% of oesophageal circumference.

NON-DRUG TREATMENT
Dietary advice by dietician.
Weight reduction is recommended if overweight.
All patients with alarm symptoms, i.e. weight loss, haematemesis and malaena, dysphagia and anaemia, should have endoscopy at the earliest opportunity.

DRUG TREATMENT
Empiric therapy for GORD can be instituted provided there are no alarm symptoms.
• aluminium hydroxide/magnesium trisilicate 250/500 mg, oral, 1–2 tablets to be chewed 1 hour before and 3 hours after meals and at night, for 4 weeks
OR
cimetidine, oral, 400 mg twice daily

CAUTION
Cimetidine has a high potential for drug interactions when used concomitantly with other drugs.

Antacids
There is little evidence that alginate and dimethicone (simethicone) are more useful than simple antacids. This is for intermittent disease without alarm symptoms, i.e. no weight loss, no blood vomiting and under 45 years of age.

PPIs
A trial with a PPI confirms acid related disease. Only if no alarm symptoms:
• omeprazole, oral, 40 mg/day for 4 weeks
CHAPTER 1  ALIMENTARY TRACT

Recurrence of symptoms.
Endoscopic confirmation of disease.

LOS ANGELES A OR B
Restart PPI:
•  omeprazole, oral, 20 mg/day
  Decrease to 10 mg/day after 4 weeks.

Try to step down to long-term H₂-blocker therapy:
•  cimetidine, oral, 400 mg twice daily

LOS ANGELES C OR D
Restart PPI:
•  omeprazole, oral, 20 mg/day
  Decrease to 10 mg/day after 4 weeks.

Note:
These patients usually need maintenance PPI therapy.

BARRETT’S OESOPHAGUS
Restart PPI:
•  omeprazole, oral, 20 mg/day

Note:
These patients usually need maintenance PPI therapy.
There is no convincing evidence that long-term treatment of Barrett’s oesophagus reduces dysplasia and or progression to malignancy.

REFERRAL CRITERIA
  o  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 huge 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 GIT resulting in recurrent symptoms of pain, constipation and/or diarrhoea and bloating.
CHAPTER 1  ALIMENTARY TRACT

NON-DRUG TREATMENT
Reassure patient that there is no serious organic disorder, after limited investigations. High fibre/bran diets may be tried for patients with constipation. Warn about temporary increased flatus and abdominal distension. High fibre/bran diets are not effective for GLOBAL IBS (i.e. all symptoms). Dietary advice by dietician.

DRUG TREATMENT
Not specifically indicated. Based on patients predominant symptoms. Short-term symptomatic treatment for diarrhoea and/or constipation.

Laxatives only for constipation specific, see Section 1.1.3: Constipation/ Faecal Impaction. Antidiarrhoeals only for diarrhoea specific, 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.

The prognosis of acute pancreatitis can be estimated using Ranson’s 11 prognostic signs:

On admission
1  age > 55 years
2  serum glucose > 11.1 mmol/L
3  serum LDH > 350 units/L
4  AST > 250 U
5  WBC > 16 000/microL

48 hours after admission
6  Hct decrease > 10%
7  serum urea > 1.8 mmol/L
8  serum Ca < 2 mmol/L
9  PaO₂ < 60 mmHg
10 base deficit > 4 mEq/L
11 estimated fluid sequestration > 6 L
Mortality increases with the number of positive signs:
- < 3 positive signs: mortality rate < 5% (mild)
- 3–4 positive signs: mortality rate 15–20% (moderate)
- > 6 positive signs: mortality rate – up to 100% (severe)

Pancreatitis associated with necrosis and haemorrhage has a mortality rate of ≥ 10–50%.

**NON-DRUG TREATMENT**
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.

**DRUG TREATMENT**

**Analgesia**
- 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, followed by 60–120 mL diluted in 1 L sodium chloride solution 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**
For severe acute pancreatitis, i.e. Ranson > 4:
- Broad spectrum IV antibiotics, e.g.:
  - benzylpenicillin (Penicillin G), IV, 2 million units 6 hourly
  **PLUS**
  - gentamicin, IV, 5 mg/kg once daily
  **PLUS**
  - metronidazole, oral, 400 mg 8 hourly

**OR**
- 3rd generation cephalosporin, e.g.:
  - cefotaxime, IV, 1 g 12 hourly
  **PLUS**
  - metronidazole, oral, 400 mg 8 hourly

**REFERRAL**
- all patients with moderate or severe pancreatitis
CHAPTER 1 ALIMENTARY TRACT

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.

NON-DRUG TREATMENT
Abstinence from alcohol reduces abdominal pain in early stages of the disease. Small frequent meals, and restricted fat intake – reduce 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.

DRUG TREATMENT
Treatment is aimed at:
- pain
- malabsorption
- endocrine function. See Section 8.5.2: Insulin Dependent Diabetes Mellitus (IDDM) Type 1.

Analgesia
See Section 12.1: Chronic Pain.

Note:
Pancreatic enzymes may reduce pain by negative feedback on pancreatic secretion.

Malabsorption
Start treatment when steatorrhea > 7 g (or 21 mmol) fat in faeces/24 hours while on a 100 g fat per day diet. Reduce dietary fat to less than 25 g/meal.

- lipase/protease 8 000/25 000 units, oral
  lipase: 30 000 units
  PLUS
  trypsin: 10 000 units during 4 hours post prandial
  Aim for 5% of normal maximum output.

Supplements of fat soluble vitamins may be indicated.
1.1.10 PEPTIC ULCER

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 then be assessed at scope by rapid urease testing (RUT) or biopsy.

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

DRUG 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 in the future. Empiric eradication of H. pylori is not recommended.

Proton pump inhibitor (PPI)
• omeprazole, oral, 40 mg/day
  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.
CHAPTER 1 ALIMENTARY TRACT

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

Proton pump inhibitor (PPI)
• omeprazole, oral, 20 mg/day
  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 elderly or concomitant disease. Maintenance therapy with proton pump inhibitor, e.g.:
• omeprazole, oral, 20 mg/day. Specialist initiated.

1.2 HEPATIC DISORDERS

1.2.1 HEPATITIS, NON-VIRAL
K70.9
* 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.

NON-DRUG TREATMENT
Diet: protein restricted if features of liver failure are present. Excessive protein restriction may accentuate catabolism.
Alcohol is inadvisable in any form of hepatitis.
Avoid other hepatotoxic agents.
Monitor blood glucose regularly because hypoglycaemia is common.

DRUG TREATMENT
HEPATITIS DUE TO INFECTIONS
Antibiotic therapy based on culture.

ALCOHOL INDUCED HEPATITIS
Even if no bleeding:
• vitamin K₁, IM/IV, 5–10 mg daily for 10 days
• thiamine, oral, 100 mg/day
Other vitamins if indicated.
CHAPTER 1

**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/day
  Taper down to a suitable maintenance dose.
**PLUS**
- azathioprine, oral, 0.5–1 mg/kg/day

**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 has occurred.

**1.2.2 LIVER FAILURE**

**NON-DRUG TREATMENT**
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.

**DRUG TREATMENT**
On admission to change pH of large bowel:
- lactulose, oral, 10–30 mL
Thereafter, to attain 2–3 soft stools a day:
- lactulose, oral, 10–30 mL 3 times daily
  Titrate dose to 2–3 soft stools a day.

**EVEN IF NO BLEEDING**
- vitamin K₁, IM/IV, 5–10 mg daily for 10 days

Other vitamins if indicated.
Multivitamin supplements should be considered and may be indicated.
CHAPTER 1  

**ALIMENTARY TRACT**

**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  

**DESCRIPTION**
The complications of portal hypertension are:
- variceal bleeds
- ascites and fluid overload
- encephalopathy
- spontaneous bacterial peritonitis in patients with ascites

**NON-DRUG TREATMENT**
Ascites: salt restriction, i.e. < 2 g/day.
Monitor weight regularly and bed rest.
Encephalopathy: low protein diet. Protein restriction indicated. 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.

**DRUG TREATMENT**

**ASCITES, OEDEMA**
If no response to strict bed rest after 2–3 days:
- spironolactone, oral, 50–200 mg/day  
  Titrate to higher dosages with caution.
  Optimal dose: 400 mg/day.
  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/day, 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/day.

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
CHAPTER 1 ALIMENTARY TRACT

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 hemodynamic 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 3 times daily

OESOPHAGEAL VARICES
To reduce the risk of bleeding:
• propranolol, oral 10–20 mg 12 hourly

1.3 DIARRHOEA, GASTROINTESTINAL AND LIVER INFECTIONS

1.3.1 CHOLERA
A00.9
* Notifiable disease.

DESCRIPTION
Diarrhoea due to Vibrio cholerae, often in outbreaks.

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

DRUG TREATMENT
• ciprofloxacin, oral, 1 g immediately as a single dose

1.3.2 ACUTE INFLAMMATORY DIARRHOEA (DYSENTERY)
A03.9

DESCRIPTION
Diarrhoea with neutrophils, blood and/or mucus. Causes include shigella, salmonella and campylobacter.

NON-DRUG TREATMENT
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 advised.
CHAPTER 1 ALIMENTARY TRACT

DRUG 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 \textit{E. coli}.

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

DRUG TREATMENT
• loperamide, oral, 4 mg immediately, followed by 2 mg after each loose stool
  Maximum dose: 16 mg/day.

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 \textit{Clostridium difficile} can be demonstrated on stool samples.

NON-DRUG TREATMENT
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.

DRUG 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:
• 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*.

NON-DRUG TREATMENT
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.

DRUG 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.

NON-DRUG TREATMENT
Fluid and electrolyte replacement in severe diarrhoea.

DRUG 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 HEPATITIS, VIRAL
B19.9
* Notifiable disease

DESCRIPTION
Hepatitis is 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.
CHAPTER 1  
ALIMENTARY TRACT

NON-DRUG TREATMENT

ACUTE HEPATITIS

Bed-rest until acute phase is over.

Alcohol should be avoided during the illness and for several months after clinical recovery. In cases of hepatitis B sexual contacts should be serologically screened. If they are seronegative (Anti-HBs negative) then they should receive hepatitis B active immunisation.

DRUG 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, includes 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

<table>
<thead>
<tr>
<th>Source patient</th>
<th>HBsAG positive</th>
<th>HBsAG negative</th>
<th>HBsAG unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccination status and antibody response status of HCW</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| unvaccinated or vaccination incomplete | • HBIG, IM, 500 units *  
• HB vaccine (3 doses at monthly intervals) | • Initiate Hep B vaccination (month 0, 1 and 6) | • HBIG, IM, 500 units*  
• HB vaccine (3 doses at monthly intervals) |
| vaccinated AND HBsAb > 10 units/mL* | No treatment | No treatment | No treatment |
| vaccinated AND HBsAb < 10 units/mL | • HBIG, IM, 500 units  
• Repeat HB vaccine (3 doses at monthly intervals) | No treatment | • HBIG, IM, 500 units*  
• Repeat HB vaccine (3 doses at monthly intervals) |

* HBIG and first dose of vaccine to be given simultaneously, but at different sites.

# If the delay in obtaining HBsAb results is more than 24 hours initiate treatment as for vaccinated AND HBsAb < 10 units/mL.
CHAPTER 1 ALIMENTARY TRACT

1.3.9 LIVER ABSCESS, PYOGENIC

K75.0

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

NON-DRUG TREATMENT
Drainage is essential in all cases. This should preferably be done percutaneously by inserting a catheter under ultrasound guidance.

DRUG TREATMENT
Empiric antibiotic therapy
• benzylpenicillin (Penicillin G), IV, 2 million units every 6 hours
PLUS
• gentamicin, IV, 5 mg/kg/day
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.

1.3.10 LIVER ABSCESS, AMOEBIC

A06.4

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

NON-DRUG TREATMENT
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.

DRUG TREATMENT
• metronidazole, oral, 400 mg 8 hourly for 10 days
1.3.11 PERITONITIS

DESCRIPTION
Infection of the peritoneum, usually secondary to a surgical cause such as perforated bowel. In this setting polymicrobial infection with anaerobes and Enterobacteriaceae is usually found. Primary or spontaneous bacterial peritonitis is much less common and usually complicates ascites in patients with portal hypertension. This is not usually polymicrobial but due generally to Enterobacteriaceae such as E. coli. Spontaneous bacterial peritonitis is often culture-negative but is diagnosed by ascitic neutrophil count > 0.25 x 10⁹/L (250 cells/ mm³).

NON-DRUG TREATMENT
SECONDARY PERITONITIS
Intravenous fluids and nasogastric suction.

Prompt surgical intervention is essential.

DRUG TREATMENT
Empiric antibiotic therapy
For surgical causes of peritonitis:
• benzylpenicillin (Penicillin G), IV, 2 million units every 6 hours
PLUS
• gentamicin, IV, 5 mg/kg/day
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

2.1 ANAEMIA, APLASTIC
D61.9

DESCRIPTION
Anaemia caused by bone marrow failure.

DIAGNOSTIC CRITERIA
Clinical
- pallor
- petechiae
- purpura
- bleeding
with frequent or severe infections.

Investigations
Pancytopenia, with anaemia, leucopenia and thrombocytopenia.
Hypoplastic bone marrow on trephine biopsy.

NON-DRUG TREATMENT
All blood products should be used sparingly and all patients should be discussed urgently with a regional haematology centre.
Limit the use of blood and blood products as the patient may be sensitised for future bone marrow transplant.
Blood products as needed, i.e. leucodepleted packed red cells and/or single donor leucodepleted platelets.

DRUG TREATMENT
If neutropenic and febrile, see Section 2.2: Febrile Neutropenia.

REFERRAL
- all cases of suspected aplastic anaemia for consideration such as bone marrow transplants or ATG and ciclosporin
Stabilise patient, if necessary with blood products before transport, but after consultation with an expert.

2.2 FEBRILE NEUTROPENIA
D70

DESCRIPTION
Documented fever 38°C plus absolute neutrophil count 0.5 x 10⁹/L from any cause.

This is a medical emergency as these patients can rapidly develop features of severe sepsis (multi-organ failure and/or hypotension).
CHAPTER 2 BLOOD AND BLOOD FORMING ORGANS

NON–DRUG TREATMENT
Treat the underlying cause of neutropenia, if applicable.
Withdraw any drug that may cause neutropenia.
Blood cultures must be taken prior to antimicrobial therapy.

DRUG TREATMENT
For patients with febrile neutropenia within 48 hours of admission:
3rd generation cephalosporin, e.g.:
• ceftriaxone, IV, 1 g daily
PLUS
• gentamicin, IV, 5 mg/kg daily
Duration of therapy:
• If neutrophil count increases to > 0.5 x 10^9/L, continue for 2 days after fever has settled.
• If neutrophil count remains ≤ 0.5 x 10^9/L, continue for 7 days after fever has settled.

If fever develops after 48 hours of admission:
• piperacillin/tazobactam, IV, 4.5 g 8 hourly
 OR
 cefepime, IV, 1 g 12 hourly
 OR
 A carbapenem, e.g.:
 meropenem, IV, 1 g 8 hourly

REFERRAL
• persistent fever for 5 days, despite above measures
• for further investigation and management of the underlying cause

2.3 ANAEMIA, HAEMOLYTIC

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. 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 antiglobin) is usually positive with autoimmune haemolysis.
CHAPTER 2 BLOOD AND BLOOD FORMING ORGANS

Investigate for auto-immune disease or malignancy, such as lymphoma.

NON-DRUG TREATMENT
Do not transfuse prior to appropriate investigations, unless anaemia is life threatening. Coombs-positive haemolytic anaemia may require expert blood cross matching.

In G6PD deficiency, avoid drugs known to cause haemolysis, including aspirin, sulfonamides (including trimethoprim/sulfamethoxazole), dapsone and primaquine. In patients with cold agglutinin all transfusions need to be given through a blood warmer to avoid cold induced haemolysis.

DRUG TREATMENT
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 level and lactic dehydrogenase serum values, taper dose over a period of 2–4 weeks to 30 mg daily.
  Thereafter further reduction should be slower to prevent disease recurrence.
  Prednisone treatment can be stopped when the Coomb’s reaction becomes negative.

If inadequate response:
ADD
• azathioprine, oral, 2.5 mg/kg daily may be required for several months
  Titrate to Hb response.
  Monitor for neutropenia.

Patients who fail drug treatment should be considered for splenectomy.

REFERRAL
In consultation with a specialist:
  o no response to drug treatment
  o other causes of haemolytic anaemia

2.4 ANAEMIA, IRON DEFICIENCY
D50.9

DESCRIPTION
Anaemia due to iron deficiency. Common causes of iron deficiency are poor nutritional intake and blood loss.
CHAPTER 2
BLOOD AND BLOOD FORMING ORGANS

HYPOCHROMIC MICROCYTIC ANAEMIA

Investigations
Iron studies are necessary to confirm the iron deficiency.
Document a haematological response to iron therapy.

NON-DRUG TREATMENT
Identify and treat the cause.
Dietary adjustment.

DRUG TREATMENT
ORAL IRON SUPPLEMENTATION
If GIT intolerance occurs, this can be obviated by taking the preparation with meals,
at the expense of a decrease in absorption.
A reticulocytosis begins on the 3rd or 4th day after therapy, peaks at approximately day
ten and lasts between 12 and 21 days.
The haemoglobin rise is ± 0.1 g/dL/day or 2 g/dL every 3 weeks.

Therapeutic
• iron, elemental, oral, 100–200 mg daily, e.g.:
  ferrous sulphate compound, oral, 170 mg three times daily
  Treat until haemoglobin normalises.
After the haemoglobin has returned to normal, treatment should be continued for
6 months in order to adequately replenish the iron stores.

Prophylaxis
E.g. during pregnancy.
• ferrous sulphate compound, oral, 170 mg daily
With failure to respond to iron therapy, consider the following:
  o non-compliance, i.e. failure to take tablets
  o continued blood loss
  o wrong diagnosis/another cause of anaemia
  o malabsorption
  o mixed deficiency concurrent folate or vitamin B12 deficiency
  o use of slow release preparations

PARENTERAL IRON
Intravenous iron is seldom required.
The use of parenteral iron may be associated with anaphylaxis, which may be fatal.
Parenteral iron is only indicated where oral iron is:
  o ineffective, e.g. malabsorption
  o impractical, e.g. active Crohn’s disease
  o where there is a need to replenish body iron rapidly e.g. late pregnancy or patients
    on haemodialysis and erythropoietin therapy
BLOOD TRANSFUSION
Indicated in patients with:
- anaemia leading to cardiac failure or severe dyspnoea
- active, ongoing bleeding
- where rapid correction of anaemia is required prior to performing an invasive procedure or surgery

2.5 ANAEMIA, MEGALOBLASTIC

DESCRIPTION
Anaemia caused by a deficiency of folate and/or vitamin B₁₂.

Investigations
- Elevated MCV (mean corpuscular volume) and MCH (mean corpuscular haemoglobin).
- Macro-ovalocytes on blood smear; polynuclear neutrophils, thrombocytopenia with giant platelets.
- Decreased serum vitamin B₁₂ or red blood cell folate.
- Pancytopenia in severe cases.
- Intrinsic factor antibody test in vitamin B₁₂ deficiency, and anti-parietal cell antibodies to document pernicious anaemia.

NON-DRUG TREATMENT
Dietary modifications to ensure adequate intake of folate and vitamin B₁₂. Food fortification of staple foods such as flour, etc.
Try to avoid blood transfusion. Only transfuse in consultation with a specialist. Identify and treat the underlying cause, e.g. antibiotics for intestinal overgrowth with bacteria.

DRUG TREATMENT
After specimens for folate and B₁₂ levels have been taken, start with folic acid, vitamin B₁₂ and potassium supplementation. Monitor serum potassium. When results are available, adjust management as follows:

Folic acid deficiency
- folic acid, oral, 5 mg daily until haemoglobin returns to normal
- Prolonged treatment may be required for malabsorption states.

Vitamin B₁₂ deficiency
- vitamin B₁₂, IM, 1 mg (1 ampoule) daily for 3–5 days, then weekly for a further 1–3 doses (total of 6 mg) or 1 g given on alternate days 3 times a week for 2 weeks, then two monthly for life, except in clear nutritional deficiency where the individual can modify their diet
CHAPTER 2 BLOOD AND BLOOD FORMING ORGANS

Note:
Response to treatment is associated with an increase in strength and improved sense of well-being.
Reticulocytosis begins 3 to 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.
Failure to respond, consider the following:
- co-existing folate and/or iron deficiency
- infection
- hypothyroidism
- myelodysplasia
- incorrect diagnosis

Hypokalaemia and salt retention may occur early in course of therapy. Monitor serum potassium. Thrombocytosis may also be seen.

PROPHYLAXIS
Vitamin B₁₂
Indicated for patients after total gastrectomy and ileal resection.

Folic acid
Indications:
- 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 crisis, and infection.

THE PAIN CRISIS/ VASO-OCCulsive 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
CHAPTER 2 BLOOD AND BLOOD FORMING ORGANS

- symmetrically in several limbs
- 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 electropheresis.

NON-DRUG TREATMENT
Bed rest and/or hospitalisation.
Give oxygen.

DRUG TREATMENT

Analgesia
For severe pain:
- morphine, IV, 10–15 mg 4 hourly

Fluids
Keep well hydrated with:
- sodium chloride 0.9% or sodium chloride 0.9% with dextrose 5%, IV

All patients:
- folic acid, oral, 5 mg daily

REFERRAL
- all for chronic management in a specialised centre

2.7 MYELODYSPLASTIC SYNDROMES

DESCRIPTION
A group of disorders characterised by refractory cytopenia’s due to bone marrow failure. Anaemia is very common and patients become easily symptomatic particularly if they have ischaemic heart disease. In some patients these disorders may develop increasing number of blasts and even acute leukaemia.

Investigations
Evidence of cytopenia, with normal B12 and folic levels and substantial morphological dysplasia on the blood smear.
Bone marrow examination confirms dysplasia of the blood elements and the presence of cytogenetic abnormalities.

DRUG TREATMENT
It is advised that transfusion should be with leucodepleted red cells and/or platelets to delay immunisation, as clinically indicated.
CHAPTER 2  BLOOD AND BLOOD FORMING ORGANS

Bone marrow transplantation can be curative in younger patients. If neutropenic and febrile, see Section 2.2: Febrile Neutropenia.

REFERRAL
- all patients for further investigation and management

2.8 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 differ 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.

2.8.1 HAEMOPHILIA A AND B, VON WILLEBRAND’S DISEASE

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).

Sub classification (factor VIII and IX deficiency):

<table>
<thead>
<tr>
<th>Class</th>
<th>Clotting factor</th>
<th>% of normal</th>
<th>Signs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>VIII or IX</td>
<td>5–25%</td>
<td>Occasional bleeds</td>
</tr>
<tr>
<td>Moderate</td>
<td>VIII or IX</td>
<td>2–5%</td>
<td>Less frequent bleeds post trauma/dental extraction</td>
</tr>
<tr>
<td>Severe</td>
<td>VIII or IX</td>
<td>&lt;1–2%</td>
<td>Trauma/spontaneous bleeds</td>
</tr>
</tbody>
</table>
CHAPTER 2 BLOOD AND BLOOD FORMING ORGANS

Complications include haemarthrosis with later chronic arthropathy; intracranial haemorrhage, soft tissue and muscle haematomas.

DIAGNOSTIC CRITERIA

Clinical
Major bleeds:
- CNS
- advanced joint and soft tissue
- gastrointestinal
- hip and iliopsoas
- neck and throat
- forearm compartments
- severe injury

Minor bleeds:
- early joint bleed
- mouth and gum
- muscle
- epistaxis
- soft tissue
- haematuria

Pain/tingling in the joints suggests bleeding into the joint in a known haemophiliac complaining of pain.

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.

NON-DRUG TREATMENT
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)

ACUTE BLEEDS INTO JOINTS
Apply ice packs.
Bed rest and rest of affected joint/limb until pain free and no further bleeding.
No weight bearing.
Splint (no circumferential casting).

DRUG TREATMENT
Avoid IM injections.
Exercise great caution when taking blood specimens.
Avoid aspirin and NSAIDS.
Taking blood from femoral veins is absolutely contra-indicated.
CHAPTER 2  BLOOD AND BLOOD FORMING ORGANS

HAEMOPHILIA

Bleeding episodes are treated with factor replacement therapy and spontaneous bleeding is usually controlled if the patient’s factor level is raised above 20% of normal. For major surgery, serious post-traumatic bleeding or when haemorrhage is occurring at a dangerous site (such as the CNS), however, the factor level should be elevated to 100% and then maintained above 50% when acute bleeding has stopped, until healing has occurred.

For pain, give analgesia at appropriate doses.

HAEMOPHILIA WITH NO INHIBITORS

Factor VIII deficiency (with no inhibitor present)

Bleeding episodes are treated with factor replacement therapy and spontaneous bleeding is usually controlled if the patient’s factor level is raised above 20% of normal. For major surgery, serious post-traumatic bleeding or when haemorrhage is occurring at a dangerous site, such as the CNS, however, the factor level should be elevated to 100% and then maintained above 50% when acute bleeding has stopped, until healing has occurred.

• lyophilised factor VIII concentrate, IV, administered 12 hourly for 1–3 days until pain free and full movement of joint/limb is restored
  
  Dose:
  Desired % increase in factor x body weight x 0.5
  e.g. 50% x 60 kg x 0.5 = 1 500 units

Factor IX deficiency (with no inhibitor present)

• lyophilised factor IX concentrate, IV, administered once daily for 1–3 days
  
  Dose:
  Desired % increase in factor x body weight x 1
  e.g. 50% x 60 kg x 1 = 1 300 units

HAEMOPHILIA WITH INHIBITORS

Refer for assessment and planning with a haematologist.

• factor VIII inhibitor-bypassing activity (FEIIBA) under haematologist supervision only

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 4 times daily for two minutes.
CHAPTER 2 BLOOD AND BLOOD FORMING ORGANS

Mucous membrane bleeds
- tranexamic acid, oral, 25 mg/kg 6 hourly
  Contraindicated in haematuria, factor IX deficiency, and with prothrombin complex concentrate.

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
  OR
desmopressin, intranasal, 10–20 mcg, once or twice daily

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

VON WILLEBRAND’S DISEASE

Mild bleeding
E.g. epistaxis and menorrhagia.
Antifibrinolytics, e.g.:
- tranexamic acid, oral, 1 g 4 times daily

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, intranasal, 10–20 mcg, once or twice daily

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 every 12 hours
  OR
lyophilised factor VIII concentrate, IV, 30–50 units/kg/day administered twice daily
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.
CHAPTER 2 **BLOOD AND BLOOD FORMING ORGANS**

**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

2.9 **IDIOPATHIC THROMBOCYTOPENIC PURPURA (ITP)**

**DESCRIPTION**
A common bleeding disorder due to immune destruction of platelets.
Exclude drug-induced thrombocytopenia, e.g. penicillins, cephalosporins, quinine, rifampicin and heparin.

**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 and may show large platelets.
Do INR and APTT, which should be normal in ITP.
Bone marrow aspirate and trephine bone marrow biopsy prior to starting steroids.
Patients with suspected ITP should be tested for SLE and for HIV infection, as ITP frequently is a precursor of SLE and may also be associated with HIV infection.

**NON-DRUG TREATMENT**
Avoid:
- medication that affects platelet function, e.g. NSAIDs and aspirin
- platelet transfusions unless life-threatening bleeds
- contact sport, injury and trauma
- dental procedures in acute phase
- IM injections
Reassure the patient that that resolution usually occurs in acute ITP.
Medic alert bracelet.
Platelet transfusions may be given if surgery is required or in life threatening bleeding.

**DRUG TREATMENT**

**ACUTE ITP**
- prednisone, oral, 2 mg/kg daily
  - Taper dose once response is achieved, usually within 10–14 days.
  - It may take a few months before prednisone is eventually discontinued.

**Platelet transfusions**
Platelet transfusions are indicated in acute active bleeding or before procedures.
In an adult, 1 mega-unit of single donor, leucocyte depleted platelets is usually
CHAPTER 2  BLOOD AND BLOOD FORMING ORGANS

sufficient to control the bleeding initially. Platelet transfusions have very short benefit in this condition as platelets are rapidly destroyed by the immune system.

HIV associated immune thrombocytopenia is an indication for antiretroviral therapy, regardless of CD4 counts.

REFERRAL

- local incapacity to manage the condition
- surgical treatment
  - Splenectomy should be considered in poor responders to oral corticosteroids, after consultation with haematologist.
  - Splenectomy is recommended in patients who still have platelet counts < 30 x 10^9/L after 3 months of steroid therapy or who require unacceptably high doses of corticosteroids (which are likely to produce adverse effects) to maintain a platelet count > 30 x 10^9/L.
  - Before splenectomy: pneumococcal (polysaccharide) vaccine.
  - After splenectomy: prophylactic penicillin should be used for 2 years.
- for consideration of gammaglobulin or pulse steroids
- ITP complicated by severe haemorrhage, bleeding into vital organs or an intracranial haemorrhage
- ITP that fails to resolve in 6–12 months on adequate treatment, i.e. chronic ITP

2.10 THROMBOTIC THROMBOCYTOPENIC PURPURA (TTP)

DESCRIPTION

A fulminating, generally lethal disorder characterised by:

- a Coombs'-negative haemolytic anaemia with severely fragmented red blood cells, i.e. microangiopathic haemolytic anaemia
- thrombocytopenic purpura
- fever
- renal failure
- and fluctuating, often bizarre neurologic manifestations.

Trombocytopenia and haemolysis with fragmented red blood cells may also occur in HIV infection, neoplasms with widespread metastases and in toxemaia of pregnancy.

NON-DRUG TREATMENT

Patients often respond to infusions of fresh frozen plasma if the required volume can be tolerated. Doses of 30 mL/kg are useful until response obtained and then tapered slowly to prevent recurrence of haemolysis. If there is no clinical improvement or patients are unable to tolerate plasma volume, and the equipment is available, plasmapheresis can induce rapid remissions.
While the patient is receiving plasma therapy, give:
• prednisone, oral, 1–2 mg/kg daily
  Taper dose once response is achieved.

2.11 THROMBOCYTOSIS/THROMBOCYTHEMIA
D75.2/D47.3

DESCRIPTION
Thrombocytosis refers to a platelet count > 600 x 10^9/L. The three most common causes of reactive thrombocytosis include:
  o bleeding
  o infection
  o iron deficiency, where the thrombocytosis responds to treatment of the underlying cause.

Thrombocythemia refers to a platelet count > 1 000 x 10^9/L.

Thrombocytosis/thrombocythemia may manifest clinically with either thrombosis or bleeding. Bleeding is more likely to occur with higher platelet counts.

Investigate the underlying cause of:
  o thrombocytosis, usually reactive or secondary cause
  o thrombocythemia, usually underlying myeloproliferative disorder, including essential thrombocythemia
  and manage accordingly.

DRUG TREATMENT
Aspirin and NSAIDs are contraindicated if the platelet count is > 1 000 x 10^9/L.

To reduce the thrombotic risk, especially in patients younger than 60 years with no previous thrombosis or haemorrhage and platelets < 1 000 x 10^9/L:
• aspirin, soluble, oral, 150 mg daily

REFER
  o all patients
2.12 ACQUIRED COAGULATION DEFECTS

2.12.1 DISSEMINATED INTRAVASCULAR COAGULATION (DIC)

MANAGEMENT
Identify and treat the underlying cause. If bleeding, platelet concentrates, cryoprecipitate, and fresh frozen plasma contain the haemostatic factors and inhibitors of blood coagulation commonly depleted in patients with DIC.

SUPPORTIVE THERAPY
In general, patients should be transfused with blood components when they have bleeding and depleted haemostatic factors. Cryoprecipitate provides a more concentrated source of fibrinogen (150–200 mg/unit) and red cell transfusions may be required.

The use of heparin or antiplatelet drugs to inhibit the coagulation process is usually not indicated because bleeding may, in some cases, be aggravated.

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

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

Fibrinolytic inhibitors should not be considered because failure to lyse thrombi in organs such as the kidney may have adverse effects.

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: ±280 mL/unit.

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

Perform frequent estimation of the platelet count and coagulation screening tests.
CHAPTER 3
CARDIOVASCULAR SYSTEM

3.1 ACUTE CORONARY SYNDROMES

3.1.1 ST ELEVATION MYOCARDIAL INFARCTION (STEMI)

DESCRIPTION
Chest pain that is associated with elevated cardiac markers and ECG changes either ST elevation or new LBBB.

NON-DRUG TREATMENT
Rest, reassurance.
Oxygen 40% if clinically hypoxic.
Early ambulation.

DRUG TREATMENT
Inhibit platelet thrombi or aggregation:
• aspirin, soluble, oral, 300 mg immediately, followed by 150 mg daily

PLUS
To relieve spasm and pain, and to reduce preload:
• isosorbide dinitrate, SL, 5 mg immediately
  May be repeated at 5-minute intervals for 3 or 4 doses.

PLUS
Thrombolysis
Streptokinase should be used for acute myocardial infarction with ST elevation if history of onset is less than 6 hours. Beyond 6 hours treat as NSTEMI (see below).

For new left bundle branch block:
• streptokinase, IV, 1.5 million units diluted in 200 mL sodium chloride 0.9%, infused over 30–45 minutes

Do not use heparin if streptokinase is given.
Contraindications:
  o absolute
    ▪ streptokinase used within the last year
    ▪ CVA within the last 3 months
    ▪ history of recent major trauma
    ▪ previous allergy
    ▪ bleeding within the last month
    ▪ aneurysms
    ▪ surgery or head injury within the preceding month
    ▪ active bleeding or known bleeding disorder
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- relative
  - refractory hypertension
  - warfarin therapy
  - pregnancy
  - traumatic resuscitation
  - recent retinal laser treatment
  - subclavian central venous catheter
  - TIA in the preceding 6 months

For persistent pain and if oral therapy is insufficient:
- glycercyll trinitrate, IV, 1–2 mcg/kg/minute titrated over 8 hours
  In exceptional cases, may be repeated for a total duration of 24 hours.
  No survival benefit with the use of this agent.

PLUS
To relieve pain:
- morphine, IV, 1–2 mg/minute
  Dilute 10 mg up to 10 mL with sodium chloride solution 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 is indicated.

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

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
Angina 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.

NON-DRUG TREATMENT
Rest, reassurance.
Oxygen 40% if clinically hypoxic.
Early ambulation.
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DRUG TREATMENT
Inhibit platelet thrombi or aggregation:
• aspirin, soluble, oral, 300 mg immediately, followed by 150 mg daily
PLUS
To relieve spasm and pain and to reduce preload:
• isosorbide dinitrate, SL, 5 mg immediately
  May be repeated at 5-minute intervals for 3 or 4 doses.
PLUS
Thrombolysis is not indicated except if new left bundle branch block – see above.
For acute myocardial infarction with no ST elevation:
• heparin, IV bolus, 5 000 units, follow with 1 000–1 200 units hourly
  Continue infusion for 3–5 days.
  OR
  Low molecular weight heparin (LMWH), e.g.:
  enoxaparin, IV, 1 mg/kg 12 hourly for two days. Specialist initiated.
For persistent pain and if oral therapy is insufficient:
• glyceryl trinitrate, IV, 1–2 mcg/kg/minute titrated over 8 hours
  In exceptional cases, may be repeated for a total duration of 24 hours.
  No survival benefit with the use of this agent.
PLUS
To relieve pain:
• morphine, IV, 1–2 mg/minute
  Dilute 10 mg up to 10 mL with sodium chloride solution 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 is indicated.

3.1.3 CHRONIC MANAGEMENT OF STEMI / NSTEMI / UA

NON-DRUG TREATMENT
Stop smoking.
Appropriate risk reduction diet.
Rehabilitation programme.
Risk stratification and modification, including attention to smoking and lipid lowering strategies.
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DRUG TREATMENT
Continue medical management.

This is a high-risk condition for CVD and is an indication for a statin for patients with proven lesions.
HMGCoA reductase inhibitors, e.g.:
• simvastatin, oral, 10 mg/day. Specialist initiated.
  This therapy requires good initial evaluation, ongoing support for patients and continuous evaluation to ensure compliance.
  Random cholesterol should be measured at baseline.
  If < 7.5 mmol/L – initiate therapy.
  If > 7.5 mmol/L – initiate therapy and refer for further assessment.
  Therapy should be initiated together with appropriate lifestyle modification and adherence monitoring.

ß-blocker:
• atenolol, oral, 50 mg/day

CARDIAC FAILURE
If heart failure develops, replace atenolol with:
• carvedilol, oral. Specialist initiated.
See Section 3.3: Congestive Cardiac Failure.

REFERRAL
• myocardial infarction related mitral regurgitation or VSD
• ongoing chest pain or post-infarct angina
• refractory ventricular tachyarrhythmias

3.1.4 ANGINA PECTORIS, STABLE

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

NON-DRUG TREATMENT
Lifestyle modification.
Intensive health education.
Modify reversible risk factors.

DRUG TREATMENT
Long-term prophylaxis for thrombosis:
• aspirin, soluble, oral, 150 mg daily
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PLUS
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 per minute.

If β-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
  OR
  nifedipine slow release, oral, 30 mg daily

Step 3
ADD
• isosorbide mononitrate, oral, 10–20 mg twice daily
  OR
  isosorbide dinitrate, oral, 20–40 mg, twice daily
  At 8:00 and 14:00 for both drugs in order to provide a nitrate free period to prevent tolerance.
  Modify for night shift workers.

This is a high-risk condition for CVD and is an indication for a statin for patients with proven lesions.

HMGCoA reductase inhibitors, e.g.:
• simvastatin, oral, 10 mg/day. Specialist initiated.
  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.

REFERRAL
  o when diagnosis is in doubt
  o failed medical therapy
3.1.5 Atherosclerotic Peripheral Disease

**DESCRIPTION**
History and palpation of pulses confirms diagnosis.

**NON-DRUG TREATMENT**
Smoking cessation is essential and is the single most important intervention to prevent progression.
Exercise within exercise tolerance and other lifestyle modifications.

**DRUG TREATMENT**
For prevention of platelet thrombi and aggregation:
- aspirin, soluble, oral, 150 mg daily

This is a high-risk condition for CVD and is an indication for a statin for patients with proven lesions.
HMGCoA reductase inhibitors, e.g.:
- simvastatin, oral, 10 mg/day. Specialist initiated.
  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.

**REFERRAL**
- ongoing vascular insufficiency, which may be surgically reversible

3.2 Cardiac Arrhythmias/Dysrhythmias

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

3.2.1 Narrow QRS Complex (Supraventricular) Tachyarrhythmias

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

ATRIAL FLUTTER
P waves visible before QRS.
Commonly occurs, usually 2:1. (± 150 per minute).
P waves, usually negative in Lead II precede QRS, blocked P in ST segment or hidden by QRS.
Vagal stimulation with ECG may reveal blocked P waves.

AV JUNCTIONAL RE-ENTRY TACHYCARDIAS
Usually paroxysmal.
Often young with normal heart.
AV nodal re-entry or WPW syndrome.
P waves usually not visible (hidden by QRS).

ATRIAL TACHYCARDIAS
Rare.
Often incessant
May cause heart failure (tachycardia cardiomyopathy).
P before QRS (often long PR) or hidden in T.

ATRIAL FIBRILLATION

DRUG TREATMENT
INITIAL
Anticoagulate with warfarin.

Control the ventricular rate with one of the following:
• digoxin, oral, 0.25 mg daily
  Use only in heart failure.
CHAPTER 3  CARDIOVASCULAR SYSTEM

• atenolol, oral, 50–100 mg daily
  Contraindicated in asthmatics; caution in heart failure.

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

LONG-TERM
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
  Use:
    o Prophylaxis in chronic atrial fibrillation
    o Prior to cardioversion to sinus rhythm
    o In lone atrial fibrillation of persons 65 or older.
If the patient has a prosthetic valve,
ADD
• aspirin, soluble, oral, 150 mg daily

CAUTION
Use warfarin only if INR can be monitored regularly.
If not, consider aspirin.

Rate control
Continue as above.
Digoxin only controls rate at rest and is insufficient on its own.
If used long-term, combine with a β-blocker.
In the elderly and patients with renal impairment:
• digoxin, oral, 0.125 mg initial dose
  Adjust dosages according to trough levels within the therapeutic range.
  Do levels only if the patient has been on the drug for at least 10 days.

• atenolol, oral, 50–100 mg daily

Prevention of recurrent paroxysmal atrial fibrillation
Only in patients with severe symptoms despite the above measures:
• amiodarone, oral, 200 mg three times daily for 1 week, followed 200 mg twice daily
  for one week and thereafter 200 mg daily. Specialist initiated.
  Precautions:
    o halve dosage of warfarin and monitor INR closely, until stable
    o avoid concomitant digoxin
    o monitor thyroid function every 6–12 months as thyroid abnormalities may develop
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ATRIAL FLUTTER

NON-DRUG TREATMENT
Synchronised DC cardioversion, 200 J, after sedation with:
• diazepam, IV, 10–20 mg
If flutter has been present longer than 48 hours, defer cardioversion for 4 weeks after anticoagulation with warfarin, unless severe symptoms or heart failure require urgent conversion.

DRUG TREATMENT
None is nearly as effective as DC cardioversion.
Most drugs have serious side effects. Do not use verapamil as it will not convert flutter to sinus rhythm and may cause serious hypotension.
Anticoagulants if sustained.

LONG-TERM TREATMENT
Recurrent atrial flutter is an indication for referral. Many can be cured by radiofrequency catheter ablation.

AV JUNCTIONAL RE-ENTRY TACHYCARDIAS

NON-DRUG TREATMENT
Vagal manoeuvres: Valsalva or carotid sinus massage. The patient should be supine and as relaxed as possible, to avoid competing sympathetic reflexes.

DRUG TREATMENT
If vagal manoeuvres fail:
• adenosine, rapid IV bolus, 6 mg through a good IV line, followed by a bolus of 10 mL sodium chloride 0.9% to ensure that it reaches the heart before it is broken down. Half life: ± 10 seconds.
Run the ECG for 1 minute after the injection.
If 6 mg fails, repeat with 12 mg.
If the drug reaches the central circulation before it is broken down the patient will experience flushing, sometimes chest pain and anxiety.
If the tachycardia fails to terminate without these symptoms, the drug did not reach the heart.

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

Verapamil and digoxin are contraindicated in WPW syndrome.
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LONG-TERM TREATMENT
Teach the patient to perform vagal manoeuvres, Valsalva is the most effective.
For infrequent, non-incapacitating symptoms:
ß–blocker, e.g.:
• atenolol, oral, 50–100 mg daily

If asthmatic, but normal heart:
• verapamil, oral, 80–120 mg three times daily

REFERRAL
NARROW QRS COMPLEX (SUPRAVENTRICULAR) TACHYARRHYTHMIAS
• poor rate control
• severe persistent symptoms
• patients with severe symptoms

REGULAR NARROW QRS (SUPRAVENTRICULAR) TACHYCARDIAS
• frequent or severe symptoms for curative radiofrequency catheter ablation
• all WPW syndrome (sinus rhythm ECG shows delta waves) for radiofrequency catheter ablation

3.2.2 WIDE QRS (VENTRICULAR) TACHYARRHYTHMIAS

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

A REGULAR WIDE QRS TACHYCARDIAS
are ventricular until proved otherwise.
Regular wide QRS supraventricular tachycardias are uncommon.

B SUSTAINED (> 30 SEC) IRREGULAR WIDE QRS TACHYCARDIAS
are usually due to atrial fibrillation with bundle branch block, or pre-excitation (WPW syndrome).

C NON-SUSTAINED (< 30 SEC) IRREGULAR WIDE QRS TACHYCARDIAS
are usually ventricular.
They are common in acute myocardial infarction.

D 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, ± hypokalaemia.

A REGULAR WIDE QRS TACHYCARDIAS
Refer all cases after resuscitation and stabilisation.
Emergency DC cardioversion is mandatory with a full protocol of CPR.
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NON-DRUG TREATMENT
Cardio-pulmonary resuscitation (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).

DRUG 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 VT recurs after cardioversion, or if spontaneous termination/recurrence.

• amiodarone, IV, 5 mg/kg infused over 30 minutes
  Follow with:
  • amiodarone, oral, 800 mg/day for 7 days
    then 600 mg/day for 3 days
    followed by a maintenance dose of 200–400 mg/day, depending upon clinical judgement.
  Also the drug of choice in acute arrhythmia with myocardial infarction, CCF
  and other conditions with VT.
  Also benefits Supraventricular tachycardia (SVT).
  Disadvantage: serious long-term side effects and long half-life.
  Patients require regular monitoring by specialist for complications – See Section 3.2.1.

OR
Only in a haemodynamically stable patient:
• lidocaine, IV, 50–100 mg (1–2 mg/kg) initially and at 5 minute intervals if required
  to a total of 200–300 mg
Thereafter, for recurrent ventricular tachycardia only:
• lidocaine, IV infusion, 1–3 mg/minute for 24–30 hours
  Lidocaine will only terminate ± 30% of sustained ventricular tachycardias, and
  may cause hypotension, heart block or convulsions.

For emergency treatment of ventricular tachycardia, DC cardioversion is first-line therapy, even if stable.
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B SUSTAINED (> 30 SECONDS) IRREGULAR WIDE QRS TACHYCARDIAS

If the QRS complexes have a pattern of typical right or left bundle branch block, with a rate < less than 170/minute, treat as for atrial fibrillation. See Section 3.2.1

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

Do not treat with drugs.

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

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

Most are ventricular.

In acute myocardial infarction, only treat non-sustained ventricular tachycardia if it causes significant haemodynamic compromise. Ensure the serum potassium level is above 4 mmol/L.

DRUG TREATMENT

- amiodarone, IV, 5 mg/kg infused over 30 minutes. Specialist initiated.
  Follow with:
  - amiodarone, oral, 800 mg/day for 7 days
    - 600 mg/day for 3 days,
    - followed by a maintenance dose of 200–400 mg/day, depending upon clinical judgement.
  Also the drug of choice in acute arrhythmia with myocardial infarction, CCF and other conditions with ventricular tachycardia.
  Also benefits Supraventricular tachycardia (SVT).
  Disadvantage: serious long-term side effects and long half-life.
  Patients require regular monitoring by specialist for complications – See Section 3.2.1.

OR

Only in a haemodynamically stable patient:

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

Thereafter, for recurrent ventricular tachycardia only:

- lidocaine, IV infusion, 1–3 mg/minute for 24–30 hours
  Lidocaine will only terminate ± 30% of sustained ventricular tachycardias, and may cause hypotension, heart block or convulsions.

In the absence of acute ischaemia or infarction, consider torsades de pointes, due to QT prolonging drugs.
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D  TORSADES DE POINTES VENTRICULAR TACHYCARDIA (VT)

NON-DRUG TREATMENT
Cardioversion/defibrillation, as necessary.
Torsades complicating bradycardia: temporary pacing.

DRUG TREATMENT
Stop all QT-prolonging drugs.
Correct serum potassium.

•  magnesium sulphate, IV, 2 g over 5–10 minutes
If recurrent episodes after initial dose of magnesium sulphate:
•  magnesium sulphate, IV, 2 g over 24 hours

Torsades complicating bradycardia:
•  adrenaline infusion to raise heart rate to > 100 per minute (if temporary pacing unavailable).

REFERRAL
○ all cases of wide QRS tachycardia, after resuscitation and stabilisation

3.2.3 HEART BLOCK (SECOND OR THIRD DEGREE)
I44.2

DESCRIPTION
The majority of cases occur in patients over 60 years 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.

NON-DRUG TREATMENT
Emergency cardio-pulmonary resuscitation.
External pacemaker should be available in all secondary hospitals and must be preceded by appropriate analgesia.

DRUG TREATMENT
Analgesia if external pacemaker:
•  morphine, IM, 10–15 mg 3–6 hourly
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AV nodal block with narrow QRS complex escape rhythm only:
• atropine, IV bolus, 0.6–1.2 mg
  May be repeated until a pacemaker is inserted.
  Use in a patient with inferior myocardial infarct and hypotension and second degree AV block.
  It is temporary treatment of complete AV block before referral (urgently) for pacemaker.

OR For resuscitation of asystole:
• adrenaline 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

HEART BLOCK IS A MEDICAL EMERGENCY.
REFER URGENTLY!

- all cases with a heart rate below 40 beats/minute after resuscitation and stabilisation
- 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.

3.2.4 SINUS BRADYCARDIA

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

Sinus bradycardia < 50/minute or sinus arrest with slow escape rhythm, accompanied by hypotension, strongly suggest a treatable underlying cause:
- acute inferior myocardial infarct
- hyperkalaemia, especially if wide QRS and/or peaked T waves
- drugs, especially combination of verapamil and β-blocker or digoxin
- hypothermia
- hypoxia

Treat the cause. Consider atropine if inferior infarct.
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3.2.5 SINUS ARREST

Refer all to a cardiologist.

3.3 CONGESTIVE CARDIAC FAILURE (CCF)

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
- constrictive pericarditis
- thyroid disease
- thiamine deficiency
- valvular heart disease
- ischaemic heart disease

NON-DRUG TREATMENT

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.

DRUG TREATMENT

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

Digoxin has only been shown to reduce hospitalisation.

1. Diuretics

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 if also renal failure.

Note:

Unless patient is clinically fluid overloaded, reduce the dose of diuretics before adding an ACE-inhibitor.
CHAPTER 3  CARDIOVASCULAR SYSTEM

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 only be used short term to correct documented low serum potassium level.

2. ACE–inhibitor, e.g.:
   • enalapril, oral, 2.5 mg 12 hourly up to 10 mg 12 hourly

If ACE-inhibitor intolerant:
   • hydralazine, oral
     Initial dose: 25 mg 4 times a day.
     Maximum dose: 200 mg/day.

 PLUS
   • isosorbide dinitrate, oral
     Initial dose: 20 mg 3 or 4 times a day.
     Maximum dose: 160 mg/day.

3. 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

4. β-blockers
For all stable patients with heart failure who tolerate it.
Patients should not be fluid overloaded or have low blood pressure prior to initiation of therapy.
   • carvedilol, oral. Specialist initiated.
     Initial dose: 3.125 mg/day.
     Increase after two weeks to 3.125 g twice daily, if tolerated.
     Increase at two-weekly intervals by doubling the daily dose until a maximum of 25 mg twice daily, if tolerated.
     If not tolerated, i.e. worsening of cardiac failure manifestations, reduce the dose to the previously tolerated dose.
     Up-titration can take several months.

5. Digoxin
Symptomatic CCF due to systolic dysfunction.
   • digoxin, oral, 0.125 mg daily

Patients at high risk of digoxin toxicity are:
   o the elderly
   o patients with poor renal function
   o hypokalaemia
   o low body weight

Digoxin trough blood levels (before the morning dose) should be maintained between 0.65 and 1.5 nmol/L.
CHAPTER 3  CARDIOVASCULAR SYSTEM

6. Anticoagulants
Heparin for DVT prophylaxis.
For patients admitted to hospital, unless contraindicated:
• heparin, SC, 5 000 units 8 hourly

Warfarin: See Section 3.2.1
• warfarin, oral, 5 mg daily
  Control with INR to therapeutic range, i.e. between 2.0 and 2.5.

7. Anti-arrhythmic drugs
See Section 3.2: Cardiac Arrhythmias.
Only for potentially life-threatening ventricular dysrhythmias.
Always exclude electrolyte abnormalities and drug toxicity first.

8. Thiamine
Consider in all unexplained heart failure.

REFERRAL
○ where specialised treatment and diagnostic work-up is needed and to identify treatable and reversible causes

3.4 ENDOCARDITIS, INFECTIVE
I09.1

NON-DRUG TREATMENT
Bed rest.
Early surgical intervention in acute fulminant and prosthetic valve endocarditis is often indicated.

DRUG 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 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.
CHAPTER 3  CARDIOVASCULAR SYSTEM

EMPIRIC THERAPY

Native valve

- benzylpenicillin (Penicillin G), IV, for 4 weeks
  4 million units 4 hourly OR 5 million units 6 hourly*
  PLUS
  - gentamicin, IV, 1.5 mg/kg 12 hourly for 2 weeks
  If staphylococcal infection is suspected (acute onset):
  ADD
  - cloxacillin, IV, 3 g 6 hourly

- vancomycin, IV, 15 mg/kg 12 hourly
  PLUS
  - rifampicin, oral, 7.5 mg/kg 12 hourly for 6 weeks
  PLUS
  - gentamicin, IV, 1.5 mg/kg 12 hourly for 2 weeks

*For the administration of penicillin a 4-hourly regimen or constant infusion regimen is preferable. Six hourly dosing should only be used when dictated by staffing realities.

DIRECTED THERAPY (NATIVE VALVE)

<table>
<thead>
<tr>
<th>Streptococcal</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Fully susceptible to penicillin</td>
<td>• benzylpenicillin (Penicillin G), IV, for 4 weeks</td>
</tr>
<tr>
<td>MIC &lt; 0.2 mg/L</td>
<td>4 million units 4 hourly OR 5 million units 6 hourly*</td>
</tr>
<tr>
<td>Moderately susceptible</td>
<td>• benzylpenicillin (Penicillin G), IV, for 4 weeks</td>
</tr>
<tr>
<td>MIC 0.2–0.5 mg/L</td>
<td>4 million units 4 hourly OR 5 million units 6 hourly*</td>
</tr>
<tr>
<td></td>
<td>PLUS</td>
</tr>
<tr>
<td></td>
<td>• gentamicin, IV, 1.5 mg/kg 12 hourly for 2 weeks</td>
</tr>
<tr>
<td>Moderately resistant</td>
<td>• benzylpenicillin (Penicillin G), IV, for 4 weeks</td>
</tr>
<tr>
<td>MIC 0.5–2 mg/L</td>
<td>4 million units 4 hourly OR 5 million units 6 hourly*</td>
</tr>
<tr>
<td>Entero cocci and Abiotrophia</td>
<td>PLUS</td>
</tr>
<tr>
<td>spp. (nutritionally variant</td>
<td>• gentamicin, IV, 1.5 mg/kg 12 hourly for 4 weeks</td>
</tr>
<tr>
<td>streptococci)</td>
<td>Six weeks of therapy may be required in cases with a history of &gt; 3 months, or mitral or prosthetic valve involvement.</td>
</tr>
<tr>
<td>Fully resistant</td>
<td>• vancomycin, IV, 15 mg/kg 12 hourly</td>
</tr>
<tr>
<td>MIC &gt; 2 mg/L</td>
<td>PLUS</td>
</tr>
<tr>
<td></td>
<td>• gentamicin, IV, 1.5 mg/kg 12 hourly for 4 weeks</td>
</tr>
</tbody>
</table>
CHAPTER 3  CARDIOVASCULAR SYSTEM

Staphylococcal (cloxacillin/methicillin sensitive)

| S. aureus | • cloxacillin, IV, 3 g 6 hourly for 4 weeks  
|           | With optional addition:  
|           | • gentamicin, IV, 5 mg/kg/day for the first  
|           | 3–5 days  
|           | The benefit of adding an aminoglycoside has not been established.  
| coagulase-negative staphylococci | • cloxacillin, IV, 3 g 6 hourly for 4 weeks  
|           | PLUS  
|           | • gentamicin, IV, 2.5 mg/kg 12 hourly for 2 weeks  

In the rare occurrence of a penicillin sensitive staphylococcus, penicillin should be used in preference to cloxacillin.

Staphylococcal (cloxacillin/methicillin resistant)

| S. aureus | • vancomycin, IV, 15 mg/kg 12 hourly for 4 weeks  
| coagulase-negative staphylococci | • vancomycin, IV, 15 mg/kg 12 hourly for 4 weeks  
|           | PLUS  
|           | • rifampicin, oral, 7.5 mg/kg 12 hourly for 4 weeks  
|           | PLUS  
|           | • gentamicin, IV, 1.5 mg/kg 12 hourly for 2 weeks  

ENDOCARDITIS PROPHYLAXIS

Cardiac conditions

Selected procedures are listed and are not meant to be all-inclusive.

Endocarditis prophylaxis is recommended for:

- patients with prosthetic valves or with surgically constructed cardiac shunts
- patients who have had endocarditis previously
- all patients with congenital cardiac disease other than those with an isolated secundum atrial septal defect
- patients with valvular dysfunction, including those with mitral valve regurgitation due to prolapse
- patients with hypertrophic cardiomyopathy

Endocarditis prophylaxis is not recommended for:

- patients with surgically repaired secundum atrial septal defect, ventricular septal defect, or patent ductus arteriosus who are more than 6 months post-operative and have no murmur
- patients who have undergone coronary artery bypass grafting
- patients with mitral valve prolapse but no regurgitation
- patients with functional murmurs or who have had rheumatic fever but have no valvular dysfunction
- patients with pacemakers
CHAPTER 3  CARDIOVASCULAR SYSTEM

Dental or surgical procedures
Selected procedures are listed and are not meant to be all-inclusive. Procedures for which endocarditis prophylaxis should be given include:

- dental procedures known to cause bleeding (but not fillings or adjustment of braces)
- tonsillectomy or adenoidectomy (but not tympanostomy)
- surgical operations that involve intestinal or respiratory mucosal incisions
- rigid, but not flexible, bronchoscopy
- oesophageal dilatation, or sclerotherapy for oesophageal varices
- biliary tract surgery, or ERCP in the presence of obstruction
- cystoscopy, urethral dilatation or prostatic surgery
- urethral catheterisation in a patient with a urinary tract infection
- incision and drainage of infected tissue
- vaginal delivery in the presence of suspected infection such as with prolonged rupture of membranes or manipulative vaginal deliveries

Procedures for which endocarditis prophylaxis not recommended**

- shedding of primary teeth
- endotracheal intubation
- cardiac catheterisation
- endoscopy with or without gastrointestinal biopsy
- urinary catheterisation in the absence of infection
- if infection is not suspected: Caesarean section or vaginal hysterectomy, dilatation and curettage, uncomplicated vaginal delivery, therapeutic abortion, sterilisation procedures, or insertion or removal of intrauterine devices

**In patients who have prosthetic heart valves, a previous history of endocarditis, or surgically constructed systemic-pulmonary shunts or conduits, physicians may choose to administer prophylactic antibiotics even for low-risk procedures that involve the lower respiratory, genitourinary or gastrointestinal tracts.

Antibiotic Prophylaxis
Oral cavity, respiratory tract or oesophageal procedures:

- amoxicillin, oral, 2 g one hour before the procedure
  Repeat dose 6 hours later.
  OR
  Penicillin allergy:
  clindamycin, oral, 600 mg one hour before the procedure

If patient cannot take oral:

- ampicillin, IV/IM, 2 g 30 minutes before the procedure
  Repeat dose 6 hours later.
  OR
  Penicillin allergy:
  vancomycin, IV, 1 g
CHAPTER 3  CARDIOVASCULAR SYSTEM

Genitourinary or gastrointestinal procedures:
Also for patients with prosthetic heart valves or previous infective endocarditis.

• ampicillin, IV/IM, 2 g 30 minutes before the procedure
  Repeat dose 6 hours later.
  OR
  Penicillin allergy:
  vancomycin, IV, 1 g

PLUS

• gentamicin, IV/IM, 1.5 mg/kg 30 minutes before the procedure
  Do not exceed 120 mg.

REFERRAL

o complications such as renal failure and progressive cardiac failure
o for surgical intervention, e.g. emergency valve replacement
o assessment for post treatment valve replacement

3.5 HYPERTENSION

KEY POINTS

o Hypertension control has shown to have significant benefit for patients.
o Co-existent risk factors should be detected and treated.
o Assess cardiovascular risk.
o Lifestyle modification and patient education are essential in all patients.
o Drug treatment for SBP >140 mmHg; DBP > 90 mmHg.
  First line:
  Low dose thiazide diuretic, unless compelling indication for another class.
  Second line:
  Add one of the following: ACE-inhibitor or calcium channel blocker.
  Third line:
  Add one of the second line drugs, which has not already been used, or β-blocker

  Immediate drug 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

Treat these risk factors:

o diabetes mellitus
o hypertension
o obesity
o smoking
CHAPTER 3  CARDIOVASCULAR SYSTEM

- dyslipidaemia
- family history of primary hypertension or premature cardiovascular disease in men less than 55 years and in women less than 65 years
- physical inactivity
- pre-existing disease (target organ damage)
- left ventricular hypertrophy
- ischaemic heart disease (angina or prior myocardial infarction)
- heart failure
- transient ischaemic attacks
- stroke
- chronic kidney disease/impairment
- retinopathy
- peripheral arterial disease

INVESTIGATIONS
- if overweight, body weight and waist circumference should be recorded at each visit when BP is measured:
  - Men: 100 cm
  - Women: 88 cm
- do urine test strip analysis for protein, blood and sugar at presentation
  - If normal, repeat urine test strip every 6 months.
  - If abnormal, do spot albumin creatinine ratio. Repeat yearly.
- if haematuria > 1+, investigate further
- if glycosuria, exclude diabetes mellitus
- if known diabetic, HbA1C
- random total cholesterol
- if diabetic, do spot albumin creatinine ratio, which should be repeated yearly
- perform a resting electrocardiogram for left ventricular hypertrophy or ischaemia
- assess renal function by calculating creatinine clearance
  - GFR calculated using the Cockcroft and Gault formula:
    \[
    \text{CrCl (mL/minute)} = \frac{(140-\text{age}) \times \text{weight (kg)}}{0.82 \times \text{plasma Cr (micromol/L)}} \]
  - * in males
  - * In females, multiply plasma Cr by 0.85 instead of 0.82.

GOALS OF TREATMENT
- aim for SBP <140 mmHg and DBP < 90 mmHg
- aim for the blood pressure 130/80 mmHg or lower in patients with diabetes, chronic kidney disease with GFR < 60, proteinuria > 1 g/24hours or equivalent albumin creatinine ratio, congestive heart failure
- hypertensive emergency (pulmonary oedema, encephalopathy), reduce mean arterial pressure by 25% in first 2 hours
CHAPTER 3   CARDIOVASCULAR SYSTEM

NON-DRUG TREATMENT
LIFESTYLE MODIFICATION
All persons with hypertension should be encouraged to make the following lifestyle changes as appropriate:

- maintain ideal weight, i.e. BMI < 25
- weight reduction in the overweight patient, i.e. BMI > 25
- salt restriction (e.g. remove the salt from the table, gradually reduce added salt in food preparation, avoid processed foods), with increased potassium intake from fresh fruits and vegetables
- reduce alcohol intake to no more than 2 standard drinks/day
- 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 3–5 times/week
- smoking cessation

DRUG TREATMENT
Initial drug choices in patients qualifying for treatment is dependent on presence of compelling indications.

DRUG TREATMENT CHOICES WITHOUT COMPELLING INDICATIONS
Treat if BP > 140/90 mmHg

First line
Low dose thiazide diuretic e.g.:
- hydrochlorothiazide, oral, 12.5 mg daily

Second line
If target blood pressure is not reached after two months, add one of the following: ACE-inhibitor or calcium channel blocker

Third line
If target blood pressure is not reached after two months, add one of the second line drugs which has not already been used or a ß-blocker.
## CHAPTER 3  CARDIOVASCULAR SYSTEM

### DRUG TREATMENT CHOICES - WITH COMPPELLING INDICATIONS

<table>
<thead>
<tr>
<th>COMPELLING INDICATIONS</th>
<th>DRUG CLASS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angina</td>
<td>• β-blocker</td>
</tr>
<tr>
<td></td>
<td>• calcium channel blocker</td>
</tr>
<tr>
<td>Prior myocardial infarct or coronary artery disease</td>
<td>• β-blocker</td>
</tr>
<tr>
<td></td>
<td>• ACE-inhibitor</td>
</tr>
<tr>
<td></td>
<td>If β-blocker contraindicated:</td>
</tr>
<tr>
<td></td>
<td>• verapamil</td>
</tr>
<tr>
<td>Post myocardial infarction</td>
<td>• β-blocker</td>
</tr>
<tr>
<td></td>
<td>• ACE-inhibitor</td>
</tr>
<tr>
<td>Heart failure</td>
<td>• ACE-inhibitor</td>
</tr>
<tr>
<td></td>
<td>• carvedilol</td>
</tr>
<tr>
<td></td>
<td>• spironolactone</td>
</tr>
<tr>
<td></td>
<td>• furosemide</td>
</tr>
<tr>
<td>Left ventricular hypertrophy</td>
<td>• ACE-inhibitor</td>
</tr>
<tr>
<td>Stroke</td>
<td>• hydrochlorothiazide</td>
</tr>
<tr>
<td></td>
<td>• ACE-inhibitor</td>
</tr>
<tr>
<td>Diabetes type 1 or 2 with or without evidence of</td>
<td>• ACE-inhibitor, usually in combination with a diuretic*</td>
</tr>
<tr>
<td>microalbuminurin or proteinuria</td>
<td></td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>• ACE-inhibitor, usually in combination with a diuretic</td>
</tr>
<tr>
<td>Isolated systolic hypertension</td>
<td>• hydrochlorothiazide</td>
</tr>
<tr>
<td></td>
<td>• calcium channel blocker</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>See Chapter 6</td>
</tr>
<tr>
<td>Prostatism</td>
<td>• alpha-blocker</td>
</tr>
</tbody>
</table>

* In 60-80% of patients a combination of the drugs above is needed.

### RISK STRATIFICATION AND TREATMENT

The criterion for management is that BP has been measured and recorded as elevated over a two-month period for high-normal and stage 1 hypertension.

**High normal:** SBP 130–139 mmHg and/or DBP 85–89 mmHg

- **no risk factor, TOD/CCD:**
  - Low risk: lifestyle modification for 6–12 months only.
- **≥ 1 major risk factor; no TOD/CCD:**
  - Low risk: lifestyle modification for 6 months only.
- **TOD/CCD, diabetes mellitus with or without other risk factors:**
  - High risk: lifestyle modification and drug therapy for those with heart failure, diabetes mellitus or chronic kidney disease.
CHAPTER 3  CARDIOVASCULAR SYSTEM

Stage I (Mild): SBP 140–159 mmHg and/or DBP 90–99 mmHg
- no risk factor, TOD/CCD:
  Low risk: lifestyle modification for 3 months only and then drug therapy as resources permit.
- ≥ 1 major risk factor, no TOD/CCD:
  Medium risk: lifestyle modification for 3 months only then drug therapy as resources permit.
- TOD/CCD, diabetes mellitus with or without other risk factors:
  High risk: lifestyle modification and drug therapy for those with heart failure, diabetes mellitus or chronic kidney disease.

Stage II (Moderate): SBP 160–179 mmHg and/or DBP 100–109 mmHg
- no risk factor, TOD/CCD:
  Medium risk: lifestyle modification and recheck BP within 2 weeks, then start drug therapy.
- ≥ 1 major risk factor, no TOD/CCD:
  Medium risk: lifestyle modification and recheck BP within 2 weeks, then start drug therapy.
- TOD/CCD, diabetes mellitus with or without other risk factors:
  Very high risk: lifestyle modification and drug therapy for those with heart failure, diabetes mellitus or chronic kidney disease.

Stage III (Severe): SBP ≥ 180 mmHg and/or DBP ≥ 110 mmHg
May need referral*.
- no risk factor; TOD/CCD
- ≥ 1 major risk factor; no TOD/CCD
- TOD/CCD; diabetes mellitus with or without other risk factors:

Asymptomatic severe hypertension (very high risk):
- Recheck BP after 1 hour.
- Start drug therapy with 2 agents.
- Hypertensive urgency and emergency can occur in this group and should be treated as indicated below and in the text.

Hypertensive urgency (very high risk):
- Start drug therapy with 2 agents.

Hypertensive emergency (very high risk):
- Parenteral drug therapy in a high care facility.

If not at goal blood pressure:
- Optimise dosages or add additional drugs until goal blood pressure is achieved.
- Consider consultation with a specialist.

Note:
- check adherence to drug treatment
- advise patient to take medication on the day of the clinic visit, as missing a dose can be a reason for a high BP reading
- 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
CHAPTER 3  CARDIOVASCULAR SYSTEM

CAUTION
Lower BP over a few days.
A sudden drop in BP can be dangerous, especially in the elderly.
BP should be controlled within 3–6 months.

Risk assessment: 10 year risk of MI > 20%:
HMGCoA reductase inhibitors e.g.:
• simvastatin, oral, 10 mg daily. Specialist initiated.
  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.

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:
• the patient is compliant with therapy, and the blood pressure is refractory, i.e.
  > 140/90 mmHg, while on drugs from three different classes, one of which being 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

3.5.1 HYPERTENSION, SEVERE

DESCRIPTION
Asymptomatic severe hypertension.

These patients are asymptomatic and have severe hypertension with or without
evidence of TOD.
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.
Follow-up carefully and refer as needed.

3.5.2 HYPERTENSIVE URGENCY

DESCRIPTION
This level of hypertension is symptomatic with evidence of TOD or grade III/IV
retinopathy (malignant/accelerated hypertension). There are no immediate life threatening
neurological or cardiac complications such as are seen in the hypertensive emergencies.
Thrombotic (ischaemic) stroke and intracerebral haemorrhage should be managed
according to the South African Stroke Therapy Clinical Guideline.
Do not lower BP in acute stroke or use antihypertensive medication unless
SBP > 220 mmHg or DBP > 120 mmHg, as a rapid fall may aggravate cerebral
ischaemia and worsen the stroke.
CHAPTER 3  CARDIOVASCULAR SYSTEM

If the BP is above these levels then treatment should aim not to lower the BP by more than 15–20% in the first 24 hours.

Treatment may be given orally but if the patient is unable to swallow then the use of parenteral drugs may be warranted.

DRUG 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 used in very low doses initially. Avoid if there is severe hyponatraemia (serum Na < 130 mmol/L).
- ß-blockers
- diuretics may potentate the effects of the other classes of drugs when added.
  Furosemide should be used if there is renal insufficiency or signs of pulmonary congestion.

3.5.3 HYPERTENSIVE CRISIS, HYPERTENSIVE EMERGENCY

DESCRIPTION

This is a rare life-threatening situation which requires immediate lowering of BP usually with parenteral therapy.
The true emergency situation should preferably be treated by an appropriate specialist.

The 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)
- excessive circulating catecholamines: e.g. phaeochromocytoma – rare cause of emergency; food or drug interaction with monoamine oxidase inhibitors
- eclampsia and severe pre-eclampsia
- acute kidney failure with encephalopathy
- acute aortic dissection

DRUG TREATMENT

Admit the patient to a high-care setting for parenteral 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
- labetalol, IV, 2 mg/minute to a total dose of 1–2 mg/kg
  Caution in acute pulmonary oedema.
CHAPTER 3  

CARDIOVASCULAR SYSTEM

OR
If myocardial ischaemia and CCF:
• glycercyl trinitrate, IV, 5–10 mcg/minute

Furosemide
• furosemide, IV, 40–80 mg
  Acts only for 6 hours.
  Potentiates all of the above drugs.

ORAL THERAPY
Use only if intravenous drugs are not available.

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.
  Do not use if bilateral artery stenosis or in pregnancy.

3.6 RHEUMATIC HEART DISEASE
109.9

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

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

DRUG TREATMENT

ACUTE RHEUMATIC FEVER
For eradication of streptococci in throat:
• benzathine benzylpenicillin (depot formulation), IM, 1.2 million units one dose
  OR
  phenoxyethylpenicillin, oral, 500 mg 12 hourly for 10 days

Penicillin allergy:
• 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.
CHAPTER 3  CARDIOVASCULAR SYSTEM

- benzathine benzylpenicillin (depot formulation), IM, 1.2 million units every 21–28 days (3–4) weeks
  OR
  phenoxy methylpenicillin, oral, 250 mg 12 hourly

Penicillin allergy:
- erythromycin, oral, 250 mg 12 hourly

PROPHYLAXIS FOR INFECTIVE ENDOCARDITIS
See Section 3.4: Infective Endocarditis

REFERRAL
- where surgery is contemplated
- management of intractable heart failure or other non-responding complications
- pregnancy

3.7 VENOUS THROMBO-EMBOLISM

DESCRIPTION
Formation and consequences of thrombi in the venous system.

Classical factors are stasis, endothelial damage and hypercoagulability, which result in local and distant complications, e.g. pulmonary embolism.

NON-DRUG TREATMENT
Advice on prophylaxis should be emphasised.
Eliminate all predisposing factors.
Prevent deep vein thrombosis.

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

Note:
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 negative.

DRUG TREATMENT

ACUTE TREATMENT
Thrombolytic therapy is indicated only in patients with angiographically confirmed early pulmonary embolism where haemodynamic stability cannot be achieved. Heparin initially, plus simultaneous warfarin. After 4–6 days, heparin is usually stopped and oral warfarin continued, depending on a therapeutic INR value being reached.
CHAPTER 3  CARDIOVASCULAR SYSTEM

For proximal venous thrombosis and/or pulmonary embolism:
• heparin, IV, 5 000 units as a bolus, followed with IV infusion of 30 000–35 000 units/day
  Control dose with APTT to keep it 1.5–2.5 times normal.
  OR
Low molecular weight heparin (LMWH), e.g.:
  enoxaparin, SC, 1 mg/kg 12 hourly, for 5–10 days
  Round off the dose to the nearest 20 mg.
  PLUS/FOLLOW WITH
• warfarin, oral, 5 mg/day
  Control with INR to keep within therapeutic range.
  Continue warfarin for 3–6 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, it should be replaced with heparin.

PROPHYLAXIS
Prophylaxis depends on clinical circumstances.

Short term prophylaxis is indicated in high risk hospitalised patients with, e.g.:
  o age > 60 years
  o obesity
  o congestive heart failure
  o chronic lung disease
  o varicose veins
  o immobility/paralysis
  o prior venous thrombo-embolism
  o thrombophilia (inherited or acquired)
  o active cancer
  o acute ischaemic stroke
  o inflammatory bowel disease
  o acute MI
  o nephrotic syndrome
  o central venous catheter
  o oestrogen therapy
  o prior ischaemic stroke with residual paresis

• heparin, SC, 5 000 units 8–12 hourly
Relative/absolute contraindications to prophylactic heparin:
  o active bleeding
  o significant renal insufficiency
  o heparin-induced thrombocytopenia
  o recent intraocular or intracranial surgery
  o lumbar puncture or epidural anesthesia within 12 hours

REFERRAL
  o complicated cases
4.1 ACNE

DESCRIPTION
Acne is an inflammatory condition of the hair follicle. Blockage of the follicle leads to comedone formation:
- open comedones – black heads
- closed comedones – white heads.
Secondary changes lead to scarring and inflammation:
- pustules
- papules
- nodules
- cysts and sinuses.
All forms of acne can cause scars.
Post inflammatory hyperpigmentation may be disfiguring, especially in pigmented skin. This will gradually fade once the acne is controlled.
Response to treatment may be slow and treatment may need to be continued for months to years.

NON-DRUG TREATMENT
Regular normal gentle cleansing with soap and water is usually adequate for skin hygiene in patients with acne.
Avoid greasy or oily topical products such as moisturisers that block the hair follicle openings.
Diet plays no role in acne.

DRUG TREATMENT
- benzoyl peroxide 5%, topical, apply to affected areas as needed
AND/OR
For inflammatory acne:
- doxycycline, oral, 100 mg daily, for at least 3 months, after which review patient

Doxycycline impairs the efficacy of oral contraceptives.
Additional non-oestrogen measures may have to be used.

Topical retinoids
Indicated in non-inflammatory acne and where benzoyl peroxide is ineffective. The main action is to control comedone formation.
Introduce gradually as nighttime applications to limit skin irritant effects, which are worse if used during day (UVL aggravation).
Topical retinoids should not be used in pregnant women.

• tretinoin gel/cream, topical. Specialist initiated.

REFERRAL
o severe and recalcitrant acne should be referred to a dermatologist

4.2 CELLULITIS AND Erysipelas
L03.9

DESCRIPTION
Skin and subcutaneous infections with pain, swelling and erythema. Regional lymphadenitis may be present. Erysipelas has a raised demarcated border, whilst the border is indistinct in cellulitis.

NON-DRUG TREATMENT
Elevate the affected limb to reduce swelling.

DRUG TREATMENT
For pain:
• ibuprofen, oral, 400–800 mg 8 hourly
  OR
  paracetamol, oral, 1 g 6 hourly when needed

Antibiotic therapy
If intravenous antibiotics are given initially patients should be switched to oral agents as soon as there is clinical improvement. Antibiotics should be given until infection is cleared, usually for 7–10 days.

Note:
Patients with necrotising fasciitis require broad-spectrum antibiotics, as these infections are often polymicrobial.

• flucloxacillin, oral, 500 mg 6 hourly
  OR
  In severely ill patients:
  • cloxacillin, IV, 1 g 6 hourly

Penicillin allergy:
• clindamycin, oral, 300 mg 8 hourly
  OR
  clindamycin, IV, 600 mg 8 hourly

RECURRENT CELLULITIS
Investigate and treat any underlying cause for the infection such as lymphoedema eczema, leg ulcer and stasis.
CHAPTER 4  
Dermatology

Prophylaxis
Frequent recurrent cellulitis in patients with lymphoedema:
• benzathine benzylpenicillin (depot formulation), IM, 1.2 million units every 28 days

Penicillin allergy:
• erythromycin, oral, 250 mg 12 hourly

URGENT REFERRAL
○ for debridement if necrotising fasciitis is suspected, i.e. gangrene, gas in the tissues or haemorrhagic bullae

REFERRAL
○ to surgeon for non-response

4.3 Impetigo
L01.0

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

NON-DRUG TREATMENT
Good personal and household hygiene to avoid spreading the infection and to reduce carriage of organisms.

DRUG TREATMENT
Daily cleansing with an antiseptic, e.g.:
• potassium permanganate 1:10 000 aqueous solution

Antibiotic therapy
• flucloxacillin, oral, 250 mg 6 hourly for 5–10 days

Penicillin allergy:
• erythromycin, oral, 500 mg 6 hourly for 5–10 days

4.4 Abscesses (Furuncles, Boils and Carbuncles)
L02.9

DESCRIPTION
Localised bacterial skin infection of hair follicles or dermis, usually with S. aureus. The surrounding skin becomes:
○ swollen ○ hot
○ red ○ tender to touch
CHAPTER 4  

DERMATOLOGY

Note:
Boils in diabetic or immunocompromised patients require careful management.

NON-DRUG TREATMENT
Encourage general hygiene.
Apply local hot compresses three times daily until the boil/abscess starts draining.
Drainage of abscess is treatment of choice, surgical incision being performed only after the lesion is mature.

DRUG TREATMENT
Antibiotic therapy
Is only indicated if there are systemic features of infection or marked surrounding cellulitis.
• cloxacillin, IV, 1 g 6 hourly
Follow with:
• flucloxacillin, oral, 500 mg 6 hourly
Penicillin allergy:
• clindamycin, oral, 300 mg 8 hourly for 5 days

4.4.1 BOILS, RECURRENT

DESCRIPTION
Usually due to staphylococcal carrier state.
Investigate for diabetes mellitus.

NON-DRUG TREATMENT
Incision and drainage is the mainstay of treatment.
Good personal hygiene.

DRUG TREATMENT
Scalp and body washes with antiseptics, e.g.:
• povidone iodine, topical for 1 week

4.5 ECZEMA

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.

NON-DRUG TREATMENT
Avoid exposure to trigger or precipitating factors, where applicable.
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Good personal hygiene with regular washing to remove crusts and accretions and avoid secondary infection.
Avoid irritants such as strong detergents, antiseptics, foam baths, woollen and synthetic clothing and pets.

Respect patient preference for cream or ointment topical treatment.  
Wet wraps help control eczema and pruritus but do not use for infected eczema.  
Diet modification has no role in atopic eczema treatment unless double blind challenge testing proves sensitivity.

DRUG TREATMENT

MILD CASES - MILD DISEASE INVOLVING LIMITED AREAS

To relieve skin dryness:
• aqueous cream, topical, applied daily

To control eczema:
• betamethasone 0.1%, topical, applied daily
  Wean to emollients, e.g. emulsifying ointment as tolerated.

Maintenance therapy, once eczema is controlled:
• aqueous cream or emulsifying ointment, topical, applied daily

MODERATE TO SEVERE CASES

To control eczema:
• betamethasone 0.1%, topical, applied daily for 5–7 days  
  Avoid facial areas, especially around the eyes.
Thereafter:
• hydrocortisone 1%, topical, applied daily as tolerated for a further 5–7 days  
  Wean to emollients, e.g. emulsifying ointment as tolerated.

INFECTED ECZEMA

This is usually due to staphylococcus.
Antiseptic cream, e.g.:
• povidone iodine 5%, topical, applied for 24 hours  
  Continue with topical steroids thereafter.

Antibiotic therapy
• flucloxacillin, oral, 500 mg 6 hourly for 5 days

For penicillin allergy:
• clindamycin, oral, 300 mg 8 hourly
For relief of itch if there is an urticarial component:
- chlorpheniramine, oral, 4 mg 3 times daily, as needed
  OR
- cetirizine, oral, 10 mg daily
  OR
- promethazine, oral, 25 mg at night as needed in severe cases

REFERRAL
- severe, non-responsive or complicated cases

4.6 ERYTHEMA MULTIFORME, STEVENS JOHNSON SYNDROME, TOXIC EPIDERMAL NECROLYSIS

DESCRIPTION
A continuum ranging from mild Erythema Multiforme (EM), to Stevens Johnson Syndrome (SJS) and then to the most severe and potentially lethal Toxic Epidermal Necrolysis (TEN).
Drugs (EM, SJS, TEN) and herpes simplex or mycoplasma infections (EM) are the main causes of these rashes.

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

NON-DRUG TREATMENT
Supportive and symptomatic management as for burn cases.
Identify and remove the offending agent.
Monitor vital organ function in severe cases, especially liver function tests.
All patients require a medical alert disc.
Exclude systemic involvement, e.g. liver, kidney, bone marrow and lung.
Skin hygiene; daily cleansing and bland, non-adherent dressings as needed.
Regular supervised oral, genital and eye care to prevent synechia and scarring.

DRUG TREATMENT
PRINCIPLES OF MANAGEMENT
Manage as for Burns.
See Section 20.2.1: Burns.
The foundation of management is supportive, good nursing and the prevention of infection.

Fluids
Replace fluids.
Oral is preferred but intravenous fluid therapy may be required in significant dehydration.

Corticosteroids
There is no convincing evidence that steroids are of benefit and in TEN steroids may even cause harm.
**The use of systemic corticosteroids is therefore not recommended.**
CHAPTER 4  
DERMATOLOGY

Antibiotic therapy
Systemic antibiotics may be indicated, depending on results of culture grown from skin swabs, blood and urine.

Analgesia
Appropriate and adequate analgesia for the severe pain associated with dressing changes.

REFERRAL
- all cases with systemic features, mucosal involvement or extensive cutaneous involvement

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, fibroed 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.

NON-DRUG TREATMENT
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, povidone-iodine, fusidic acid, clioquinol, antihistamine creams, colophony, etc.
If the ulcer is oedema/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:
- slough removal
- surgery for varicose veins
- arterial insufficiency
- skin grafting.
CHAPTER 4  
DRUG TREATMENT  
Dermatology

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

- amoxicillin/clavulanic acid, oral, 625 mg 8 hourly for 10 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 exuding, infected wounds:
- potassium permanganate 1:10 000 aqueous solution or povidone-iodine

For wounds complicated by pseudomonas species:
- acetic acid 0.5%

**Dressings**
These are individualised and selected relative to the type of ulcer and the presence and degree of infection, slough, necrosis, exudate and granulation tissue present. Non-stick hydrocolloid dressings ensuring a moist wound environment free of products toxic to cells, which promote debridement and healing should be used for uninfected ulcers.

**REFERRAL**
- recalcitrant cases

---

**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.

**NON-DRUG TREATMENT**
Counselling regarding precipitating factors and chronicity. Encourage sun exposure as tolerated.
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DRUG TREATMENT

LOCAL PLAQUES

• salicylic acid 2–10% in white soft paraffin, topical, applied three times daily until scale is removed
  Then:
  • liquor picis carbonis 5–10%, topical
  OR
corticosteroid, topical
  OR
modified Adamson’s/Brown ointment, topical

• dithranol 0.1–1% in soft paraffin, topical, applied daily for 10–60 minutes followed by careful removal of the ointment and showering or bathing. Specialist initiated. Occasionally up to 3% may be used.
  Use only after supervised demonstration of its application and removal with detergent.
  This is an irritant - avoid contact with eyes, tender areas or open wounds.
  Clothes, furniture and household surfaces are easily and permanently stained by dithranol.

SEVERE LOCALISED OR GENERALISED PUSTULAR PSORIASIS

To be prescribed by a dermatologist only:
  o corticosteroids, topical or oral
  o acitretin
  o methotrexate

SEVERE PSORIASIS

To be prescribed by a dermatologist only:
  o calcipotriol
  o UVB
  o PUVA
  o azathioprine
  o acitretin
  o hydroxycarbamide
  o methotrexate

SCALP PSORIASIS

• betamethasone 0.05% lotion, topical, applied once daily

REFERRAL

  o no response to treatment
  o severe complications
  o uncertain diagnosis

4.9 URTICARIA

DESCRIPTION
A transient itchy inflammatory skin and mucosal condition recognised by a wheal and flare reaction for which there are many causes. In most chronic cases the precipitant
CHAPTER 4 DERMATOLOGY

for the urticaria will never be 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.

NON-DRUG TREATMENT
A good history is key to identifying triggers of urticaria that should be avoided. Limit exposure to triggers such as non-immune mast cell degranulators, which aggravate and prolong urticaria, e.g. codeine, NSAIDs, salicylates, etc.

DRUG 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.

- chlorpheniramine, oral, 4 mg 3 times daily, as needed
  OR
cetirizine, oral, 10 mg daily, preferably in the evening

The use of oral corticosteroids should be avoided.

PAPULAR URTICARIA
For relief of itch and sedation:

- chlorpheniramine, oral, 4 mg 3 times daily, as needed
  OR
cetirizine, oral, 10 mg daily
  OR
promethazine, oral, 25 mg at night as needed in severe cases

REFERRAL
  o recalcitrant cases

4.10 FUNGAL INFECTIONS
B35

DESCRIPTION
The skin may be infected by yeasts or fungi and the clinical presentation varies with organism, body site infected and the body’s response to the infection. Most infections are due to anthropomorphic species that infect humans primarily. Yeasts such as Candida spp (intertrigo, thrush) and Pityrosporum spp (tinea/pityriasis vesicolor, folliculitis) are common. Dermatophyte (tinea) infections are common and do not necessarily imply underlying disease.
CHAPTER 4  DERMATOLOGY

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

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

DRUG TREATMENT

CANDIDA
Imidazole, e.g.:
• clotrimazole, topical, applied twice daily until clear of disease

PITYROSPORUM
• selenium sulphide 2% suspension, topical, applied once weekly to all hair bearing surfaces Allow to dry and leave for 24 hours before rinsing off. Repeat for 3 weeks.

DERMATOPHYTES
Imidazole, e.g.:
• clotrimazole, topical, applied twice daily until clear of disease

For mild cases:
• benzoic acid 6%/salicylic acid 3% (Whitfield’s ointment), topical, applied twice daily

Systemic antifungal therapy
Duration of therapy:
4 weeks: only for extensive, incapacitating and recurrent skin infections
8 weeks: for scalp and hair infections
3–6 months: for finger and toe nail infections

Big toe nail infections do not respond to therapy. Topical treatment is generally ineffective for hair and nail infections. Recurrent infections are not uncommon if repeat exposure is not prevented.
• griseofulvin, oral, 10 mg/kg daily

REFERRAL
• recalcitrant and non-responding infections
• systemic infections
CHAPTER 4  

DERMATOLOGY  

4.11 VIRAL INFECTIONS  

4.11.1 WARTS  

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

NON-DRUG TREATMENT  
Cryotherapy.  
Patients with anogenital warts should be checked for the presence of other STIs.  

DRUG TREATMENT  
Cutaneous warts  
Treatment seldom indicated.  

Anogenital warts  
• podophyllin 20% in Tinct. Benz. Co., topical  
  Apply to affected areas and leave on for a few hours.  
  Wash off with water and then repeat once a week until lesions disappear.  

4.11.2 SHINGLES (HERPES ZOSTER)  

See Section 9.11: Zoster (shingles)
CHAPTER 5
GYNAECOLOGY

5.1 DYSMENORRHOEA
N94.4

NON-DRUG TREATMENT
Surgical treatment for persistent pain despite medical treatment: laparoscopy, diagnostic and therapeutic in the younger patient.

DRUG TREATMENT
Symptomatic relief:
• paracetamol, oral, 1 g up to 4 times daily
OR
• ibuprofen, oral, 400 mg 3 times daily

For severe pain:
ADD
• combined oral contraceptives

REFERRAL
• young women with pain not responding to conventional treatment
• older women with persistent pain

5.2 GENITAL PROLAPSE AND URINARY INCONTINENCE
N81

Note:
All patients should be referred for specialist care. Baseline investigations can, however, be done at lower level.

NON-DRUG TREATMENT
Surgical procedures as dictated by the diagnosis at specialist care. For stress incontinence – pelvic floor exercises.

DRUG TREATMENT
Infections, and underlying conditions, as appropriate and as dictated by the diagnosis.

For detrusor hyperactivity/instability as demonstrated on urodynamic studies:
• amitriptyline, oral, 10 mg at night as an initial dose
  Increase by 10–25 mg 1–2 times daily.
  Maximum dose: 75 mg daily.
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REFERRAL
- all patients with prolapse
- patients not responding to therapy
- incontinence:
  - stress incontinence as surgical repair will be likely
  - total incontinence as fistulation has to be excluded
  - urge incontinence resistant to drug treatment after 3 months' duration as first line medical treatment then seems to be unsuccessful
  - mixed incontinence as seen with both stress as well as urge incontinence present as surgery will play a role

5.3 INFERTILITY
N97.9

NON-DRUG TREATMENT
Counselling.
Lifestyle modification, e.g. weight optimisation, smoking cessation and regular sexual intercourse.
Investigation of semen analysis and prolactin levels.
Laparoscopy and/or hysterosalpingography (Specialist supervision).

DRUG TREATMENT
Treat the underlying disease.

For induction of ovulation:
- clomifene, oral, 25–50 mg daily for 5 days on days 5–9 of the cycle. Specialist only.
  Monitor the progress of ovulation.

For hyperprolactinaemia after further investigation:
- bromocriptine, oral, 2.5 mg at night. Specialist only.

5.4 MENOPAUSE AND PERIMENOPAUSAL SYNDROME
N95.9

NON-DRUG TREATMENT
Counselling.

DRUG 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:
The most important contra-indication for HRT is a previous hormone dependent malignant tumor of breast or endometrium.
Relative contraindications to HRT include:
- coronary heart disease
- stroke
- breast cancer
- previous thrombo-embolism.
In all these instances consult a specialist.

When considering use of HRT in women without menopausal symptoms, or for long-term use, alternative treatment should be considered.

**INTACT UTERUS (NO HYSTERECTOMY)**
HRT can be offered as sequentially opposed oestrogens or continuously opposed oestrogens. Continuously opposed oestrogen has the advantage of less breakthrough bleeding. Treatment should be planned for 5 years but reviewed annually.

Sequentially opposed:
- conjugated oestrogens, oral, 0.625 mg for 11 days followed by the addition of medrogestone 5 mg for 10 days
  OR
Continuous opposed:
- conjugated oestrogens, oral, 0.625 mg plus medrogestone 2.5 mg daily

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 can be offered as oestrogen only. Oestrogen supplementation to prevent postmenopausal osteoporosis requires long-term treatment.

- estradiol valerate, oral, 1–2 mg daily
  OR
  conjugated oestrogens, oral, 0.3 mg daily or 0.625 mg on alternative days up to 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
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5.5 MISCARRIAGE
O00–O08

It is recommended that Manual Vacuum Aspiration be used in place of curettage where evacuation of the uterus is suggested, in cases of uncomplicated incomplete miscarriage. The equipment to do this should be available at all hospitals where gynaecological procedures are done.

5.5.1 BLIGHTED OVUM/ANEMBRYONIC PREGNANCY
O02.0

NON-DRUG TREATMENT
Counselling.
Evacuation of the uterus.

DRUG TREATMENT
To ripen the cervix:
\* misoprostol, oral/vaginal, 400 mcg as a single dose

5.5.2 RETAINED/MISSED MISCARRIAGE ALSO UNCOMPLICATED INCOMPLETE MISCARRIAGE IN THE FIRST TRIMESTER
O02.1

NON-DRUG TREATMENT
Counselling.
Evacuation of the uterus after ripening the cervix.

DRUG TREATMENT
To ripen the cervix:
\* misoprostol, oral/vaginal, 400 mcg as a single dose

5.5.3 MIDTRIMESTER MISCARRIAGE (FROM 13–22 WEEKS GESTATION)
O03.9

NON-DRUG TREATMENT
Counselling.
Evacuation of the uterus after the fetus has been expelled.

DRUG TREATMENT
For augmentation:
\* misoprostol, vaginal, 400 mcg immediately
Follow with:
\* misoprostol, oral, 200 mcg every 2 hours until expulsion of the products of conception

Warning
Uterine rupture may occur in women with previous Caesarean sections. Caution for this group and those of high parity: use lower the dose of misoprostol or alternative methods such as extra-amniotic saline infusion without misoprostol.
If misoprostol is not available (less effective):
• oxytocin, IV, 20 milliunits/minute
  Reduce rate if strong contractions are experienced.
  Dilute 20 units in 1 L sodium chloride 0.9%, i.e. 20 milliunits/mL solution.
  **Note:**
  Check serum sodium if used for more than 24 hours because of the danger of dilutional hyponatraemia.

Analgesia for all patients undergoing suction termination, e.g.:
• morphine, IV, 10 mg

If mother is Rh-negative:
• anti-D immunoglobulin, IM, 100 mcg as a single dose

**REFERRAL**
- uterine congenital abnormalities
- suspected cervical incompetence
- recurrent midtrimester miscarriages (3 consecutive spontaneous miscarriages) with minimal pain and bleeding
- congenital anomalies of the fetus
- immunological problems
- diabetes mellitus
- parental genetic defects and SLE or other causes of autoimmune disease

### 5.5.4 SEPTIC MISCARRIAGE

**NON-DRUG TREATMENT**
Counselling.
Evacuation of uterus and surgical management of complications.

**DRUG TREATMENT**
• oxytocin, IV, 20 milliunits/minute
  Reduce rate if strong contractions are experienced.
  Dilute 20 units in 1 L sodium chloride 0.9%, i.e. 20 milliunits/mL solution.
  **Note:**
  Check serum sodium if used for more than 24 hours because of the danger of dilutional hyponatraemia.

**Antibiotic therapy**
• ampicillin, IV, 1 g immediately, followed by 1 g 6 hourly
**PLUS**
• gentamicin, IV, 5 mg/kg daily
**PLUS**
• metronidazole, IV, 500 mg 8 hourly
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Change to oral treatment after improvement:
• amoxicillin/clavulanic acid, oral, 625 mg 8 hourly for 5 days
PLUS
• doxycycline oral, 100 mg 12 hourly for 10 days

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

Penicillin allergy:
• clindamycin, IV, 600 mg 8 hourly
PLUS
• gentamicin, IV, 5 mg/kg daily

Change to oral treatment after improvement:
• clindamycin, oral, 450 mg 8 hourly for 5 days
PLUS
• doxycycline, oral, 100 mg 12 hourly for 10 days
PLUS
• ciprofloxacin, oral, 500 mg 12 hourly for 5 days

If patient has severe sepsis, consideration should be given for urgent hysterectomy.

REFERRAL
- evidence of trauma
- no response to treatment

5.5.5 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

5.6 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 female genital tract.
Sequelae are:
- recurrent infections if inadequately treated
- infertility
- increased probability of ectopic pregnancy
- chronic pain, i.e. dyspareunia, dysmenorrhoea, and low back pain
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Early death may result from sepsis, late death may follow a ruptured ectopic pregnancy. Chronic PID may follow if the abnormalities persist with hydro/pyosalpinx, adhesions to bowel and to the uterus.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Manifestations</th>
<th>Treatment objectives</th>
</tr>
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</table>
| Stage I                            | o local adnexal tenderness  
| Acute/uncomplicated salpingitis    | o no peritoneal tenderness                     | o cure  
|                                   |                                                     | o prevent spread  
|                                   |                                                     | o prevent HIV                               |
| Stage II                           | o local adnexal tenderness  
| Salpingitis + peritonitis          | o peritoneal irritability, e.g. rebound, guarding, etc. | o cure  
|                                   |                                                     | o preserve fertility  
|                                   |                                                     | o prevent complications                     |
| Stage III                          | o as stage II PLUS  
| Tubal occlusion + pus + distention | o palpable mass May need ultrasound to detect if there is much tenderness.  
|                                   | o mass larger than pyosalpinx, posterior to uterus, i.e. Douglas pouch | o maintain ovarian function  
|                                   | o infertility may result                         | o facilitate surgery                        |
| Stage IV                           | o septicaemia  
| Rupture to peritoneal cavity       | o collapse                                     | o preservation of life  
|                                   |                                                     | o rapid surgical exploratory laparotomy      |

Non-Drug Treatment

All patients with stage II–IV must be hospitalised for parenteral antibiotic therapy. Frequent monitoring of general abdominal and pelvic signs is essential.

Note:
Remove IUCDs.
Test and 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:
 o the diagnosis is uncertain  
 o rupture seems imminent  
 o there is no adequate response after 48 hours of appropriate therapy  
 o the patient deteriorates on treatment  
 o after 4–6 weeks there still is a large or symptomatic pelvic mass
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DRUG TREATMENT

STAGE I
• doxycycline, oral, 100 mg 12 hourly for 7 days
PLUS
• ciprofloxacin, oral, 500 mg immediately as a single dose
PLUS
• metronidazole, oral, 2 g immediately as a single dose

STAGE II–IV
• benzylpenicillin (Penicillin G), IV, 2 million units 6 hourly
PLUS
• gentamicin, IV, 5 mg/kg daily
PLUS
• metronidazole, oral, 400 mg 8 hourly
  OR
• metronidazole, IV, 500 mg 8 hourly
PLUS
• doxycycline, oral, 100 mg 12 hourly for 14 days
  Start as soon as patient is able to take oral medication.

Continue intravenous therapy until there is definite clinical improvement.
Thereafter, change to:
• amoxicillin/clavulanic acid, oral, 625 mg 8 hourly should be added to the doxycycline
to complete 14 days therapy

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

Penicillin allergy:
• clindamycin, IV, 900 mg 8 hourly
PLUS
• gentamicin, IV, 5 mg/kg daily

Continue intravenous therapy until there is definite clinical improvement.
Thereafter, change to:
• doxycycline, oral, 100 mg 12 hourly
PLUS
• metronidazole, oral, 400 mg 8 hourly for 14 days

REFERRAL
  o stages III and IV should be managed in consultation with a gynaecologist
CHAPTER 5 GYNAECOLOGY

5.7 TERMINATION OF PREGNANCY (TOP)

Gestational age is based on the estimated size of the uterus rather than dates. Ultrasound examination is not essential.

SUMMARY OF CHOICE OF TERMINATION OF PREGNANCY ACT

WOMEN ELIGIBLE
Up to 12 weeks by dates: on request.
13–20 weeks by dates: If doctor 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 by dates: Doctor and second doctor or registered midwife is satisfied that there is danger to the mothers’ life, severe fetal malformation or risk of fetal injury.

Venue
Facility designated by the Member of the Executive Council on provincial level.

PRACTITIONER
Up to 12 weeks by dates: doctor or midwife with appropriate training.
More than 12 weeks by dates: 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 13–20 weeks (above), spouse/guardian cannot prevent TOP by withholding consent.

5.7.1 GESTATION BY DATES, UP TO 12 WEEKS

NON-DRUG TREATMENT
Counselling.
Outpatient procedure by nursing staff with specific training.
Manual vacuum aspiration of the uterus.
CHAPTER 5 GYNAECOLOGY

DRUG TREATMENT
If difficulty with cervical dilation is expected, e.g. if prostagandin preparation has not been used, a paracervical block may be considered.

- misoprostol, SL/PV, 400 mcg 2 hours before routine vacuum aspiration of the uterus

If woman commits to come back for follow-up, an alternative is medical abortion with a prostoglandin analogue, e.g.:
- misoprostol, SL/PV, 800 mcg daily for 2 doses, e.g.:
  - 800 mcg PV on day 1. Supply 800 mcg for sublingual use at home on day 2 and review with ultrasound on day 3.
  - If does not abort completely, i.e. < 20% of cases, vacuum evacuation of the uterus on day 3.

  Side effects: pain due to uterine contractions.
  Bleeding may persist for up to 1 week.

Routine analgesia for vacuum aspiration.
If recovery facilities are not available:
- paracetamol, oral, 1 g 30 minutes before aspiration procedure
AND
- ibuprofen, oral, 800 mg 30 minutes before aspiration procedure

If recovery facilities are available:
- pethidine, IM, 100 mg 30 minutes before aspiration procedure
  OR
  - morphine, IM, 10 mg 30 minutes before aspiration procedure

Continue oral analgesia above as required for 48 hours.
- paracetamol, oral, 1 g 6–8 hourly
AND
- ibuprofen, oral, 800 mg three times a day

5.7.2 GESTATION BY DATES, 13 TO 20 WEEKS

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

NON-DRUG TREATMENT
Evacuation of the uterus, (preferably vacuum aspiration) if abortion is not complete.
CHAPTER 5  
Gynaecology

DRUG TREATMENT

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

- misoprostol, SL/PV, 200–400 mcg 12 hourly until expulsion

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.
  - Attach sodium chloride 0.9% 1 L with giving set to catheter.
  - Infuse sodium chloride 0.9% at 50 mL/hour.

After cervical dilation or bleeding has commenced:
- oxytocin, IV, 20 units in 1 L sodium chloride 0.9%
  - Infuse at a rate of 125 mL/hour.

Note:
  - Check serum sodium if used for more than 24 hours because of the danger of dilutional hyponatraemia.
  - Most women deliver in 48 hours, some need manual removal of placenta.
  - Side effects: heavy bleeding and pain due to uterine contractions.

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

Analgesia
- pethidine, IM, 100 mg 4 hourly as needed
  - morphine, IM, 10 mg 4 hourly as needed

Avoid NSAIDs.

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
CHAPTER 5  GYNAECOLOGY

5.8 UTERINE BLEEDING, ABNORMAL
N91–N93

NON-DRUG TREATMENT
Surgical procedures as dictated by the diagnosis.
Perform endometrial ultrasound and sampling in women over 45 years of age.
Actively exclude organic causes for abnormal uterine bleeding.

DRUG TREATMENT
Dysfunctional uterine bleeding implies no organic cause present.

ARREST OF ACUTE HAEMORRHAGE
High dose combined oral contraceptive:
• levonorgestrel/ethinyl oestradiol 250/50 mcg, oral, 1 tablet every 6 hours for 2–3 days, thereafter 1 tablet daily for three months
  Placebos in the pack should be taken to regularise the menstrual cycle after the bleeding has stopped.

OR
For excessively heavy anovulatory dysfunctional bleeding:
Progestogen
• norethisterone, oral, 5 mg 4 hourly for 24–48 hours
  OR
  medroxyprogesterone acetate, oral, 5 mg three times daily for 24–48 hours
Thereafter follow guidelines for restoring cyclicity.

OR
Oestrogen
• conjugated oestrogens, IM/IV, 25 mg
  In cases of severe haemorrhage, repeat once if necessary after 6–12 hours.
  • tranexamic acid, oral, 1 g 4 times daily on days 1–4 of the cycle. Specialist initiated.
After bleeding has stopped, continue with a combined contraceptive tablet 3 times daily for 7 days and then 1 tablet once daily for 3 months.

FOR RESTORING CYCLICITY
For women in the reproductive years:
• combined oral contraceptive, oral, 1 tablet daily for 3–6 months

OR
As alternative to combined oral contraceptives:
Progestesterone only:
• medroxyprogesterone acetate, oral, 10 mg 3 times daily for 10 days, starting on day 14 of the cycle
  OR
  norethisterone, oral, 5 mg 3 times daily for 10 days, starting on day 14 of the cycle
Repeat every 3 weeks for restoring cyclicity, use for 3 months.
For perimenopausal women, if uterus present, HRT:
- conjugated oestrogens, oral, 0.625 mg daily for 11 days followed by the addition of medrogestone 5 mg for 10 days
  Use for 3–6 months.

For dysmenorrhoea and abnormal bleeding:
ADD
- ibuprofen, oral, 200 mg 3 times daily for 2–3 days
CHAPTER 6
OBSTETRICS

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

6.1 ANAEMIA IN PREGNANCY
D64.9

DESCRIPTION
Haemoglobin (Hb) of less than 10 g/dL.

NON-DRUG TREATMENT
Lifestyle adjustment to prevent nutritional deficiency.
Avoid “pica”, i.e. eating sand.

DRUG TREATMENT

PROPHYLAXIS
• ferrous sulphate compound, oral, 170 mg daily

PLUS
• folic acid, oral, 5 mg daily
Iron and folic acid supplementation should be continued during lactation.
Other causes of anaemia should be treated according to the diagnosis.

FOLIC ACID DEFICIENCY
• folic acid, oral, 5 mg daily

Treat until Hb is normal. Hb is expected to rise by at least 0.2 g per week if diagnosis is correct.
Associated vitamin deficiencies should be identified and treated accordingly.

IRON DEFICIENCY
• ferrous sulphate compound, oral, 170 mg 2–3 times daily
  Continue for 3 months after the Hb reaches normal to replenish iron stores.

REFERRAL
○ symptomatic anaemia
○ no response to management
○ anaemia due to causes other than haematinic deficiency

6.2 DEHYDRATION/KETOSIS

DESCRIPTION
Subclinical dehydration is often missed in labour.
CHAPTER 6

NON-DRUG TREATMENT
Encourage adequate oral fluid intake.

DRUG TREATMENT
Mild dehydration
Give oral fluids.

Moderate/severe dehydration
Intravenous fluids, 250 mL/hour.

Re-evaluate hydration hourly.
Intravenous dextrose in excess of 6 g/hour may cause fetal hyperinsulinism and hyponatraemia. Limit dextrose given IV as follows:
up to 125 mL/hour: dextrose 5%
any additional fluid: sodium chloride 0.9%

6.3 DIABETES MELLITUS AND GLUCOSE INTOLERANCE IN PREGNANCY

O24
Ideally this should be managed by a specialist.

DESCRIPTION

Diabetes mellitus in pregnancy
Fasting blood glucose: ≥ 6.9 or ≥ 11 mmol/L 2 hours after 75 mg glucose load.

Impaired glucose tolerance
Blood glucose 7.8–11 mmol/L 2 hours after 75 g glucose load.

NON-DRUG TREATMENT
Diet
Diabetic diet of not less than 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.

DRUG TREATMENT
Insulin requirements may increase with increasing gestation and later readmission may be necessary.
Six-point blood sugar profiles, i.e. pre- and 1–2 hour post-breakfast, lunch and supper.

Normal Profiles
Preprandial levels < 5.0 mmol/L and postprandial < 7.5 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 at:

- Preprandial levels: 3.5–5.5 mmol/L
- 2 hour postprandial: ≤ 7 mmol/L

When adequate glucose monitoring cannot be maintained, e.g. 24-hour profile in hospital every 1–2 weeks, and the risk of hypoglycaemia is unpredictable, these targets may need to be less stringent, e.g.:

- 2 hour postprandial: 7.8 mmol/L

Preferable 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 postprandial levels.

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

To maintain preprandial levels:

- Intermediate acting insulin, 10 units

To maintain the postprandial levels:

- Insulin, soluble, short acting, 5 units with all 3 meals

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

Where the above ideal regimen is not feasible
Twice-daily regimen with biphasic insulin.
Empiric starting dose if previous insulin requirements not known:

- Daily dose = 0.2 units/kg/day, ⅔ with breakfast and ⅓ with supper.
- Titrate daily to achieve target blood glucose as above.

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

- Insulin, soluble, short acting, continuous IV infusion, 10 units plus 20 mmol potassium chloride in 1 L dextrose 5% at an infusion rate of 100 mL/hour, i.e. 1 unit of insulin/hour
  - If blood glucose < 4 mmol/L, discontinue insulin.
  - If > 9 mmol/L, increase to 20 units/L.

The postpartum insulin requirements decrease rapidly.
During the first 48 hours blood sugar levels are maintained by 4-hourly blood glucose measurement and regular short-acting insulin administration.
CHAPTER 6 OBSTETRICS

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

The newborn is at risk of:
- hypoglycaemia (very common),
- respiratory distress,
- hyperbilirubinaemia,
- congenital abnormalities.

Postpartum contraception
Tubal ligation should be considered.
Consider:
- low-dose combined contraceptive in well-controlled cases
- progestogen-only preparation or intra-uterine device if the control is unstable.

6.4 HEART DISEASE IN PREGNANCY

DESCRIPTION
During labour the load on the heart is particularly high and any increased load should be prevented.

Refer for specialist assessment.

NON-DRUG TREATMENT
Screen for infections and anaemia, which may aggravate the cardiac condition.
Spontaneous delivery is usually preferable to Caesarean section, unless there are obstetric reasons for surgery.
Nurse in semi-Fowler position.
Restrict intravenous fluids.
Assist second stage of labour with forceps or vacuum extraction if does not progress rapidly.

Contraception, including the option of tubal ligation should be discussed after delivery in all women with significant heart disease.
Women having had serious complications during pregnancy should be advised not to become pregnant again.
A heart valve prosthesis must be considered a relative contraindication to pregnancy.

DRUG TREATMENT
Anticoagulation
Indications for prophylactic anticoagulation during pregnancy:
- more than one previous episode of venous thromboembolism
- one previous episode without a predisposing factor, or with evidence of thrombophilia
- valvular disease with atrial fibrillation
- women with prosthetic heart valves
CHAPTER 6

TREATMENT

First trimester

• heparin, IV, 5 000 units as a bolus, followed by 1 000–1 200 units/hour as an infusion
  OR
  heparin, SC, 10 000 units twice daily
  Control dose with APTT to keep it 1.5–2.5 times normal.
  OR
  Low molecular weight heparin (LMWH), e.g:
  enoxaparin, SC, 1 mg/kg twice daily

Women with prosthetic valves should receive LMWH ONLY if antifactor Xa levels can be monitored weekly.
Pre-dosing level 0.6 units/mL and a 4-hour peak level of 1–1.2 units/mL.

Second trimester

• warfarin, oral, 5 mg daily
  Control with INR to keep within the therapeutic range (2–3).

After 36 weeks

• heparin, IV, 5 000 units as a bolus, followed by 1 000–1 200 units/hour as an infusion
  OR
  heparin, SC, 10 000 units twice daily
  Control dose with APTT to keep it 1.5–2.5 times normal.
  Stop heparin on the morning of elective Caesarean section or when in established labour, and re-start after delivery.

PROPHYLAXIS

First and third trimester

• heparin, SC, 5 000 units twice daily

Antibiotics

Endocarditis prophylaxis is not indicated following uncomplicated vaginal delivery or Caesarean section.

Procedures for which endocarditis prophylaxis is not recommended:
  o if infection is not suspected
  o Caesarean section or vaginal hysterectomy
  o dilatation and curettage
  o uncomplicated vaginal delivery
  o therapeutic abortion
  o sterilisation procedures
  o insertion or removal of intrauterine devices
CHAPTER 6 OBSTETRICS

Procedures for which endocarditis prophylaxis is indicated include:

- vaginal delivery in the presence of suspected infection such as with prolonged rupture of membranes or manipulative vaginal deliveries

Refer Section 3.4: Endocarditis, Infective.

CARDIAC FAILURE
As for non-pregnant women, except that ACE-inhibitors are contra-indicated.

If a vasodilator is needed:

- hydralazine, oral, 25 mg 4 times daily
  - Maximum dose: 200 mg/day.

PLUS

- isosorbide dinitrate, oral, 20 mg, 3–4 times daily
  - Maximum dose: 160 mg/day.

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:

- furosemide, IV, 20 mg with delivery of the baby
  - Monitor for 48 hours thereafter for pulmonary oedema.

6.5 HYPEREMESIS GRAVIDARUM

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

Exclude:

- medical causes, e.g. thyrotoxicosis
- molar pregnancy

NON-DRUG TREATMENT
Counselling.
Frequent small, dry meals.
Avoid fatty and spicy foods.
Restrict oral intake for 24–48 hours, but ensure adequate intravenous hydration.
Baked fresh ginger root, 250 mg four times daily may have benefit.

DRUG TREATMENT
Correct electrolyte imbalance with IV fluids.

- pyridoxine, oral, 25 mg 8 hourly
- metoclopramide, oral/IV, 10–20 mg 6 hourly as needed
- vitamin B complex, IV, 10 mL
CHAPTER 6

OBSOTETRICS

In refractory cases:
• prednisone, oral, 20–40 mg daily
OR
If oral route unsuitable:
• dexamethasone, IM/IV, 4–8 mg daily

6.6 PRE-ECLAMPSIA/ECLAMPSIA

DESCRIPTION
DBP > 90 mmHg on two occasions or > 110 mmHg on one occasion, after 20 weeks’ gestation
PLUS
proteinuria > 300 mg/24 hours, or 500 mg/L, or
urinary protein-creatinine ratio > 0.034 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.

NON-DRUG TREATMENT
Prevention
Advise adequate dietary calcium (1 200 mg daily).
Bed rest, preferably in hospital.
Lifestyle adjustment and diet.
Monitor BP, urine output, renal and liver function tests, platelet count, proteinuria and foetal condition.
Consider delivery when risks to mother outweigh risks of prematurity to baby.

DRUG TREATMENT
• 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 also susceptible to pulmonary oedema. Consequently, hypotension is a risk during anaesthesia. Careful infusion of IV fluids is important. Blood-loss at Caesarean section should be limited.

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. Excessive IV fluids should be avoided; there is no need for IV fluid loading in labour.

Assisted delivery is advocated to prevent the woman from bearing down.
CHAPTER 6

PRE-ECLAMPSIA

Prevention
For women at high risk of pre-eclampsia, e.g. pre-eclampsia in a previous pregnancy, chronic hypertension or severe hypertension:
• aspirin, soluble, oral, 75 mg daily

Calcium supplementation
There is clear evidence from randomised trials that calcium supplementation for women with inadequate dietary calcium reduces the risk of pre-eclampsia.
1 g elemental calcium/day, e.g.:
• calcium carbonate 168 mg tablets, oral, 6 tablets daily with food
  Administer at least 4 hours before or after iron supplementation.

Treatment
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 twice daily, increase to 500 mg 4 times daily
  Maximum dose: 2 g/day
AND/OR
• nifedipine, extended release, oral, 30 mg daily, increase to 60 mg daily
AND/OR
• hydralazine, oral, 25 mg 3 times daily, increase to 50 mg 4 times daily

In women with pre-eclampsia in a previous pregnancy, in chronic hypertension or severe hypertension, once blood pressure is controlled:
ADD
• aspirin, soluble, oral, 75 mg daily

ECLAMPSIA
This treatment is recommended for:
• imminent eclampsia
• eclampsia
• severe pre-eclampsia, particularly in the presence of complications
PLUS
• magnesium sulphate, IM, 2 doses of 5 g with 1 mL lidocaine 1% followed by 5 g, 4 hourly
  Continue until 24 hours after delivery.

In high-care setting:
• magnesium sulphate, IV, 4 g in 20 mL sodium chloride 0.9% over 20 minutes
Follow with:
• magnesium sulphate, IV infusion, 1 g/hour

Check knee reflexes, and if absent or respiratory rate < 16/minute, stop magnesium sulphate and consider calcium gluconate:
• calcium gluconate 10%, IV, 10 mL given slowly at a rate not exceeding 5 mL/minute

If urine output < 100 mL/ 4 hours, stop magnesium sulphate.
CHAPTER 6

ECLAMPTIC SEIZURE IN PROGRESS

• clonazepam, slow IV, 1 mg

Notify the person who will resuscitate the child that a benzodiazepine has been given to the mother.

REFERRAL

○ all cases of eclampsia to a high or intensive care facility

6.7 HYPERTENSION IN PREGNANCY

O10.9

NON-DRUG TREATMENT

Lifestyle modification
The average weight gain during the last 2 trimesters is 2 kg/month. If the prepregnancy BMI is > 25%, weight gain of less than this should be attempted.
Salt restriction, e.g. remove the salt from the table, avoid processed foods and gradually reduce added salt in food preparation. Increase potassium intake from fresh fruits and vegetables.
No alcohol should be taken.
Follow a prudent eating plan, i.e. low fat, high fibre and unrefined carbohydrates, with adequate fresh fruit and vegetables.
Regular moderate exercise, e.g. 30 minutes brisk walking 3–5 times/week.
Stop smoking.
Fetal surveillance by symphysis-fundus height (SFH) growth carefully monitored and antepartum fetal heart monitoring at least weekly after 28 weeks.

Induction of labour should be considered in:
○ cases with BP persistently $>160/110$ mmHg,
○ pregnancy of 37 weeks duration or more, or
○ in the presence of maternal or fetal compromise, e.g. poor SFH growth and oligohydramnios, etc.

DRUG TREATMENT

See treatment of pre-eclampsia.

6.7.1 HYPERTENSIVE EMERGENCY

Preload with:

• sodium chloride 0.9%, IV infusion, 300 mL

• nifedipine, oral, 5–10 mg, half-hourly if needed until SBP < 170 mmHg and DBP < 110 mmHg
  Swallow whole.
  Do not chew, bite or give sublingually.

OR

hydralazine, oral, 25 mg every half-hour if needed until SBP < 170 mmHg and DBP < 110 mmHg
CHAPTER 6

Obstetrics

If unable to take oral:
• labetalol, IV infusion, 2 mg/minute to a total of 1–2 mg/kg

6.8 JAUNDICE IN PREGNANCY

DESCRIPTION
Jaundice associated with pregnancy may be due to one of the following:
• intrahepatic cholestasis of pregnancy,
• acute fatty liver of pregnancy (acute yellow atrophy of the liver),
• as a result of severe pre-eclampsia or eclampsia,
• as a result of hyperemesis gravidarum.
Consider non-pregnancy related causes of jaundice, e.g. hepatitis.

REFERRAL
• all, as certain causes of jaundice in pregnancy have a high mortality

6.9 LABOUR INDUCTION

If induction is medically indicated.

NON-DRUG TREATMENT
Reassurance.

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.

DRUG TREATMENT

Cervix favourable
• oxytocin, IV, 2 milliunits/minute
  Titrate dose to achieve desired response.
• Dilute 2 units oxytocin in 1 L Ringer–Lactate solution to make a solution of 2 milliunits/mL.
CHAPTER 6 OBSTETRICS

Cervix unfavourable
Prostaglandins, e.g.:
• dinoprostone gel, intravaginally, 1–2 mg
OR
dinoprostone tablets, intravaginally, 0.5–1 mg
OR
misoprostol, vaginal, 25 mcg,
after 4 hours follow with:
  misoprostol, oral, 25 mcg 2-hourly until in labour.

In nulliparous women, if no response to first 2 doses:
increase to 50 mcg 2 hourly. Vaginal dose may be omitted.
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 25 mL 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 section and relatively contraindicated in grand multiparous women.
Note:
Misoprostol is not registered for this indication in South Africa.
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.

6.10 LABOUR PAIN, SEVERE

NON-DRUG TREATMENT
Antenatal counselling.
Psychological support from family member, friend or volunteer ‘doula’.
Keeping women informed about the progress of labour, and reassurance with careful
explanation of the procedures performed, may reduce the need for analgesic drugs.
Anticipate the need for analgesia rather than waiting for severe distress.

DRUG TREATMENT
• morphine, slow IV, 10 mg, at the onset of a uterine contraction
  OR
  pethidine, slow IV, 100 mg at the onset of a uterine contraction

• promethazine, slow IV/IM, 25 mg
  OR
  morphine, IM, 10 mg 4 hourly
  OR
  pethidine, IM, 100 mg 4 hourly
Titrate dose and dose frequency according to pain.
Supplement with premixed nitrous oxide 50%/ oxygen 50% in late first stage.
CHAPTER 6 Obstetrics

Absorption from intramuscular injections during labour is poor. The preferable route is IV.

For intrauterine death
Use analgesia as frequently as requested.
• morphine, IV/IM, 10–15 mg 3–4 hourly
  Titrate dose and dose frequency according to pain.

Regional anaesthetic, epidural anaesthesia or caudal block
• bupivacaine without adrenaline
  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
• morphine or pethidine, as appropriate.
• ibuprofen, oral, 400 mg three times daily with meals

6.11 POSTPARTUM FEVER

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.

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

DRUG 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, IV, 500 mg 8 hourly
    OR
    metronidazole, oral, 400 mg 8 hourly
  PLUS
• gentamicin, IV, 5 mg/kg/day in a single daily dose
CHAPTER 6

After defervescence, intravenous ampicillin can be changed to:
• amoxicillin, oral, 500 mg 8 hourly

6.12 POSTPARTUM HAEMORRHAGE

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

NON-DRUG TREATMENT
Massage 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.

DRUG TREATMENT
Prevention
Active management of the 3rd stage of labour:
• oxytocin, IM, 10 units
AND
controlled cord traction.

TREATMENT
Resuscitate.
• oxytocin, IV, 20–40 units in 1 L sodium chloride 0.9% at 60 drops/minute
If necessary:
ADD
• ergometrine, IM/IV, 0.2–0.5 mg

OR
• oxytocin 5 units plus ergometrine 0.5 mg, IM/IV
Avoid ergometrine in women with hypertension or cardiac disease, except in severe cases where the benefit is considered to outweigh the risk.
Ergometrine may be repeated as needed up to a maximum of 1 mg in 24 hours.

For non-responsive cases
• dinoprost 5 mg/mL, intramyometrial
Dilute 1 mL to 10 mL.
Give 2 doses of 1 mL of dilute solution at different sites.
CHAPTER 6  
OBSTETRICS

6.13 PRETERM LABOUR AND PRETERM RUPTURE OF MEMBRANES

DESCRIPTION
Preterm: < 37 weeks gestation.
Most problems occur at < 34 weeks’ gestation.
Confirm ruptured membranes by sterile vaginal speculum examination if not clinically obvious.
Preterm labour confirmed by regular uterine contractions with progressive cervical changes.

NON-DRUG TREATMENT
Assess fetal wellbeing.
Estimate fetal weight.
Deliver if amnioinitis suspected.

DRUG TREATMENT
Pre-hydrate before administration of nifedipine:
• sodium chloride 0.9%, IV, 500 mL
  Continue with 125 mL/hour during treatment.

• nifedipine, oral, 20 mg
  If contractions persist, follow with 10 mg after 30 minutes then 10 mg 4 hourly for up to 24 hours.

OR
If gestation below 30 weeks:
• indomethacin, oral, 50 mg
  If contractions persist, follow with 25 mg 4 hourly for 24–48 hours.

To improve fetal lung maturity at 26–34 weeks:
• betamethasone, IM, 12 mg, 2 doses 24 hours apart
  OR
dexamethasone, IM, 12 mg, 2 doses 24 hours apart
  A single dose of steroid may be repeated weekly if the mother remains at risk of imminent preterm birth and the gestation is < 32 weeks.

Antibiotics
Indicated routinely for ruptured membranes and selectively for preterm labour with intact membranes if high risk for infection.
• amoxicillin, oral, 500 mg 8 hourly
PLUSS
• metronidazole, oral, 400 mg 8 hourly for 10 days

OR
CHAPTER 6 OBSTETRICS

- 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
- a fetus requiring neonatal intensive care: weight <1 500 g or gestation less than 34 weeks
- a fetus requiring specialised treatment after birth, e.g. surgery
- severely ill mother

6.14 RHESUS INCOMPATIBILITY

NON-DRUG TREATMENT
Amniocentesis (after 22 weeks) is indicated if atypical antibodies are found in the mother’s serum.
Test for maternal serum antibodies at ‘booking’, 28 and 34 weeks’ gestation.

DRUG TREATMENT
Maternal serum antibodies absent
During pregnancy, give prophylactic anti-D immunoglobulin to the mother within 72 hours of a potentially sensitising event.

After an abortion, threatened miscarriage or amniocentesis:
- anti-D immunoglobulin, IM, 50 mcg

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

At birth, determine the Rh status of the cord blood and request a Coombs’ test:
Cord blood Rh negative - no treatment.
Cord blood Rh positive, Coombs negative:
- anti-D immunoglobulin, IM, 100 mcg

If a large feto-maternal transfusion is suspected:
- anti-D immunoglobulin, IM, 300 mcg for every 25 mL transfusion
  Maximum dose: 1 200 mcg
  PLUS
  Do a maternal blood Kleihauer test.

Rh positive, Coombs positive. In these cases the mother will also have antibodies.
No anti-D immunoglobulin.
CHAPTER 6

Maternal serum antibodies present
A titre less than 1:16 - repeat in 4 weeks’ time.
A titre of 1:16 or more - refer to a specialist for further management.
In units where middle cerebral artery Doppler studies are available, cordocentesis for
Hb estimation and packed cell transfusion should be performed once the Doppler
indicates fetal anaemia.

6.15 SUPPRESSION OF LABOUR, ACUTE (TOCOLYSIS)
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.

DRUG TREATMENT
ß2-stimulant, e.g.:
• hexoprenaline, slow IV, 5–10 mcg over 10 minutes
  Stop the injection if the maternal pulse > 120/minute.

6.16 SYPHILIS
A53.9

DIAGNOSTIC CRITERIA
Positive syphilis serology (RPR).

NON-DRUG TREATMENT
Inform contact(s).

DRUG TREATMENT
• benzathine benzylpenicillin (depot formulation), IM, 2.4 million units weekly for
  3 doses

Penicillin allergy:
• erythromycin, oral, 500 mg 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.
CHAPTER 7
NEPHROLOGICAL/UROLOGICAL DISORDERS

7.1 NEPHROLOGY SECTION

7.1.1 CHRONIC KIDNEY DISEASE (CKD)
D64.9

DESCRIPTION
Kidney damage for > 3 months defined by structural or functional abnormalities of the kidney, with or without a decreased GFR (see below). It manifests by:
- pathological abnormalities, e.g. biopsy proven glomerular disease, or
- markers of kidney damage, including:
  - abnormalities in the composition of blood or urine e.g. proteinuria or haematuria, or
  - abnormalities in imaging tests e.g. small kidneys on ultrasound.

GFR < 60 mL/minute for > 3 months with or without kidney damage. GFR calculated using the Cockcroft and Gault formula:
\[
\text{CrCl (mL/minute)} = \frac{(140-\text{age}) \times \text{weight (kg)}}{0.82 \times \text{plasma Cr (micromol/L)}}
\]
*In males
*In females, multiply plasma Cr by 0.85 instead of 0.82.

Common causes of CKD include:
- hypertension
- diabetes
- glomerular disease (idiopathic, HIV, Hepatitis B and C and systemic lupus erythematosus)
- polycystic kidney disease

Chronic kidney disease can be entirely asymptomatic.

TREATMENT AND PREVENTION STRATEGIES ACCORDING TO STAGES
Adverse outcomes of chronic kidney disease can often be prevented or delayed through early detection and treatment of risk factors and CKD. Earlier stages of chronic kidney disease can be detected through routine laboratory measurements. The presence of chronic kidney disease should be established, based on presence of kidney damage e.g. sonar or renal biopsy; and level of kidney function e.g. estimating GFR (see staging below). The diagnosis of CKD is made irrespective of diagnosis i.e. Glomerulonephritis or Diabetic Nephropathy.
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.

**STAGING OF KIDNEY DISEASE**

<table>
<thead>
<tr>
<th>Stage/ glomerular filtration rate (mL/minute/1.73)</th>
<th>Description</th>
<th>Action</th>
</tr>
</thead>
</table>
| Stage 0 or GFR > 90                              | at increased risk CKD (with CKD or CVD risk factors) | screening  
|                                                 |             | CKD risk reduction  
|                                                 |             | CVD risk reduction |
| Stage 1 or GFR > 90                              | kidney damage with normal or I GFR | diagnose and treat comorbid conditions  
|                                                 |             | slow progression  
|                                                 |             | CVD risk reduction |
| Stage 2 or GFR 60–89                             | kidney damage with mild I GFR | estimate progression |
| Stage 3 or GFR 30–59                             | moderate I GFR | evaluate and treat complications |
| Stage 4 or GFR 15–29                             | severe I GFR | prepare for kidney replacement therapy |
| Stage 5 or ESRD or GFR < 15 or on dialysis      | kidney failure requiring renal replacement therapy  
|                                                 | End Stage Renal Disease (ESRD) | renal replacement therapy, i.e. dialysis or transplant if uraemia present |

**NON-DRUG TREATMENT**

Limit salt intake.  
Low protein diet until CKD stage 4.  
Reduce CVD risk factors – See Section 3.5: Hypertension  
See Sections:  
7.1.3: Glomerular Disease and Nephritic Syndrome  
7.1.4: Glomerular Disease and Nephrotic Syndrome  
7.1.6: End Stage Renal Disease (ESRD) - CKD Stage 5

**DRUG TREATMENT**

The following interventions may delay progression of renal disease.

**PROTEINURIA REDUCTION**

Determine the amount of proteinuria and assess the risk for deterioration with a 24-hour urinary protein excretion rate (PER) or spot albumin creatinine ratio (mACR), (i.e. mg/mmol is done if urine dipsticks is negative for protein otherwise use protein creatinine ratio (PCR), i.e g/mmol if urine dipsticks positive for protein).  
The ideal target is: proteinuria < 300 mg/24 hours or albumin creatinine ratio < 100 mg/mol or PCR < 0.10 g/mmol.  
Aim for a stable or increasing GFR and declining proteinuria.
CHAPTER 7  NEPHROLOGICAL/URINARY DISORDERS

Note:
A normal decline in GFR is observed with ageing at a rate of 1 mL/minute/year after 45 years. Changes in renal structural should be stable or improve as evidenced by imaging tests or kidney biopsy.

ACE inhibitor
Start an ACE-inhibitor and up titrate to the maximum dose, if tolerated. A decline in function may occur but observe patient every 1–2 weekly to allow GFR to settle. There is no level of GFR/creatinine at which an ACE-inhibitor is contraindicated, but use with caution in advanced CKD. However, if GFR/creatinine continues to decline after 4–6 weeks of treatment, consider stopping the ACE-inhibitor. Consult a specialist if necessary.
Check serum potassium when:
- using higher doses of ACE-inhibitor and
- CKD stage 3 or greater is present.
If ACE-inhibitor cannot be used, use other antiproteinuric drugs, i.e. β-blocker and/or nondihydropyridine CCBs, e.g. verapamil.
Note: These drugs are not as good as ACE-inhibitors for proteinuria reduction.
Optimise blood pressure control with additional antihypertensive agents, BP control results in a lowering of proteinuria and slower decline in GFR. Target BP < 130/80 mmHg.

HYPERLIPIDAEMIA
When hyperlipidaemia is a co-existent risk factor, add an HMGCoA reductase inhibitor (statin), e.g.:
- simvastatin, oral, 10 mg daily

DIABETES MELLITUS
In diabetics, optimise control. Avoid oral hypoglycaemics if GFR is < 60 because of the risk of lactic acidosis with metformin and prolonged hypoglycaemia with long acting sulphonylureas.

As CKD stages progress the following problems may become difficult to treat:

HYPERTENSION
See Section 3.5: Hypertension
Note: BP control results in a lowering of proteinuria and slower decline in GFR. Mortality increases when SBP < 100 mmHg in dialysis patients.

FLUID OVERLOAD AND OEDEMA
- furosemide, oral
  When GFR < 60 mL/minute, titrate to a maximum of 500 mg twice daily.
CHAPTER 7  Nephrological/Urological Disorders

Furosemide is no longer indicated when the patient is anuric.
Furosemide is ineffective when patient is on dialysis and anuric.
Beware of over diuresis at lower stages of CKD i.e. Stages 4 or lower.

HYPOCALCAEMIA AND HYPERPHOSPHATAEMIA
The aim is to lower phosphate levels and maintain normal calcium levels to ensure calcium phosphate product < 4.4 i.e. Ca x PO₄ in mmol/L to prevent calcium deposition in vessels and tissue which aggravates vascular disease.

The following drug treatment should be initiated by a specialist as patients may require parathyroid surgery to control calcium and phosphate:

For low serum phosphate and calcium:
• calcium carbonate, oral, 500–1 500 mg/day in divided doses with meals or between meals. Specialist initiated.

For hyperphosphataemia uncontrolled on calcium carbonate:
• aluminium hydroxide, oral, 20 mL three times daily. Specialist initiated.
  To prevent dementia-associated aluminium toxicity, do not use for longer than 3 months.

For hyperparathyroidism, initiate when when PTH levels > 2–3 times normal:
• calcitriol, oral, 0.25–4 mcg in divided doses. Specialist initiated.
  Monitor Ca++ and PO₂ and PTH levels regularly.

ANAEMIA ASSOCIATED WITH CKD IN HOSPITALS WITH DIALYSIS UNITS
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, IV. Specialist initiated.
  The use of oral iron is insufficient to correct iron stores.
  AND
• erythropoietin, SC/IV. Specialist nephrologist initiated.

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

ACIDOSIS AND HYPERKALAEMIA
See Section 7.1.5: Acute Renal Failure.

REFERRAL
- CKD Stage 4 – GFR < 30 mL/minute
- CKD Stage 3 – GFR < 60 mL/minute where complications exist which require drugs not available at secondary hospital e.g. hyperparathyroidism and anaemia
- unknown cause of kidney failure or as per glomerular disease below
- uncontrolled hypertension with CKD stage 3 or more
CHAPTER 7 NEPHROLOGICAL/URETICAL DISORDERS

Patients who qualify for dialysis or who have complications should be referred early to ensure improved outcome and survival on dialysis. i.e. GFR < 30.
Dialysis should ideally be started when the patient is mildly symptomatic and before nutritional status begins to deteriorate.

7.1.2 GLOMERULAR DISEASES (GN) N00–N08

DESCRIPTION
Many different diseases act on the glomeruli and may be a result of a primary insult to the kidney, or may be secondary to a systemic disorder. The effects of glomerular damage are relatively similar whatever the cause and can present with:
- reduced GFR
- proteinuria
- haematuria
- hypertension and oedema.

Nephrotic syndrome is the advanced clinical syndrome associated with severe protein leakage and fluid overload.
Nephritic syndrome is the advanced clinical syndrome of haematuria associated with glomerular injury, sodium and water retention or hypoalbuminaemia.

REFERRAL
All patients with:
- unexplained haematuria on two consecutive visits
- nephritic syndrome, i.e. acute glomerulonephritis
- proteinuria > 1 g/24 hours or equivalent on spot protein urine test and/or nephrotic syndrome for possible kidney biopsy
  - Not accurate in presence of heart failure, urinary tract infection, menstruation or sepsis.
- uncontrolled hypertension with CKD
- severe kidney dysfunction, i.e. reduced GFR – CKD Stage 4 < 30 mL/minute
- progressive decline in kidney function
- nephrotic syndrome associated with:
  - thrombo-embolic complications
  - complications of longstanding hyperlipidaemia
  - gross fluid retention
- all new patients with nephrotic and nephritic syndrome for biopsy and blood investigations depending on type of glomerular disease suspected or found

Where facilities are available investigation and management is usually done with guidance or referral to a nephrologist.
CHAPTER 7  NEPHYROLOGICAL/UCROLOGICAL DISORDERS

7.1.3 GLOMERULAR DISEASE AND NEPHRITIC SYNDROME
N01/N03

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

NON-DRUG TREATMENT
Regulate fluid and electrolyte balance. Monitor weight closely.
Dietary modification if severe kidney dysfunction e.g.: restrict protein, potassium and phosphorus intake.
Avoid nephrotoxins: e.g. drugs excreted by the kidney and NSAIDs.
Treat severe hypotension and hypertension adequately to prevent renal failure or worsening of renal failure
See Section 7.1.1: Chronic Kidney Disease (CKD).

DRUG 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.

General management:
See Section 7.1.1: Chronic Kidney Disease (CKD).

For streptococcal infection of the throat and skin to prevent acute post-streptococcal glomerulonephritis:
• phenoxymethylpenicillin, oral, 500 mg 12 hourly for 10 days
Penicillin has no role in established post-streptococcal glomerulonephritis.

7.1.4 GLOMERULAR DISEASE AND NEPHROTIC SYNDROME
N04

DESCRIPTION
Glomerular disease characterised by:
• severe proteinuria, i.e.:
  • 2.5 g/day, or greater
  • as determined by a spot urine protein measurement, i.e. protein creatinine ratio (PCR).
  Note: mACR is only used if urine dipsticks is negative for protein.

and
• resultant clinical picture which includes:
  • oedema
  • hypoproteinaemia and
  • hyperlipidaemia.
The cause cannot be determined accurately without a biopsy.
CHAPTER 7 Nephrological/Urological Disorders

NON-DRUG TREATMENT
Regulate salt and fluid intake.
Weigh daily.
Postural BP for monitoring fluid loss and to prevent excessive diuresis.
Evaluate proteinuria with albumin creatinine ratio (ACR):
  o initially – weekly
  o when discharged – monthly, until stable
  o every 3–6 months – 24 hour urine, if possible
Evaluate electrolytes frequently, especially in the early period of diuresis as patients may require potassium.

DRUG 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.
Specialist therapy may include a variety of immunosuppressive agents.

General management to prevent deterioration of GFR:
See Section 7.1.1: Chronic Kidney Disease (CKD).

THROMBOTIC COMPLICATIONS
See Section 3.7: Venous Thrombo-Embolism.

Beware of renal and deep vein thromboses (RVT and DVT).
RVT is rarely symptomatic with flank pain, haematuria, raised LDH.
High risk patients:
  o immobile patient
  o those with membranous nephropathy diagnosed on renal biopsy
  o albumin < 20 g/L or fibrinogen > 6 g/L

In patients with intractable nephrotic syndrome and serum albumin < 20 g/L despite therapy, consider anticoagulation with warfarin, until condition has improved.

DIALYSIS
May be indicated for worsening renal failure and pulmonary oedema – See indications for acute dialysis below.

7.1.5 ACUTE RENAL FAILURE (ARF)

DESCRIPTION
This is reversible kidney failure, most commonly as a result of:
  o pre-renal ARF, e.g. dehydration and fluid loss
  o intra-renal kidney ARF, e.g. acute tubular necrosis or acute glomerulonephritis
  o post-renal ARF, e.g. cervical cancer and ureteric obstruction.
CHAPTER 7 NEPHROLOGICAL/ UROLOGICAL DISORDERS

Often combinations of above occur, i.e. dehydration with pre-renal ARF and resultant ischaemia causing intra-renal kidney ARF from acute tubular necrosis (ATN).

NON-DRUG TREATMENT
Establish cause of ARF with good history and clinical examination. Treat all patients as if renal failure is potentially reversible.

DRUG TREATMENT

PRIMARY THERAPY- HOW TO AVOID DIALYSIS

1. Identify patients at risk
Risk factors include:
- volume depletion
- hypotension
- elderly
- contrast media
- myoglobinuria
- previous hypertension
- cirrhosis
- haemoglobinuria
- post op or post procedures
- previous renal dysfunction
- diabetes
- heart failure
- alcoholism
- HIV

Evaluate current drug treatment and stop all potential nephrotoxins e.g. certain antibiotics and NSAIDs.

2. Early referral and consultation with expert/experienced clinician
- hypotensive episode
- reduced urine output
- Cr > 180 micromol/L
- worsening creatinine e.g. doubling of serum creatinine over 24 hours

3. Aggressive fluid replacement and optimise volume status
   • sodium chloride 0.9%

If associated acidosis, see fluid preference below.

Note:
No proven role for:
- mannitol
- calcium channel blockers
- theophylline
- dopamine

4. 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 1–4 hours
   OR
   furosemide, IV, 250 mg 6 hourly for 24 hours administered over at least 20 minutes
   Maximum dose: 1 g/24 hours.
CHAPTER 7 NEPHROLOGICAL/UROLOGICAL DISORDERS

Note:
May convert oliguric to non-oliguric RF.
Can be used at 1–4 mg/hour.
No mortality advantage in clinical trials.
An increased incidence of seizures has been reported.

5. Avoid nephrotoxic agents or those agents that may become nephrotoxic when GFR is reduced
Withdraw nephrotoxic drugs, e.g. aminoglycosides, NSAID’s and ACE-inhibitors, especially when volume depletion is present.

6. Modify doses of drugs, if applicable
Check all drugs for possible dose adjustment.

7. Treat sepsis, if present

URAEMIC EMERGENCIES
1. Fluid overload/pulmonary oedema
   • furosemide, preferably IV, 250 mg 6 hourly for 24 hours administered over at least 20 minutes
   Maximum dose: 1 g/24 hours.
   Refer immediately if no improvement.

2. Acidosis
   If pH < 7.25 or CO₂ < 15 and the patient is stable and not dehydrated:
   • Shohl’s solution, oral, 10–30 mL three times daily after meals.
     Adjust dose according to response.
     citric acid 140 g
     sodium citrate 98 g
     water to 1 L
     1 mL = 1 mmol of alkali
   If not overhydrated or if severe acidosis or ill:
   • sodium bicarbonate 4.2%, IV, 50 mL in 1 L dextrose 5%.
     Maximum dose: 300 mL sodium bicarbonate per L dextrose 5%.
     Up to 3–4 L/24 hours depending on requirements i.e. clinical condition or CVP measurement.

   CAUTION
   Avoid fluid overload.

3. Bleeding
   Urgent dialysis is required if patient is bleeding, e.g. from gums or GIT. If not on dialysis, refer immediately for dialysis or start if available.
   Dialysis may not stop ‘uraemic bleeding’ immediately.
   Blood transfusion is indicated but only for blood loss or low Hb.
CHAPTER 7 Nephrological/Urological Disorders

For uraemic gastritis, proton pump inhibitor, e.g.:
• omeprazole
  GFR 10–50: decrease dose by 50%
  GFR < 10: decrease dose by 75%

Note:
For haemodialysis: suggest give dose after dialysis.
For chronic ambulatory peritoneal dialysis: no adjustment is required.

4. Hyperkalaemia
Serum K⁺ > 7mmol/L or K⁺ 5.5–7 with ECG changes.

Emergency measures are normally a prelude to rather than a substitute for dialysis.

• calcium gluconate 10%, slow IV bolus, 10 mL
  Maximum dose: 40 mL.

• dextrose 50%, IV infusion, 100 mL with insulin, soluble 10 units over 10–20 minutes
  Repeat 2 hourly as necessary.
  Monitor HG Ts every 30 minutes.
  OR
  dextrose 50%, continuous IV infusion, 100 mL with insulin, soluble 10 units at 5–10 L/hour
  Monitor HG Ts hourly.

For longterm or chronic, nonurgent need for potassium removal:
• sodium polystyrene sulfonate, oral, 15 g with 15 mL lactulose, 6 hourly
  Do not administer aluminium hydroxide and sodium polystyrene sulfonate simultaneously.
  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 after 24 hours, urgent dialysis is required.

5. Hypertension
Treat if present and especially if evidence clinically of hypertensive end organ damage.
See Section 3.5: Hypertension.

6. Hyperphosphataemia
To decrease absorption of phosphate in acute renal failure
• aluminium hydroxide 300 mg/5 mL, oral, 15–30 mL 8 hourly
CHAPTER 7  Nephrological/Urological Disorders

ACUTE DIALYSIS
Ideally, all cases should be discussed with a specialist.

Indications
- unsuccessful primary therapy:
  - oliguria or anuria
  - metabolic imbalance, e.g. acidosis: pH < 7.1 and/or TCO₂ or HCO₃ < 12 mmol/L
  - hyperkalaemia > 7 mmol/L
  - fluid overload, especially pulmonary oedema
  - severe dysnatraemia Na > 160 or < 115 mmol/L
- uraemic complications, e.g. pericarditis, encephalopathy and bleeding
- drug overdose, dialysable toxin only

Good and effective removal by haemodialysis can occur with only a few agents. A decision to be made by a specialist based on clinical scenario.

The HIV and Hepatitis B and C status of all patients receiving intermittent haemodialysis must be available within 24 hours. If haemodialysis is required acutely, the machine is chemically disinfected and isolated from further use until the Hepatitis B status is known.

Note:
HIV is not known to be transmitted through dialysis if machine is cleaned according to standard protocol after use. All known cases of transmission have occurred when standard disinfection procedures have been breached.

Types of dialysis/renal replacement therapy (RRT)
This depends only on the type of resources available:
- peritoneal dialysis
  - Specifically indicated in the following conditions:
    - primary malignant hypertension with ARF
    - acute on chronic RF
    - head injury
- haemodialysis, intermittent
- continuous veno-venous haemodialysis and haemofiltration (ICU only) or, sustained low-efficiency dialysis (SLED)

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
- severe fluid overload
- suspected glomerular disease or cause of ARF is unknown
- determination of cause
- failure to recover kidney function after 3 weeks on dialysis or after suspected cause has been treated or withdrawn
CHAPTER 7  Nephrological/Urological Disorders

7.1.6 End Stage Renal Disease (ESRD) - CKD Stage 5

N18.0

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

NON-DRUG TREATMENT
Appropriate dietary control of metabolic needs, electrolyte, fluid status and serum
phosphate and calcium.
Restrict protein, salt, phosphate and potassium.

DRUG TREATMENT
Avoid magnesium and aluminium containing substances.
Manage fluid balance on an individual basis.
Adjust all drug doses for the level of renal function, most will be GFR < 10.

HYPERTENSION
See Section 3.5: Hypertension

Note:
Mortality increases when SBP < 100 mmHg and > 150 mmHg in dialysis patients.
Slightly higher BPs are acceptable in patients on dialysis.

Indications and uses of furosemide – See Section 7.1.1: Chronic Kidney Disease
(CKD) (Fluid overload and oedema).

FLUID OVERLOAD OR OEDEMA
Fluid restriction or greater fluid removal via ultrafiltration on dialysis.
See Section 7.1.1: Chronic Kidney Disease (CKD).

HYPOCALCAEMIA, HYPERPHOSPHATAEMIA AND HYPERPARATHYROIDISM
See Section 7.1.1: Chronic Kidney Disease (CKD).

ANAEMIA ASSOCIATED WITH CKD OR ESRD
See anaemia associated with CKD.

ACIDOSIS AND HYPERKALAEMIA
This is usually controlled by dialysis.
In cases of acute derangement, see Section 7.1.5: Acute Renal Failure.

OTHER
There are other unique problems associated with CKD 5 (ESRD) and dialysis which
require specialist care e.g. pruritus, vascular access.
CHAPTER 7  NEPHROLOGICAL/UROLOGICAL DISORDERS

REFERRAL
- all ESRD patients should be referred to a specialist facility with the resources and expertise to manage ESRD patients
- all ESRD patients who qualify for long term dialysis programs

7.1.7 NATIONAL GUIDELINES FOR CHRONIC DIALYSIS

Public sector dialysis facilities in South Africa are limited because of the expense and shortages of resources. Transplantation is cost effective with good rehabilitation prospects for the patient and thus the major principle for acceptance for renal replacement therapy is the suitability for renal transplantation.

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.

The following co-morbid conditions should be considered as contra-indications for transplantation in the South African public sector:
- age > 60 years
- diabetics with significant non-renal complications or diabetic > 50 years
- malignancy
- severe cardiac failure or inoperable coronary artery disease
- HIV positive unless stable on HAART
- severe COPD or bronchiectasis
- chronic, persistent or active hepatitis due to hepatitis B or C
- patients with cirrhosis diagnosed by liver biopsy
- persistent non-compliance
- any serious underlying disorder in which transplantation is contra-indicated
- BMI > 35 kg/m²
- serious psychiatric conditions or substance abuse
- unwillingness to undergo transplantation

The following factors are relative contraindications for transplantation but not absolute exclusion criteria:
- patients with positive Hepatitis B surface antigen
- distance from the transplant centre and unavailability of transport
- BMI ≥ 30–35
CHAPTER 7  NEPHROLOGICAL/UROLOGICAL DISORDERS

7.1.8 URINARY TRACT INFECTION (UTI)

DESCRIPTION
Infection of the urinary tract, which, because of the anatomical continuity of the system, involve part or all of the urinary tract. More rarely, perinephric tissues may be involved. Upper UTI is a more serious condition and requires longer and sometimes intravenous treatment.

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

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

NON-DRUG TREATMENT
It is advised that to avoid recurrence of UTI consider the following:
- treat constipation if associated with UTI
- double/triple voiding with vesico-ureteric reflux
- void after intercourse and before retiring at night
- do not postpone voiding when urge to micturate occurs
- change from use of diaphragm or spermicides to an alternative type of contraception

DRUG 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.

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

UNCOMPPLICATED CYSTITIS
- ciprofloxacin, oral, 500 mg as single dose

For pregnant women:
- amoxicillin/clavulanic acid, oral, 375 mg 8 hourly for 7 days

COMPLICATED CYSTITIS
- ciprofloxacin, oral, 500 mg 12 hourly for 7 days

ACUTE PYELONEPHRITIS
Admit all patients with severe acute infections, defined as vomiting or sepsis or diabetes or HIV.
Chapter 7 Nephrological/Urological Disorders

Ensure adequate hydration with intravenous fluids. Ideally, all hospitalised patients should have an ultrasound, and especially in high risk patients e.g. diabetics.

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, 5 mg/kg/day
Switch to oral therapy as soon as 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 patient is able to take oral fluids:
- ciprofloxacin, oral, 500 mg 12 hourly for 7 days
  - CrCl: 10–50 mL/minute 75% of normal dose
  - CrCl: < 10 mL/minute 50–75% 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
Recurrence of bacteruria with the same organism within 3 weeks of completing treatment may be due to:
- antibiotic resistance
- inadequate duration of therapy, e.g. prostatitis
- underlying structural abnormality, e.g. benign prostatic hyperplasia with bladder outflow obstruction, renal cysts and pyogenic abscess

Reinfection
Eradication of bacteruria by appropriate treatment, followed by infection with a different organism.
Constitutes 80% of recurrent infections.

Send urine for microscopy, culture and sensitivity as treatment is dictated by the results.
CHAPTER 7  NEPHROLOGICAL/UROLOGICAL DISORDERS

NON-DRUG TREATMENT
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 is appropriate.

DRUG TREATMENT

PROPHYLAXIS
> 3 infections/year to reduce risk of recurrence requires continuous prophylaxis for 6–12 months or even 2 years:
• nitrofurantoin, oral, 100 mg at night
  Beware of pulmonary fibrosis.
  Limit for 6 months only.
  OR
  trimethoprim/sulphamethoxazole 80/400 mg, oral, 1 tablet at night
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
Screen and treat the sexual partner.

TREATMENT
Treat according to microscopy, culture and sensitivity.

REFERRAL
• septicaemia not responding to treatment
• uncertain diagnosis
• recurrent infection where no facilities exist for adequate culture of urine
• further investigation in women with relapses, especially outside pregnancy
• all men with recurrent UTI, i.e. > 3 infections/year

7.1.10 PROSTATITIS

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
• acutely tender prostate on rectal examination
CHAPTER 7  NEPHROLOGICAL/UROLOGICAL DISORDERS

CHRONIC NON-BACTERIAL PROSTATITIS
Is a diagnosis of exclusion (failure to respond to antibiotics), and is associated with perineal, suprapubic, penile and testicular pain.

DRUG TREATMENT
Acute bacterial prostatitis
In men < 35 years:
• ciprofloxacin, oral, 500 mg as single dose
Followed by:
• doxycycline, oral, 100 mg 12 hourly for 7 days

In men > 35 years:
• 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, the collecting system, bladder, prostate and urethra. Glomerular disease is suggested if proteinuria is present as well as casts on routine microscopy. Schistosomiasis (bilharzias) is a common cause of haematuria.

NON-DRUG TREATMENT
All patients must have a urine microscopy evaluation to determine the origin of the haematuria.
Isomorphic: suggests urinary tract below the kidney i.e. pelvis to urethra.
Dysmorphic: suggests intra-renal and glomerular origin.

Exclude schistosomiasis.

Note:
The presence of blood on urine test strips does not indicate infection and should be investigated as above.
CHAPTER 7 Nephrological/Urological Disorders

DRUG TREATMENT
Only if evidence of associated urinary tract infection, i.e. positive leukocytes or nitrites on urine test strips.
See Section 7.1.9: Urinary Tract Infection (UTI).
See Section 7.1.2: Glomerular Disease.

SCHISTOMIASIS
For *S. haematobium* and *S. mansoni*:
- praziquantel, oral, 40 mg/kg as a single dose
  **Note:**
  Breastfeeding women should stop breastfeeding on the day of drug administration and for the next 48 hours.

REFERRAL
- all cases of haematuria
- all cases not responding to specific drug treatment
- suspected glomerular disease - to a nephrologist
- gross macroscopic haematuria with no response to primary therapy and with drop in haemoglobin

7.2.2 BENIGN PROSTATIC HYPERPLASIA

DESCRIPTION
Benign prostatic hyperplasia is a noncancerous (benign) growth of the prostate gland. It occurs usually in men over 50 years. Cause is often unknown and believed to be changes in hormone levels associated with aging.

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

DRUG TREATMENT
When surgery is not feasible or not preferred:
- doxazosin, oral, 2–4 mg daily
  **Titrate to a maximum dose of 8 mg daily.**
  The first dose should be taken at night to prevent symptomatic postural hypotension.
  **OR**
  prazosin, oral, 1 mg at night, initial dose
  Increase to 2 mg twice daily.
CHAPTER 7  NEPHROLOGICAL/UROLOGICAL DISORDERS

REFERRAL
- renal failure
- for biopsy if associated constitutional symptoms or weight loss
- hydronephrosis
- recurrent urinary tract infections
- raised PSA > 4 ng/mL
- urinary retention
- urge incontinence
- suspected prostate cancer on digital rectal examination
- suspected TB of prostate gland on biopsy
- haematuria
- bladder calculi

7.2.3 BLADDER DYSKINESIA
N39.4

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

NON-DRUG TREATMENT
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.

DRUG TREATMENT
For detrusor hyperactivity demonstrated on urodynamic studies:
• imipramine oral, 25–50 mg 3 times daily
PLUS
• propantheline, oral, 15 mg 3 times daily for 12 weeks. Urologist initiated.
  Follow with 30 mg at night.
  Higher doses may be required.
OR
  oxybutynin, oral, 2.5–5 mg 3 times daily. Urologist initiated.

REFERRAL
- for confirmation of diagnosis
- complications

7.2.4 IMPOTENCE
F52.2

DESCRIPTION
The inability to attain and maintain an erect penis with sufficient rigidity for vaginal penetration. Organic causes include neurogenic, vasculogenic, endocrinological as well as many systemic diseases and medications.
CHAPTER 7  NEPHROLOGICAL/UROLOGICAL DISORDERS

NON-DRUG TREATMENT
Thorough medical and psychosexual history. Examination should rule out gynaecomastia, testicular atrophy or penile abnormalities. Consider the removal drugs that may be associated with the problem. A change in lifestyle or medications may resolve the problem.

DRUG TREATMENT
Treat the underlying condition.

In patients with proven testosterone deficiency:
• testosterone. Specialist initiated.

REFERRAL
o where an organic disease or medical condition is suspected as a cause to urologist or appropriate specialist if surgical intervention is need then, e.g. penile prostheses, vascular surgery and pelvic fractures

7.2.5 RENAL CALCULI
N20.2

DESCRIPTION
This is 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.

NON-DRUG TREATMENT
Acute stage
Oral fluids administered liberally. IV 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/day, especially in warm climates.

DRUG TREATMENT
Analgesia for pain.

For hypocitraturia:
• potassium citrate mixture BP, oral, 10–15 mL, well diluted with water, 3 times daily for 10 days. Repeat as necessary.

For uric acid stones (not necessarily gout):
• potassium citrate mixture BP, oral, 10–15 mL, well diluted with water, 3 times daily for 10 days. Repeat as necessary
PLUS
• allopurinol, oral, 300 mg at night
  Start at 100 mg, uptitrate to 300 mg.
The treatment is long-term to prevent recurrence.
CHAPTER 7 Nephrological/Urological Disorders

For mild metabolic hyperoxaluria (MMO):
• pyridoxine, oral, 25–75 mg daily

PLUS
• calcium carbonate, oral, 500–1 000 mg 3 times daily with meals for a few weeks

For renal hypercalciuria (absorptive type):
• hydrochlorothiazide, oral, 50 mg daily for 1 month
  May be repeated.

REFERRAL
  o in acute setting for suspected or diagnosed obstruction and/or ongoing pain
  o complicating urinary tract sepsis
  o renal damage or insufficiency i.e. presence of CKD at time of diagnosis or afterwards
  o recurrent calculi
  o if medical problem is suspected to be the cause e.g. chronic UTI and Crohn’s disease and expertise to make diagnosis does not exist
CHAPTER 8
ENDOCRINE SYSTEM

8.1 ACROMEGALY
E22

This condition should be managed at a tertiary centre.

REFERRAL
Patients should be referred to a hospital with endocrine and neurosurgery facilities. Transsphenoidal hypophysectomy is the accepted form of therapy. Radiotherapy post operatively if required in most cases (with large tumours).

8.2 ADRENAL INSUFFICIENCY (ADDISON’S DISEASE)
E27

DESCRIPTION
Primary adrenocortical insufficiency.

CLINICAL PRESENTATION
Acute crisis:
- hypotensive shock
- fever
- GIT disturbances
- dehydration
- weakness
- depressed mentation
- hypoglycaemia
- hyponatrema
- hyperkalaemia
- acidosis

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

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

INVESTIGATIONS
08:00 cortisol level
- > 550 nmol/L: excludes the diagnosis
- < 100 nmol/L: highly suggestive of Addison’s disease
- 100–550 nmol/L is indeterminate and may require an ACTH stimulation test which is done on referral to a centre with the appropriate expertise and access to the investigational agent.

Posttest level should be > 550 nmol/L or double the pre-test level.
This can be done with adrenocorticotropic hormone, which stimulates maximal adrenocortical secretion:
- ACTH, IM, 1 mg with blood sampling at 45 minutes
CHAPTER 8  ENDOCRINE SYSTEM

DRUG TREATMENT

ACUTE CRISIS
Exclude sepsis.
• hydrocortisone, IV, 100–500 mg 6 hourly as required
  Gradually taper to maintenance dose according to patient's clinical status.
Add mineralocorticoid therapy when maintenance doses reached.

To maintain adequate intravascular volume:
• sodium chloride 0.9%, IV
  Several litres may be required in the first 24–48 hours.

To reduce the risk of hypoglycaemia:
• dextrose, IV/oral

CHRONIC
As maintenance therapy:
• hydrocortisone, oral
  10–20 mg in the morning.
  5–10 mg at night.
OR
  prednisone, oral, 5–7.5 mg daily

For patients who remain symptomatically hypotensive:
• fludrocortisone, oral, 50–100 mcg daily
  Monitor therapy with:
    o symptoms: improvement in fatigue and GIT disturbances
    o blood pressure: normotensive and no postural drop
    o electrolytes: normal Na+ and K+

Note:
All patients should wear an alert bracelet.
All patients must receive increased doses of glucocorticoids during times of “stress”
i.e. acute illness, surgery, trauma, etc.

For severe stress:
• hydrocortisone, IV, 100 mg 6 hourly

REFERRAL
o all suspected cases for full evaluation

8.3 ANDROGEN DEFICIENCY
E29.1

DESCRIPTION
Deficient testosterone production or action due to hypothalamic/pituitary hypofunction
or due to primary testicular failure.
CHAPTER 8  ENDOCRINE SYSTEM

INVESTIGATIONS
- 09:00 am serum testosterone
- LH and FSH
- further investigations to determine cause to be undertaken after referral

Monitoring therapy
- PSA
- Haematocrit and haemoglobin
- Serum testosterone should be performed on the day of intramuscular injections just before administration to determine trough levels
- Lipids

DRUG TREATMENT
Individualise dosage and review doses on clinical response.
- testosterone, IM, 200–300 mg every 2–4 weeks

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 which is elevated
Low dose dexamethasone suppression test to confirm Cushing’s syndrome and high dose to try to determine aetiology:
- betamethasone or dexamethasone, oral, 1 mg
  Administer at 23:00 or 24:00.
  Measure plasma cortisol at 07:00 or 08:00 in the morning.
  In normal patients morning cortisol will be suppressed to ≤ 138 nmol/L.
  Patients with Cushing’s syndrome will have morning cortisol level of at least 248 nmol/L and will not suppress their cortisol.

NON-DRUG TREATMENT
Patient’s general condition may be supported by appropriate administration of a high protein intake.

DRUG TREATMENT
Consider potassium replacement if hypokalaemic.

REFERRAL
- all cases for investigation of aetiology and appropriate management
CHAPTER 8  
ENDOCRINE SYSTEM

8.5 DIABETES MELLITUS

DESCRIPTION

Types
- type I: Insulin-Dependent Diabetes Mellitus (IDDM)
- type 2: Non-Insulin Dependent Diabetes Mellitus (NIDDM)
- pancreatic diabetes mellitus
- gestational diabetes mellitus – See Section 6.3: Diabetes Mellitus and Glucose Intolerance in Pregnancy

NON-DRUG TREATMENT

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.
Cessation of smoking and discourage commencement of smoking.
Increased physical activity within limits i.e. aerobic exercise 3 times per week for 30–40 minutes.
Education for foot care.

MONITORING

- glycated haemoglobin preferably 3 monthly in all diabetics
- blood glucose at every visit
- weight and blood pressure at every visit
- potassium, creatinine and lipids annually
- funduscopy annually
- proteinuria annually

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<th>Acceptable</th>
<th>Additional action suggested</th>
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<td>&gt; 27</td>
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REFERRAL

- inability to advise optimal metabolic control
- complications that cannot be managed on site, especially ophthalmic, e.g. cataracts and proliferative retinopathy
CHAPTER 8  ENDOCRINE SYSTEM

8.5.1 NON-INSULIN DEPENDENT DIABETES MELLITUS (NIDDM) – TYPE 2

The management includes:
- treatment of hyperglycaemia
- treatment of hypertension and dyslipidaemia after risk-assessment. See Section 3.5: Hypertension
- prevention and treatment of microvascular complications
- prevention and treatment of macrovascular complications

DRUG TREATMENT

ORAL BLOOD GLUCOSE LOWERING DRUGS

Oral drugs are indicated when individualised glycaemic targets are not met by the combination of dietary modifications and physical activity/exercise.

In some cases, oral drugs are indicated at the first presentation of diabetes i.e. fasting blood glucose level of more than 15 mmol/L.

These agents may be used as monotherapy or in combination therapy targeting different aspects in the pathogenesis of hyperglycaemia in type 2 diabetes mellitus, i.e. increased insulin production and release, decrease insulin resistance and/or decrease hepatic glucose production.

Monotherapy with any of the drugs should be the initial choice. Use of stepped-care approach is recommended to clinicians.

Combination therapy using oral agents with different mechanisms of action is indicated if monotherapy with one of the agents has failed.

When oral combination therapy fails, insulin should be added to the treatment regimen or replace the oral agents.

Secondary failure of oral agents is said to be common, i.e. 5–10% of patients annually.

If overweight, i.e. BMI > 25 kg/m², metformin should be the first choice.

Sulphonylurea derivatives: glibenclamide or gliclazide

- glibenclamide, oral, 2.5 mg daily with breakfast
  
  Dose increments if the blood or urine glucose is uncontrolled:
  
  Increase with 2.5 mg daily at two-weekly intervals.
  
  Maximum dose: 15 mg daily.
  
  If 7.5 mg or more is needed, divide the total daily dose into 2, with the larger dose in the morning.

OR

If an alternative is required, e.g. in the elderly and patients with renal impairment:

- gliclazide, oral, 40 mg daily with breakfast
  
  Dose increments if the blood or urine glucose is uncontrolled:
  
  Increase with 40 mg daily at two-weekly intervals.
  
  Maximum dose: 160 mg twice daily.
  
  If 80 mg or more is needed, divide the total daily dose into 2.
CHAPTER 8  ENDOCRINE SYSTEM

Biguanides: metformin
• metformin, oral, 500 mg daily
  Dose increments if the blood or urine glucose is uncontrolled:
  Increase to 500 mg twice daily after two weeks.
  Increase to 850 mg twice daily after another two weeks if needed.
  Maximum dose: 850 mg three times daily.
Contra-indicated in:
  patients with a serum creatine of ≥ 50 micromol/L
  uncontrolled congestive cardiac failure
  impaired liver function

INSULIN THERAPY IN TYPE 2 DIABETES
See insulin protocols as in type 1 diabetes mellitus below.
Insulin therapy is indicated in:
  o secondary failure with oral drugs, i.e. combination/substitution insulin therapy
  o peri-operative period especially major or emergency surgery
  o severe kidney or liver failure
  o pregnancy
  o latent autoimmune diabetes in adults

Oral agents should not be used in Type 1 diabetes, severe kidney and hepatic impairment.
The regimen and dose of insulin therapy vary from patient to patient.
Two forms of insulin therapy are often used in combination with oral blood glucose
lowering drugs:
  o intermediate or long acting insulin plus oral agents or
  o premixed combination of short acting with intermediate acting insulin.
At initiation of insulin therapy, appropriate advice on self-blood glucose monitoring
(SBGM) and diet should be given.

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

8.5.2 INSULIN DEPENDENT DIABETES MELLITUS (IDDM)
  TYPE 1

The management includes:
  o maintenance of glycaemic control within acceptable limits
  o prevention of chronic complications
  o prevention of acute complications, e.g. hyperglycaemic and hypoglycaemic coma

INSULIN PROTOCOLS
• insulin, soluble, short acting, SC, three times daily, 30 minutes prior to meals
  Regular human insulin.
  Onset of action: 30 minutes.
  Peak action: 2–5 hours.
  Duration of action: 5–8 hours.
CHAPTER 8 ENDOCRINE SYSTEM

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

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

SELECTION OF INSULIN

Basal bolus insulin
All type 1 diabetics should preferentially be managed with combined intermediate-acting (basal) and short-acting soluble insulin (bolus), the so-called basal bolus regimen.
This consists of pre-meal short acting insulin and bedtime intermediate acting insulin not later than 22:00.
The initial total daily insulin dose should be calculated as 0.6-units/kg body weight.
The total dose is divided into 50% basal insulin and 50% bolus insulin split equally for each meal. The dose is then adjusted on an individual basis.

Pre-mixed insulin
Twice daily pre-mixed insulin, i.e. a mixture of intermediate/short acting soluble insulin does not provide as good control but is a practical option for patients who cannot monitor blood glucose frequently.

INSULIN DELIVERY DEVICES
Due to cost, prefilled disposable pens should be reserved for special categories of patients, e.g. visually impaired patients and patients on the basal bolus regimen.

HOME GLUCOSE MONITORING
• patients on basal bolus insulin should measure glucose at least daily
• all type 2 patients on insulin should be given up to 25 strips per month for home glucose monitoring

GLUCAGON
Type 1 diabetics on tight control, i.e. basal bolus, who are judged to be at high risk of hypoglycaemia should have a glucagon hypoglycaemia kit and both the subject and the family should be educated how to use this emergency therapy.

8.6 DIABETIC EMERGENCIES

8.6.1 HYPOGLYCAEMIA
E83.5

DIAGNOSIS
CLINICAL
See above.
CHAPTER 8       ENDOCRINE SYSTEM

BIOCHEMICAL
Act on finger prick blood glucose. Confirm with laboratory measurements.

TREATMENT
1. Start immediately.
   • dextrose 50%, rapid IV injection, 50 mL

2. Assess clinical and biochemical response over the next 5–10 minutes.

3. Establish a large bore intravenous line and keep open with:
   • dextrose 10%, IV

4. If no clinical response give a second injection of:
   • dextrose 50%, IV, 50 mL

5. To prevent recurrent hypoglycaemia, continue infusion with:
   • dextrose 10%, IV infusion, at a rate of ± 1 L in 6 hours

6. 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.

7. If intravenous glucose cannot be given, for any reason, give:
   • glucagon, IM, 1 mg
   Blood glucose will take 10–15 minutes to rise.

8. 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, and admit to hospital for observation and for education, etc, to prevent further hypoglycaemic episodes.

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

RECURRENT HYPOGLYCAEMIA
Consider the following in the case of recurrent hypoglycaemia:
  o inappropriate management, e.g. too much insulin or too high dose of sulphonylurea
  o poor compliance
  o alcohol abuse
  o factitious administration of insulin
  o the honeymoon period of Type 1 diabetes
  o the advent of renal failure
  o hypoglycaemic unawareness
  o pancreatic diabetes

Other causes of hypoglycaemia should also be considered e.g. associated Addison’s disease or hypopituitarism.
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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. Evidence exists that in some cases this situation can be restored to normal with avoidance of hypoglycaemia.

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

DIABETIC COMAS – RECOGNITION AND CLINICAL PROFILES

DKA often occurs in the younger age and develops over hours to days. There may be vomiting, abdominal pain and acidic breathing.
- blood glucose usually < 40
- blood ketones are positive
- serum osmolality < 350 mOsm/L.

HONK is a syndrome characterised by impaired consciousness, sometimes accompanied by seizures, extreme dehydration and severe hyperglycaemia, that is not accompanied by severe ketoacidosis. It usually occurs in the elderly type 2 diabetic and develops over days to weeks.
- blood glucose usually > 40
- blood ketones usually negative
- serum osmolality is > 320 mOsm/L.

Anion gap = Na – (Cl + HCO₃) (N = ± 12 : DKA > 20)
Calculated serum osmolarity = 2 (Na + K) + glucose + urea (N = 275–285 mOsm/L)

NON-DRUG TREATMENT

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

DRUG 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.
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Fluid therapy thereafter is calculated to replace the estimated deficit in 48 hours, ± 5 mL/kg/hour.
Reduction in serum osmolality should not exceed 3 mOsm/kg/hour.

Correct sodium for blood glucose.
Rough guide: divide glucose by 3 and add to sodium value.

If plasma Na+ > 140 mmol/L:
• sodium chloride 0.45%, IV

If plasma Na+ < 140 mmol/L:
• 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.

**Potassium**

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

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

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

Maximum potassium dose: 40 mmol/hour.
Monitor 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 starts excreting urine

**INSULIN THERAPY**

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

**PROTOCOL 1**: continuous intravenous infusion
• insulin, soluble, short acting, IV infusion, 50 units in 200 mL sodium chloride 0.9%
  1 mL of solution = 4 units insulin
  • initial infusion: 0.1 unit/kg/hour
  Usually 5–7 units/hour: 20–28 mL/hour.
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- 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 3–4 mmol/L/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 with glucose test strips.

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 glycaemia alone!

PROTOCOL 2: hourly intramuscular bolus injections
Where intravenous infusion cannot be safely administered:
- Insulin, soluble, short acting
  - Loading dose: 0.5 units/kg body weight.
  - Give half the dose as an intravenous bolus injection and the other half IM.
  - Dilute 100 units with sodium chloride 0.9% to 10 mL i.e. 10 units/mL.
  - Do not give with an insulin syringe and needle as this would be subcutaneous.
  - Subsequent hourly doses: ± 5–10 units IM every hour (i.e. 0.1 units/kg/hour) and titrated against the bedside capillary glucose level.

Criteria for resolution of DKA
Note:
Plasma glucose level is not the main criteria. Ketosis and acidosis must be resolved.

PROGRESS MANAGEMENT
Continue protocols 1 or 2 until the acidosis has resolved and:
- The patient is able to eat
- When subcutaneous insulin therapy can be instituted either at previous doses or, for newly diagnosed diabetes at 0.5–1 unit/kg total daily dose divided into at least two doses with mixed short and long acting insulin (biphasic insulin 2/3 in the morning and 1/3 at night).

Infusion must overlap with subcutaneous regimen for 1–2 hours to avoid reversion to acidosis.

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

CEREBRAL OEDEMA
May occur with over-aggressive fluid replacement.
If treatment is necessary, See Section 14.11.1: Brain Oedema due to Tumors and Inflammation.
CHAPTER 8  ENDOCRINE SYSTEM

8.7 MICROVASCULAR COMPLICATIONS (NERVES, KIDNEYS, EYES)
E10.2/E10.3/E10.4

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

There are three major categories:
- peripheral neuropathy
- autonomic neuropathy
- acute onset neuropathies

DRUG TREATMENT
Improve glycaemic control.
Exclude or treat other contributory factors:
- alcohol excess
- vitamin B₁₂ deficiency, if suspected
- uraemia

Pain
- paracetamol, oral, 1 g every 6 hours as needed
- amitriptyline, oral, 10–25 mg at night increasing to 75 mg, if necessary

If ineffective, consider adding:
- carbamazepine, oral, 100 mg daily increasing to 200 mg twice daily if necessary

Gastroparesis
- metoclopramide, oral, 10 mg three times daily before meals
  If ineffective consult a specialist.

8.7.1 DIABETIC KIDNEY DISEASE
N18
See Section 7.1.1 Chronic Kidney Disease (CKD).

8.7.2 DIABETIC FOOT ULCERS
L97

NON-DRUG TREATMENT
Metabolic control and treatment of comorbidity.
Relieve pressure: non-weight bearing is essential.
Smoking cessation.
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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.

DRUG TREATMENT
SUPERFICIAL ULCER WITH EXTENSIVE INFECTION
Debridement with removal of all necrotic tissue.

Antibiotic therapy
For polymicrobial infection.
Topical antibiotics are not indicated.
Duration of therapy: 10 days but longer courses may be necessary.
• amoxicillin/clavulanic acid, oral, 625 mg 8 hourly

SEVERE INFECTION
• cloxacillin, IV, 2 g 6 hourly
PLUS
• metronidazole, oral, 400 mg, 8 hourly
PLUS
• gentamicin, IV, 5 mg/kg/day
Penicillin allergy:
• clindamycin, oral, 150 mg 8 hourly
PLUS
• gentamicin, IV, 5 mg/kg/day
Renal impairment
Replace gentamicin plus cloxacillin with 3rd generation cephalosporin, i.e.:
• ceftriaxone, IV, 2 g daily
PLUS
• metronidazole, oral, 400 mg, 8 hourly

REFERRAL
o arterial revascularisation procedures

8.8 MACROVASCULAR COMPLICATIONS

SECONDARY PREVENTION
Diabetic patients with a history of myocardial infarction, vascular bypass, stroke or transient ischemic attack, peripheral vascular disease, claudication, or angina.
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PRIMARY PREVENTION
Any diabetic patient with an additional cardiovascular risk factor, e.g. age > 40 years, cigarette smoking, hypertension, obesity, albuminuria, hyperlipidaemia, or a family history of coronary heart disease.
- aspirin, soluble, oral, 75–150 mg daily

HYPERTENSION
See Section 3.5: Hypertension

DYSLIPIDAEMIA
See Section 8.9: Dyslipidaemia

8.9 DYSLIPIDAEMIA

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 CAD e.g. hypertension, smoking, diabetes, must be looked for and treated. Underlying secondary causes of dyslipidaemia, e.g. excess alcohol intake, hypothyroidism, should be identified and corrected. The goal of treatment should be clearly explained to the patient and the risks conferred by untreated dyslipidaemia should be emphasised.

NON-DRUG TREATMENT
Lifestyle modification:
- dietary strategies are effective
  - substituting unsaturated fats (mono-and polyunsaturated fats) for saturated fats
  - consuming a diet high in fruits, vegetables, nuts and whole refined grains
- smoking cessation
- increase physical activity
- maintain ideal body weight

DRUG TREATMENT
INDICATION FOR DRUG THERAPY
- ischaemic heart disease
- peripheral vascular disease
- atherothrombotic stroke
- a risk of MI of greater than 20% in 10 years
Such high-risk patients will benefit from lipid lowering (statin) therapy irrespective of their baseline LDL-C levels.
CHAPTER 8  

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**CALCULATION OF ABSOLUTE RISK OF MYOCARDIAL INFARCTION OVER 10 YEARS (IN THE ABSENCE OF ISCHAEMIC HEART DISEASE AND MONOGENETIC DYSLIPIDAEMIA)**

To derive the absolute risk as percentage of subjects who will have a myocardial infarction over 10 years: Add the points for each risk category (men – section A; women – section B).

The risk associated with the total points is then derived from section C (for men and women).

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CHAPTER 8 ENDOCRINE SYSTEM

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<td>Diabetic</td>
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* Use the highest reading of either diastolic or systolic pressure (mmHg).

**Section C: Risk** (% of cohort defined by the score who will have a myocardial infarction in 10 years)

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<th>Women (%)</th>
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</table>

The score is gender dependent: for example, 6 points for men and 10 for women both have a 10% risk.

**CARDIOVASCULAR**

The main indication for lipid modifying medication is to reduce cardiovascular risk. 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.

**NON-CARDIOVASCULAR**

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

The basic principles are:
- control or reverse possible secondary factors, e.g. alcohol excess and diabetes
- introduce a very low fat diet
- lipid modifying drug therapy.
  - Fibric acid derivatives are the drugs of choice for severe hypertriglyceridaemia.

**Choice of drug**

Depends on the type of lipid disturbance:
- predominant hypercholesterolaemia: HMGCoA reductase inhibitors (statin)
- mixed hyperlipidaemia: HMGCoA reductase inhibitors (statin) or Fibric acid derivatives
- predominant hypertriglyceridaemia: Fibric acid derivatives

If lifestyle modification does not achieve lipid goals within 3 months:
HMGCoA reductase inhibitors (statins) that lowers LDL by at least 25%, e.g.:
- simvastatin, oral, 10 mg daily
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OR
Fibrin acid derivatives e.g.:
• bezafibrate, oral, 400 mg daily
Fibrin acid derivatives should be used for patients with moderate to severe fasting hypertriglyceridaemia and for patients on ARV therapy i.e. triglycerides > 10 mmol/L.

People with protease inhibitor induced dyslipidaemia fulfilling the above criteria should be treated with a fibrin acid derivative because of adverse drug reactions with statins.

REFERRAL
o people with FH
o suspected severe familial dyslipidaemias

8.10 HYPERCALCAEMIA, INCLUDING PRIMARY HYPERPARATHYROIDISM
E83.5/E21.0

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

AETIOLOGY
o ambulatory patients: hyperparathyroidism is the most common cause in > 90% of cases.
o in hospitalised patients: malignancies are the most common cause (65% of cases).
  Hyperparathyroidism accounts for another 25%.
o granulomatous disease (Sarcoid)
o immobilisation in those with high bone turnover

INVESTIGATIONS
Draw blood for PTH and a simultaneous calcium and albumin.
A detectable PTH in the presence of hypercalcaemia indicates primary hyperparathyroidism.

DRUG TREATMENT
HYPERCALCAEMIA
Patients with hypercalcaemia should be kept well hydrated and may need several litres of fluid.
Avoid thiazide diuretics as it increases serum calcium concentration.

For hypercalcaemia plus symptoms:
• sodium chloride solution 0.9%, IV infusion, 4–6 L/24 hours
PLUS
• furosemide, IV, 10–20 mg 6–12 hourly
  Observe urine output carefully.

Furosemide should not be given until the patient is well hydrated.
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If after 24 hours and adequate hydration and still symptomatic, serum calcium is still over 3 mmol/L:

ADD

Bisphosphonates (specialist initiated) e.g.:
- pamidronic acid, IV infusion, according to plasma calcium concentration, 30 mg over 1–4 hours
  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.

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

REFERRAL
- when a diagnosis of hyperparathyroidism is confirmed

8.11 HYPOCALCAEMIA
E83.5

DESCRIPTION
When serum calcium (corrected for albumin) fall 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: calcium, albumin, phosphate, urea, creatinine, magnesium and PTH.

DRUG TREATMENT
Directed at underlying cause.
For hypoparathyroidism:
- calcium, elemental, oral, 500–1500 mg/day

For acute hypocalcaemia with neurological problems:
- calcium gluconate 10%, IV, 10 mL administered over 15–30 minutes
  This may be repeated and/or add calcium gluconate 10%, 20–30 mL to 1 L dextrose 5% and infuse over 12–24 hours.
  Monitor closely with ECG.
- alfacalcidol, oral, 1–3 mcg daily

Renal failure
See Section: 7.1.1: Chronic Kidney Disease (CKD).
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REFERRAL
- If cause is uncertain
- If hypoparathyroidism considered and PTH analysis required as above

8.12 HYPOTHYROIDISM
E30.9

CAUSES
Common causes of primary hypothyroidism are thyroiditis, post-surgery and post-radiodine.
Secondary hypothyroidism may be due to any cause of anterior hypopituitarism.

INVESTIGATIONS
TSH and T4 initially and for monitoring adequacy of therapy.

DRUG TREATMENT
- levothyroxine, oral, 100 mcg daily
  - If TSH and T4 are low this suggests hypopituitarism. Give hydrocortisone replacement before starting levothyroxine.
  - 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 T4, after 2–3 months and adjust dose if required.
  - TSH levels will take several months to stabilise.
  - Once stable check T4 and TSH annually.

HYPOTHYROIDISM IN PREGNANCY
About 60% of hypothyroid pregnant women need an increase in thyroxine therapy in the second and third trimesters. Check TSH monthly and increase thyroxine doses to keep serum TSH levels low normal. After delivery, revert to pre-conception doses.

8.13 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.

NON-DRUG TREATMENT
Adequate energy and protein intake.
Adequate dietary calcium (>1 g/day) intake 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.
Avoid excessive alcohol, i.e. > 10 drinks/week.
Avoid falls:
- avoid sedating drugs especially in the elderly
- manage visual, mental and/or balance impairment
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- weakness
- sarcopenia
- environmental hazards
- history of falls

**DRUG TREATMENT**

**Calcium supplementation**
Preferably dietary, but few achieve RDA and supplements usually required.
- calcium, elemental, oral, 500–1 000 mg daily
  Calcium carbonate to be taken with meals. Other calcium salts can be taken between meals.

**Vitamin D supplementation**
In the elderly, the institutionalised and those who wear protective clothes:
- vitamin D, oral, 400–800 units/day
When concomitant osteomalacia is present:
- vitamin D, oral, 50 000 units every 1–2 weeks

**Hormone Replacement Therapy**
See Section 5.4: Menopause and Perimenopausal Syndrome.

**REFERRAL**
- to establish diagnosis (bone densitometry)
- for initial assessment
- initiation and monitoring response to therapy and 18–24 monthly BMD
- fractures suspected to be due to osteoporosis after initial management for consideration of bisphosphonate therapy

### 8.14 OSTEOMALACIA / RICKETS

M83.9

**DESCRIPTION**
A disorder of mineralisation of newly synthesised bone matrix.

**REFERRAL**
- all

### 8.15 PAGET’S DISEASE

M88.9

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

**NON-DRUG TREATMENT**
Most cases are mild and asymptomatic and no treatment is required.
CHAPTER 8

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 pain resulting from fracture or complicating osteosarcoma.

DRUG TREATMENT
After referral for diagnosis and initiation of therapy.
For pain:
• ibuprofen, oral, 400 mg 8 hourly

REFERRAL
o basal skull involvement
o severe pain not responding to NSAIDs
o Pagetic fracture

8.16 PITUITARY DISORDERS

8.16.1 PROLACTINOMA

DESCRIPTION
Prolactinoma is the most common functioning pituitary tumour.

INVESTIGATIONS
o serum prolactin

Note:
There are numerous causes of hyperprolactinaemia other than a prolactinoma, e.g. drugs, physiological, hypothyroidism, chronic renal failure and tumors. Elevated serum prolactin levels up to 200 ng/mL may also be found in other pituitary tumours and hypothalamic-pituitary lesions with stalk compression.

DRUG 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 twice a day with food and check prolactin 4 weeks later.
  Higher doses may be needed.
  GIT side effect minimised by giving doses with food.
  If total dose of 10 mg does not normalise prolactin, refer.

URGENT REFERRAL
o compression of optic chiasm
o pituitary apoplexy

REFERRAL
o all tumours, once secondary causes of hyperprolactinaemia have been sought and excluded
CHAPTER 8  ENDOCRINE SYSTEM

8.16.2 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 due to hypothalamic dysfunction, which may result in hypothyroidism and/or hypoadrenalism and/or hypogonadism.

NON-DRUG TREATMENT
Surgery is required for large tumours, pituitary apoplexy, and hormone secreting tumours (prolactinoma excluded).
An alert bracelet is needed.

DRUG TREATMENT

ACUTE CRISIS
Treat as for Acute crisis in section 8.2: Adrenal Insufficiency (Addison’s Disease).

CHRONIC
See Section 8.2: Adrenal Insufficiency (Addison’s Disease)

HYPOADRENALISM
See Section 8.2: Adrenal Insufficiency (Addison’s Disease)

HYPOGONADISM
Individualise dosage and need for replacement.
Women:
As for postmenopausal HRT: See Section 5.4.

Men:
•  testosterone, IM, 300 mg every 3–4 weeks

REFERRAL
• all diagnosed patients for initial assessment

8.16.3 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 and are most often idiopathic.
CHAPTER 8

ENDOCRINE SYSTEM

NON-DRUG TREATMENT
Rehydration with water or hypotonic fluids.

DRUG TREATMENT
Replacement therapy
- desmopressin aqueous solution 100 mcg/mL, 10–40 mcg (0.05–0.4 mL)
  daily, delivered nasally:
  - nasal spray, 10 mcg/spray (0.1 mL) once or twice daily
  OR
  - nasal solution, 5–20 mcg once or twice daily via calibrated plastic catheter
  OR
  desmopression, oral, 0.2–1.2 mg daily
  Optimal dose: 0.1–0.2 mg three times daily

ACUTE MANAGEMENT
Post operatively:
- vasopressin, IV, 1–4 mcg once or twice daily
  Larger doses can lead to water overload and hyponatraemia.

REFERRAL
- all diagnosed patients
  Water deprivation and vasopressin test is necessary to confirm the diagnosis.
  Careful monitoring on therapy is essential to ensure appropriate dose by way of electrolytes and exclusion of fluid overload.

8.17 PHEOCHROMOCYTOMA
C74.9

DESCRIPTION
Catecholamine-secreting tumour of the adrenal medulla.

CLINICAL PRESENTATION
Always consider in hypertensive patients that have paroxysmal symptoms:
- headaches
- diaphoresis
- palpitations
- anxiety
- tremor
- recurrent chest discomfort
- sweating
- GIT symptoms
There is marked interindividual variation of symptoms.
These hypertensive patients may have orthostatic changes in blood pressure.

DIAGNOSIS
24 hour urine containing HCl, normetanephrine (NMA), vanillylmandelic acid (VMA),
should be twice normal.
CHAPTER 8  ENDOCRINE SYSTEM

Test is best to be done after a paroxysm 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.

Who to screen
- young hypertensives
- hypertensive patients with paroxysmal symptoms
- patients with:
  - a labile BP
  - a family history of a phaeochromocytoma
  - radiologic evidence of an adrenal mass

NON-DRUG TREATMENT
Surgical removal of the tumour.

DRUG TREATMENT
Alpha blocker, e.g.:
- doxazocin, oral

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

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

8.18 PRIMARY ALDOSTERONISM

DESCRIPTION
Increased aldosterone production usually due to an adrenal adenoma (65%, Conn's Syndrome) or idiopathic bilateral adrenal hyperplasia (30%).

CLINICAL
Always suspect in a patient with resistant hypertension or hypertension and hypokalaemia.

DIAGNOSIS
Plasma 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 prior to testing. Stop spironolactone for 6 weeks prior to testing. Because of limited specificity, a positive screening test result should be followed by a confirmatory test and a negative random ratio test does not necessarily exclude the diagnosis.
CHAPTER 8  

ENDOCRINE SYSTEM  

DRUG TREATMENT  
ADRENAL ADENOMA  
Adrenalectomy:  
• spironolactone, oral, 100–200 mg daily  

BILATERAL HYPERPLASIA  
Standard anti-hypertensive therapy.  

REFERRAL  
o all patients to an endocrinologist or a hypertension centre for confirmation of the diagnosis and further treatment  

8.19 HYPERTHYROIDISM  
E05  

DESCRIPTION  
Most common cause of hyperthyroidism is Graves' disease, which is an autoimmune condition resulting from the presence of TSH stimulating auto–antibodies.  

INVESTIGATION  
Request TSH and T₄.  If TSH suppressed and T₄ normal, request in addition T₃.  The usual biochemical abnormalities, however, are:  
Diffuse goiter with bruit (Graves')  
Ophthalmopathy  
Pretibial myxoedema  
Family history  
Thyroiditis  
Toxic multinodular  
Goiter small to large  
Older patients  
Obstructive surgery  
Cardiac manifestations  
Thyroid nodule  
Moves on swallowing.  

If diagnosis is uncertain: request thyroid uptake scan: If uptake is:  
o elevated or diffuse: Graves' disease  
o markedly decreased: Thyroiditis  
o patchy, normal or increased: Toxic multinodular goiter  

REFERRAL  
o consultation with a specialist is recommended in all cases  
o for thyroid scan if necessary  
o thyroid associated ophthalmopathy  
o when radioactive iodine or surgery is contemplated
CHAPTER 8

ENDOCRINE SYSTEM

8.19.1 GRAVES' HYPERTHYROIDISM

E05.0

**DRUG TREATMENT**

- carbimazole, oral, 30–45 mg once daily
  - Titrate dose according to thyroid hormone levels (T₄).
  - Duration of therapy: 12–18 months.

β–blockers

Used to counteract excessive sympathetic symptoms, e.g. palpitations.
Dose is titrated by the heart rate.
Give for 2–4 weeks.
- propranolol, oral, 20–40 mg twice daily
  - Titrate dose upwards as needed.
  - OR
    - atenolol, oral, 50 mg daily

Radioactive iodine

In the setting of Graves’ disease radioactive iodine may be administered for failed medical therapy and may be indicated for patients with coexistent heart disease. It is contraindicated in active thyroid associated ophthalmopathy.

**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 T₄. 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 neutropaenia with carbimazole, a FBC must be done in patients presenting with an infection or sore throat.

Post-radioiodine TSH and T₄ should be checked at 6 weeks, 3, 6, 9 and 12 months and annually thereafter until either hypothyroidism occurs or patient remains euthyroid for ± 3–4 years. Although uncommon, hypothyroidism can occur years later.

8.19.2 TOXIC MULTINODULAR GOITER

E05.2

**DRUG TREATMENT**

Radioactive iodine

Radioactive iodine is the treatment of choice. Medical therapy is indicated initially for patients with underlying heart disease to achieve euthyroidism prior to radioactive iodine. Surgery is restricted to patients with obstructive symptoms.
8.19.3 SINGLE TOXIC NODULES
E05.1

DRUG TREATMENT

Radioactive iodine
Smaller nodules are best managed with radioactive iodine while larger nodules may require surgery.

β–blockers
Used to counteract excessive sympathetic symptoms, e.g. palpitations. Dose is titrated by the heart rate. Give for 2–4 weeks.
• propranolol, oral, 20–40 mg twice daily
 Titrate dose upwards as needed.
  OR
  atenolol, oral, 50 mg daily

8.19.4 THYROIDITIS
E06

DRUG TREATMENT

β–blockers
Used to counteract excessive sympathetic symptoms, e.g. palpitations. Dose is titrated by the heart rate. Give for 2–4 weeks.
• propranolol, oral, 20–40 mg twice daily
  Titrate dose upwards as needed.
  OR
  atenolol, oral, 50 mg daily

NSAIDs, e.g.:
• ibuprofen, oral, 400 mg three times daily
  OR
  For painful subacute thyroiditis (De Quervain’s):
  • prednisone, oral, 40 mg daily. Specialist consultation.

8.19.5 THYROID CRISIS
E05.5

DRUG TREATMENT

IV fluids as indicated.
• carbimazole, oral, 30 mg 6 hourly followed after 30 minutes by 10 drops of Lugol’s iodine in milk 3 times daily
  Start with second dose of carbimazole and continue until crisis is controlled.

PLUS
• propranolol, oral, 60–120 mg 6 hourly
  Treat precipitating illness and infection.
  ICU admission is desirable.
CHAPTER 9
SYSTEMIC AND NOSOCOMIAL INFECTIONS

9.1 HOSPITAL-ACQUIRED INFECTIONS

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 prior to 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 is essential.

9.1.1 INTRAVASCULAR LINE INFECTIONS

DESCRIPTION
Common organisms:
- coagulase negative staphylococci
- S. aureus.

The line should always be withdrawn. In many cases, especially 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.

DRUG 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: 4 weeks required. Switch to oral flucloxacillin after 14 days may be acceptable.
- candida: 2 weeks after resolution of fever

- cloxacillin, IV, 2 g 6 hourly
For confirmed S. aureus infection, duration of therapy is 4 weeks.

After 14 days, switch to:
- flucloxacillin, oral, 500 mg 6 hourly

OR
If penicillin allergy or known high rate of cloxacillin resistance:
- vancomycin, IV, 1 g 12 hourly
CHAPTER 9  SYSTEMIC AND NOSOCOMIAL INFECTIONS

CANDIDAEMIA
- amphotericin B, IV, 0.7 mg/kg daily
  OR
  If renal failure or intolerance of amphotericin B:
- fluconazole, oral, 800 mg, immediately followed by 400 mg daily

9.1.2 SURGICAL WOUND INFECTIONS

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

DRUG TREATMENT
Empiric antibiotic therapy
If surrounding cellulitis or systemic sepsis:
- cloxacillin, IV, 2 g 6 hourly

Penicillin allergy:
- vancomycin, IV, 1 g 12 hourly

9.1.3 HOSPITAL-ACQUIRED PNEUMONIA

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
- cloxacillin-resistant S. aureus is mainly found in ICU
Microbiologic specimen: blood culture and sputum/tracheal aspirate.

DRUG 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:
- vancomycin, IV, 1 g 12 hourly
  OR
  - clindamycin, IV, 600 mg 8 hourly
  PLUS
  - ciprofloxacin, oral, 500 mg 12 hourly
CHAPTER 9  

SYSTEMIC AND NOSOCOMIAL INFECTIONS

VENTILATOR ASSOCIATED PNEUMONIA
Choice will depend on local susceptibility patterns. One or more of the following antibiotics/classes need to be available:

- piperacillin/tazobactam, IV, 4.5 g 8 hourly
  OR
  cefepime, IV 1 g 12 hourly
  OR
  A carbapenem, eg.: meropenem, IV, 1 g 8 hourly

9.1.4 URINARY TRACT INFECTIONS

DESCRIPTION
Common organisms:
- resistant aerobic Gram-negative organisms
Microbiologic specimen: blood culture and MSU/CSU.

DRUG TREATMENT
Empiric antibiotics:
- amikacin, IV, 15 mg/kg daily
  OR
  ciprofloxacin, oral, 500 mg 12 hourly
Duration of therapy 7–14 days.

9.2 ADULT VACCINATION

<table>
<thead>
<tr>
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<td>Influenza vaccine</td>
<td>COPD, frail elderly, high risk patients, healthcare workers with direct patient contact</td>
<td>Contraindication: egg allergy. Dose: IM, 0.5 mL. Repeat annually.</td>
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<td>Pneumococcal vaccine (23 valent polysaccharide)</td>
<td>patients without a spleen, chronic cerebrospinal fluid (CSF) leak</td>
<td>Contraindication: pregnancy. Booster: every 5 years. Dose: SC/IM, 0.5 mL.</td>
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<td>Hepatitis B vaccine</td>
<td>high risk groups, e.g. hospital personnel or sexual contacts of infected patients, sexual assault</td>
<td>Dose: IM, 1 mL immediately then 1 mL after 1 month and 1 mL 6 months after first dose.</td>
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<td>Tetanus toxoid vaccine</td>
<td>Booster when there is a high risk for tetanus e.g. contaminated wound or pregnant women to prevent neonatal tetanus.</td>
<td>Dose: IM, 2.5 mg/0.5 mL.</td>
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<tr>
<td>Rubella vaccine</td>
<td>Pre-conception in non-immunised women</td>
<td>Contraindication: pregnancy. Dose: SC, 0.5 mL.</td>
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N39.0

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Common organisms:
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CHAPTER 9

SYSTEMIC AND NOSOCOMIAL INFECTIONS

9.2.1 RABIES VACCINATION

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/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 HDCV:

- rabies inactivated whole virus vaccine, IM, 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 RIG:

- rabies immunoglobulin (RIG), 20 units/kg on day 0 or within 7 days after exposure
  Half the dose is infiltrated around the wound and give the rest IM.
  It is recommended that RIG 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 NOT PREVIOUSLY IMMUNISED

- rabies inactivated whole virus vaccine, IM, 1 dose on day 0 and day 3
  In these cases RIG (see above) is not given.
  Caution: anaphylaxis.
  If patient presents after 48 hours, double initial dose on day zero.
## CHAPTER 9   SYSTEMIC AND NOSOCOMIAL INFECTIONS

<table>
<thead>
<tr>
<th>Risk category</th>
<th>Type of exposure</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>o touching or feeding animal</td>
<td>o none if reliable history</td>
</tr>
<tr>
<td></td>
<td>o licking intact skin</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>o nibbling uncovered skin</td>
<td>o wound treatment</td>
</tr>
<tr>
<td></td>
<td>o superficial scratch without bleeding</td>
<td>o give rabies vaccine</td>
</tr>
<tr>
<td></td>
<td>o licking broken skin</td>
<td>o do not give anti-rabies immunoglobulin, except in HIV infected people</td>
</tr>
<tr>
<td></td>
<td></td>
<td>o stop vaccination if laboratory tests of animal are negative for rabies or animal, i.e. dog or cat remains well after 10 days observation.</td>
</tr>
<tr>
<td>3</td>
<td>o bites or scratches</td>
<td>o wound treatment</td>
</tr>
<tr>
<td></td>
<td>o penetrating skin and drawing blood</td>
<td>o give rabies vaccine</td>
</tr>
<tr>
<td></td>
<td>o licking of mucous membranes</td>
<td>o give anti-rabies immunoglobulin (RIG)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>o give tetanus toxoid vaccine and antibiotic</td>
</tr>
<tr>
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<td>o stop vaccination if laboratory tests of animal are negative for rabies or animal, i.e. dog or cat remains well after 10 days observation.</td>
</tr>
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</table>

**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
- fever
- pain
- arthralgia
- erythema
- arthritis
- swelling or itching at the injection site
- angioedema
- systemic reactions
- nausea
- vomiting
- malaise
**CHAPTER 9  SYSTEMIC AND NOSOCOMIAL INFECTIONS**

**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**
A23.10
*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.

**DRUG TREATMENT**
- 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, 15 mg/kg/day 12 hourly for 6 weeks

**9.4 HAEMORRHAGIC FEVER SYNDROME**
A98.0

Serve 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 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
- other causes for DIC / bleeding tendency.
CHAPTER 9 SYSTEMIC AND NOSOCOMIAL INFECTIONS

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:
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.

DRUG TREATMENT
INITIAL MANAGEMENT
A detailed travel and clinical history is crucial. If VHF is still considered, patient is to be isolated in a single room and proper precautions taken 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
- waterproof boots or 2 pairs of overshoes, one over the other
Alternate diseases (See above) should be excluded by means of appropriate laboratory testing, keeping safety precautions in mind.
Patients should be supported with packed red cells and fresh frozen plasma, as required.
Testing for VHF may be required, both to confirm and rule out the possibility of VHF - this is arranged with the NICD (See above), before sending the specimens, as specific precautions apply.
It is required to keep record and follow up all patient contacts.

9.5 HYDATID DISEASE

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.

DRUG TREATMENT
- albendazole, oral, 15 mg/kg/day up to 400 mg twice daily for 28 days
  Repeat cycle twice with 14 days break between courses.
CHAPTER 9  SYSTEMIC AND NOSOCOMIAL INFECTIONS

With medical therapy as above, cure is achieved in about a third, improvement in about a third and no response in about a third of cases.

Definitive treatment with surgery or PAIR (percutaneous aspiration injection and re-aspiration) is preferred for accessible lesions.
Before PAIR or surgery:
• albendazole, oral, 15 mg/kg/day up to 400 mg twice daily for 14–28 days

REFERRAL
o all cases to a centre with experience in surgery and PAIR

9.6 MALARIA, SEvere

*This is a notifiable disease.

See primary care book for uncomplicated malaria and non-falciparum malaria.

DESCRIPTION
P. falciparum malaria with one or more of the following features:
• impaired consciousness
• convulsions
• vomiting
• severe anaemia (Hb < 7 g/dL)
• haemoglobinuria
• deep jaundice
• renal dysfunction
• heavy parasitaemia (≥ 5%)
• ARDS
• shock
• acidosis
• hypoglycaemia

NON-DRUG TREATMENT
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.

DRUG 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.

Complete the 7-day course with:
• quinine, oral, 600 mg 8 hourly
  If the patient is experiencing side effects such as tinnitus and vertigo, reduce the dose to 600 mg 12 hourly.
CHAPTER 9  SYSTEMIC AND NOSOCOMIAL INFECTIONS

Monitor for hypoglycaemia and dysrhythmias.
Monitor treatment response with regular blood smears.
A dramatic reduction should appear after 48 hours.
An increase in parasitaemia may occur at 24 hours due to sequestration of parasites.

Note:
Gametocytes may appear after this stage – this does NOT mean failure of therapy.
Only the reappearance or failure to clear trophozoites means failure.

PLUS
To prevent the development of resistance:
• doxycycline, oral, 200 mg immediately, starting on day 3 of quinine treatment or as soon as able to take oral medication, and then 100 mg daily for 7 days
  OR
  In pregnancy, starting on day 3 of quinine treatment or as soon as able to take oral medication:
  clindamycin, oral, 600 mg twice daily for 7 days starting on day 3 of quinine treatment

REFERRAL
o patient in need of ventilation or dialysis if these are unavailable on site

9.7 TETANUS
A35
*This is a notifiable disease.

NON-DRUG TREATMENT
Maintain airway.
Monitor ECG and blood pressure.
Maintain and replace IV fluids.
Wound management is essential with debridement and removal of any foreign bodies.

DRUG 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.

Where muscle relaxation is required:
• alcuronium, IV, 10 mg/2 mL, as needed
  This 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
CHAPTER 9  SYSTEMIC AND NOSOCOMIAL INFECTIONS

For passive immunisation:
• tetanus immunoglobulin, human, 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
  at 6 months

For fever, combine with mechanical cooling:
• paracetamol, oral, 1 g 6 hourly

For shock, dehydration, maintenance of hydration:
• IV fluids, plasma volume expanders

As prophylaxis for deep vein thrombosis:
• heparin, SC, 5 000 units 8 hourly

To alleviate pain.
• morphine, slow IV, 10 mg up to 10 mL with sodium chloride 0.9% administered over 45 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 ± 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 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.

DRUG TREATMENT
• doxycycline, oral, 100 mg 12 hourly for 7 days

In pregnancy:
• clindamycin, oral, 600 mg twice daily for 7 days
  In severe cases, initiate therapy with 1–2 days of doxycycline.
CHAPTER 9  
SYSTEMIC AND NOSOCOMIAL INFECTIONS

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

DESCRIPTION
Systemic infection due to *S. typhi* or related organisms (e.g. *S. paratyphi*). Initial symptoms are abdominal pain, headache and fever with diarrhoea only developing late. Bacteraemia is common initially, subsequently stool culture has the highest yield.

NON-DRUG TREATMENT
Transfusion is indicated for severe haemorrhage.
Replace fluid and electrolytes.

DRUG TREATMENT
• ciprofloxacin, oral, 500 mg 12 hourly for 10 days
  
  OR
  
  If oral therapy not possible, start with:
  ceftriaxone, IV, 2 g/day

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
  o 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)

B01.8
See also primary care guidelines.

NON-DRUG TREATMENT
Cool, wet compresses or tepid water baths.
Body hygiene to prevent secondary infection.
Advise against scratching.
CHAPTER 9  SYSTEMIC AND NOSOCOMIAL INFECTIONS

DRUG TREATMENT
Antiviral therapy is only required in complicated cases, e.g. chickenpox pneumonia, neurological involvement and chickenpox in immunocompromised patients.

- aciclovir, IV, 10 mg/kg 8 hourly administered over one hour for 7 days
  The course can be completed with oral aciclovir 800 mg five times daily.

Prevention of transmission to susceptible health workers is the responsibility of the employer/individual.

For non-immune pregnant women and a non-immune worker who is immunologically compromised:
- 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).

NON-DRUG TREATMENT
Isolate from immunocompromised or pregnant non-immune individuals (who may develop severe chickenpox).
Offer HIV test in patients < 50 years of age.

DRUG TREATMENT
Antiviral therapy, for:
- zoster in immunocompromised patients, provided that active lesions are still being formed
- in immunocompetent individuals provided they present within 72 hours of onset:
  - aciclovir, oral, 800 mg five times daily for 7 days

For zoster with secondary dissemination or neurological involvement:
- aciclovir, IV, 10 mg/kg over one hour, every 8 hours, for 7 days
  The course can be completed with oral aciclovir 800 mg five times daily.

Topical therapy
Do not use calamine lotion.

Eye involvement:
- aciclovir, ophthalmic ointment
CHAPTER 9          SYSTEMIC AND NOSOCOMIAL INFECTIONS

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.
• erythromycin, oral, 500 mg 6 hourly

Pain control
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.:
• ibuprofen, oral, 400 mg 3 times daily
AND/OR
• paracetamol, oral, 1 g 6 hourly
AND/OR
If pain is severe or not adequately controlled:
• morphine, IV
  See Section 12.1: Chronic Pain

Post-herpetic neuralgia
Early initiation of amitriptyline or carbamazepine is recommended.
See Section 12.1: Chronic Pain.

REFERRAL
• to an ophthalmologist if there is ocular involvement with ophthalmic zoster (if the tip of the nose is involved then ocular involvement should be suspected)
10.1 OPPORTUNISTIC DISEASES

10.1.1 CANDIDIASIS OF OESOPHAGUS/TRACHEA/BRONCHI

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 together with oral thrush.

NON–DRUG TREATMENT
Maintain adequate hydration.

DRUG TREATMENT
• fluconazole, IV/oral, 200 mg daily for 14 days
   The usual route is oral, but give IV if patient unable to swallow.
   An early relapse should be treated with a 4-week course of fluconazole as above.
   Note:
   Fluconazole prophylaxis is discouraged.

In case of failed therapy:
• amphotericin B, slow IV infusion, 0.7 mg/kg/day in dextrose 5 % over 4 hours for 14 days
   The nephrotoxicity of amphotericin B is minimised by ensuring adequate hydration.
   Regular, e.g. 3 times a week, monitoring of potassium, magnesium and renal function is essential.

REFERRAL DOWN
○ to antiretroviral treatment center

10.1.2 CRYPTOCOCCOSIS

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.
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NON–DRUG TREATMENT
Therapeutic lumbar puncture is of critical importance in cryptococcal meningitis as the intracranial pressure is frequently elevated – this should be done with pressure monitoring, removing sufficient CSF (maximum 18 mL) to lower pressure to 18 cm H2O. Therapeutic lumbar puncture should be done daily until there is improvement.

DRUG TREATMENT
- amphotericin B, slow IV infusion, 0.7 mg/kg/day in dextrose 5 % over 4 hours for 14 days
  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.
  The nephrotoxicity of amphotericin B is minimised by ensuring adequate hydration.
  Regular, e.g. 3 times a week, monitoring of potassium, magnesium and renal function is essential.

Follow with:
- fluconazole, oral, 400 mg daily for 8 weeks

SECONDARY PROPHYLAXIS
Continue for at least 6 months and until CD4 count increases to > 200 on HAART or life long if patient is not on HAART.

Note:
In patients on concomitant TB therapy, CSF should be culture negative before reducing the dose to 200 mg daily as rifampicin reduces the plasma levels of fluconazole.

- fluconazole, oral, 200 mg daily

REFERRAL
SPECIALIST OR TERTIARY
- focal neurological signs – CT scans required to exclude other pathology e.g. toxoplasmosis

DOWN
- to antiretroviral treatment centre

10.1.3 CRYPTOSPORIDIOSIS DIARRHOEA
B20.8

DESCRIPTION
Chronic diarrhoea due to Cryptosporidium parvum. Disease lasting > 4 weeks is AIDS-defining (WHO clinical stage 4).

NON–DRUG TREATMENT
Rehydration with oral rehydration solution (ORS).
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DRUG TREATMENT

There is no specific antimicrobial therapy for cryptosporidiosis. As with other opportunistic
diseases it responds well to HAART.

Antimotility agents are partially effective, e.g.:
• loperamide, oral, 4 mg initially, followed by 2 mg as required up to four times daily

REFERRAL
DOWN
○ to antiretroviral treatment centre

10.1.4 CYTOMEGALOVIRUS (CMV)

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
Retinitis must be diagnosed by an ophthalmologist.
GIT and other organ involvement must be diagnosed on biopsy.
CNS disease must be diagnosed by PCR of CSF.

DRUG 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.
Patients should be commenced on HAART as soon as possible after initiating ganciclovir
in order to prevent recurrent disease. Initial therapy with systemic ganciclovir should
be considered 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.
FBC should be monitored regularly during therapy. Other drugs associated with bone
marrow suppression (particularly zidovudine) should be avoided.

BIOPSY PROVEN GIT DISEASE AND OTHER ORGAN DISEASE
• ganciclovir, IV, 5 mg/kg 12 hourly for 14–21 days. Specialist initiated.

CNS
Initial treatment
• ganciclovir, IV, 5 mg/kg 12 hourly for 14–21 days. Specialist initiated.
CHAPTER 10 HIV AND AIDS

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 on HAART

REFERRAL
SPECIALIST OR TERTIARY CENTER
○ all
DOWN
○ to antiretroviral treatment centre

10.1.5 ISOSPORIASIS
A07.3

DESCRIPTION
Diarrhoea due to Isospora belli. Disease lasting > 4 weeks is AIDS-defining (WHO clinical stage 4).

NON–DRUG TREATMENT
Rehydration with oral rehydration solution (ORS).

DRUG TREATMENT
• trimethoprim/sulfamethoxazole 80/400, oral, 4 tablets 12 hourly for 10 days

SECONDARY PROPHYLAXIS
Continue for at least 6 months and until CD4 count increases to > 200 on HAART or lifelong if patient is not on HAART:
• trimethoprim/sulfamethoxazole 80/400, oral, 2 tablets daily

REFERRAL
DOWN
○ to antiretroviral treatment centre

10.1.6 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 and bone marrow. AIDS-defining illness (WHO clinical stage 4).

DRUG TREATMENT
• clarithromycin, oral, 500 mg 12 hourly. Specialist initiated.
PLUS
• ethambutol, oral, 15–20 mg/kg/day
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Treatment can be stopped when treatment has been continued for at least 12 months AND the CD4 count has increased to > 100 on HAART.

REFERRAL DOWN
- to antiretroviral treatment centre

10.1.7 PNEUMOCYSTIS PNEUMONIA
B20.6

DESCRIPTION
Interstitial pneumonitis due to *Pneumocystis jiroveci* (formerly *carinii*). AIDS-defining illness (WHO clinical stage 4).

NON–DRUG TREATMENT
Oxygen by face mask or CPAP as necessary.

DRUG TREATMENT
- trimethoprim/sulfamethoxazole 80/400, oral, 6 hourly for 21 days
  - < 60kg three tablets
  - > 60kg four tablets

Note:
Monitor FBC and potassium when on high dose therapy.

Trimethoprim/sulfamethoxazole desensitisation
Patients with a history of trimethoprim/sulfamethoxazole hypersensitivity should be considered for desensitisation.
Desensitisation should not be considered for patients with hypersensitivity that is life threatening such as Stevens–Johnson 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 trimethoprim/sulfamethoxazole suspension in 200 mL sodium chloride 0.9% or dextrose 5% solution.
1 mL dilute solution = 0.004/0.02 mg trimethoprim/sulfamethoxazole

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<td>0</td>
<td>0.004/0.02 mg</td>
<td>1 mL of dilute solution</td>
</tr>
<tr>
<td>1</td>
<td>0.04/0.2 mg</td>
<td>10 mL of dilute solution</td>
</tr>
<tr>
<td>2</td>
<td>0.4/2 mg</td>
<td>0.05 mL of syrup or 100 mL of dilute solution</td>
</tr>
<tr>
<td>3</td>
<td>4/20 mg</td>
<td>0.5 mL of syrup</td>
</tr>
<tr>
<td>4</td>
<td>40/200 mg</td>
<td>5 mL of syrup or ½ tablet</td>
</tr>
<tr>
<td>5</td>
<td>160/800 mg</td>
<td>2 single strength or 1 double strength tablet</td>
</tr>
</tbody>
</table>
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Alternatives, in case of allergy, intolerance, etc.:
• clindamycin, oral, 600 mg 8 hourly for 21 days

PLUS
• primaquine, oral, 15 mg daily for 21 days
  Exclude G6PD deficiency before initiating therapy.

For hypoxic patients:
• prednisone, oral, 80 mg daily for 5 days, then taper over 14 days

SECONDARY PROPHYLAXIS
Continue for at least 6 months and until CD4 count increases to > 200 on HAART or life long if patient is not on HAART.
• trimethoprim/sulfamethoxazole 80/400, oral, 1 tablet daily

Alternatives, in case of allergy, intolerance, etc.:
• dapsone, oral, 100 mg daily

REFERRAL
SPECIALIST OR TERTIARY CENTRE
• intolerance to second line regimen
  DOWN
• to antiretroviral treatment centre

10.1.8 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). Diagnosis is confirmed by response to therapy, which occurs in 7–14 days.

DRUG TREATMENT
• trimethoprim/sulfamethoxazole 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 on HAART or life long if patient is not on HAART.
• trimethoprim/sulfamethoxazole 80/400, oral, 1 tablet daily
  See trimethoprim/sulfamethoxazole desensitisation above.

REFERRAL
SECONDARY OR TERTIARY
• intolerance to trimethoprim/sulfamethoxazole
  Note:
  Attempt desensitisation first.
  DOWN
• to antiretroviral treatment centre
10.2 ANTIRETROVIRAL THERAPY

Highly active antiretroviral therapy (HAART) consists of three or more antiretroviral drugs that are capable of suppressing HIV replication when used together. The usual HAART regimen contains two nucleoside reverse transcriptase inhibitors together with either a non-nucleoside reverse transcriptase inhibitor or a protease inhibitor. High levels of adherence are essential for long-term success with HAART. The national guidelines for public sector use of HAART are based largely on the 2002 WHO guidelines. Treatment with HAART is a rapidly changing field. Therefore the guidelines are likely to change, particularly with the advent of new therapies.

Medical indications for initiating HAART in adults:
- CD4 count < 200 $10^6$/L
- WHO stage 4 disease (excluding tuberculosis – see below)

PSYCHOSOCIAL INDICATORS OF READINESS FOR HAART
- It is essential that patients have good insight into the need for long-term therapy and high levels of adherence.
- Structures need to be in place to provide adherence support for patients.
- Patients should be encouraged to disclose their HIV status to somebody close to them and this person should act as a treatment supporter. If this is not possible then the patient should join a support group.
- Depression must be treated.
- HAART must not be commenced if there is active substance abuse.

HAART REGIMENS AND MONITORING
With the antiretrovirals currently available in South Africa it is possible to have two robust HAART regimens. These should last at least five years and considerably longer than this in patients with high levels of adherence.

Regimen 1
Consists of two nucleoside reverse transcriptase inhibitors, i.e. stavudine + lamivudine plus a non-nucleoside reverse transcriptase inhibitor, either efavirenz or nevirapine. Efavirenz and nevirapine are equipotent, but have different toxicities. Efavirenz is teratogenic and should not be used in women of child-bearing potential. There is cross-resistance between efavirenz and nevirapine so there is no point switching them when virological failure occurs.

- stavudine, oral, 40 mg 12 hourly
  - If < 60 kg: 30 mg 12 hourly.
AND
- lamivudine, oral, 150 mg 12 hourly
PLUS
- efavirenz, oral, 600 mg at night
OR
  - nevirapine, oral 200 mg daily for the first 2 weeks increasing to 200 mg 12 hourly thereafter
Regimen 2
Consists of two alternative nucleoside reverse transcriptase inhibitors, i.e. zidovudine and didanosine plus the protease inhibitor combination, i.e. lopinavir/ritonavir. The small dose of ritonavir in this preparation acts as a potent enzyme inhibitor in order to boost the level of lopinavir.

- zidovudine, oral, 300 mg 12 hourly
  AND
- didanosine, oral, 400 mg once daily on an empty stomach
  If < 60 kg: 250 mg 12 hourly
PLUS
- lopinavir/ritonavir 400/100, oral, 3 capsules 12 hourly

Efficacy monitoring
Monitor CD4 count and viral load 6 monthly. The viral load will indicate when resistance is developing and when regimens need to be changed. The viral load should become lower than the detectable limit by 6 months. If this does not happen on the first regimen then this is nearly always due to poor adherence. Consider switching to the second line regimen when the viral load rises to > 5 000 copies/mL, assuming that the initial response was good. The CD4 response is more variable, with an average increase of around 150 cells in the first year.

Toxicity monitoring
Laboratory monitoring for toxicity varies with the individual antiretroviral drug. Refer to the national guideline.

USING HAART IN PATIENTS WITH TUBERCULOSIS
A wide range of immune suppression occurs in HIV infected patients in areas where tuberculosis is endemic. Tuberculosis itself should not be a criterion for starting HAART, even though some forms of tuberculosis are considered AIDS illnesses. If tuberculosis develops before HAART is started, the CD4 count determines when HAART should be started:
CD4 > 200
Defer HAART until after tuberculosis has been treated. HAART should only be started then if the CD4 drops to below 200 or another AIDS-defining illness occurs.
CD4 50–200
Complete 2 months of antituberculous therapy, i.e. two months for an initial episode of tuberculosis, before commencing HAART.
CD4 < 50 or severe AIDS defining illness
Commence ARV therapy after 2 weeks of TB therapy.

If the patient develops TB when on HAART then the HAART regimen must not be discontinued but modified because of drug interactions (see below).

There are significant shared side effects of HAART and TB therapy. HAART can also lead to paradoxical deterioration of TB. In addition there are significant drug
interactions. Rifampicin acts as an enzyme inducer, leading to increased metabolism of many drugs:
  o nucleoside reverse transcriptase inhibitors, e.g. zidovudine, are not affected
  o non-nucleoside reverse transcriptase inhibitors, e.g. efavirenz and nevirapine, levels are modestly reduced. These can be used with rifampicin. Efavirenz is preferable as the evidence is less good with nevirapine.
  o protease inhibitor levels are dramatically reduced. Only ritonavir, a powerful enzyme inhibitor, is capable of overcoming this at higher doses. Additional ritonavir 300 mg 12 hourly added to lopinavir/ritonavir 400/100mg will result in adequate protease inhibitor levels.

MANAGEMENT OF SELECTED ANTIRETROVIRAL SIDE EFFECTS

Hyperlipidaemia
Protease inhibitors can cause dyslipidaemia, with raised LDL cholesterol and triglycerides. Criteria for initiating therapy are the same as for HIV seronegative subjects. See Section 8.9: Dyslipidaemia. Statins should not be used as protease inhibitors inhibit the metabolism of most statins resulting in extremely high levels. Patients who fail to respond to diet should be treated with a fibric acid derivative, e.g.:
  • bezafibrate, oral, 400 mg at night

Hyperlactataemia
Symptomatic hyperlactataemia without acidosis occurs in 1–2% of patients on long-term NRTIs per annum. Lactic acidosis is rare, i.e. ± 0.1% per annum. The risk of lactate elevation differs among the NRTIs approximately as follows:
  didanosine > stavudine > zidovudine > lamivudine

Risk factors for hyperlactaemia include:
  o females
  o obesity
  o prolonged use of NRTIs
  o development of NRTI-induced peripheral neuropathy or fatty liver

The clinical symptoms of hyperlactataemia are non-specific and may include:
  o nausea
  o vomiting
  o abdominal pain
  o weight loss
  o malaise
  o liver dysfunction (due to steatosis)
  o tachycardia

A high index of suspicion is necessary. Lactate levels need to be sent on ice and processed rapidly. Alternatively, point of care finger prick lactate monitoring can be done. Acid base status should be checked.
Patients with lactate levels 2–5 mmol/L who are relatively well:
Therapy can be altered by selecting NRTIs that are less associated with lactataemia or, in the case of stavudine, by reducing the dose and monitor by serial lactate measurements (initially weekly) for approximately three months.

Patients with lactate levels > 5 mmol/L:
Withdraw HAART and commence alternative antiretroviral therapy once hyperlactatemia has resolved to less than 2 mmol/L which may take up to three months. This should be commenced at ARV treatment centre. Symptoms typically resolve very slowly. If there is acidosis then admission to a high care unit is recommended.

Lactic acidosis carries a poor prognosis. Treatment is supportive. It is essential to exclude other causes of lactic acidosis, especially sepsis. Consideration can be given to high dose vitamin B, especially riboflavin and thiamine. However, it is unknown whether these may have a role in therapy.

In most cases of severe symptomatic hyperlactataemia or lactic acidosis NRTIs should be stopped and not used again. However some authorities feel that once symptoms settle NRTIs that are less associated with hyperlactataemia could be used. If this is done then it is essential to monitor lactate levels serially, i.e. monthly for 3 months.

**Immune reconstitution inflammatory syndrome (IRIS)**
Within 3 months of initiating HAART some patients experience an immunopathological response to opportunistic diseases, which may be previously undiagnosed or diagnosed and on effective therapy.

IRIS is associated with an abnormal inflammatory response that can cause recurrence of symptoms in patients on treatment for an opportunistic infection, paradoxical deterioration despite therapy or unusual inflammatory presentations. IRIS is particularly common in patients with tuberculosis and occurs mainly when HAART is started with low CD4 counts and when opportunistic infections are partially treated, e.g. within 2 months of starting treatment for tuberculosis or cryptococcal meningitis.

Diagnosis is often difficult as new opportunistic diseases or drug resistance need to be excluded. HAART and therapy for the opportunistic infection should continue. Symptomatic therapy, e.g. paracetamol or NSAIDs is helpful for fever or pain. Short courses of high dose corticosteroids have been used, but should **ONLY** be considered for life-threatening manifestations, e.g. compression of major structures by enlarging lymph nodes, expanding CNS tuberculomata and worsening meningitis, as there are no controlled trials.

**10.3 POST-EXPOSURE PROPHYLAXIS, OCCUPATIONAL**

Antiretroviral therapy may prevent the risk of acquiring HIV following a significant occupational exposure.

It is essential to adequately document occupational exposures 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 or by 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 a 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 and are high risk exposures:

- 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, within minutes, 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
- lamivudine, oral, 150 mg 12 hourly for 4 weeks

**high-risk, expanded three-drug regimen**
- lopinavir/ritonavir 133/33, oral, 3 capsules 12 hourly

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.
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<table>
<thead>
<tr>
<th>Exposure</th>
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<th>10.4 POST-EXPOSURE PROPHYLAXIS FOR PENETRATIVE ANAL OR VAGINAL SEXUAL ASSAULT</th>
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<td>no PEP</td>
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<td>mucosal splash/non-intact skin</td>
<td>consider 2 drug regimen</td>
<td>2 drug regimen</td>
</tr>
<tr>
<td>percutaneous (sharps)</td>
<td>2 drug regimen</td>
<td>2 drug regimen</td>
</tr>
<tr>
<td>percutaneous (needle in vessel or deep injury)</td>
<td>2 drug regimen</td>
<td>3 drug regimen</td>
</tr>
</tbody>
</table>

PEP is not well tolerated. Adverse events occur in about half and therapy is discontinued in about a third. The highest rates of adverse events occur with 3 drug regimens. Most of the adverse events are not life threatening. Headache, nausea and malaise are the commonest adverse events. In cases where adverse events are intolerable a clinician experienced in managing HIV should be consulted for alternative antiretroviral drugs.

**Monitoring after occupational exposure**

Laboratory monitoring is done to exclude acquisition of HIV infection and, for those given PEP, to monitor toxicity. Healthcare workers should be tested 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, which should be done in a laboratory, usually an enzyme immuno-assay or ELISA, rather than with a clinic-based rapid test in order to ensure adequate documentation. Healthcare workers should be instructed 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, after 2 and 4 weeks on antiretroviral therapy.

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, expanded three-drug regimen:
**ADD**
- lopinavir/ritonavir, oral, 400/100 mg 12 hourly

Laboratory monitoring should be the same as for occupational PEP. Other important aspects of care for the rape survivor should not be forgotten, i.e. contraception, treatment for sexually transmitted infections, counseling and forensic specimens.
CHAPTER 11
SURGICAL ANTIBIOTIC PROPHYLAXIS

GENERAL PRINCIPLES

• the need for prophylactic antibiotic therapy is based on the risk of wound contamination
• antibiotic prophylaxis is not required for clean operations/procedures in immunocompetent patients, who have minimal risk of contamination. In all other situations, prophylaxis should be considered.
• the drug chosen should be active against the pathogens most likely to be associated with wound 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

<table>
<thead>
<tr>
<th>TYPE OF SURGERY</th>
<th>ANTIBIOTIC USED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular surgery</td>
<td>• cefazolin, IV, 1 g</td>
</tr>
<tr>
<td>Lower limb amputation</td>
<td>• cefazolin, IV, 1 g PLUS</td>
</tr>
<tr>
<td></td>
<td>• metronidazole, IV, 500 mg</td>
</tr>
<tr>
<td>Orthopaedic surgery</td>
<td>• cefazolin, IV, 1 g</td>
</tr>
<tr>
<td>Head and neck surgery</td>
<td>• cefazolin, IV, 1 g For procedures involving the oropharyngeal mucosa: ADD</td>
</tr>
<tr>
<td></td>
<td>• metronidazole, IV, 500 mg</td>
</tr>
<tr>
<td>Abdominal surgery</td>
<td>• cefazolin, IV, 1 g</td>
</tr>
<tr>
<td>Upper GIT</td>
<td></td>
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</tbody>
</table>
### Type of Surgery

<table>
<thead>
<tr>
<th>Type of Surgery</th>
<th>Antibiotic Used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal and appendix</td>
<td>• cefazolin, IV, 1 g PLUS</td>
</tr>
<tr>
<td></td>
<td>• metronidazole, IV, 500 mg</td>
</tr>
<tr>
<td></td>
<td>If perforation has occurred, treat patient for infection with a course of appropriate antibiotics.</td>
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<tr>
<td>Biliary</td>
<td>Only for high risk patients:</td>
</tr>
<tr>
<td></td>
<td>• cefazolin, IV, 1 g PLUS</td>
</tr>
<tr>
<td></td>
<td>• metronidazole, IV, 500 mg</td>
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<tr>
<td></td>
<td>• cefazolin, IV, 1 g PLUS</td>
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<td></td>
<td>• metronidazole, IV, 500 mg</td>
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<td></td>
<td>• cefazolin, IV, 1 g PLUS</td>
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<td></td>
<td>• metronidazole, IV, 500 mg</td>
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<td></td>
<td>For procedures involving the oropharyngeal mucosa:</td>
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<tr>
<td></td>
<td><strong>ADD</strong></td>
</tr>
<tr>
<td></td>
<td>• metronidazole, IV, 500 mg</td>
</tr>
<tr>
<td>Pelvic surgery</td>
<td>• cefazolin, IV, 1 g PLUS</td>
</tr>
<tr>
<td></td>
<td>• metronidazole, IV, 500 mg</td>
</tr>
<tr>
<td>ENT surgery</td>
<td>• cefazolin, IV, 1 g PLUS</td>
</tr>
<tr>
<td></td>
<td>For procedures involving the oropharyngeal mucosa:</td>
</tr>
<tr>
<td></td>
<td><strong>ADD</strong></td>
</tr>
<tr>
<td></td>
<td>• metronidazole, IV, 500 mg</td>
</tr>
<tr>
<td>Nephro-urological surgery</td>
<td>• cefazolin, IV, 1 g PLUS</td>
</tr>
<tr>
<td></td>
<td>Treat patients with preoperative bacteriuria according to MCS.</td>
</tr>
<tr>
<td>Ophthalmic surgery</td>
<td>• chloramphenicol 0.5% ophthalmic drops, instil 1 drop</td>
</tr>
<tr>
<td></td>
<td>2–4 hourly for 24 hours prior to surgery</td>
</tr>
<tr>
<td>Neurosurgery</td>
<td>• cefazolin, IV, 1 g</td>
</tr>
</tbody>
</table>

**Severe β-lactam allergy**

Use in place of cefazolin and cefazolin plus metronidazole.
Clindamycin has good anaerobic cover.
• clindamycin, IV, 300 mg

**Colorectal, Biliary or Pelvic Surgery**

• clindamycin, IV, 300 mg
**Plus**
• gentamicin, IV, 3 mg/kg
CHAPTER 12
PAIN

12.1 PAIN, CHRONIC

DESCRIPTION
Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage.
Pain is always a subjective experience.
The perception of pain is modulated by the patient’s mood, morale and the meaning the pain has for the patient.

ASSESSMENT OF PAIN
Pain needs to be recognised and assessed before it can be managed appropriately.
All patients with chronic pain require a thorough physical assessment as well as psychiatric/psychological assessment to rule out depression and/or a somatoform pain disorder.
Consider using a visual analogue scale.
Self-report of pain is the key to pain assessment.
Patient evaluation includes complaints of pain, functional status, medication use and possible overuse, and comorbid illness.
Pain control should be reviewed regularly in each patient.

NON-DRUG TREATMENT
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.
Discuss the management with the family.
Address all factors that may contribute to pain and associated symptoms, e.g. family stress, anxiety and sleep deprivation. Address family anxiety.
Use therapies, e.g. massage, splints, physiotherapy etc, where appropriate.

DRUG 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 analgesics in addition to tricyclic antidepressants or antiepileptics.
Concerns regarding addiction should not compromise adequate pain control with opioids.
Utilise the least invasive route of medication administration, preferably orally.
CHAPTER 12 PAIN

ANALGESICS

For chronic pain, analgesics must be administered regularly and not as “when required” (pm). Additional short acting analgesia may be required 30 minutes prior to pain inducing activity such as physiotherapy.

Monitor pain control and seek advice if pain is not promptly and adequately controlled. It is useful to combine different classes of medicines, the combination of which will be determined by the severity, type and control of pain.

1. Non-opioid drugs
   - paracetamol, oral, 1 g 6 hourly

2. Non-steroidal anti-inflammatory drugs (NSAIDS)
   Can be used in combination with paracetamol or opioids.
   E.g.:
   - ibuprofen, oral, 400–800 mg three times a day with meals
     An additional nighttime dose of a NSAID may be required.

3. Opioid drugs
   Increase doses of opioids according to the individual need to overcome pain. Take into account the development of tolerance. The correct dose is that which relieves patient’s symptoms and, except for tramadol, may exceed the recommended dose used in other pain relief settings. Assess patient frequently.
   - morphine, short acting, oral
     Starting dose: 10–20 mg 4–6 hourly.
     Increase dose by 50% every 24 hours if pain control is sub-optimal.
     Reduce the dosing interval if there is regular breakthrough pain.
     Manage nausea.
     OR
     morphine, long acting, oral, 30–60 mg 12 hourly
     Titrate to desired effect.
     OR
     tramadol, oral, 50 mg, 4–6 hourly as a starting dose.
     May be increased to a maximum of 400 mg daily.

As opioids cause constipation, laxatives should be used prophylactically, e.g.:
   - lactulose, oral, 20 mL daily as required

ADJUVANT THERAPY

Adjuvant agents can enhance pain control by targeting specific pain mechanisms.
   - nerve injury pain
   - burning paresthesia
   - neuropathic pain
   - nerve root compression
   - HIV neuropathy
   - chemotherapeutic nerve injuries
CHAPTER 12 PAIN

In addition to analgesia as above:
• amitriptyline, oral, 10–25 mg at night
  Titrated up to 75 mg at night.
AND/OR
• carbamazepine, oral, 100 mg every 12 hours for two weeks then 200 mg every 12 hours
  Titrate 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, 10 mg every 8 hours

For pruritus or nausea:
• promethazine, oral/IV, 10 mg 6 hourly

For anxiety:
• diazepam, oral, 2–5 mg every 12 hours

For colic:
• hyoscine butylbromide, IV/oral, 10 mg 6–8 hourly

REFERRAL
○ pain resistant to medical management

There is no place for invasive/life supporting measures in terminal patients. Discuss end of life events with patients to relieve their anxiety and avoid unnecessary referrals.
13.1 ARTHRITIS, RHEUMATOID

NON-DRUG TREATMENT
Manage by co-ordinated multidisciplinary care.
The primary outcome is to improve and maintain functional status.
The early use of the non-drug methods of management especially nursing, physiotherapy and occupational therapy, is essential.
Acute flare-ups: rest affected joints and consider the use of day and/or night splints.

DRUG TREATMENT
Evaluate all patients with suspected RA for Disease-Modifying Anti-Rheumatic Medication (DMARD). All patients with suspected RA should be seen at an early stage by an appropriate specialist.

Disease-modifying anti-rheumatic medication (DMARD), e.g.:
- methotrexate,
- chloroquine sulphate
- sulfasalazine

Use DMARDs only with regular monitoring for toxicity. This applies particularly to the retinal toxicity caused by chloroquine and to the adverse effects of methotrexate i.e. bone marrow, liver toxicity, etc.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>chloroquine</td>
<td>Beware of G6PD deficiency.</td>
</tr>
<tr>
<td></td>
<td>Do ophthalmic examination every six months.</td>
</tr>
<tr>
<td>sulfasalazine</td>
<td>Liver function and FBCs 2–4 weekly for first 3 months then every 3–6 months.</td>
</tr>
<tr>
<td>methotrexate</td>
<td>Liver function and FBCs prior to and every 12 weeks during treatment.</td>
</tr>
<tr>
<td></td>
<td>Use with caution in alcoholics and patients with renal disease.</td>
</tr>
</tbody>
</table>

Titrate dose of sulfasalazine and methotrexate gradually to maintenance dose.

- methotrexate, oral, 7.5 mg/week. Specialist consultation.
  Increase dose gradually to 20 mg per week.
  PLUS
  folic acid, oral, 5 mg/week with methotrexate
AND/OR
- chloroquine sulphate, oral, 150 mg (as base) for 5 days of each week
AND/OR
- sulfasalazine, oral, 500 mg twice daily, initial dose
  Increase dose to 1 g twice daily.
**CHAPTER 13  MUSCULOSKELETAL SYSTEM**

**Oral corticosteroids**
Indicated for:
- severe synovitis not controlled by other means
- the elderly threatened by functional dependence
- intolerable morning stiffness
- marked systemic component
- as bridging therapy while waiting for DMARDs to take effect

May be used at high doses, for an acute flare, for short periods i.e. 2 weeks.

- prednisone, oral, 40–60 mg daily for 2 weeks
  Thereafter gradually reduce the dose to 5–10 mg daily.
  The continued need for systemic steroids always needs periodic review.

Patients requiring corticosteroids for longer than 3 months should be educated to take in enough calcium in their diet or if necessary, give:
- calcium elemental, oral, 1 g daily
If necessary:
**ADD**
- vitamin D, oral, 800 units daily or 50 000 units twice a month
Monitor serum calcium twice a month.

**Pain alleviation**
- paracetamol, oral, 1 g 6 hourly as needed

**NSAIDs**
Use for active inflammation with pain.
NSAIDs are used for symptomatic control only as they have no long-term disease modifying effects.
Once the diagnosis has been established, do not use as monotherapy. The anti-inflammatory action of the NSAIDs may take 2–4 weeks to become evident.
Reduced NSAID dosages must be used in the elderly.
NSAIDs are relatively contra-indicated in patients with significantly impaired renal function, i.e. GFR < 60.

Concomitant use of more than one oral NSAID has no additional clinical benefit and only increases toxicity.
The addition of paracetamol is of benefit.

- ibuprofen, oral, 800 mg 3 times daily
  If not tolerated: 400 mg three times daily.
  **OR**
  diclofenac, oral, 50 mg 3 times daily
  If not tolerated: 25 mg three times daily.
  **OR**
  naproxen, oral, 500 mg twice daily
CHAPTER 13  MUSCULOSKELETAL SYSTEM

An extra nighttime dose of a NSAID may be added to some patients with severe nocturnal pain/morning stiffness.

**Note:**
When an added nighttime 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 nighttime dose will often exceed the recommended total daily NSAID dose. If a reduction in daytime dose cannot occur then the use of the nighttime 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 NSAIDs. Specialist consultation.

Adjunct for pain control:
- amitriptyline, oral, 25 mg at night
  - Titrate dose according to response.
  - Maximum dose: 75 mg at night.
  - Use with caution in patients with angle closure glaucoma, prostatic hypertrophy and the elderly.
  - Initial dose in the elderly: 10 mg at night.

**Intra-articular corticosteroids**
Consider if needed selected cases.
To be prescribed and administered by a specialist only.
Not more than 2–3 injections per year per joint is recommended.
- methylprednisolone acetate, 20–80 mg
  - OR
    - betamethasone depot, 0.75–6 mg, depending on joint size

**URGENT REFERRAL**
- tendon rupture
- protrusion acetabuli

**REFERRAL**
- for joint replacement and/synovectomy

**13.2 ARTHRITIS, SEPTIC AND OSTEOMYELITIS, ACUTE**
M00.9/M86.1

**NON-DRUG TREATMENT**
Rest and immobilisation.
Surgical drainage: always consider early drainage by orthopaedic surgeon.
CHAPTER 13  MUSCULOSKELETAL SYSTEM

DRUG TREATMENT

Empiric antibiotic therapy
Therapy is directed against *S. aureus* unless there 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
  - Penicillin allergy:
  - vancomycin, IV, 1 g 12 hourly

For gonococcus:
- ceftriaxone, IV, 1 g daily
  - Penicillin allergy:
  - ciprofloxacin, oral, 500 mg 12 hourly until resolved, i.e. ± 4 weeks

Analgesia
- paracetamol, oral, 1 g 6 hourly as needed
  - OR
  - NSAID until pain subsides e.g.:
  - ibuprofen, oral, 400 mg 8 hourly
    - OR
    - diclofenac, oral, 25 mg 8–12 hourly

Monitor activity of disease clinically and by serial weekly CRP measurements.

REFERRAL
- for early drainage by orthopaedic surgeon
- if pyrexia persists in spite of adequate antibiotic therapy, a subperiosteal abscess must be looked for and drained by an orthopaedic surgeon
- growth plate involvement
- chronic osteomyelitis and its complications
- pathological fractures

13.3 OSTEO-ARTHROSIS AND OSTEO-ARTHRITIS

M19.9

NON-DRUG TREATMENT
Weight reduction.
Exercise, postural and non-weight bearing.
Rest during acute painful episodes.
Support and alleviate weight bearing of affected joints i.e. walking stick.
Consider physiotherapy and/or occupational therapy.
CHAPTER 13  MUSCULOSKELETAL SYSTEM

DRUG TREATMENT
When only pain relief is required:
• paracetamol, oral, 1 g 6 hourly as needed
If ineffective:
ADD
NSAIDs e.g:
• ibuprofen, oral, 400–800 mg three times daily
As these patients have concomitant medical conditions, NSAIDs must be used with caution in, e.g. the elderly and those with cardiovascular, gastrointestinal disease or renal function impairment.

REFERRAL
o for consideration of joint replacement
o intractable pain
o neurogenic compression

13.4 GOUT
M10.9

NON-DRUG TREATMENT
ACUTE ATTACK
Rest and immobilisation.
CHRONIC GOUT
Lifestyle modification, including continued high fluid intake. Dietary purine restriction is of limited value.
Avoid excessive alcohol intake.
Avoid diuretics if possible, or use the lowest dose possible.

DRUG TREATMENT
ACUTE GOUT
Short course, high dose NSAIDs, e.g.:
• naproxen, oral, 750 mg immediately then 500 mg 12 hourly for 24–48 hours
OR
diclofenac, oral, 75 mg immediately, then 50 mg 8 hourly for 24–48 hours
Thereafter halve the dose for the duration of the attack.
OR
ibuprofen, oral, 800 mg 8 hourly, for 24–48 hours
Thereafter halve the dose for the duration of the attack.

In patients with renal impairment, or dehydration, NSAIDs should be avoided and corticosteroids used instead.
Where NSAIDs cannot be used:
• prednisone, oral, 40 mg daily for 3–5 days

CHRONIC GOUT
Avoid known precipitants and drugs that increase uric acid, if possible, e.g.:
• low dose aspirin
• ethambutol
• pyrizinamide
CHAPTER 13 MUSCULOSKELETAL SYSTEM

- diuretics, especially hydrochlorothiazide 25 mg or greater
  Remove 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
  - serum urate > 0.52 mmol/L

When the acute attack has settled completely, i.e. after 3 weeks:
  • allopurinol, oral, 100 mg daily
    Increase monthly by 100 mg according to urate blood levels.
    Titrate dose to reduce serum urate to < 0.4 mmol/L.
    Average dose: 300 mg/day.
    Maximum dose: 400 mg daily.
    The elderly and patients with renal impairment require lower doses.

ADD
  For the first 1–3 months:
  If not contra-indicated, an NSAID, e.g.:
    • ibuprofen, oral, 400 mg 8 hourly
    OR
    diclofenac, oral, 25 mg 8–12 hourly
    OR
  If an NSAID is contra-indicated or not tolerated:
    • colchicine, oral, 0.5 mg twice daily for up to 3 months

Do not stop uric acid lowering drugs during an acute attack.

REFERRAL
  - no response to treatment
  - non-resolving tophaceous gout

13.5 SERONEGATIVE SPONDYLARTHITIS
  M45–49

DESCRIPTION
  A group of diseases in which there is a predominant asymmetrical lower-limb seronegative arthritis and sacro-iliitis. Many are associated with skin, mucous membrane, cardiac or bowel disease. There are HLA associations.
CHAPTER 13  MUSCULOSKELETAL SYSTEM

Diseases included are Reactive Arthritis, Ankylosing Spondylitis, Reiter’s Syndrome, Psoriatic Arthropathy, the arthritis associated with Ulcerative Colitis and Crohn’s disease, Behcet’s syndrome, Whipples disease.

Initiate treatment with NSAIDs.

REFERRAL
All with:
- severe arthritis
- deformity at diagnosis
- failure of therapy

13.5.1 ARTHRITIS, REACTIVE  M13.9

DESCRIPTION
An acute nonpurulent arthritis complicating an infection elsewhere in the body. A spondyloarthritis following enteric or urogenital infections and occurring predominantly in individuals with HLA-B27 antigen, usually 1–4 weeks prior to the arthritis. It is a clinical diagnosis with no laboratory test or radiographic findings. It is usually self-limiting, however joint symptoms may persist in 30–60% of patients.

DRUG TREATMENT
Start with a high dose and titrate downwards if not needed or if not tolerated.
- ibuprofen, oral, 800 mg 3 times daily
  If not tolerated: 400 mg three times daily.
  OR
diclofenac, oral, 50 mg 3 times daily
  If not tolerated: 25 mg three times daily.
  OR
naproxen, oral, 500 mg 12 hourly

Prompt appropriate treatment of acute chlamydial urethritis may prevent subsequent attacks; i.e.:
- doxycycline, oral, 100 mg 12 hourly for 10 days

REFERRAL
- if steroids are required
CHAPTER 13  MUSCULOSKELETAL SYSTEM

13.6 SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

These patients need to be managed by a specialist.

NON-DRUG TREATMENT
Education regarding the disease and complications.
Avoid cigarette smoking as it is a trigger for lupus.
Avoidance of sunlight exposure.
Avoid medications implicated in triggering or causing deterioration of SLE.
Sun protective barrier creams are often indicated.
Regularly monitor urine for blood and protein.
Advice regarding family planning as pregnancy may cause a lupus flare.

DRUG TREATMENT
MILD DISEASE
Pain alleviation
• paracetamol, oral, 1 g 6 hourly as needed

AND/OR
• ibuprofen, oral, 800 mg 3 times daily
  If not tolerated: 400 mg three times daily.
  OR
  diclofenac, oral, 50 mg 3 times daily
  If not tolerated: 25 mg three times daily.
  OR
  naproxen, oral, 250–500 mg twice daily

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 longer than 3 months should be educated to take
in enough calcium in their diet or if necessary, give:
• calcium, elemental, oral, 1 g daily
If necessary:
ADD
• vitamin D, oral, 800 units daily or 50 000 units twice a month
  Monitor serum calcium twice a month.

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, 1–2 mg/kg daily
  OR
  cyclophosphamide, oral, 100–200 mg daily or 1–3 mg/kg daily
CHAPTER 13  MUSCULOSKELETAL SYSTEM

DISEASE LIMITED TO THE SKIN AND JOINT
• chloroquine sulphate, oral, 150–300 mg (base) daily for 5 days a week
  Regular ophthalmic examination, i.e. every 6 months.

SEVERE RAYNAUD’S PHENOMENON
Long acting dihydropyridine calcium channel blocker, e.g.:
• amlodipine, oral, 5 mg daily

ANTIPHOSPHOLIPID ANTIBODY SYNDROME
• aspirin, soluble, oral, 150 mg daily

Patients with previous thrombo-embolic episodes should be adequately anticoagulated with lifelong warfarin.

Hormonal therapy
The use of the oral contraceptive is controversial. Until there is clarity it is advisable to:
  o avoid oestrogens in patients with lupus
  o use only progesterone.

REFERRAL
  o all patients for initial assessment
  o lupus flare
  o severe nephritis
  o persistent haematological derangements i.e. thrombocytopenia
14.1 CEREBROVASCULAR DISEASE

14.1.1 STROKE

NON-DRUG TREATMENT
Optimal hydration and nutrition – nasogastric tube if patient cannot swallow. Precautions should be taken 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. Syphilis serology.

DRUG TREATMENT
The disease requires good initial evaluation, ongoing support for patients and continuous evaluation to ensure compliance in taking medication and diet.

All cases not on anticoagulation:
• aspirin, soluble, oral, 150 mg daily

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. Low dose subcutaneous heparin may be warranted for DVT prophylaxis. See Section 3.7: Venous Thrombo-Embolism

HYPERTENSION
In the first 72 hours following stroke, it is usual for blood pressure to be elevated. It is important to remember that excessive lowering of blood pressure may worsen neurological damage. Do not lower BP in acute stroke or use antihypertensive medication unless the SBP > 220 mmHg or the DBP > 120 mmHg, as a rapid fall may aggravate cerebral ischaemia and worsen the stroke. If the BP is above these levels then treatment should aim not to lower the BP by more than 15–20% in the first 24 hours.

Aggressive control of hypertension following stroke limits the risk of recurrent events. Treat according to guidelines. See Section 3.5: Hypertension.
CHAPTER 14  NEUROLOGICAL DISORDERS

DYSLIPIDAEMIA
Patients with a thrombotic stroke with not more than moderate disability (Rankin Grade 3, i.e. who need some help but can walk without any assistance) need HMGCoA reductase inhibitors (statins) for secondary prevention, irrespective of the LDL level e.g.:
• simvastatin, oral, 10 mg daily
A baseline cholesterol should be done though to exclude severe major gene defects.

If dyslipidaemia is present, manage appropriately with diet and drug treatment. See Section 8.9: Dyslipidaemia.

Treat secondary pulmonary and urinary tract infections early and appropriately.

REFERRAL
• patients with atypical clinical presentation
• patients with TIA who may warrant carotid endarterectomy
• young patients, i.e. < 40 years, with stroke, for evaluation of aetiology
• spontaneous subarachnoid haemorrhage who are surgical candidates, i.e. conscious patients
• suspected cerebellar haemorrhage

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 either by lumbar puncture, demonstrating xanthochromia or neurological imaging.

NON-DRUG TREATMENT
Maintain normal hydration and electrolyte status.
Control blood pressure.
Should patient improve later, refer.

DRUG TREATMENT
Analgesia if level of consciousness is not impaired:
• 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.

REFERRAL
• all patients with minimal impairment of consciousness level for angiography and appropriate neurosurgical management
• for neurological imaging: Patients in whom the diagnosis has to be confirmed radiologically and where a lumbar puncture may be considered hazardous.
14.2 DELIRIUM

DESCRIPTION
Confusional states/delirium are characterised by altered consciousness, accompanied by impairments in orientation to time and place but seldom to person. Such presentations may fluctuate and be accompanied by disturbed behaviour e.g. agitation/stuporose as well as experiencing of visual/tactile or gustatory hallucinations and even paranoid ideation. The onset will represent a significant change in the patient’s mental state.

In acute psychosis, schizophrenia, mania and drug included psychosis, the level of consciousness is unchanged, whereas it is altered in delirium and dementia.

Clouding of consciousness has many causes including infections, metabolic and nutritional disturbances, organ failure, inappropriate reaction to or toxicity of medicines and alcohol withdrawal. Focal neurological causes include meningitis, brain abscess, subdural haemorrhage and brain tumour, amongst others.

Two forms of delirium exists:
- hypoactivity with decreased alertness
- hypoactivity with increased alertness, restlessness and agitation

NON-DRUG TREATMENT
Reassure the patient and protect him/her from injury. An attendant, e.g. family member, should be present at all times.
Take measures to prevent falls from high beds. Cot sides are dangerous.
Adequate sedation is more appropriate than restraint.

Monitor and manage fluid, blood sugar and electrolyte status. The fluid balance is very important.

DRUG TREATMENT
Avoid unnecessary drugs.
Treat underlying conditions according to guidelines.

Sedatives are essential e.g.:
- clonazepam, IM, 2 mg
  OR
  lorazepam, IM, 2 mg
  Maximum daily dose: 6 mg.
  OR
  diazepam, IV, 10–20 mg slowly at rate of not more than 5 mg/minute

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.
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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.

Hallucinations:
• haloperidol, IV, 0.5–5 mg initially
  May be repeated at 50–60 minute intervals to a maximum of 20 mg daily.
Depending on response, continue with:
• haloperidol, oral, 0.5–5 mg 3 times daily

To prevent Wernicke’s encephalopathy:
• thiamine, oral/IM, 100 mg daily

REFERRAL
• if the underlying condition warrants referral

14.2.1 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
• 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.

NON-DRUG TREATMENT
The above points under Delirium management apply. 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.

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Consider meningitis as part of the differential diagnosis in febrile patients. Consider referring appropriate patients for a formal withdrawal and rehabilitation programme.

DRUG 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 are the sedative-hypnotic of choice:

- 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 required is 10–20 mg, but up to 60 mg is occasionally required.

OR

Where intravenous access is not possible:

- clonazepam, IM, 2 mg as a single dose

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.

Haloperidol

Neuroleptic medicines, such as haloperidol are associated with a lower threshold for developing seizures. Consider only for severe agitation and restlessness and are only 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.

Once patient has responded and is able to take oral medication:

- haloperidol, oral, 0.5–5 mg 4–8 hourly

Especially when administering glucose-containing fluids:

- thiamine, oral/IM, 100 mg daily
14.3 DEMENTIA

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 more evident.
Patients need to be investigated for treatable (reversible) systemic, neurological and psychiatric illnesses.
Transient worsening of condition may be due to metabolic disorders, infections and drug side effects.

NON-DRUG TREATMENT
Appropriate care and support, according to level of impairment.
Ambulatory care is preferred to hospitalisation, if feasible.
Family counselling and support.

DRUG TREATMENT
Management is mainly symptomatic.

To control the restless patient:
• haloperidol, oral, 0.5–1 mg 3 times daily with the higher dose at night if required

PELLAGRA
Due to deficiency of niacin/nicotinamide.
Features may include dermatitis, diarrhoea and dementia.
• nicotinamide, oral, 100 mg three times daily

AIDS DEMENTIA
May be treatable with ARVs.
Exclude opportunistic diseases of CNS.

REFERRAL
• patients, in whom a treatable underlying condition is suspected, for specialised investigations including a CT scan

14.4 EPILEPSY

NON-DRUG TREATMENT
Record keeping in a seizure diary recording dates and if possible the times of the seizures. 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 the doctor
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Take adequate history to define the type of epilepsy.

DRUG 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. Patients with a history of myoclonic seizures or typical absences should preferably be treated with sodium valproate, as these seizures may be aggravated by the use of either phenytoin or carbamazepine. Regular monitoring of drug levels is not useful except:
- to confirm toxicity in a symptomatic patient
- to confirm poor adherence
- with poor control and self reported adherence
- when contemplating dose increments beyond doses exceeding 5 mg/kg/day or 400 mg/day with phenytoin

A single unprovoked seizure is usually not an indication for treatment. Appropriate advice regarding birth control bearing in mind adherence issues and potential drug-drug interactions.

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, 200 mg twice daily for first 2 weeks, then 300 mg twice daily, increasing at fortnightly intervals to a maximum dose 600 mg twice daily as required
  OR
- phenytoin, oral, 4.5–5 mg/kg on lean body mass daily
  Dose changes over 300 mg should only be done in no more than 50 mg increments at intervals no shorter than 2 weeks.

Once adherence has been addressed and a second line agent is required, consider monotherapy:
- sodium valproate, oral, 200–300 mg twice daily, starting dose
  Increase, as required, every 2 weeks to a maximum daily dose of 1 200 mg twice daily. Sodium valproate should be considered as primary antiepileptic therapy in HIV patients needing antiretroviral therapy because of fewer drug interactions.

Phenytoin is not recommended as first line agent because of sedation, but may be used in selected patients e.g. mental retardation.

Phenytoin, phenobarbital 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.
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Combination antiepileptic drugs should only be used in consultation with a specialist.

OTHER EPILEPSY TYPES
Manage in consultation with a specialist.
Ethosuximide, lamotrigine and clonazepam may be indicated for long-term management.

STATUS EPILEPTICUS
See Section 14.4.1: Status Epilepticus.

PREGNANCY
Optimal control of epilepsy on single agent is 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 leads to changing drug levels – adjust dose according to levels.

Pregnant women:
ADD
• folic acid, oral, 5 mg daily

REFERRAL
• all new onset epileptics for neuroimaging, if unavailable locally
• epileptics who are poorly controlled on adequate treatment
• for consideration of combination therapy
• epilepsy with unexplained neurological symptoms or signs

14.4.1 STATUS EPILEPTICUS
G41

DESCRIPTION
Persistent seizures, without regaining consciousness.

NON-DRUG TREATMENT
Start treating immediately – do not wait for results of special investigations.
Maintain cardiorespiratory status.
Maintain fluid, electrolyte and blood sugar status.
Blood specimen for electrolytes and anticonvulsant levels.

DRUG TREATMENT
Seizure control should occur within 60 minutes to prevent permanent brain damage.
INITIAL TREATMENT
• diazepam, IV, 10–20 mg, not faster than 2 mg/minute
  OR
  clonazepam, IV, 1 mg
  May be repeated after 5 minutes.
  Maximum dose: 4 mg.
  OR
  lorazepam, IV/IM, 4 mg
  OR
  If there is no venous access:
  diazepam, rectal, 10 mg using the contents of an ampoule
  OR
  clonazepam, IM, 1 mg
  OR
  midazolam, buccal, 5–10 mg using the contents of an ampoule

AND
• phenytoin, IV, 20 mg/kg diluted in sodium chloride 0.9% (and not dextrose) administered not faster than 50 mg/minute preferably with cardiac monitoring. If arrhythmias occur, interrupt the infusion temporarily and reintroduce slowly. If there is no venous access, give same dose orally or via nasogastric tube. Flush the tube after administering phenytoin.

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 dose by 1 mg/kg every 12 hours.

Higher initial maintenance doses of phenytoin may be needed in patients that have had thiopental sodium. Doses should be guided by daily therapeutic drug monitoring until phenytoin levels have stabilised after pentothal sodium has been weaned.

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.

Long term maintenance therapy: See Section 14.4: Epilepsy.
14.5 HEADACHE AND FACIAL PAIN SYNDROMES

14.5.1 MIGRAINE

DESCRIPTION
Episodic headache, usually focal in nature, which may occur with or without an aura in the majority of cases (80% of cases). It is usually accompanied by nausea and vomiting. Several variants of migraine also occur.

NON-DRUG TREATMENT
Reassure patient that that this is a benign condition. Attempt to identify food allergies and try to diminish patterns of tension. Health education.

DRUG TREATMENT

ACUTE TREATMENT
Initiate therapy during the attack or at the very onset of the headache. Analgesics, e.g.:
- paracetamol, oral, 1 g immediately, then 4 hourly if needed
- aspirin, soluble, oral, 600 mg, immediately then 4 hourly if needed
- ibuprofen, oral, 800 mg immediately then 8 hourly if needed

For nausea:
- metoclopramide, oral/IM, 10 mg 3 times daily

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 poorly tolerate therapy for acute attacks.
- 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.
- atenolol, oral, 50–100 mg daily
  Note:
  Evidence for using atenolol for this indication is limited.
  Only about half of patients will respond to one of these agents.

REFERRAL
- patient with additional neurological signs or additional risk factors for an alternate diagnosis, such as immune deficiency. These patients require brain imaging.
CHAPTER 14 NEUROLOGICAL DISORDERS

- 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

14.5.2 CLUSTER HEADACHE
G44.0

DESCRIPTION
Repetitive episodes of excruciating headache typically of short duration (up to 2 hours) in clusters for weeks to months at a time. Typically the headache is of sudden onset, unilateral during the specific cluster and quickly reaches a climax. Associated redness of the eye with lacrimation and rhinorrhea occurs.

NON-DRUG TREATMENT
Oxygen inhalation may abort some episodes.

DRUG TREATMENT
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.

If no response to prednisone, refer.

REFERRAL
- inadequate response to treatment

14.5.3 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, impinging on the trigeminal nerve.

DRUG 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
CHAPTER 14 NEUROLOGICAL DISORDERS

14.5.4 TENSION HEADACHE
G44.2

DESCRIPTION
Headache over the back of the head, but sometimes over the entire head, being described as a tight band around the head, usually worse in the afternoon.

NON-DRUG TREATMENT
Consider use of relaxation techniques. The importance of this diagnosis is the exclusion of other, more sinister conditions. Exclude analgesia overuse headache.

DRUG TREATMENT
• amitriptyline, oral, 25–75 mg at night

REFERRAL
○ atypical pain, suggestive of alternate diagnosis
○ poor response to therapy

14.5.5 IDIOPATHIC (BENIGN) INTRACRANIAL HYPERTENSION (PSEUDOTUMOUR CEREBRI)
IG93.2

DESCRIPTION
Patients present with signs (papilloedema) and symptoms (chronic headache and sometimes eventual visual loss due to persistent papilloedema) of raised intracranial pressure without any structural intracranial abnormality or abnormal CSF composition. To make this diagnosis, the presence of raised CSF pressure > 20 cm H2O at lumbar puncture and the absence of structural lesions or hydrocephalus with neuro-imaging. This is a diagnosis of exclusion.

NON-DRUG TREATMENT
Not all patients require definite treatment. Regular monitoring of visual fields is crucial. Weight loss (15%). Repeated lumbar punctures. Consider surgery for progression of visual effects, despite medical therapy, visual loss at onset or severe papilloedema.

DRUG 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
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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

14.6 INFECTIOUS AND PARASITIC CONDITIONS

14.6.1 MENINGITIS
G02.8*

DIAGNOSIS
Lumbar puncture for chemistry and bacteriology / fungal investigation should be done in all cases.
Computed tomography needs to be done first, in all patients with:
- focal neurological signs present
- recent onset of seizures
- papilloedema
- reduced level of consciousness
- significant uncontrolled bleeding tendency

In cases where lumbar puncture is delayed or cannot be done, commence empirical antibiotic therapy after taking samples for blood cultures. Attempt the lumbar puncture later, once possible.

NON-DRUG TREATMENT
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.

DRUG TREATMENT
All patients require sufficient analgesia.

- paracetamol, oral, 1 g 6 hourly
  AND/OR
- ibuprofen, oral, 800 mg immediately, then 400 mg 8 hourly thereafter
  AND/OR
- morphine, IV, 1–2 mg/minute to a maximum total dose of 10 mg
  Dilute 10 mg up to 10 mL with sodium chloride solution 0.9%.
  This may be repeated 4 hourly.
  Beware of respiratory depression in patients with reduced level of consciousness.
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BACTERIAL MENINGITIS
*N. meningitidis and H. influenzae Type B are notifiable conditions.

For non-meningococcal aetiology
• dexamethasone, IV, 10 mg 6 hourly for 4 days
  OR
  betamethasone, oral, 10 mg 6 hourly for 4 days
  Give prior to initiation of antibiotics or less than 30 minutes after initiation of therapy. Stop if meningococcus is cultured.

Bacterial aetiology unknown, community acquired
• ceftriaxone, IV, 2 g 12 hourly for 10 days
  OR
  cefotaxime, IV, 2 g 8 hourly for 10 days

Meningococcal
For confirmed meningococcal disease only:
• benzylpenicillin (Penicillin G), IV, 20–24 million units daily in 4–6 divided doses for one week

Prophylaxis of contacts:
Only for close household contacts. Only healthcare workers who have resuscitated patient/s before treatment for 24 hours should receive prophylaxis.
• ciprofloxacin, oral, 500 mg immediately as a single dose

Pneumococcal
This organism may be associated with other respiratory disease or CSF leaks.
If sensitive:
• benzylpenicillin (Penicillin G), IV, 20–24 million units daily in 4–6 divided doses for 10 days

If any degree of resistance is present or cannot be excluded:
• ceftriaxone, IV, 2 g 12 hourly for at least 10 days
  OR
  cefotaxime, IV, 2 g 8 hourly for at least 10 days

Penicillin allergy
Consult a microbiologist.

Note:
Chloramphenicol sensitivity testing is not routinely done on Pneumococcus cultures. Penicillin resistant strains of Pneumococcus are usually also resistant against chloramphenicol.
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For meningococcus, *pneumococcus* or *haemophilus* if organism is sensitive:
- chloramphenicol, IV, 1 g 6 hourly

OR

For resistant *pneumococcus*:
- vancomycin, IV, 40 mg/kg daily

PLUS
- rifampicin, oral, 600 mg 12 hourly

HOSPITAL ACQUIRED/POST SURGERY MENINGITIS

Frequent causes are pseudomonas and staphylococcus.
Refer.

TUBERCULOUS MENINGITIS

CSF findings are extremely variable. Initially polymorphs 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/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, 10 mg 12 hourly
  OR
  - betamethasone, oral, 10 mg 12 hourly
  - Taper dose over 6–12 months.
  - Dexamethasone has been shown to reduce mortality but not morbidity.

Standard combination tuberculosis therapy according to National protocol.
See Section 16.10: Tuberculosis, Pulmonary.
Duration of therapy: 9 months.

CRYPTOCOCCAL MENINGITIS

HIV positive cases:
See Section 10.1.2: Cryptococcosis.

In HIV negative patients the aim is to cure the infection, whilst in HIV infection the aim is to suppress the infection until the immune restoration occurs with antiretroviral therapy.

- amphotericin B, IV, 0.7 mg/kg daily for up to 6 weeks
  The nephrotoxicity is minimised by ensuring adequate hydration.
  Regular, 3 times a week, monitoring of potassium and renal function is essential.

OR

- amphotericin B, IV, 0.7 mg/kg daily for 2 weeks
  Follow with:
  - fluconazole, oral, 400 mg daily for 8 weeks
  - Fluconazole should only be commenced when CSF is culture negative.
  - In patients with underlying immune suppression, fluconazole 200 mg daily should then be continued for 12 months.

Follow up is important, as relapse rates are high.
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Therapeutic lumbar puncture
This should be considered as the intracranial pressure is often elevated with a communicating hydrocephalus.
See Section 10.1.2 Cryptococcosis

14.6.2 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.

HERPES SIMPLEX ENCEPHALITIS
Clinical features are fever, change in behaviour and seizures, either focal or generalised. Evidence of mucocutaneous involvement is not usually present. Lumbar puncture shows the features above, but may additionally be haemorrhagic in nature. Diagnosis is made on the basis of the above features, particularly if temporal focus is shown on neurological imaging or EEG. HSV PCR on CSF is diagnostic.

DRUG TREATMENT
Analgesia, i.e.:
• paracetamol, oral, 1 g 6 hourly
AND/OR
• ibuprofen, oral, 800 mg immediately, then 400 mg 8 hourly thereafter
AND/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
• 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. Despite this, patients may frequently be left with neurological sequelae.
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Treat seizures appropriately with phenytoin/carbamazepine. See Section 14.4: Epilepsy. It is important to initiate therapy and then refer to centre where neuro-imaging or EEG is available.

REFERRAL
- patients not responding or worsening in condition, i.e. decrease in consciousness and cranial nerve palsies, despite appropriate therapy for neuro-imaging
  - This especially in cases of tuberculous meningitis, who may develop hydrocephalus and require an urgent shunting procedure.
- patients with shunts

14.6.3 MENINGOVASCULAR SYPHILIS
A52.1

DIAGNOSIS
Lumbar puncture typically shows lymphocytosis with combination of positive RPR/FTA-absorption on CSF. RPR in CSF is usually of low titre, and may be negative. Elevated IgG index may be helpful. Negative blood FTA excludes the diagnosis of neurosyphilis.

DRUG TREATMENT
- benzylpenicillin (Penicillin G), 20 million units daily in 4–6 divided doses for 10 days
  - Penicillin allergy:
    - Consider desensitisation at a referral centre.

14.6.4 BRAIN ABSCESS
A06.6

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.

DRUG TREATMENT
Empiric antibiotic therapy
- ceftriaxone, IV, 2 g 12 hourly
  - OR cefotaxime, IV, 2 g 8 hourly
PLUS
- metronidazole, oral, 400 mg 8 hourly
  - OR metronidazole, IV, 500 mg 8 hourly
Adjust according to sensitivity after surgical drainage.

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## NEUROLOGICAL DISORDERS

### REFERRAL
- All as patients require urgent neurosurgery opinion and treatment

### 14.6.5 ANTIMICROBIAL PROPHYLAXIS IN PATIENTS WITH HEAD INJURIES

**S06.00**

**DRUG TREATMENT**

**BASAL SKULL FRACTURES**

Antibiotic prophylaxis is not indicated.

**PENETRATING BRAIN INJURIES**

Antibiotics are given for therapy.

3rd generation cephalosporin, e.g.:

- ceftriaxone, IV, 2 g 12 hourly

### 14.6.6 NEUROCYSTICERCOSIS

**B69.0**

**DIAGNOSIS**

Patients may present with seizures and/or focal neurological deficit. Typical cystic lesions are seen on neuro-imaging.

**NON-DRUG TREATMENT**

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, of which the intensity 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.:

- dexamethasone, oral 8 mg daily for 8 days in divided doses

  **OR**

  betamethasone, oral 8 mg daily for 8 days in divided doses

Anticonvulsants, if required.

See Section 14.4: Epilepsy

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14.7 MOVEMENT DISORDERS

G25.9

DESCRIPTION
Abnormalities of movement/initiation of movement, divided into those with lack of movement (hypokinesia or bradykinesia), or those with excessive movements (hyperkinesia).

REFERRAL
- to differentiate functional from organic disorders
- tardive diskinesia
- 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

14.7.1 PARKINSONISM

G20

DESCRIPTION
Parkinsonism is a syndrome characterised by tremor, rigidity, bradykinesia and postural disturbances. It may be primary, i.e. Parkinson's disease, or secondary, i.e. drug-induced.

TREATMENT OBJECTIVES
Minimise disabling symptoms.
Prevent complications and avoid serious drug-induced side effects.
To exclude secondary forms.

NON-DRUG TREATMENT
Educate the patient.
General supportive therapy and advice about lifestyle modification, physiotherapy and occupational therapy.

DRUG TREATMENT
Note:
Set therapeutic targets so that the patient is not overtreated.

Predominant tremors
Anticholinergics, e.g.:
  - trihexyphenidyl, oral, 1–2 mg daily
    Start with the lowest dose and titrate upwards.
    Maximum dose: 15 mg/day in 3–4 divided doses.
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Bradykinesia, rigidity and postural disturbance
- carbidopa/levodopa 25/100 mg, oral, 1 tablet 3 times daily. Specialist initiated. Increase by 1 tablet every 1–2 days until the desired response is achieved or maximum dose of 8 tablets per day is reached. 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, oral, ½ tablet 3 times daily. Specialist initiated. Increase by ½ tablet every 1–2 days until the desired effect is achieved or a maximum dose of 8 tablets per day is reached.

Dopamine agonists, e.g.:
- bromocriptine, oral, 1.25 mg daily for 1 week. Specialist initiated. Increase according to response:
  - week 2: 2.5 mg daily
  - week 3: 2.5 mg twice daily
  - week 4: 2.5 mg 3 times daily
  - week 5: 5 mg 3 times daily

Drug-induced extrapyramidal syndrome
Anticholinergic agent, e.g.:
- trihexyphenidyl, oral, 1–2 mg daily Increase to 6–10 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 with treatment
- increasing on/off phenomenon

14.7.2 ESSENTIAL TREMOR
G25.0

NON-DRUG TREATMENT
Rule out and manage alternate conditions, 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.

DRUG TREATMENT
If tremor is severe and interfering with normal daily activity:
- ß-blocker, e.g.:
  - atenolol, oral, 50–100 mg daily
CHAPTER 14  NEUROLOGICAL DISORDERS

14.7.3 MYOCLONUS
G25.3

DESCRIPTION
Irregular, involuntary movements due to muscle jerks, which may be due to myoclonic seizures, but may follow injuries to brain and thus not always of ictal nature.

REFERRAL
○ all patients

14.7.4 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.

DRUG TREATMENT
To be prescribed by a specialist only.
• haloperidol, oral, 0.5–5 mg 2–3 times daily
  OR
  sodium valproate, oral, 500 mg daily
  Maximum dose: 2 500 mg daily in divided doses.

14.8 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 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 chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). This should be referred for assessment.

NON-DRUG TREATMENT
Observe rate of progression.
If the disease is progressing fairly rapidly, i.e. deterioration noted over 7 days or less, admit and monitor ventilatory status carefully with spirometry, as intubation and ventilatory support may be required.
Remove the cause where possible, i.e. drug-induced, alcohol, control of diabetes.
Specialised nursing care and dedicated physiotherapy may be indicated.
Chronic cases may develop contractures, weakness affecting gait, become wheel chair-bound and develop chronic bedsores if not managed appropriately.
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DRUG TREATMENT
Most cases respond to management of the underlying disease process or removal of the aetiological agent.

NEUROPATHIC PAIN
• amitriptyline, oral, 25–75 mg daily
  OR
carbamazepine, oral, 200–1 200 mg daily in divided doses

ISONIAZID–INDUCED POLYNEUROPATHY
• pyridoxine, oral, 75 mg daily for 3 weeks, followed by 25–50 mg daily

POST-HERPES ZOSTER NEUROPATHY
Note:
Aciclovir has not been shown to be beneficial in treating this condition.
• amitriptyline, oral, 25–75 mg daily
AND/OR
• carbamazepine, oral 200–1 200 mg daily dose in divided doses

BELLS’ PALSY
There is insufficient evidence on the efficacy of either corticosteroids or aciclovir.

WERNICKES’ SYNDROME
• thiamine, IM, 100 mg
  OR
thiamine, IV, 100 mg in 1 L fluid
  Follow with oral.
  Other nutritional deficiencies are commonly associated and should be treated.

ACUTE PORPHYRIA ATTACK
Mild abdominal pain
• paracetamol, oral, 1 g 6 hourly

Severe abdominal pain
Opiates, i.e.:
• morphine, IV, 10–15 mg 4 hourly as required

Nausea and vomiting
• metoclopramide, oral/IM/IV, 10 mg and maintain adequate fluid balance

Tachycardia and hypertension
First correct hypovolaemia, if present, then consider β-blockade.
CHAPTER 14  NEUROLOGICAL DISORDERS

Seizures
• clonazepam, IV, 1 mg slowly
  Repeat as required.
  Observe patient for progressive neuropathy as in Gullain Barré Syndrome.

ANTI-RETROVIRAL AGENT INDUCED PERIPHERAL NEUROPATHY
Most commonly due to stavudine or didanosine, especially if also receiving isoniazid.
Where appropriate/indicated, consider replacing:
  • stavudine with zidovudine
  • didanosine with lamivudine.
Without changing the ARV regimen, many cases respond to:
• amitriptyline, oral, 25–75 mg daily

HIV ASSOCIATED NEUROPATHY
This occurs in advanced cases and does not improve significantly on antiretroviral therapy.
Manage neuropathic pain as above.

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, aspiration,
  as well as for diagnostic confirmation

14.9 ACUTE MYELOPATHY
G99.2*

DESCRIPTION
Patients present with a sudden onset of flaccid paraparesis, with associated sensory loss, i.e. a sensory level may be present. There are numerous causes and it is important to exclude neoplastic and infectious conditions, i.e. granulomas and abscesses, causing external compression of the spinal cord. Incontinence and autonomic instability may be present.
Lesions, such as intervertebral disk prolapse, and mass lesions below the spinal cord (L1) may present with Cauda equina syndrome. These cases usually have asymmetrical weakness. Incontinence is a marker of severity.

REFERRAL
• all patients for urgent imaging
14.10 MULTIPLE SCLEROSIS
G35

DESCRIPTION
A demyelinating disease of the central nervous system, characterised by episodic 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.

REFERRAL
- all patients

14.11 OEDEMA, CEREBRAL
G93.6

DESCRIPTION
Swelling of brain parenchymal tissue, due to vasogenic, cytotoxic and osmotic causes. Only the vasogenic causes, such as brain tumours and inflammation, respond to corticosteroids. Consider mannitol for brain oedema in traumatic brain injury causing raised intracranial pressure, pending neurosurgical intervention. Brain oedema following stroke does not respond favourably to drug treatment.

14.11.1 BRAIN OEDEMA DUE TO TUMOURS AND INFLAMMATION

NON DRUG TREATMENT
Supportive management. See Section 14.1.1: Stroke.

DRUG TREATMENT
Treat the underlying cause. This is especially important with brain oedema associated with systemic conditions, such as electrolyte disturbances and organ failure. Patients with primary brain tumours or brain metastases should be considered for specific treatment of the tumour, which includes surgery and/or radiotherapy.
• dexamethasone, IV, 4 mg 6 hourly, initially
  OR
  betamethasone, oral/IV, 4 mg 6 hourly
  Discontinue if no response has occurred after 48 hours.
  Taper dose according to response and duration of therapy.
14.11.2 BRAIN OEDEMA DUE TO TRAUMATIC INJURY
S06.1

NON DRUG TREATMENT
Refer patient for neurosurgical opinion, if indicated.
Supportive management. See Section 14.1.1: Stroke.

DRUG 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.
CHAPTER 15
PSYCHIATRIC DISORDERS

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 the family as well as 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 experience impairments in psychosocial functioning.

NON-DRUG TREATMENT
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 compliance and knowledge of the condition.
In severe cases, psychiatrist directed electroconvulsive therapy may be required.

DRUG TREATMENT
MANIC OR MIXED EPISODES
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.
AND/OR
Benzodiazepine, repeat as necessary, to achieve containment, e.g.:
• clonazepam, IM, 2 mg
  OR
  lorazepam, IM, 2 mg
  OR
  diazepam, IV, 10 mg
Switch to oral once containment is achieved.
CHAPTER 15  PSYCHIATRIC DISORDERS

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.

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.

Maintenance therapy
Indicated where/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 prior to initiating lithium therapy.
- lithium, oral, 5 mg/kg 12 hourly
  Dose range: 400–1 200 mg/day given 12 hourly.
  Monitor trough (predose) plasma levels after 5 days.
  Therapeutic plasma level: 0.4–0.8 mmol/L.
  Where required uptitrate the dose by 5 mg/kg 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 blood levels and therapeutic drug levels of lithium do not differ greatly, and patients should therefore be closely monitored.

OR
Under specific circumstances such as, past or family history of response and rapid cycling, i.e. moving between mood states:
- sodium valproate, oral, 20 mg/kg/day in 2–3 divided doses

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 12 hourly
  Time of onset: 6–8 weeks.

Second line
ADD
- fluoxetine, oral. In consultation with psychiatrist.

Note:
Do not use monotherapy antidepressants in bipolar patients.
Increased 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**
• sodium valproate, oral, 20 mg/kg/day in 2–3 divided doses
**AND/OR**
• carbamezepine, oral, 600–1 000 mg/day
  Initial dose: 100 mg twice daily.
  Uptitrate dose by 200 mg/day every 4 days to avoid adverse effects.

**Maintenance therapy**
Following manic episodes.
Continue either lithium or sodium valproate.
Consider stopping haloperidol and benzodiazepines (always taper).
Patients who experience subthreshold symptoms or breakthrough mood episodes (depressive symptoms) may require the addition of an antidepressant.
Treatment of major depressive episodes: See Section 15.3: Depressive Disorder, Major.

**REFERRAL**
In certain circumstances it may be necessary to refer patients to psychiatric services, these include:
• mixed or rapid cycling biplolar disorder
• depressive episodes in bipolar patients not responding to second line treatment
• manic episodes not responding to treatment

### 15.2 CONFUSIONAL STATES/DELIRIUM

**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. agitation/stuporose as well as experiencing of visual/tactile or gustatory hallucinations and even paranoid ideation. The onset will present as a significant change in the patient’s mental state.

**Note:**
Many acute medical emergencies can present as delirium or apparent acute psychosis.
CHAPTER 15

PSYCHIATRIC DISORDERS

NON-DRUG TREATMENT
Hospitalisation is mandatory for physical and environmental support.
Control the acute disturbance.
Laboratory testing/medical investigations where indicated i.e. to exclude/diagnose
underlying medical problem which is the primary management where delirium has
been diagnosed.

DRUG TREATMENT

Treat medical condition if present.

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 and Neuroleptic Malignant
  Syndrome.
  Dosing may vary according to clinical circumstances, e.g. lower doses with the
  elderly or where HIV or HIV related dementia is known or suspected.

AND/OR
Benzodiazepine, repeat as necessary, to achieve containment, e.g.:
• lorazepam, IM, 2 mg
  OR
  clonazepam, IM, 2 mg
  OR
  diazepam, IV, 10 mg
Switch to oral 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.

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.
15.3 DEPRESSIVE DISORDER, MAJOR
F32.9

DESCRIPTION
Major depression is characterised by a depressed mood (sadness) accompanied by loss of interest and decreased experiencing of pleasure as well as social withdrawal. Disturbances, i.e. reduction of 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 should have been present for at least two weeks and impact on the person's ability to function normally.

NON-DRUG TREATMENT
Treatment is bio-psycho-social.
Exclude precipitating medical conditions, e.g. cerebrovascular disease or hypothyroidism.
Psychotherapy, usually cognitive-behaviour therapy.
Family therapy and psycho-education of patient and family.
Review of social factors.
Electroconvulsive therapy is indicated under specific circumstances.

DRUG TREATMENT
Antidepressant therapy
All antidepressants take 4–6 weeks to achieve their maximum effect. In some patients may experience an initial response may be experienced within the first 1–2 weeks. There is little evidence to support combination drug treatments.
Tricyclic Antidepressants (TCA) and Selective Serotonin Reuptake Inhibitors (SSRI) are of equal efficacy.
The choice of therapy is guided by comorbid states, e.g. cardiovascular disease and in the elderly. In patients with CV disease, avoid TCA and in the elderly caution with TCA and SSRI.
Following remission continue the pharmacotherapy for at least another 6 months. Thereafter, review the need for ongoing therapy. When discontinuing the medication, taper off slowly to avoid discontinuation symptoms. If there is a recurrence, reinstitute the continuation 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 only be treated by a specialist due to the increase risk of suicide ideation when treated with SSRIs.
CHAPTER 15

MAJOR DEPRESSIVE DISORDER

First line
Tricyclic antidepressants, e.g.:
• amitriptyline, oral, at bedtime
  Initial dose: 25 mg, increase by 25 mg/day at 3–4 day intervals.
  Maximum dose: 150 mg/day.
  Doses in excess of 150 mg: consult a psychiatrist.
  OR
  imipramine, oral, at bedtime. Specialist initiated.
  Initial dose: 25 mg, increase by 25 mg/day at 3–4 day intervals.
  Maximum dose: 150 mg/day.
  Doses in excess of 150 mg: consult a psychiatrist.

OR
Selective serotonin reuptake inhibitors:
• 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. Specialist initiated.

If a sedating antidepressant is required or 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 before starting with citalopram after stopping fluoxetine.

REFERRAL
  no response to treatment

15.4 DYSTHYMIC DISORDER

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 the presentation 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.

NON DRUG TREATMENT
As for Major Depressive Disorder.

DRUG TREATMENT
As for Major Depressive Disorder.
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REFERRAL

no response to treatment

15.5 GENERALISED ANXIETY DISORDER

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.

NON-DRUG TREATMENT
Crisis management may be needed.
Psychotherapy, e.g. supportive and cognitive-behaviour therapy.
Most patients can be treated as outpatients, but some may need to be admitted.

DRUG 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 the 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 twice daily.
  Duration of therapy: up to 2 weeks tapering off to zero within 6 weeks.

Maintenance therapy
SSRI:
• fluoxetine, oral, 20–40 mg daily. Specialist initiated.
  Duration of therapy: variable, although the condition tends to be chronic.
  Extended drug 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.
Drug abuse may occur.
Combination therapy with more than one benzodiazepine is not indicated.

REFERRAL

ongoing symptoms
non/poor response to 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 patients' day and interfere with daily functioning. Generally the features are distressing to the patient.

REFERRAL
- all

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, possible 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.

NON-DRUG TREATMENT
Psycho-education and reassurance.
Psychotherapy, e.g. cognitive-behaviour therapy.
Always consider the possibility of an underlying medical condition, e.g. thyrotoxicosis, etc.

DRUG 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, IV/oral, 2–5 mg as a single dose
- clonazepam, IM/oral, 0.5–1 mg immediately

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.
CHAPTER 15 \hspace{1cm} PSYCHIATRIC DISORDERS

Treatment of choice: SSRI, e.g.:
- fluoxetine, oral
  Start with the lowest possible dose available because of increased sensitivity to side effects.
  Duration of therapy: variable, initially 6 months–1 year.
  Extended drug treatment over many years and even life-long may be necessary, except where cognitive-behaviour therapy has been successful.
  Relapses may occur when treatment is discontinued.

REFERRAL
- recurrent panic attacks/panic disorder

15.8 ACUTE STRESS DISORDER AND POSTTRAUMATIC STRESS DISORDER

F43.1

DESCRIPTION
Acute stress and posttraumatic 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 either 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 of the 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.

NON DRUG TREATMENT
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.

DRUG TREATMENT
Acute management
For anxiety and insomnia:
Benzodiazepines, repeated as necessary to control symptoms, e.g.:
- diazepam, IV/oral, 2–5 mg as a single dose
  OR
- clonazepam, IM/oral, 0.5–1 mg immediately
CHAPTER 15  PSYCHIATRIC DISORDERS

Maintenance antidepressant therapy
Indicated for features of Posttraumatic Stress Disorder as well as the possibility of an emergent, co-morbid, 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 be experiencing 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 the 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

DESCRIPTION
Schizophrenia is characterised by psychotic episodes, and is typically accompanied by a deterioration in social and occupational functioning as well functioning generally i.e. tasks of daily living such as hygiene and grooming. Whilst the presentations may be acute, typically the sufferer’s illness tends to have a chronic course.

NON-DRUG TREATMENT
Supportive psychotherapy and psycho-educational group therapy for patients and family members.
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DRUG 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 anti-psychotic
effect.

AND/OR
Benzodiazepine, repeat as necessary, to achieve containment, e.g.:
• lorazepam, IM, 2 mg
  OR
diazepam, IV, 10 mg
  OR
clonazepam, IM, 2 mg

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 be schizophrenic:
• 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
  for the patient.

Prophylactic anticholinergics:
• orphenadrine, oral, 50 mg twice daily
If dystonic reactions develops:
• biperiden, IM, 2 mg
  Do not further administer antipsychotic.
  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, cease 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/day
    OR
    chlorpromazine, oral, 75–300 mg/day in divided doses
  OR
  If adherence is a problem:
    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 ruled out:
  Refer for consideration of clozapine or other antipsychotics including “atypicals”.
  • clozapine, oral, 300–450 mg daily. Psychiatrist initiated.
    Titrate doses.
    Frequent WCC monitoring – See package insert.
    OR
    risperidone, oral, 1–4 mg daily. Psychiatrist initiated.
    OR
    sulpiride, oral, 600–800 mg/day in divided doses. Psychiatrist initiated.
  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 twice daily.
    Do not prescribe more than 150 mg/day.
    Use with caution in the elderly as it may cause confusion and urinary retention.
    OR
    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**
  o for consideration of clozapine or other atypical antipsychotics if haloperidol and
  chlorpromazine fail and adherence is a problem
  o psychotic patients with uncertain diagnosis
  o patients who relapse and refuse treatment or become aggressive or suicidal, refer
    to the Mental Health Care Act in terms of involuntary treatment
  o patients with complications due to medication which cannot be managed easily
CHAPTER 15

PSYCHIATRIC DISORDERS

15.11 WITHDRAWAL FROM SUBSTANCES OF ABUSE

15.11.1 ALCOHOL

F10.4

NON-DRUG TREATMENT
Admit patients with:
- convulsions
- psychosis
- suicidal ideation
- significant medical comorbidity such as heart failure, 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.

DRUG 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 twice daily for 2 days
  then 5 mg daily for 2 days
  then stop.

COMPLICATED WITHDRAWAL
See Section 14.2.1: Alcohol Withdrawal Delirium (Delirium Tremens)

15.11.2 OPIATES E.G. HEROIN

F11.2

Withdrawal is generally poorly tolerated, but not dangerous, except in very frail debilitated patients or during the first trimester of pregnancy.

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 3 times daily as required
For diarrhoea:
• loperamide, oral, 4 mg immediately, then 2 mg after each loose stool

Mild

MODERATE TO SEVERE WITHDRAWAL
Hospitalise patient.

Substitution treatment
Methadone syrup is used under specialist guidance, ideally in a specialist centre. The dose is determined by titrating it according to the level of tolerance. Methadone may be used in conjunction with symptomatic treatment to reduce the methadone requirement.

Day 1
Only if clinical signs of withdrawal are present:
• methadone, oral, 10 mg (= 25 mL)
  If symptoms are still present after 1 hour, give another 5–10 mg.
  If symptoms are still present after 1 hour, give a repeat dose of 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.

15.11.3 STIMULANTS INCLUDING METHAMPHETAMINES AND COCAINE
F14.2.

NON-DRUG TREATMENT
These patients usually do not require admission.
Beware of depression and assess suicide risk.

DRUG TREATMENT
No substitute drug available for detoxification.

For severe anxiety, irritability and insomnia, short-term benzodiazepines, e.g.:
• diazepam, oral, 5–10 mg 3 times daily for 5–7 days
CHAPTER 15    PSYCHIATRIC DISORDERS

15.11.4 METHAQUALONE AND/OR CANNABIS
F12.2

Only for intolerable withdrawal symptoms:
• diazepam, oral, 5 mg as needed
  Maximum dose: 20 mg daily.

15.11.5 BENZODIAZEPINES
F13.2

NON-DRUG TREATMENT
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.

DRUG TREATMENT
Replace short-acting benzodiazepine with an equivalent diazepam (long acting
benzodiazepine) dose.
Approximate equivalent doses to diazepam 5 mg are:
  o chlordiazepoxide 15 mg
  o lorazepam 1 mg
  o alprazolam 0.25 mg
  o bromazepam 1.5 mg
  o flunitrazepam 0.5 mg
  o nitrazepam 5 mg
  o oxazepam 15 mg
  o temazepam 15 mg
  o zopiclone 7.5 mg
  o 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.
CHAPTER 16
RESPIRATORY SYSTEM

16.1 ASTHMA, ACUTE

NON-DRUG TREATMENT
Prevent exposure to known allergens and inhaled irritants.
Oxygen if hypoxic.
Ensure adequate hydration.

DRUG TREATMENT
\(\beta_2\)-stimulants, e.g.:
- salbutamol or fenoterol, MDI, 1–2 mg immediately via larger volume spacer
  
  \(1\text{ mg} = 1\ 000\text{-}2\ 000\ \text{mcg} = 10\text{-}20\text{ puffs of } 100\ \text{mcg}\)
  
  If patient responds, follow with 200 mcg 4–6 hourly.

  OR
  - salbutamol, nebulised, 2.5–5 mg, administered:
    - undiluted and nebulise over 3 minutes
    - or
    - diluted with sodium chloride 0.9% to a total volume of 4–5 mL and nebulise over 20 minutes
  
  Repeat 4–6 hourly.

  OR
  - fenoterol, nebulised, 1.25–2.5 mg undiluted administered over 3 minutes
  
  Repeat 4–6 hourly.

Take cognisance of the proper use of available nebulisers.
Continue with this inhalation until peak flow returns to 80% of predicted, or of personal best.

In very severe cases, and in patients not responding to standard dosages, these dosages may be given more frequently, i.e. every 20 minutes for 1 hour or continuously, after which patient should be reassessed clinically, and by peak flow meter and pulse oximetry/oxygen saturation and monitoring of pulse, BP and respiratory rate.

Consider admission to an intensive care unit in life-threatening asthma, when there is no response to treatment, as intubation and ventilatory support may be required.

Corticosteroids
Patients having an acute attack of asthma, unless the attack is very mild and the response to \(\beta_2\)-stimulants very rapid:
- prednisone, oral, 40 mg immediately
Follow with:
- prednisone, oral, 20–40 mg daily for 7–10 days

OR
In patients who cannot use oral therapy:
- hydrocortisone, IV, 100 mg immediately
Once oral medication can be taken, follow with:
• prednisone, oral, 20–40 mg daily for 7–10 days
  Monitor response closely by measurement and clinical signs. Exclude causes of intractable asthma.
  If there is a good response, prednisone can be discontinued abruptly after 7–14 days. If used for longer, dosage must be tapered and then stopped.

THEOPHYLLINE NAÏVE PATIENTS
Aminophylline should be reserved for severely ill cases and/or cases not responding to initial bronchodilator or corticosteroid therapy.

In a Cochrane review aminophylline has not been shown to be beneficial in acute asthma in adults who are given sufficient nebulised β₂-stimulants. It is a toxic drug and is not a first line drug in the treatment of asthma, but it may have a role in cases not responding to initial bronchodilator and corticosteroid therapy. Because of its toxicity, blood levels must be monitored if it is used. Potassium levels should be monitored and corrected at initiation and continuously during treatment.

Patients not currently using oral theophylline preparations:
• aminophylline, IV, 6 mg/kg loading dose administered over 10–20 minutes Specialist initiated.
  Maintenance dose: 0.6 mg/kg/hour diluted in 200 mL sodium chloride 0.9% administered as a continuous infusion. The dose should be titrated to a plasma level of 10–20 mcg/mL, if therapeutic drug monitoring is available.

Patients currently using oral theophylline preparations:
No loading dose is needed. Commence immediately with:
• aminophylline, IV, 0.6 mg/kg/hour diluted in 200 mL sodium chloride 0.9% administered as a continuous infusion. The dose should be titrated to a plasma level of 10–20 mcg/mL, if therapeutic drug monitoring is available.

Anticholinergics, e.g.:
For the duration of the acute attack, until peak flow returns to 80% of predicted or of personal best:
• ipratropium bromide, MDI, 40–120 mcg 3–4 times daily via large volume spacer
  OR
  ipratropium bromide, nebulised, 0.5 mg 4 hourly
  Dilute 2 mL in 3 mL sterile sodium chloride solution 0.9%.
CHAPTER 16  RESPIRATORY SYSTEM

REFERRAL
- severe non-responding bronchospasm
- patients presenting with repeated asthma exacerbations
- patients with previous life-threatening exacerbations
- when there are unsatisfactory social and personal factors, e.g. inadequate access to health care, unavailability of transport, difficult home conditions or difficulty with the home management plan

16.2 ASTHMA, CHRONIC PERSISTENT

J45

NON-DRUG TREATMENT
Patient education.
Eliminate/decrease exposure to triggers, e.g. house dust mite, pollens, grasses, pets, smoke, fumes, etc.
Psychological support.

DRUG TREATMENT
Concomitant use of preparations of the same pharmacological classification is hazardous and must be avoided.
Nocturnal asthma and/or regular need for bronchodilators are usually indicative of poor control of asthma. Consider adjustment of treatment.

Note:
All regular nebulised therapy should be prescribed by a specialist.
Correct use of inhaler therapy 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
Administer all inhaled corticosteroids via a spacer.
Indicated in all patients with daytime symptoms > twice a week or nocturnal symptoms > once a month.
If no peak flow or other lung function test assessment available:
- budesonide, inhaled, 200 mcg twice daily
  Maximum total daily dose: 1 200 mcg.
  Doses in excess of 800 mcg daily are reserved for specialist only, and should not normally be used as higher dosages cause significant metabolic adverse effects.
  OR
  beclomethasone, inhaled, 200 mcg twice daily
  Maximum total daily dose: 1 000 mcg.
  Doses in excess of 1 500 mcg daily are reserved for specialist only, and should not normally be used as higher dosages cause significant metabolic adverse effects.
As reliever/rescue therapy:

**β₂-stimulants**, e.g.:
- salbutamol, MDI, 100–200 mcg, 4–6 hourly as necessary
  
  Do not exceed dose in chronic asthma except in acute severe attacks, as higher doses may be hazardous, especially in the elderly and those with cardiac disease.

  **OR**
  
  salbutamol, nebulised, 2.5–5 mg, administered:
  - undiluted and nebulise over 3 minutes
  - diluted with sodium chloride 0.9% to a total volume of 4–5 mL and nebulise over 20 minutes
  
  Repeat 4–6 hourly.

Exercise-induced asthma may be an isolated symptom of asthma and may require the use of an inhaled β₂-stimulant 15–20 minutes before exercise.

**Note:**
Nebulised bronchodilator therapy is not recommended for chronic maintenance therapy of asthma, except under specialist direction.

**If insufficient response to salbutamol:**
ADD

**Anticholinergics**, e.g.:
- ipratropium bromide, MDI, 40–120 mcg 6–8 hourly. Specialist initiated.

**If asthma is still not well controlled:**
ADD
- theophylline slow release, oral. Specialist initiated.
  
  Initial dose: 150–200 mg 12 hourly followed by increments of 150–200 mg/day every third day, if tolerated.
  
  Maximum dose: 14 mg/kg daily or 900 mg daily.
  
  Higher dosages of theophylline should ideally be guided by blood level monitoring where available.
  
  The elderly are more susceptible to theophylline toxicity. Theophylline dosages need to be reduced by ± 30%.

  Combinations of xanthine derivatives with ephedrine-like substances and sedatives have no place in the treatment of asthma.
  
  Oral theophylline has a limited place in the treatment of asthma after insufficient response to inhaled β₂-stimulants and corticosteroids in sufficient doses and should be prescribed only on the basis of proven benefit via pulmonary function testing in individual patients.

  Ongoing use of theophylline should be re-evaluated periodically. If there is no benefit after 4 weeks, discontinue theophylline.
CHAPTER 16 RESPIRATORY SYSTEM

If asthma is still not well controlled:
ADD
Long acting β-agonist, e.g.:
• salmeterol, inhaled, 50 mcg twice daily. Specialist only.
  OR
  formoterol, inhaled, 12 mcg twice daily. Specialist only.
A three month trial of long acting beta agonist therapy, verified by lung function assessments, is indicated in treatment-compliant patients who have a demonstrated adequate technique in the use of inhalers and whose asthma is uncontrolled with high doses of inhaled corticosteroids, regular inhaled β₂-stimulant and ipratropium bromide and who have theophylline dosages adjusted to therapeutic blood levels.
If clinical benefit is objectively and convincingly demonstrated by significant lung function improvement, i.e. FEV₁ increase by >10%, decreased hospitalisations, decreased exacerbations and decreased nocturnal awakenings, long acting β-agonist therapy should be continued and oral theophylline may be tried to be withdrawn.
PLUS
If required, i.e. inadequate response to high dose inhaled corticosteroids (800 mcg daily):
• prednisone, oral, 5–10 mg daily
  For short-term exacerbations in patients not responding to the above, doses of 20–40 mg daily for 7–10 days may be required.
  These patients should be referred to a tertiary centre.

Cromoglycate and nedocromil provide no additional benefit over corticosteroids.

INTERCURRENT BACTERIAL INFECTIONS
Bacterial infections are seldom present in acute exacerbations of asthma and yellow sputum is usually related to presence of eosinophils.
• amoxicillin, oral, 500 mg 8 hourly for 5–10 days
Penicillin allergy:
• doxycycline, oral, 100 mg twice daily taken with an adequate amount of fluid

REFERRAL
- to assess and confirm diagnosis when in doubt
- for treatment optimisation
- to treat complications
- patients not responding to optimal therapy
- acute severe non-responding attacks of bronchospasm

16.3 BRONCHIECTASIS

NON-DRUG TREATMENT
Patient education.
Advice on early self-referral for suspected acute infections.
Physiotherapy:
- regular and continued postural drainage is the mainstay of therapy and must be emphasised.
- demonstrate postural drainage to the patients. Check adherence to the correct technique at each visit.
- regular home physiotherapy, including cough and chest drainage techniques are the basis of therapy and must be emphasised repetitively

**DRUG TREATMENT**

**Antimicrobial therapy**
Antibiotic therapy in patients with bronchiectasis should only be used when there are features of systemic sepsis i.e.:
- temperature
- white cell count > 14 000
- significant reduction in effort tolerance and/or new infiltrates on chest X-ray

Treatment may need to be prolonged for several weeks, depending on the extent of the bronchiectasis and the organisms suspected.
In patients who do not respond or improve on treatment below, sputum culture and sensitivity should be done to determine antimicrobial resistance.

In patients otherwise stable and with mild bronchiectasis:
- amoxicillin, oral, 1 g 8 hourly for at least 10 days, or longer depending on the response

Penicillin allergy:
- doxycycline, oral, 100 mg twice 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 cultures and sensitivity determination are indicated in all cases.
- ampicillin, IV, 1 g 6 hourly

**PLUS**
- gentamicin, IV, 5 mg/kg once daily

Depending on the background resistance patterns of common organisms, the following initial therapy may be justified:
- amoxicillin/clavulanic acid, IV, 1.2 g 6 hourly

Switch to oral treatment once there is an improvement:
- amoxicillin/clavulanic acid, oral, 625 mg 8 hourly

Subsequent antibiotic therapy should be based on results of sputum investigations.
**Note:**
Treat cor pulmonale along conventional lines. See Section 3.3 Congestive Cardiac Failure.
CHAPTER 16  RESPIRATORY SYSTEM

Inhaled bronchodilators
Bronchodilators may be used as for asthma or COPD, if air flow obstruction is present. There is no indication for inhaled corticosteroids.

REFERRAL
- confirmation of the diagnosis and exclusion of a possible foreign body
- non-responsive infections
- cardiovascular and other systemic complications
- major haemoptysis
- assessment for possible surgical removal of a bronchiectatic segment

16.4 CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

J44.9

NON-DRUG TREATMENT
Lifestyle adjustment, e.g. smoking cessation.
Avoid precipitants, e.g. infections, inhaled irritants, etc.
Chest X-ray to exclude TB, carcinoma or a surgically correctable abnormality e.g. a large single bulla.
Pulmonary rehabilitation, including exercise rehabilitation and cough techniques.
Psychological support.
Educate patient and family regarding the disease.
Ensure adequate nutrition and physical conditioning.
Treat complicating infections early.

DRUG TREATMENT
Note:
Correct use of inhaler therapy technique should be demonstrated and checked regularly by way of placebo inhalers, as the majority of patients do not use their inhalers correctly.

β₂-stimulants, e.g.:
- salbutamol, MDI, 200 mcg 4–6 hourly as needed using a larger volume spacer
  OR
  salbutamol, nebulised, 2.5–5 mg, administered:
  - undiluted and nebulise over 3 minutes
  or
  - diluted with sodium chloride 0.9% to a total volume of 4–5 mL and nebulise over 20 minutes
  Repeat 4–6 hourly.

Anticholinergics, e.g.:
- ipratropium bromide, MDI with spacer, 40–120 mcg 6–8 hourly as needed

Note:
Restrict nebulised therapy.
Do not use as maintenance therapy except under specialist direction.
CHAPTER 16  RESPIRATORY SYSTEM

Theophylline

In a Cochrane review there was evidence of marginal improvement in lung function but the clinical relevance of this is unclear.

- theophylline, oral, 125–150 mg 12 hourly for three days
  Titrate upwards by 125–150 mg per day every third day.
  Maximum dose: 14 mg/kg daily or 900 mg daily, whichever is the higher.
  Doses exceeding these should be titrated upward using plasma theophylline level monitoring.
  Ongoing use of theophylline should be re-evaluated periodically. If there is no benefit after 4 weeks, discontinue theophylline.
  If the 12 hourly daily doses are different, the higher dose should be given at night.
  A slow release formulation is preferred to avoid wide trough to peak level differences during the day.
  Side effects are dose-related and include nausea, gastric intolerance, tachycardia and seizures. Titrate doses slowly upwards to reduce side effects. Titration may be interrupted or reversed to the previous tolerated dose.
  Interacts with many other drugs including antibiotics such as erythromycin and quinolones.

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.
Patients should be in a stable condition.
Monitor steroid usage by objective parameters such as FEV₁ and six minute walking test.
- prednisone, oral, 40 mg daily for 14 days
  Taper to 20 mg for a further 2 weeks, after which lung function testing needs to be repeated.
  If there is a significant improvement, reduce dose to 10 mg daily for one month while inhaled steroids are introduced. Long-term oral steroids beyond this time increase mortality and morbidity.
  If no significant improvement in lung function values, i.e. FEV₁ increase by > 12% and 200 mL, stop prednisone.

Antibiotic therapy

Exacerbations of chronic bronchitis are, in contrast to exacerbations in asthma, frequently related to bacterial infections.
CHAPTER 16  RESPIRATORY SYSTEM

5 days antibiotic treatment in these patients is often insufficient and leads to incomplete response and recurrence of symptoms.

• amoxicillin, oral, 500 mg 8 hourly for 10 days

Penicillin allergy:
• doxycycline, oral, 100 mg twice daily for 10 days

REFERRAL
○ to establish the diagnosis and an optimal treatment protocol
○ treatment-resistant acute or chronic airflow limitation
○ pre-operative assessment for surgical procedures
○ assessment regarding long-term domiciliary oxygen therapy

16.5 LUNG ABSCESS
J85

NON-DRUG TREATMENT
Physiotherapy and regular emphasis on postural drainage is of extreme importance in the management.
Instruct patient to do postural drainage for at least 10 minutes 4 times a day.
Nutritional support.

DRUG TREATMENT
• benzylpenicillin (Penicillin G), IV, 5 million units 6 hourly
PLUS
• metronidazole, oral, 400 mg 8 hourly
Follow with:
• amoxicillin, oral, 500 mg 8 hourly
PLUS
• metronidazole, oral, 400 mg 8 hourly
Until infection has clinically and radiologically resolved.

In situations where gram negative organisms are suspected or cultured and depending on the background resistance patterns of common organisms:
• amoxicillin/clavulanic acid, IV, 1.2 g 8 hourly until the patient is no longer pyrexial for 48 hours
Follow with:
• amoxicillin/clavulanic acid, oral, 625 mg 8 hourly

Penicillin allergy:
• clindamycin, IV, 600 mg 8 hourly
Follow with:
• clindamycin, oral, 300 mg 8 hourly

Duration of therapy is until there are no features of sepsis and there is no fluid level, and is usual for several weeks.
CHAPTER 16 RESPIRATORY SYSTEM

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
- surgery, if indicated, for lung abscess
- complications, such as empyema, septicaemia, haemoptysis, etc.

16.6 PNEUMONIA, COMMUNITY ACQUIRED

NON-DRUG TREATMENT
Bed rest.
Frequent monitoring of temperature, blood pressure and pulse rate in order to detect complications early and monitor response to therapy.
Attention should be given to fluid and nutritional replacements.
Oxygen via nasal prongs or facial mask.

Even in clinically classic cases of pneumonia, tuberculosis may need to be excluded by way of a sputum examination. An initial chest X-ray should routinely be followed by a follow up X-ray after the 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 only be done 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 the pneumonia the X-ray changes may be unimpressive, and may only develop fully after a few days.
A control chest X-ray is always indicated after attempted pleural fluid aspiration to exclude pneumothorax, as hydro-pneumothorax in this setting often leads to empyema with high morbidity and prolonged hospitalisation.

Empyema, detected early by a low pH and leucocytosis in pleural aspirate and a cloudy or clearly infected pleural aspirate, should be drained completely by chest tube drainage.

DRUG TREATMENT

NON-SPECIFIC/SUPPORTIVE
Adequate analgesia with paracetamol or morphine for pleuritic pain. If NSAIDs are to be used then sufficient hydration in the patient must be ensured.
Blood pressure support may be needed.

SPECIFIC
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 any of the complications, or to the incorrect choice of antibiotic, or due to an underlying bronchus obstruction (foreign body or carcinoma). These patients should be further investigated.

UNCOMPPLICATED COMMUNITY-ACQUIRED PNEUMONIA
• benzylpenicillin (Penicillin G), IV, 2 million units 6 hourly
  OR
  ampicillin, IV, 1 g 6 hourly

When temperature has settled follow with:
• amoxicillin, oral, 500 mg 8 hourly

If poor response after 48–72 hours:
ADD
• doxycycline, oral, 200 mg immediately, followed by 100 mg twice daily for 14 days
  OR
  erythromycin, oral, 500 mg 6 hourly for 14 days

Penicillin allergy:
• erythromycin, oral, 500 mg 6 hourly

HOSPITALISED PATIENTS > 65, COMORBID DISEASE, INCLUDING HIV INFECTION, DIABETES MELLITUS, CARDIAC FAILURE, KIDNEY DISEASE, ETC.
3rd generation cephalosporin e.g.:
• ceftriaxone, IV, 1 g 12 hourly

Penicillin allergy:
• moxifloxacin, oral, 400 mg daily

If poor response after 48–72 hours:
ADD
• doxycycline, oral, 200 mg immediately, followed by 100 mg twice daily for 14 days
  OR
  erythromycin, oral, 500 mg 6 hourly for 14 days

SEVERE PNEUMONIA
• ceftriaxone, IV, 1 g 12 hourly
PLUS
• erythromycin, oral, 500 mg 6 hourly

In severe penicillin allergy:
• moxifloxacin, oral/IV, 400 mg daily for 5–10 days
**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, except that patients tend to be more ill.

Aspiration pneumonia should be suspected in patients with episodic or prolonged decreased level of consciousness, e.g. in alcoholics, drug overdoses, epileptics, strokes, etc, or 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.

**DRUG TREATMENT**

*Antimicrobial therapy*

Continue therapy until there are no features of sepsis and there is no fluid level. Once the acute infection has settled, refer all patients for specialist opinion regarding surgical intervention. Gram-negative organisms are only frequently seen in nosocomial aspiration and in nursing home residents. In this setting add gentamicin for 5 days with trough level monitoring. In patients with renal impairment, use a third generation cephalosporin.

- amoxicillin/clavulanic acid, IV, 1.2 g 8 hourly until the patient is no longer pyrexial
  Follow with:
  - amoxicillin/clavulanic acid, oral, 375 mg 8 hourly
  **AND**
  - amoxicillin, oral, 500 mg 8 hourly
  **PLUS**
  - metronidazole, oral, 400 mg 8 hourly

**OR**

- benzylpenicillin (Penicillin G), IV, 2 million units 6 hourly
  **PLUS**
  - metronidazole, oral, 400 mg 8 hourly

Penicillin allergy:

- clindamycin, IV, 600 mg 8 hourly
  **PLUS**
  Aminoglycoside, e.g.:
  - gentamicin, IV, 5 mg/kg daily
CHAPTER 16 RESPIRATORY SYSTEM

REFERRAL
- 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 injury.

NON-DRUG TREATMENT
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.

DRUG TREATMENT
Antimicrobial therapy
Antimicrobial therapy is that of the primary condition.

PENETRATING CHEST WALL INJURY
- cloxacillin, IV, 2 g 6 hourly

REFERRAL
- complicated empyema requiring ultrasound guided drainage or surgical resection
- chronic empyema with pleural thickening and restrictive lung disease, requiring surgical decortication

16.9 CYSTIC FIBROSIS
E84

DESCRIPTION
A genitically inherited disease of exocrine glands, leading to thick viscid secretions, leading to recurrent respiratory tract infections and bronchiectasis and to malabsorption due to pancreatic insufficiency.

NON-DRUG TREATMENT
Premarital gene typing and counselling.
Counselling of parents.
CF support groups.
Adequate hydration and electrolyte replacement, especially in warm weather.
Early treatment of infections.
Active chest physiotherapy, i.e. frequent postural drainage.
Diet: high protein, high calorie and low fat diet.
DRUG TREATMENT
Treat each feature according to its severity.
Vitamin supplementation.

CHRONIC PANCREATITIS
Pancreatic enzymes as a combination capsule containing amylase, lipase and protease.
Dose according to response.
See Section 1.1.9: Chronic Pancreatitis.

RESPIRATORY TRACT INFECTIONS
Prophylaxis
There is no convincing evidence of a beneficial effect of the use of prophylactic antibiotics to prevent respiratory tract infections.

Established infections
It is essential to monitor sputum culture sensitivity, as antimicrobial resistance commonly develops in patients with cystic fibrosis.
For pseudomonas species or other gram negative organisms, combinations of a β-lactam antibiotic, e.g. piperacillin, or a third generation cephalosporin, such as ceftazidime or ceftriaxone, with an aminoglycoside, or ciprofloxacin may be needed depending on microbial sensitivity.
The duration of therapy is related to clinical and bacteriological response. Antibiotic treatment should be continued for 10–14 days after the clinical manifestations have subsided.
After an acute infection has cleared, patients need to be followed up at short intervals, to ensure successful outcome.

*S. aureus*
- cloxacillin, IV, 1 g 6 hourly
  OR
  flucloxacillin, oral, 500 mg 6 hourly

Proven resistance of *S. aureus* to the above, treat according to sensitivity:
- vancomycin, IV, 10 mg/kg 6 hourly
Maximum dose: 2 g daily.

Pseudomonas species
Monotherapy is acceptable as there is no convincing evidence that combination therapy has a better outcome.
- β-lactam, e.g.:
  piperacillin, IV, 300 mg/kg/day
  OR
  3rd generation cephalosporin, e.g.:
  ceftazidime, IV, 2 g 8 hourly
PLUS
- gentamicin, IV, 5 mg/kg once daily
Measure peak and trough levels.

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CHAPTER 16

OR
ciprofloxacin, oral, 750 mg twice daily
OR
ciprofloxacin, IV, 2.5–5 mg/kg 12 hourly

REFERRAL
- for confirmation of diagnosis and screening of relatives
- to plan management
- to manage complications such as:
  - malnutrition and deficiencies
  - severe haemoptysis, which may require pulmonary artery embolisation
  - recurrent pneumothorax for pleurodesis or pleurectomy
  - cor pulmonale
  - obstructive GIT complications for surgical correction

16.10 TUBERCULOSIS, PULMONARY

* 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 expanded and complicated 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 Ziehl-Nielsen stained sputum or gastric aspirate smears, positive for acid-fast bacilli (AFB) and/or culture. Sputum induction with hypertonic ultrasonic nebulised saline 5% has been shown to increase the yield of positive smear or culture. This may be of special value in the context of HIV/AIDS, as in these patients TB frequently presents without cavitation and there consequently often is a low sputum yield of organisms. In exceptional cases bronchial washings may have to be done to confirm the diagnosis.

MDR-TB is diagnosed exclusively on culture and sensitivity essays.
Directly observed therapy (DOT), short-course, using fixed medicine combinations is recommended to avoid the development of antimicrobial resistance. Treatment should be given five times per week in both the intensive (initial) and the continuation phases.

**Note:**
In order to avoid dosage errors, clinics should adhere to either a five-times per week (preferred) or a three-times per week dosage (not recommended) schedule in the follow-up treatment phase.

Fixed dose drug combinations available:

<table>
<thead>
<tr>
<th>Drug Combination</th>
<th>Dosage</th>
</tr>
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<tbody>
<tr>
<td>RH – 150/75 mg</td>
<td>RH – 300/150 mg</td>
</tr>
<tr>
<td>RH – 150/150 mg*</td>
<td>RHZE – 150/75/400/275 mg</td>
</tr>
<tr>
<td>R – Rifampicin</td>
<td>H – Isoniazid (INH)</td>
</tr>
<tr>
<td>Z – Pyrazinamide</td>
<td>E – Ethambutol</td>
</tr>
</tbody>
</table>

*RH (150/150 mg) should be used only when treatment is given THREE times weekly in the continuation phase (not recommended).

**Regimen 1 – New cases with age above 8 years and adults**
New smear-positive and new smear-negative patients with pulmonary and extrapulmonary TB:
Regimen 2 – Retreatment cases
Previously treated TB patients after cure, completion, interruption and failure:

<table>
<thead>
<tr>
<th>Pretreatment body weight</th>
<th>Two months initial phase treatment given five times a week</th>
<th>3rd month initial phase given five times a week</th>
<th>Five months continuation phase When given five times a week</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RHZE (150/75/400/275)</td>
<td>RHZE (150/75/400/275)</td>
<td>RH (150/75)</td>
</tr>
<tr>
<td></td>
<td>Streptomycin*</td>
<td></td>
<td>E (400)</td>
</tr>
<tr>
<td></td>
<td>2 tablets</td>
<td>2 tablets</td>
<td>RH (300/150)</td>
</tr>
<tr>
<td></td>
<td>500 mg</td>
<td>2 tablets</td>
<td>E (400)</td>
</tr>
<tr>
<td>30–37 kg</td>
<td>2 tablets</td>
<td>2 tablets</td>
<td></td>
</tr>
<tr>
<td>38–54 kg</td>
<td>3 tablets</td>
<td>3 tablets</td>
<td></td>
</tr>
<tr>
<td>55–70 kg</td>
<td>4 tablets</td>
<td>4 tablets</td>
<td></td>
</tr>
<tr>
<td>71 kg and over</td>
<td>5 tablets</td>
<td>5 tablets</td>
<td></td>
</tr>
</tbody>
</table>

* Do NOT give streptomycin during pregnancy and to those over 65 years.

16.11 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 a pleural 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 by ZN staining or culture 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 in the appropriate settings.

Treatment is as for pulmonary TB.

Note:
Total drainage by aspiration or under-water tube-drainage is not needed, unless an empyema develops.
A TB pleural empyema must be drained by intercostal under-water tube-drainage. There is no benefit of oral or intrapleural corticosteroids in the initial treatment phase.
REFERRAL
- non-resolving effusions. Suspect an incorrect diagnosis of TB pleurisy if the effusion does not clearly show signs of regression on the chest X-ray after at least 3 months of treatment.
- loculated TB empyema, not resolving after intercostal underwater tube drainage and needing assessment for surgical drainage.
- persistent bronchopleural fistula.

16.12 MULTIDRUG-RESISTANT (MDR) TB

**NEVER TREAT FOR MDR TB WITHOUT CULTURE AND SENSITIVITY RESULTS. ALL CASES SHOULD BE REFERRED TO A SPECIALISED CENTRE.**

**TREATMENT OF MDR TB SHOULD BE SPECIALIST INITIATED.**

DESCRIPTION
Multidrug resistant tuberculosis (MDR TB) is diagnosed when there is in vitro resistance of *M. tuberculosis* against, at least, rifampicin and isoniazid.

NON-DRUG TREATMENT
The cure rate of MDR TB in South Africa is only between 30–50% for first MDR treatments. With successive MDR treatments, the cure rates decrease considerably. Screen all close contacts for signs and symptoms of MDR TB and by sputum sampling to detect early disease.

DRUG TREATMENT TO PREVENT MDR TB
Treat all new cases of sputum positive tuberculosis with a regimen containing 4 agents for the full duration of the 2-months initial intensive phase followed by 2 agents for the full duration of the 4-months consolidation phase (see above). Never add a single agent to a TB treatment regimen that has, apparently, failed. Rather wait till 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.

Prolonged treatment, usually for at least 18 months, is required in patients diagnosed with MDR TB.

The treatment of MDR TB should be coordinated 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.

**Intensive phase: 4 monthly (daily)**

<table>
<thead>
<tr>
<th>Patient weight</th>
<th>Drug</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 50 kg</td>
<td>• kanamycin</td>
<td>750 mg</td>
</tr>
<tr>
<td></td>
<td>• ethionamide</td>
<td>500 mg</td>
</tr>
<tr>
<td></td>
<td>• pyrazinamide</td>
<td>1,000 mg</td>
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<tr>
<td></td>
<td>• ofloxacin</td>
<td>600 mg</td>
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<tr>
<td></td>
<td>• ethambutol</td>
<td>800 mg</td>
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<tr>
<td></td>
<td>OR terizadone*</td>
<td>750 mg</td>
</tr>
<tr>
<td>50–65 kg</td>
<td>• kanamycin</td>
<td>1,000 mg</td>
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<tr>
<td></td>
<td>• ethionamide</td>
<td>750 mg</td>
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<td></td>
<td>• pyrazinamide</td>
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<td></td>
<td>• ofloxacin</td>
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<td>• ethambutol</td>
<td>1,200 mg</td>
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<tr>
<td></td>
<td>OR terizadone*</td>
<td>750 mg</td>
</tr>
<tr>
<td>&gt; 65 kg</td>
<td>• kanamycin</td>
<td>1,000 mg</td>
</tr>
<tr>
<td></td>
<td>• ethionamide</td>
<td>750 mg</td>
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<td></td>
<td>• pyrazinamide</td>
<td>2,000 mg</td>
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<td>• ofloxacin</td>
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<td></td>
<td>• ethambutol</td>
<td>1,200 mg</td>
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<td></td>
<td>OR terizadone*</td>
<td>750 mg</td>
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</tbody>
</table>
Continuation phase: 12–18 months (daily), depending on culture conversion

<table>
<thead>
<tr>
<th>Patient weight</th>
<th>Drug</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 50 kg</td>
<td>• ethionamide</td>
<td>500 mg</td>
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<td></td>
<td>• ofloxacin</td>
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<td>• ethambutol</td>
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<tr>
<td>50–65 kg</td>
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<td>• ofloxacin</td>
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<td></td>
<td>• ethambutol</td>
<td>1 200 mg</td>
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<tr>
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</tr>
<tr>
<td>&gt; 65 kg</td>
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<td>750 mg</td>
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<td></td>
<td>• ofloxacin</td>
<td>800 mg</td>
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<tr>
<td></td>
<td>• ethambutol</td>
<td>1 200 mg</td>
</tr>
<tr>
<td></td>
<td>OR terizadone*</td>
<td>750 mg</td>
</tr>
</tbody>
</table>

* Use ethambutol if strain is still susceptible.
  Use terizadone if strain is resistant to ethambutol. If weight ≤ 35 kg, reduce dose to 500 mg. For patients on terizadone, give pyridoxine, oral, 150 mg daily.

In exceptional cases:
- Kanamycin may be substituted with amikacin.
- Ofloxacin may be substituted with ciprofloxacin.

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 have teratogenicity.
  In pregnant women, treatment should, therefore, be delayed until after the first trimester of pregnancy, unless the MDR is life threatening.
  Aminoglycosides are usually not used in pregnancy, as they may cause deafness in the newborn.
- Blood glucose, renal function and serum electrolytes should be carefully monitored in diabetic patients with MDR TB.
- The doses of medication used must be amended in patients with impaired renal function.

Reference: “Standardised Management of Multidrug Resistant Tuberculosis in South Africa” policy guidelines of the National Tuberculosis Control Programme of the National Department of Health.
CHAPTER 17
EAR, NOSE AND THROAT DISORDERS

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.

NON-DRUG TREATMENT
Secure the airway.
Humidified oxygen.
Adequate hydration.

DRUG TREATMENT
3rd 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, 625 mg 8 hourly for 10 days
Severe β-lactam allergy:
• chloramphenicol, IV, 1 g 6 hourly for 5–10 days

IN THE 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 1:1 000, nebulised
  Dilute to 5 mL with sodium chloride 0.9% and administer 4–6 hourly.

17.2 EPISTAXIS
R04.0

NON-DRUG TREATMENT
Control bleeding by applying digital pressure over the cartilaginous part of the nose.
Tilt head forward and not backwards to avoid pooling of blood in the posterior pharynx. Resuscitation, 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).
CHAPTER 17  EAR, NOSE AND THROAT DISORDERS

Posterior bleeding: insert a posterior nasal pack, using a Foley’s catheter. An anterior nasal pack should then be inserted. A posterior nasal pack should not be left in place for more than 48 hours. Deflate after 24 hours.

REFERRAL
- persistent bleeding
- systemic disease

17.3 RHINITIS, ALLERGIC, PERSISTENT
J30.4

NON-DRUG TREATMENT
Avoid allergens and irritants.

DRUG TREATMENT
- chlorpheniramine, oral, 4 mg three times daily

For patients intolerant to chlorpheniramine:
- cetirizine, oral, 10 mg daily

- corticosteroids, topical, aqueous nasal solution, 2 sprays in each nostril twice daily

17.4 SINUSITIS, BACTERIAL, COMPLICATED
J01.9

DESCRIPTION
Acute bacterial sinusitis complicated by extension to the orbit or intracranially. Extension to the orbit gives rise to 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 result in meningitis, subdural empyema, brain abscess, or thrombosis of cavernous sinus/cortical veins. Radiography of the paranasal sinuses, preferably by CT scan, should be done in all cases.

In immunosuppressed or diabetic patients presenting with features of bacterial sinusitis also consider fungal infections such as mucormycosis.

NON-DRUG TREATMENT
Sodium chloride 0.9% spray or irrigation of the nasal cavity may provide symptomatic relief.

DRUG TREATMENT
- ceftriaxone, IV, 2 g 12 hourly and refer

Topical nasal decongestants, e.g.:
- oxymetazoline 0.05%, intranasal, administered 8 hourly
CHAPTER 17  EAR, NOSE AND THROAT DISODERS

URGENT REFERRAL
- proptosis
- ophthalmoplegia

REFERRAL
- after initiating antimicrobial therapy to a centre where an appropriate surgical specialist, i.e. ophthalmologist, ENT specialist or neurosurgeon, is available
- suspected fungal sinusitis

17.5 OTITIS MEDIA
H66.9

NON-DRUG TREATMENT
Do not instil anything into the ear.
Avoid getting the inside of the ear wet.

DRUG TREATMENT
- amoxicillin, oral, 500 mg 8 hourly
  Uncomplicated cases: 5 days.
  Complicated cases and those with risk factors: 10 days.

Penicillin allergy:
- erythromycin, oral, 500 mg 6 hourly for 10 days
- chlorpheniramine, oral, 4 mg three times daily

For pain:
- paracetamol oral, 1 g 6 hourly as needed

REFERRAL
- perforation of the eardrum
- no response after 5 days treatment
- no pain relief
- bulging eardrum, not responding to treatment after 24 hours
- recurrent otitis media

17.6 MASTOIDITIS
H70

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.

DRUG TREATMENT
- ceftriaxone, IV, 2 g 12 hourly
CHAPTER 17  EAR, NOSE AND THROAT DISODERS

REFERRAL
- after initiating antimicrobial therapy, to a centre where mastoidectomy can be performed

17.7 OTITIS EXTERNA

17.7.1 OTITIS EXTERNA, NECROTISING
H60.9

DESCRIPTION
Necrotising otitis externa is typically associated with elderly diabetics or other immunocompromised patients. Patients complain of otalgia and otorrhea persisting more than a month, which is unresponsive to medical therapy. Nearly always due to P. aeruginosa. Cranial nerve palsies frequently occur, especially 7, but also 9, 10 and 12.

NON-DRUG TREATMENT
Debridement as indicated.
Insert dry wick such as a dried sponge, into the canal under direct vision. Remove wicks 2 days later, and replace if necessary.

DRUG 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

17.8 ABSCESS, PERITONSILLAR
J36

DESCRIPTION
Peritonsillar abscess or quinsy is a collection of pus lateral to the tonsil, i.e. underneath it pushing it toward the midline. It typically present with trismus and sore throat. Other features include:
- unilateral throat pain
- dysphagia
- drooling
- muffled voice ("hot potato" voice)
- fever

NON-DRUG TREATMENT
There are 3 main methods:
- needle aspiration of pus
- incision and drainage
- abscess tonsillectomy, either unilateral or bilateral
CHAPTER 17  EAR, NOSE AND THROAT DISODERS

DRUG TREATMENT
Antibiotic therapy
Total duration of therapy: 10 days

• benzylpenicillin (Penicillin G), IV, 2 million units 6 hourly
  Follow with:
  • phenoxyethylpenicillin, oral, 500 mg 12 hourly

Penicillin allergy:
• clindamycin, IV, 600 mg 8 hourly
  Follow with:
  • clindamycin, oral, 300 mg 8 hourly

17.9 VERTIGO, ACUTE
R42

DESCRIPTION
An acute syndrome, consisting of vertigo, nystagmus, nausea and 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 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.

NON-DRUG TREATMENT
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.
CHAPTER 17  EAR, NOSE AND THROAT DISORDERS

DRUG 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.

• chlorpheniramine, oral, 4 mg 6 hourly
  Beware of side effects, related to antimuscarine effects in patients with glaucoma and prostatic enlargement.
  Sedation may be an additional problem.

If vomiting continues:
• metoclopramide, oral, 10 mg 6–8 hourly

CEREBELLAR STROKE
See Section 14.1: Cerebrovascular Disease

REFERRAL
  o suspected intracranial mass lesions or cerebellar stroke as indicated
  o suspected vestibular neuritis
  o patients not responding to therapy for exclusion of alternative aetiology
18.1 CONJUNCTIVITIS

DESCRIPTION
Inflammation of the conjunctiva, usually due to allergy or infection (viral or bacterial). Conjunctivitis is usually bilateral. Other causes of the red eye are often unilateral.

NON-DRUG TREATMENT
Supportive therapy with cold compresses.

If it is due to an infection, counsel on the importance of:

- frequent hand washing by patients and family members
- using separate linen, towels and washcloths
- 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

DESCRIPTION
Adenovirus is the most common cause of infective conjunctivitis. It is usually bilateral. It may be associated with a upper respiratory infection. There may be preauricular lymphadenopathy.

DRUG TREATMENT
- sodium chloride 0.9%, eye washes or irrigations
  - If sodium chloride 0.9% is not available use cooled boiled water or sterile water.
- oxymetazoline 0.025%, ophthalmic drops, 6 hourly for 7 days

18.1.2 CONJUNCTIVITIS, ALLERGIC

DESCRIPTION
There is moderate to severe itching. It may be associated with hay fever or other features of allergy. There may be acute inflammation of the conjunctiva, or chronic cobblestone elevations of the tarsal conjunctiva or chronic thickening and discoloration of the perilimbal conjunctiva.
CHAPTER 18

DRUG TREATMENT

Drug treatment should be for short-term use.

For relief of mild symptoms:
- oxymetazoline 0.025%, ophthalmic drops, instill 1–2 drops 4 times daily – short term use

For relief of symptoms in moderate and severe cases:
- fluoromethalone, ophthalmic drops, instill 1–2 drops 4 times daily – short term use

For control of allergic response in chronic cases:
- sodium chromoglycate 2%, ophthalmic drops, instill 1–2 drop 4 times daily

Note:
Topical corticosteroids are contraindicated if there is no facility for slit lamp biomicroscopic examination of the eye.

18.1.3 CONJUNCTIVITIS, BACTERIAL

H13.1*

DESCRIPTION

The following organisms may be involved:
- *S. aureus*  
- *H. influenzae*  
- *S. pyogenes*  
- *Moraxella* species  
- *S. pneumoniae*  
- *N. gonorrhoeae*  
- *Pseudomonas* species

It is usually bilateral. There is a mucopurulent discharge and there may be matting of lashes in the morning. The eyelid may be swollen.

DRUG TREATMENT

- gentamicin, ophthalmic drops, instill 1 drop 4–6 hourly during the day  
  OR  
  chloramphenicol 1%, ophthalmic drops, instill 1 drop 4–6 hourly during the day  
  AND  
  chloramphenicol 1%, ophthalmic ointment, apply at night

18.2 ENDOPHTHALMITIS, BACTERIAL

DESCRIPTION

Infection of the ocular cavity, which is an emergency as it can cause serious visual disturbances. This may occur spontaneously or post-surgery.

Spontaneous endophthalmitis is generally caused by haematogenous spread in acutely ill bacteraemic patients. Usual organisms are *S. pneumoniae* and *N. meningitides*.

Post-surgical causative organisms include *S. aureus*, *P. aeruginosa*, and proteus.
**CHAPTER 18**

**EYE DISORDERS**

**DRUG TREATMENT**

**SPONTANEOUS ENDOPHTHALMITS**

- ceftriaxone, IV, 2 g daily for 7 days

**POST-SURGICAL ENDOPHTHALMITS**

Specialist initiated, vitrectomy often required.

- ceftazidime, intravitreal, 2.25 mg
- vancomycin, intravitreal, 1 mg

In addition, if there is soft tissue involvement:

- ciprofloxacin, oral, 750 mg 12 hourly may be added

**18.3 GLAUCOMA**

**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:
- most common
- 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:
- sudden onset of severe pain and eye redness, associated with nausea and vomiting
- 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.

**DRUG TREATMENT**

**OPEN ANGLE GLAUCOMA, CHRONIC**

Refer to an ophthalmology unit for treatment.
First line

ß-blocker

Non-selective, e.g.:
• timolol 0.25%, ophthalmic drops, instill 1 drop twice daily

Selective, e.g.:
• betaxolol 0.5%, ophthalmic drops, instill 1 drop twice daily
  Fewer pulmonary side effects with the use of this drug.

Second line

Prostaglandin analogues, e.g.:
• latanoprost, ophthalmic drops, instil 1 drop once daily
  Use as first line if patient has contra-indication to use of ß-blocker.
  Use in place of ß-blocker if patient has intolerable side effects with ß-blocker or
  if there is no significant reduction in IOP with ß-blocker alone.
  Use in combination with ß-blocker if there is significant reduction in IOP on ß-
  blocker, but patient still has progression of disease or target IOP is not reached
  on ß-blocker alone.

In severe cases, carbonic anhydrase inhibitors:
• acetazolamide, oral, 250 mg 6 hourly
  Use if intra-ocular pressure is not controlled on all the above – usually as a
  temporising measure before ocular surgery.

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
• timolol 0.25% or 0.5%, ophthalmic drops, instill 1 drop twice daily

Treat patient for associated pain and nausea.

Where these measures fail:
• mannitol, IV, 1.5–2 g/kg as a 20% solution over 30–60 minutes for short-term use only
  OR
  glycerin, oral, diluted to 50% solution, 1–1.5 g/kg, for short-term use only

To constrict the pupil (open the angle), once the IOP has dropped:
• pilocarpine 2%, ophthalmic drops, instill 1 drop every 6 hours

REFERRAL
• all to ophthalmology unit
CHAPTER 18  

18.4 HERPES ZOSTER OPHTHALMICUS

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. Patients < 50 years old should be offered HIV testing.

DRUG TREATMENT
• aciclovir, oral, 800 mg five times daily for 7–10 days

For neuralgic pain:
• amitriptyline, oral, 25 mg at night for 3 months

For skin lesions:
• potassium permanganate. 1:10 000 aqueous solution, topical, cleanse twice daily
PLUS
• silver sulphadiazine, topical, apply twice daily after cleansing

Follow patient weekly until skin lesions healed.

Best results are obtained if treatment is initiated within the first three days of onset of symptoms.

REFERRAL
○ fluorescein uptake by the cornea (keratitis)
○ decreased vision, i.e. a 2 line fall off in Snellen acuity in affected eye compared to healthy eye
○ afferent pupil defect
○ signs of uveitis

18.5 KERATITIS

18.5.1 KERATITIS, HERPES SIMPLEX

DESCRIPTION
Associated features: previous history often, decreased corneal sensation. Morphology: dendritic ulcer seen on staining with fluorescein.
CHAPTER 18  

EYE DISORDERS

DRUG TREATMENT
• aciclovir ophthalmic ointment inserted in the lower cul-de-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 RVD + or history of injury to eye with plant matter, need high index of suspicion for fungal infection.

DRUG TREATMENT
Treat only if access to slit lamp, otherwise refer.  
Scrape ulcer for microscopy, culture and sensitivity and modify treatment accordingly.

• ciprofloxacin, ophthalmic drops, instill 1 drop hourly for 3 days then reduce frequency to 1 drop 3–4 hourly  
  OR  
  ofloxacin, ophthalmic drops, instill 1 drop hourly for 3 days then reduce frequency to 1 drop 3–4 hourly

If gram positive cocci:
ADD
• vancomycin 25 mg/mL, topical

If fungal infection, change to:
• natamycin 5%, ophthalmic drops, instill 1 drop 1–2 hourly, initially  
  After 3–4 days 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
CHAPTER 18  
EYE DISORDERS

18.6 RETINITIS, HIV CMV  
h30.9

DESCRIPTION
CMV retinitis is seen in advanced HIV, with CD4 count < 100. The characteristic appearance is necrosis, i.e. white exudates, and hemorrhages at the edges of the exudates. Irreversible blindness occurs once the optic disk is involved.

DRUG TREATMENT
• ganciclovir, intravitreal, 200 mcg once a week  
  Once immune function has been restored with antiretroviral therapy, i.e. CD4 >100, maintenance ganciclovir can be stopped but monitor for recurrence.

18.7 UVEITIS  
H20.0

DESCRIPTION
An 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, circumciliariy 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.  
This condition should be managed at an ophthalmology unit.

DRUG TREATMENT
Cycloplegic agents, e.g.:
• homatropine 5%, ophthalmic drops, instill 1–2 drops 3–4 hourly
AND
Corticosteroids, e.g.:
• prednisolone 1%, ophthalmic drops, instill 1–2 drops 4 times daily
CHAPTER 19
POISONING

19.1 ENVENOMATION

19.1.1 INSECT BITES AND STINGS
T63

DESCRIPTION
Insect bites and stings usually have local effects. Systemic effects are rare. Local inflammatory or systemic/immunological forms of toxicity are encountered, which may vary between minor local reactions and acute anaphylaxis.

Multiple bee stings may require ICU care.

NON-DRUG TREATMENT
Observe patient for sufficient period of time, as a rapid worsening in the condition may occur and the effects of treatment may be transient.

DRUG TREATMENT
ANAPHYLAXIS
See Section 20.1: Anaphylaxis/Anaphylactic Shock.

19.1.2 SNAKE BITES
T63.0

NON-DRUG TREATMENT
Minimise movement of affected limb.
Emergency treatment by bandaging affected limb with a crepe bandage without compromising blood supply.
Observe patient closely for a period of 24 hours after contact.
Do not apply a tourniquet.
Sucking or cutting the wound has not been found to be of any benefit.

COBRA AND MAMBA
Application of a tight crepe bandage proximal to the bite-site may be life saving.
The venom of cobras and mambas bites is predominantly neurotoxic. Ventilatory and cardiovascular support may be needed in an ICU.
If venom occurs in the eyes, irrigate extensively with copious amounts of water for 15–20 minutes.

BOOMSLANG OR BERGADDER
The venom of boomslang is haemotoxic.
Observe for 36 hours.

VIPERS AND ADDERS
The venom of vipers and adders is predominantly cytotoxic.
Crepe bandaging is inappropriate in all cases of cytotoxic snakebites.
Surgical intervention, i.e. decompression surgery for established compartment syndrome and debridement of necrotic tissue should be done only when absolutely necessary and as conservatively as possible.
CHAPTER 19

DRUG TREATMENT

Cleanse wound:
• chlorhexidine 0.05% in water

Secondary infection:
• amoxicillin/clavulanic acid, oral, 375 mg 8 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

Intravenous Fluids
Reverse circulatory shock, if present.

Analgesia
For mild pain:
• paracetamol, oral, 1 g 4–6 hourly as needed
OR
For severe pain:
Opioids, e.g.:
• morphine, slow IV, 3–10 mg in increments of 2 mg
  Dilute morphine to 10 mL with water for injection or sodium chloride 0.9%.
  Beware of respiratory arrest and hypotension when administering high dose
  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 full details in package insert.
Effective against the venom of:
o puff adder
o gaboon adder
o rinkhals
o Cape cobra
o Egyptian cobra
o black necked spitting cobra
o forest cobra
o black and green mamba

It is ineffective against the venom of:
o night and berg adder and other minor adders
o boomslang
o vine and twig snakes
CHAPTER 19 POISONING

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 relatively common, especially after administration of large doses of antivenom

Criteria for antivenom administration:
- all patients with confirmed mamba bites should receive antivenom, even before onset of symptoms
- patients with confirmed gaboon adder or puff adder bites should receive antivenom at the onset of any symptoms

Signs of systemic poisoning:
- muscle weakness and/or difficulty in breathing
- difficulty in swallowing
- weakness
- double vision
- 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 extends 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

- 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 until the infusion is completed 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. May be repeated - See package insert.
CHAPTER 19  POISONING

BOOMSLANG POISONING
Envenomation rarely occurs, causing disseminated intravascular coagulation usually a few days later but has occurred within hours in isolated cases.
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 test tube and leave at room temperature for 20 minutes. Normal clotting time varies from 5–20 minutes. The initial blood clotting parameters may be normal.
It is important to follow these over a few days.
Special investigations include FBC, activated PTT, Prothrombin time (INR), fibrinogen, D-dimer and monomers.
Correct haematological abnormalities.

Boomslang antivenom
Obtainable from SA Vaccine Producers - See full details in package insert.
Do not administer polyvalent antivenom.

| 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

19.1.3 SCORPION ENVENOMATION
T63.2

DESCRIPTION
Poisonous scorpions in Southern Africa are of the Genus Parabuthus. Features useful in its identification are a relatively large tail and small pincers.
The venom typically causes immediate pain, followed by systemic symptoms within 1–4 hours. These include:
- general paraesthesias
- muscle cramps
- pain
- excessive sympathetic stimulation
Dysphagia, dysarthria and loss of pharyngeal reflexes with possibly respiratory impairment may be encountered.

NON-DRUG TREATMENT
Observe all cases for 12–24 hours.
Ventilatory support may be required in severe cases.

DRUG TREATMENT
Routine antivenom therapy is recommended only in severe cases with systemic signs.
- 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
CHAPTER 19 POISONING

Never administer antivenom without being fully prepared to manage acute anaphylaxis.

Immunisation, primary or booster:
• tetanus toxoid vaccine, IM, 0.5 mL immediately

In unimmunised or partially immunised patients:
• tetanus immunoglobulin, human, IM, 250 units

Intravenous Fluids
Reverse circulatory shock, if present.
Monitor response.

Analgesia
Analgesics such as paracetamol and opiates have not been shown to be effective.

“Ring block”
• lidocaine (lignocaine) 1–2%, 2 mL injected around the bite as local anaesthetic

Severe muscle pain and cramps:
• calcium gluconate 10%, bolus IV infusion, 10 mL over 10 minutes
  Followed by 60–120 mL diluted in 1 L sodium chloride 0.9%, administered over 12–24 hours.
  May need to be repeated frequently, i.e. every 20–30 minutes.
  Only moderately effective.

19.1.4 SPIDER ENVENOMATION

BLACK WIDOW SPIDER
Features useful in the identification of black widow spiders are black or dark brown colour with variable red markings on the dorsal aspect of the abdomen, which diminish with age and no ventral markings. Is to be differentiated from Latrodectus geometricus with a geometric hourglass shaped marking on the ventral abdomen and much less potent venom.
The venom typically causes:
• 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, as well as neurological hyperreactivity.
Pain increases with time and may last for days to a week if antivenom is not given
Secondary infection with cellulitis is a common complication.

Other spider species, may cause cytotoxic damage.

NON-DRUG TREATMENT
Observe all cases for 12–24 hours.
CHAPTER 19 POISONING

DRUG 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

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
  Followed by 60–120 mL diluted in 1 L sodium chloride 0.9%, administered over 12–24 hours.
  May need to be repeated frequently, i.e. every 20–30 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

Intravenous Fluids
Reverse circulatory shock, if present.
Monitor response.

Analgesia
For mild pain:
• paracetamol, oral, 1 g 4–6 hourly as needed
  Opioids and NSAIDS have not been shown to be effective.

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.

South African Vaccine Producers (Pty) Ltd

1 Modderfontein Road
Sandringham, Johannesburg
Tel: (011) 386 6000
Fax: (011) 386 6016
After hours: 082 905 3329
http://www.savp.co.za/

Products
Polyvalent snake venom (10 mL)
Boomslang antivenom (10 mL)
Spider antivenom (Latrodectus indistinctus) (5 mL)
Scorpion antivenom (Parabuthus spp.) (5 mL)
CHAPTER 19

19.2 EXPOSURE TO POISONOUS SUBSTANCES

GENERAL MEASURES

- Limit further exposure to toxin. In case of skin exposure, wash body and remove clothes. Showering may be useful. Eye contaminants, especially alkalis, acids and other irritants, should be removed by continuous irrigation of the eye for 15–20 minutes.
- 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.
- Limit the use of toxicology investigations to those that may influence/alter management. Avoid non-specific toxicology screens.
- Establish baseline laboratory values. Quantify toxin level in blood, to monitor progress where relevant and follow urine and electrolytes, pH and blood gases, glucose and others, as indicated.
- Maintain and follow basic clinical parameters, i.e.:
  - pulse rate
  - blood pressure
  - hydration
  - ventilation
  - patent airway and oxygenation
  - control seizures and prevent physical injury in the restless. Avoid excessive sedation.

INITIATION OF TREATMENT

Neutralise poison
Administer only if patient has ingested a potentially toxic amount of a poison which is known to be adsorbed by charcoal. Administer within 1–2 hours after ingestion of poison.
- charcoal, activated, oral, 50–100 g diluted in 300–600 mL water
  In poisoning with large amounts and/or slow release formulations, repeat at least 12.5 mg hourly.
  When mixing, add charcoal to water and not vice versa.

Alkalisation
Possible 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 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.
CHAPTER 19 POISONING

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 7.5 or higher.

Haemodialysis
PATIENT SHOULD BE REFERRED TO A TERTIARY (DIALYSIS) CENTRE.
Limited to a number of agents, i.e. salicylates, lithium (serum levels over 4.0 mmol/L), ethylene glycol, methanol, ethanol and theophylline that does not respond to initial/alternative management.

Charcoal haemoperfusion may be of benefit in cases of extremely high theophylline levels, benzodiazepine, carbamazepine and methaqualone poisoning.

REFERRAL
- severely ill patient for ventilatory/circulatory support
- relevant diagnostic testing not available, e.g. paracetamol levels
- relevant medication/antidotes is not available
- where dialysis/haemoperfusion is required
- for psychiatric evaluation

19.3 SPECIFIC POISONINGS

19.3.1 BENZODIAZEPINE POISONING
T42.4

DESCRIPTION
Patients present with depressed mental and respiratory function. Benzodiazepines are unlikely to cause significant respiratory suppression on their own.

Management is supportive. Ventilatory support may be required.

19.3.2 CARBON MONOXIDE POISONING
T58

DESCRIPTION
Poisoning caused by accidental or suicidal exposure to fires in poorly ventilated areas, combustion engines, faulty stoves and faulty heating systems.
CHAPTER 19 

POISONING

Patients present with:
- dizziness
- seizures and other CNS symptoms
- nausea
- vomiting
- retinal haemorrhages
- impaired level of consciousness
- cherry red skin and lips
- tachycardia
- ECG changes
- normal arterial PO₂ but low oxygen saturation
- high arterial carboxyhaemoglobin - test not commonly available

NON-DRUG TREATMENT

Remove patient from toxic environment.
Oxygen via facemask.
Ventilation may be needed in deeply comatose patients.

In a Cochrane review, hyperbaric oxygen therapy has not been shown to be of benefit.

DRUG TREATMENT

For seizures:
- diazepam, slow IV, 10 mg

19.3.3 INGESTION OF CAUSTIC SUBSTANCES

DESCRIPTION

Alkaline: Detergent, toilet bowl cleaners and liquid drain cleaners.

Acids: Various.
Causes tissue necrosis of gut resulting in strictures later.

NON-DRUG TREATMENT

No emesis or gastric lavage.
Rinse mouth with copious amounts of cold water.
Patients require urgent endoscopical evaluation and possible surgical intervention.

19.3.4 COCAINE POISONING

DESCRIPTION

Cocaine may be absorbed through any mucous membrane, smoked or injected intravenously. Persons who smuggle cocaine, may ingest packets of this agent.
Patients may present with one or more of the following:
- acute myocardial infarction
- cardiac dysrhythmias
- tachycardia and hypertension
- stroke
- seizures
- alterations in mood and confusion
- pulmonary oedema
- rhabdomyolysis with acute renal failure and intestinal ischaemia
CHAPTER 19  POISONING

NON-DRUG TREATMENT
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. The ECG may be normal in some cases of acute myocardial infarction.
For severe dysrythmias, DC cardioversion.
Note:
Lidocaine (lignocaine) may precipitate seizures.
ß–blockers may aggravate hypertension and myocardial ischaemia.

DRUG TREATMENT
For sedation or seizures:
• diazepam, IV, 10 mg

STATUS EPILEPTICUS
See Section 14.4.1: Status Epilepticus.
Psychosis or delirium with severe agitation:
• haloperidol, IM, 2–5 mg
  OR
  lorazepam, IM, 2 mg
Severe hypertension:
• labetalol, IV, 2 mg/minute to a maximum of 1–2 mg/kg
As relatively unopposed stimulation of alpha-receptors may result, this should be preceded by:
• chlorpromazine, IV, 25 mg

19.3.5 ETHANOL POISONING
T51.0

DESCRIPTION
Acute poisoning usually presents with:
o central nervous system depression
o hypoglycaemia
o hypothermia
o changes in fluid and electrolyte status such as hypokalaemia and hyponatraemia
High levels of ethanol may influence the osmolar gap and cause a pseudohyponatraemia.
See Section 19.3.6: Ethylene Glycol Poisoning.
Consider other causes for the patient’s condition, including hypoglycaemia and head trauma.
CHAPTER 19 POISONING

NON-DRUG TREATMENT
Supportive management aimed at maintaining stable cardiorespiratory function. Manage hypothermia.

DRUG TREATMENT
• thiamine, IV, 100 mg in 1 L dextrose 5%

19.3.6 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:
 o resembles alcohol intoxication
 o vomiting
 o later hypotension
 o cardiac failure
 o oliguric renal failure
 o significant metabolic acidosis with a large anion gap, i.e.:
   \[ ([Na^+] – [Cl^-] – [HCO_3^-] > 12) \]
 o hypocalcaemia
 o a higher measured serum osmolality when compared to the calculated equivalent
 o oxalate crystals in urine

DRUG TREATMENT
In acidotic patients, haemodialysis is the treatment of choice.

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 ± 40% (80 proof), at the above oral dose.
CHAPTER 19 POISONING

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 ultimate goal is a pH of not more than 7.2.

- sodium bicarbonate, IV, 50–100 mmol/L administered over 30–45 minutes

Note: The rapid infusion of large volumes in an already oliguric patient may precipitate pulmonary oedema and cardiac dysrhythmias.

Correct hypoglycaemia.
Correct severe or clinical evident hypocalcaemia.

19.3.7 HEAVY METALS: MERCURY, ARSENIC, GOLD, COPPER AND LEAD POISONING

T56.1/T57.0/T56.8/T56.4/T56.0

DESCRIPTION
Acute toxicity of organ-systems may be summarised as follows:

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<tr>
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<th>Pneumonitis</th>
<th>GIT</th>
<th>Blood cells</th>
<th>CVS collapse</th>
<th>Kidneys</th>
<th>Hepato toxicity</th>
<th>CNS</th>
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</table>

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 and 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.
CHAPTER 19

Penicillamine
Penicillamine also chelates metals.
Indicated in copper, mercury, arsenic, zinc and lead poisoning.
• penicillamine, oral, 0.5–1.5 g/day in 4 divided doses

19.3.8 HYDROCARBON POISONING

DESCRIPTION
Poisoning due to petroleum products, including paraffin, turpentine, petrol, mineral spirits and halogenated hydrocarbons.
Clinical signs:
  o aspiration pneumonia
  o GIT effects
  o arrhythmias
  o CNS effects

NON-DRUG TREATMENT
If contaminated, remove clothing and wash skin.
Do not attempt gastric emptying/lavage.

DRUG TREATMENT
The usefulness of activated charcoal is limited.
Observe and examine for aspiration pneumonia. Prophylactic antibiotics are not indicated.

19.3.9 IRON TOXICITY

DESCRIPTION
Iron is a commonly prescribed drug, especially in pregnancy, and causes initial gastrointestinal toxicity.
More significant exposure may be associated with:
  o metabolic acidosis
  o hypotension
  o CNS side effects
  o renal failure
  o hepatitis

DRUG TREATMENT
Chelation therapy
Patients with serum iron levels < 54 micromol/L and absence of symptoms more than 6 hours after overdose do not require chelation therapy.
CHAPTER 19  POISONING

- desferrioxamine, IV, 1–2 g every 3–12 hours to a maximum of 6 g every 24 hours

For levels > 180 micromol/L, consider exchange transfusion.

If serum iron levels are not available and the probability of this poisoning is high administer a single dose of desferrioxamine 1 g and 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.

19.3.10 POISONING WITH AMPHETAMINE DERIVATIVES

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 effects on dopaminergic and serotonergic neurons in the CNS and include:
- hyperthermia, especially with Ecstasy
- tachycardia
- hypertension
- angina pectoris and myocardial infarction
- stroke
- hyperactivity
- delirium
- tremors
- seizures and coma.

Further complications include:
- rhabdomyolysis, which presents with elevated serum creatine kinase
- hyperkalaemia
- later acute tubular necrosis
- potentially fatal hyponatraemia
- dehydration

NON-DRUG TREATMENT
Supportive management aimed at maintaining stable cardiorespiratory function. Manage hypothermia, hypoglycaemia and fluid and electrolyte status.

DRUG TREATMENT
Haemodialysis may be required for acute renal failure.

For seizures:
- diazepam, IV, 10 mg
CHAPTER 19

Severe hypertension:
• labetalol, IV, 2 mg/minute to a maximum of 1–2 mg/kg
As relatively unopposed stimulation of alpha-receptors may result, this should be preceded by:
• chlorpromazine, IV, 25 mg

19.3.11 METHANOL POISONING
T51.1

DESCRIPTION
Previously found in methylated spirits but has recently been replaced with less toxic agents. Presents with:
  o initially, CNS and GIT effects
  o later, large anion gap (> 12), metabolic acidosis, retinal toxicity and renal failure due to formic acid production.

DRUG TREATMENT
If acidotic and there is an osmolar gap, \[\text{measured osmolarity minus calculated (2} \{\text{sodium+potassium}\} + \text{urea+ glucose)}\], start dialysis urgently, if available.

If dialysis not available, use ethanol.
See Section 19.3.6: Ethylene Glycol Poisoning.

19.3.12 POISONING WITH NITRITES, NITROPRUSSIDE, NITROGLYCERINE CHLORATES, SULPHONAMIDES AND OTHERS
D74.8/D74.9

DESCRIPTION
Nitrites are used to cure meat in the informal butchery sector. Patients present with:
  o normal oxygen levels and deep central cyanosis, due to methaemoglobinemia
  o CNS depression
  o arrhythmias.
Note:
The measured PO$_2$ is normal and that only the pH and a directly measured oxygen saturation give an indication of severity.

NON-DRUG TREATMENT
Oxygen via facemask.

DRUG TREATMENT
In symptomatic cases or patients with high methaemoglobin values > 30%:
• methylene blue (tetramethyl thionine chloride) 1% dilute solution, slow IV infusion, 1–2 mg/kg administered over 5 minutes
  Repeat in 1 hour and if necessary every 4 hours up to total of 7 mg/kg.
Side effects include precordial pain, restlessness and dyspnoea.
CHAPTER 19 POISONING

In severe cases, not responding to methylene blue or if methylene blue is not available, consider exchange transfusion. Administration of ascorbic acid (vitamin C) has not been shown to be effective, mainly due to slow onset of effect.

19.3.13 OPIOID POISONING

DESCRIPTION
Poisoning due to morphine, pethidine, methadone (long-acting) and heroin ingestion. Patients present with:
- especially respiratory depression, and/or CVS-, and/or CNS depression
- miosis.
Non-cardiogenic pulmonary oedema may be present.

NON-DRUG TREATMENT
Supportive management aimed at maintaining cardiorespiratory function.

DRUG TREATMENT
- naloxone, IV, 0.4–2 mg immediately
  Repeat 0.4 mg every 5 minutes until reversal or pupils dilate.
  Total effective dose is 10 mg.
  May be administered endotracheally.
  Duration of action is short, i.e. 45 minutes. Repeat doses over 24 hours may be required.

19.3.14 ORGANOPHOSPHATE POISONING

DESCRIPTION
Poisoning due to parathion, malathion and other insecticides, possibly in hydrocarbon solvent. Absorption occurs through the skin or agent is taken orally. Patients present with muscarinic and/or 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. May be confirmed by measuring red cell pseudocholinesterase levels - serum levels are unreliable.

NON-DRUG TREATMENT
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.
CHAPTER 19

DRUG TREATMENT

- atropine, IV, 1 mg, initial dose
  Follow with 0.05 mg/kg every 15 minutes.
  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.
  Atropine therapy should not be stopped abruptly and should be weaned at a rate of no more than 1–2 mL/hour. During this phase it is important to follow the patient as a worsening in condition commonly occurs a few days following ingestion.

19.3.15 PARACETAMOL POISONING

DESCRIPTION

The liver is the main organ acutely damaged in paracetamol poisoning. Acute ingestion of doses of 7.5–15 g in a healthy adult may cause severe centrilobular hepatic necrosis. In patients on enzyme inducers, particularly alcohol, lower doses of paracetamol cause damage. Renal tubular necrosis may also develop. Hepatic and renal failure typically manifest after 2–5 days.

Clinical features

Within 0.5–24 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. Activated charcoal should be administered within 1–2 hours after overdose.

24–48 hours after overdose

Signs and symptoms may be less pronounced, but the blood chemistry may become abnormal. In severe intoxication, the clinical picture of progressive liver failure develops within 2–5 days.

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. Levels < 120 mcg/mL at 4 hours are unlikely to be associated with hepatotoxicity. For reliable hepatotoxicity risk assessment, blood for plasma paracetamol levels should be drawn 4 hours post ingestion or as possible thereafter as this represents peak levels.

If paracetamol levels are in the toxic range, defined as above the predictive graph line joining 150 mcg/mL at 4 hours and 20 mcg/mL at 15 hours after ingestion on the Rumack-Matthew nomogram, liver function tests (ALT) should be performed daily. With significant hepatitis, investigate degree of liver failure with INR and refer patient for further management, which may involve liver transplant. Patients with 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.
CHAPTER 19 POISONING

Monitor renal function and serum potassium in patients with significant toxicity.

DRUG TREATMENT

Acetylcysteine

Acetylcysteine is the antidote of choice and should be given intravenously. Although it is more effective when given within 8 hours of ingestion of paracetamol, there may be benefit even if liver failure has developed. It is never too late to administer acetylcysteine.

Indications for acetylcysteine

Administer without waiting for plasma paracetamol levels in substantial overdose, defined as 7.5 g or 125 mg/kg, whichever is smaller. Discontinue if plasma levels are in the non-toxic range.

Administer immediately if there is doubt about the time interval since ingestion. Do not use the Rumack-Matthew nomogram.

Give to patients presenting 24 hours or later after an overdose, who have detectable plasma paracetamol levels or biochemical evidence of hepatotoxicity.

Acetylcysteine therapy is necessary if the initial paracetamol level is in the toxic range.

Paracetamol toxicity develops 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 for instituting antidote therapy should be used, i.e. 25% lower than the line joining 150 mcg/mL at 4 hours and 20 mcg/mL at 15 hours.

- acetylcysteine, IV, 150 mg/kg in 200 mL dextrose 5% over 15 minutes 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 less severe cases of allergy administer the loading dose over 1–2 hours under antihistamine cover and continue at a lower infusion rate.
19.3.16 SALICYLATES OR NSAID POISONING

T39/T39.3

DESCRIPTION
Patients present with:
- nausea
- vomiting
- CNS depression
- respiratory alkalosis followed by metabolic acidosis or one or both disorders
- tinnitus
- convulsions
- non cardiogenic pulmonary oedema

Modified and reproduced from Rumack BH, Matthew H: Acetaminophen poisoning and toxicity. Paediatrics 1975; 55:871
CHAPTER 19  
POISONING

NON-DRUG TREATMENT
Consider ICU admission for pulmonary and/or cerebral oedema.

DRUG TREATMENT
Alkalisation often with potassium replacement. Exercise caution in patients with respiratory alkalosis.
Monitor closely with laboratory data, where available.

Where acidosis does not respond rapidly to sodium bicarbonate, consider haemodialysis.

19.3.17 THEOPHYLLINE POISONING
T44.9

DESCRIPTION
Patients present with:
- tachycardia and tachydysrhythmias
- vomiting
- agitation
- seizures
- nausea
- abdominal pain
- restlessness
- profound hypokalaemia

NON-DRUG TREATMENT
Monitor cardiac function and treat dysrhythmias.
Monitor and correct fluid status and other electrolyte abnormalities.

DRUG 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

In severe cases, consider charcoal haemoperfusion.

19.3.18 TRICYCLIC ANTIDEPRESSANT POISONING
T43.0

DESCRIPTION
Patients present with:
- signs of cholinergic blockade
- hypotension
- agitation progressing to coma
- both tachy- and bradyarrhythmias
- pulmonary oedema
- seizures
- profound hypokalaemia

The antimuscarinic effects of these agents may cause transient gastrointestinal ileus and urinary retention.
CHAPTER 19 POISONING

NON-DRUG TREATMENT
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.

DRUG TREATMENT
Repeated or prolonged administration of activated charcoal.

Although the evidence for this indication is limited, consider alkalinisation in severe cases with evidence of cardiac involvement, i.e. prolongation of QRS duration or QRS axis deviation on ECG and/or severe hypotension.
Note: Alkalosis and resultant hypokalaemia may aggravate cardiac dysrhythmias.

For torsade des pointes:
• magnesium sulphate, IV 2 g administered over 30 minutes, then 1 g hourly
Mange broad 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
Monitor response.
See Section 20.1.2.2: Tension Pneumothorax, Suspected

19.3.19 ANTICOAGULANT POISONING
T45.5

DESCRIPTION
Poisoning due to warfarin ingestion and ingestion of supercoumarins, e.g. rat poison and other vermin poisons.

DRUG TREATMENT
• vitamin K₁, IV/IM, 10 mg
  May be repeated depending on the INR response.
  Note the delay in effect.

Patients 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.
CHAPTER 19

POISONING

Administration of vitamin K may induce resistance to warfarin. Patients on chronic warfarin therapy and at high risk for thromboembolic complications, but who are not actively bleeding with INR between 5–9:
• vitamin K\textsubscript{1}, IV, 0.5–1 mg low dose
Resume warfarin therapy, once the INR is less than 4.0.

For INR > 9:
• vitamin K\textsubscript{1}, IV, 2.5 mg
OR
• vitamin K\textsubscript{1}, oral, 5 mg

For oral administration of low doses, the parenteral form may be used.

In all cases repeat INR in 24 hours.

SUPER COUMARINS
Treatment may be prolonged.

19.4 POISON CENTRES

<table>
<thead>
<tr>
<th>Western Cape</th>
<th>Tygerberg</th>
<th>021 931 6129</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Red Cross</td>
<td>021 689 5227</td>
</tr>
<tr>
<td>Gauteng</td>
<td>Johannesburg</td>
<td>0800 333 444</td>
</tr>
<tr>
<td></td>
<td></td>
<td>082 911</td>
</tr>
<tr>
<td></td>
<td>Garden City</td>
<td>011 495 5000</td>
</tr>
<tr>
<td></td>
<td>MEDUNSA</td>
<td>012 521 4145/4359 (office hours)</td>
</tr>
<tr>
<td>Free State</td>
<td>Bloemfontein</td>
<td>082 491 0160</td>
</tr>
<tr>
<td>KwaZulu-Natal</td>
<td>St. Augustine's</td>
<td>031 268 5559</td>
</tr>
</tbody>
</table>

Telephone numbers tested on 31 May 2006.
20.1.1 ANAPHYLAXIS/ANAPHYLACTIC SHOCK

**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.

**NON-DRUG TREATMENT**

Cardiopulmonary resuscitation.
Maintain an open airway. Intubate if necessary.
Monitor all vital parameters closely.
Check pulse and blood pressure.
Reassure and comfort patient.
Patient counselling to prevent recurrence.
Medical alert bracelet should be worn at all times.

**DRUG TREATMENT**

Administer adrenaline and hydrocortisone early to prevent circulatory collapse and severe bronchospasm.

**Intravenous fluids**

Establish a large bore intravenous line and keep open with:

- sodium chloride 0.9%, IV

If IV access not possible, administer the first dose of adrenaline IM.

- adrenaline 1:1 000, IM, 0.3–0.5 mL by deep intramuscular injection. **Not subcutaneously.**
  OR
  - adrenaline, IV, 3–5 mL of 1:10 000 solution
    Give very slowly. Start with 1 mL then repeat after every minute.
    Maximum dose: 1 mg/dose or 5 mg/day.
    To make a 1:10 000 solution: dilute 1 mL in 9 mL sodium chloride 0.9%.

**PLUS**

- hydrocortisone, IV, 200 mg, immediately

**PLUS**
CHAPTER 20  EMERGENCIES AND INJURIES

For bronchospasm
Oxygen at least 40%.
• salbutamol, nebulised, 2.5–5 mg undiluted given over 3 minutes
  Repeat 4–6 hourly.
  OR
  salbutamol 100 mcg, MDI, 2–4 puffs every 3 minutes

For severe allergic reaction, after resuscitation:
• prednisone, oral 0.5 mg/kg daily for 10 days

For urticaria, after resuscitation:
• chlorpheniramine, oral, 4 mg as a single dose

Observe all patients for at least 4–6 hours after stabilisation.

20.1.2 SHOCK

20.1.2.1 HYPOVOLAEMIA

DESCRIPTION
Loss of intravascular fluid, e.g. dehydration, haemorrhage or fluid shifts.

NON-DRUG TREATMENT
Control obvious bleeding with direct pressure. Do not use tourniquets.
Insert one or two large bore IV catheters, peripheral lines are adequate.

DRUG TREATMENT
INITIAL VOLUME RESUSCITATION
• sodium chloride 0.9%, IV, 1–2 L
  Monitor blood pressure, pulse and clinical response.

Most patients will respond to the initial fluid bolus.
If they respond initially and subsequently deteriorate, there may be an ongoing occult haemorrhage.
If no response occurs, consider:
  o occult exsanguinating haemorrhage: intra-abdominal, retroperitoneal and intrapleural
  o non-hypovolaemic shock: tension pneumothorax, myocardial contusion or myocardial infarct.

CONSIDERABLE HAEMORRHAGE
Blood transfusion is indicated.
Transfer to a specialist unit once stable.

20.1.2.2 TENSION PNEUMOTHORAX, SUSPECTED

DESCRIPTION
Patient presents with decreased or absent breath sounds, tracheal shift and elevated JVP.
CHAPTER 20  
EMERGENCIES AND INJURIES

NON-DRUG TREATMENT
If clinical signs are present:

1: Emergency management: insert a large bore needle into the 2nd interspace, mid-clavicular line, then
2: place an intrathoracic drain.

Obtain a chest X-ray as soon as possible and a control chest X-ray after intrathoracic drain insertion.

DRUG TREATMENT
PRECORDIAL PAIN
Refer urgently if myocardial infarction is suspected and confirmed on ECG and the patient remains hypotensive.
Initiate therapy with:

• aspirin, soluble, oral, 300 mg immediately

PLUS
Assuming adequate central venous pressure, inotropic drugs e.g.:

• dobutamine, IV, 2–10 mcg/kg/minute as needed to achieve desired response
  Dilute in dextrose 5% or in sodium chloride 0.9%. Lower doses may be given initially.
  Administer under constant ECG monitoring.

20.1.2.3 NEUROGENIC SHOCK
R57.8

DRUG TREATMENT
MILD TO MODERATE HYPOTENSION
For patients requiring a vasopressor agent:

• phenylephrine, IM, 25 mg, immediately

SEVERE HYPOTENSION

• phenylephrine, continuous IV infusion, 100–150 mcg/minute
  After blood pressure has stabilised, give maintenance rate of 40–60 mcg/minute.
  Dilute 10 mg or more in 200 mL sodium chloride 0.9% or dextrose 5% to make desired concentration.
  OR

For cardiac arrest, asystole and pulseless ventricular tachycardia:
  Administer CPR and/or cardioversion, with tracheal tube in place and vascular access, together with:

• adrenaline 1:1 000, IV, every 3 minutes until patient’s arrest has resolved
  OR
  adrenaline, endotracheal, 3–5 mL of 1:10 000 solution every 3 minutes until patient’s arrest has resolved
  To make a 1:10 000 solution: dilute 1 mL in 9 mL sodium chloride 0.9%.
  Restore blood volume adequately.
CHAPTER 20  EMERGENCIES AND INJURIES

20.1.2.4 SEPTIC SHOCK
A41.9

DRUG TREATMENT
The following may be required:
- adequate fluid resuscitation of up to 6 L in the first 6 hours
- additional inotropic support
- a central venous line to monitor fluid administration.

- adrenaline, IV infusion, 2–10 mcg/minute
  Dilute 4 ampoules of adrenaline (1 mg/mL) in 200 mL sodium chloride 0.9% and
  infuse at 5 mL/hour (= 2 mcg/minute).

PLUS
appropriate antibiotics

20.1.2.5 PULMONARY OEDEMA, ACUTE
J81

DESCRIPTION
A life-threatening condition with abnormal accumulation of fluid in the lungs.
Acute heart failure is a common cause.

NON-DRUG TREATMENT
Maintain open airway.
Administer oxygen.
Bed rest in Fowler’s position, unless hypotensive or comatose.
Correct electrolyte disturbances.
Determine and correct any arrhythmias.
Venesection may be required if other interventions do not succeed, but to be effective
must be done quickly by using a large bore needle, withdrawing 500 mL within 10 minutes.

DRUG TREATMENT
- furosemide, IV, 20–80 mg initial dose
  May be repeated 15 minutes later if symptoms persist.

- morphine, IV, 10 mg
  Dilute 10 mg up to 10 mL with sodium chloride 0.9% and administer 1 mg/minute
  up to a maximum of 10 mg.

Nitrate
- isosorbide dinitrate, SL, 5 mg 6 hourly or more frequently
  Monitor closely.
  OR
  glyceryl trinitrate, IV, 1–2 mcg/kg/minute diluted in sodium chloride 0.9%
  Titrare according to response.
CHAPTER 20  EMERGENCIES AND INJURIES

If hypotensive consider inotropic support, e.g.:
- dobutamine, IV infusion, 2–20 mcg/kg/minute
  Dilute in dextrose 5% in water or sodium chloride 0.9%.
  Administer under constant ECG monitoring.

20.2 INJURIES

20.2.1 BURNS

DESCRIPTION
Skin and tissue damage caused by:
- exposure to extremes of temperature
- contact with an electrical current
- exposure to a chemical agent
- radiation

ASSESSMENT OF BURNS

<table>
<thead>
<tr>
<th>Depth of burn</th>
<th>Degree</th>
<th>Surface/colour</th>
<th>Pain sensation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superficial</td>
<td>1st</td>
<td>Dry, minor blisters, erythema</td>
<td>Painful</td>
</tr>
<tr>
<td>(Partial loss of skin)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Partial A</td>
<td>2nd A</td>
<td>Blisters</td>
<td>Painful</td>
</tr>
<tr>
<td>(Superficial dermal)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Partial B</td>
<td>2nd B</td>
<td>Moist white slough, red mottled</td>
<td>Painful</td>
</tr>
<tr>
<td>(Deep dermal)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full thickness</td>
<td>3rd</td>
<td>Dry, charred whitish</td>
<td>Painless</td>
</tr>
<tr>
<td>(Deep/complete loss of skin)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NON-DRUG TREATMENT
Remove smouldering or hot clothing.
Immerse the burnt area in cold tap water to limit the extent of the burn.
Clean and dress wounds appropriately.
Early intubation if hypoxic or drop in oxygen saturation and ventilation or if soft tissue swells, as these patients frequently tend to develop respiratory failure.
Support vital organ function.
IV access should be obtained to administer intravenous fluids in e.g. shocked patients.
Look for aggravating comorbidities, e.g. seizures, hypokalaemia and renal failure.

Clean superficial burns can be managed by occlusive dressings. Do not use “burnshield” on full thickness wounds and on extensive surface area wounds.
While waiting transfer to a major burn centre, cover wound with cling wrap.
Deeper wounds may have to be excised and grafted.
Rehabilitation.
CHAPTER 20  

EMERGENCIES AND INJURIES

DRUG TREATMENT

Intravenous fluids
If required, as soon as possible:
•  sodium chloride 0.9%, IV

Anlagesia
Ensure adequate analgesia particularly at change of dressing, i.e.:
•  morphine, IV, 0.1 mg/kg as a bolus
  Thereafter titrated according to effect with a maximum of 10–15 mg every 3–4 hours.

Immunisation, primary or booster:
•  tetanus toxoid vaccine, IM, 0.5 mL immediately

Burn dressing
•  povidone iodine 5% cream  
  OR
  silver sulfadiazine cream 1%
  Cover with paraffin gauze.

•  gentamicin, ophthalmic drops, instil 1 drop 4–6 hourly during the day

GASTRIC ULCER PROPHYLAXIS
•  sucralfate, oral, 1 g 6 hourly

Note:
The pharmacokinetic profile of certain drugs may be altered and will require appropriate dose adjustments.

REFERRAL CRITERIA
•  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
CHAPTER 21
DRUGS USED FOR CERTAIN CONDITIONS

21.1 ANAESTHESIOLOGY

DRUGS FOR INDUCTION
• diazepam
• etomidate
• ketamine
• midazolam
• propofol
• thiopental sodium

INHALANTS
• halothane
• isoflurane

ANALGESICS
• fentanyl
• morphine

MUSCLE RELAXANTS AND RELATED DRUGS
• atracurium besylate
• glycopyrronium bromide
• neostigmine
• suxamethonium chloride
• vecuronium bromide

LOCAL ANAESTHETICS
• bupivacaine
• bupivacaine 5 mg/mL plus dextrose
• lidocaine 1%
• lidocaine 2%
• lidocaine 2% plus adrenaline
• lidocaine jelly
• lidocaine topical spray

OTHER DRUGS
• adenosine:
  o For rapid reversion to sinus rhythm of paroxysmal supraventricular tachycardias. Beware of atrial fibrillation or flutter with accessory pathway. Contra-indicated in 2–3 AV block. Cardiac monitoring is essential.
  o Dose: 6 mg by rapid IV injection over 1–2 seconds. If ineffective after 2 minutes, follow with 12 mg over 1–2 seconds. Follow immediately with sodium chloride 0.9%.
CHAPTER 21  DRUGS USED FOR CERTAIN CONDITIONS

• adrenaline
• antacid mixture
• atropine
• calcium, IV
• dantrolene:
  o For malignant hyperthermia.
  o Dose: 1 mg/kg by rapid IV injection.
  o Repeat as necessary to cumulative maximum of 10 mg/kg. Avoid extravasation.
• dextrose 50%, IV
• dobutamine
• esmolol
• furosemide, IV
• glyceryl trinitrate
• heparin, 5 000 units/mL
• hydrocortisone, IV
• insulin, soluble, short acting
• isosorbide dinitrate
• isosorbide mononitrate
• lanolin eye ointment, liquid
• magnesium, IV
• mannitol, IV
• metoclopramide, IV
• naloxone
• neostigmine (post op)
• oxytocin
• phenylephrine:
  o For acute hypotension, i.e. systolic < 70 mmHg, where other measures have failed, or where a tachycardia may be undesirable.
  o May decrease kidney perfusion.
  o Dose: 180 mcg/minute by IV infusion, reduced to 30–60 mcg/minute according to response.
  OR
  o In theatre: slow IV infusion of a 1 mg/mL solution; 100–500 mcg, repeated as necessary after at least 15 minutes.
• potassium, IV
• promethazine, IV
• salbutamol, inhaler
• salbutamol, IV
• sodium bicarbonate 4.2%
CHAPTER 21  DRUGS USED FOR CERTAIN CONDITIONS

21.2 TOTAL PARENTERAL NUTRITION SOLUTIONS

Normally, nourished patients will not be severely affected by going without food for as long as 7–10 days. Hence parenteral nutrition should not be considered under these circumstances unless there is a hypercatabolic state and the enteral route is not appropriate. Early consultation with a dietician is recommended for patients.

"If the gut works, use it" is useful. The gastrointestinal tract is always the preferred route.

Potential benefits of enteral nutrition include:
- prevention of gut atrophy
- reduction in bacterial translocation
- enhanced immunomodulation of antigens
- attenuation of the metabolic response to various cytokines and endotoxin.

GENERAL INDICATIONS FOR TPN

- in patients with small-bowel obstruction secondary to inflammatory adhesions
- when adequate enteral nutrition cannot be established within 1 week of hospitalisation
- in patients with enterocutaneous fistulas, both high and low

It is recommended that a TPN preparation that can be reconstituted in the ward be used in preference to those that need to be mixed in a sterile pharmacy unit.

Relative contraindications to early enteral feeding:
- bowel obstruction (absolute)
- small bowel ileus (absolute)
- short-bowel syndrome
- high-output gastrointestinal fistulas
- necrotising pancreatitis
- intra-abdominal sepsis

21.3 ORAL MICRONUTRIENTS

- ascorbic acid
- thiamine
- pyridoxine
- folic acid
- niacin
- vitamin B complex
- multivitamin (RDAs and/or selenium and zinc)
21.4 DRUGS USED IN INTENSIVE CARE UNIT

It is advisable that the following drugs are available in ICU
- adrenaline
- aminophylline, IV
- amiodarone IV and oral
- atracurium besylate
- atropine
- β–blocker, IV, long acting, e.g. atenolol
- calcium gluconate, IV
- diazepam
- dihydropyridine calcium channel blocker, long acting, e.g. amlodipine
- dobutamine
- furosemide, IV
- glyceryl trinitrate, IV
- heparin
- hydrocortisone, IV
- ipratropium bromide solution for nebulisation
- isosorbide dinitrate
- lidocaine 2%
- magnesium, IV
- mannitol
- metoclopramide, IV
- morphine
- naloxone
- neostigmine
- nifedipine
- phenylephrine
- phenytoin, IV
- potassium IV
- promethazine, IV
- salbutamol solution for nebulisation
- sodium bicarbonate 4.2%
- sodium nitroprusside
- suxamethonium chloride
- thiopental sodium
- verapamil IV
21.5 DIAGNOSTIC CONTRAST AGENTS AND RELATED SUBSTANCES

- antacid mixture
- bowel preparation, e.g. sodium phosphate
- barium sulphate suspension enema
- barium sulphate powder
- hyoscine butylbromide
- iohexol
- iopamidol
- iopromide
- ioversol 300 and 350
- lidocaine 1% jelly
- meglumine amidotrizoate plus sodium amidotrizoate
- meglumine iothalamate
- metoclopramide
- sennosides A and B mixture
- sodium bicarbonate
- sodium iopodate capsules
- sodium iothalamate infusion

21.6 INTRAVENOUS FLUID THERAPY

AIMS OF FLUID THERAPY

Aims of fluid therapy include:
- to restore blood volume
- to restore an effective circulation by correcting a contracted ECF volume
- to correct true “dehydration” i.e. expand a contracted ICF volume
- to provide for ongoing losses or “maintenance” requirements

It is important to decide at the outset which body fluid compartment has the fluid deficit so that fluid which preferentially expands that compartment may be selected. In healthy males total body water (TBW) is 60% of mass, and 50% in females. Of this, $\frac{3}{5}$ is inside cells (ICF) and $\frac{1}{5}$ outside (ECF) in plasma and interstitial fluid.

Clinical assessment of ECF volume is difficult. A typical history, and signs of low JVP, BP, and tachycardia, with marked postural changes should be sought but are often absent. Useful laboratory tests to support or confirm a clinical suspicion include a rise in haematocrit or plasma protein concentrations, and a “pre-renal” ratio of plasma urea (mmol/L) to creatinine (micromol/L), which approaches 1:10 rather than the usual 1:20. To guide therapy, an estimate should then be made of the deficit e.g. 10% or 15% of an ECF volume of ± 10 L or 15 L.

Contraction of the ICF compartment (“shrunken cells”) is present when there is hypernatraemia. As a rough guide, the percentage increase in plasma Na concentration is equal to the percentage of the ICF water deficit.
SELECTION OF INTRAVENOUS FLUID

In general, infusion of hypotonic fluids should be avoided.
Firstly, most hospitalised patients who are ill will have non-osmotic release of ADH. They may therefore be unable to deal with a water load and are prone to develop acute hyponatraemia. The clinical effects will be most severe in patients with small muscle mass (females, malnutrition) or high brain-to-skull volume (children, young adults).
Secondly, the water requirements to replace “insensible losses” in inactive, hospitalised patients are often over-estimated, unless there is clearly fever and increased sweating.

Note:
Most patients with hyponatraemia on presentation will have chronic hyponatraemia (duration > 48 hours). The major danger here is that of serious brain damage from too-rapid correction of plasma Na concentration.

When there are “swollen cells” in the setting of acute hyponatraemia (< 48 hours duration), therapy in the symptomatic patient is to raise the ECF osmolality rapidly by administration of hypertonic saline. Most of these cases will develop in hospital or will be seen in the setting of psychogenic polydipsia, marathon running or “ecstacy” use.

If the ECF volume is being expanded, isotonic fluid is required.
The default choice in most circumstances is isotonic saline, i.e.:
• sodium chloride 0.9%
There should be a good reason for selecting another option.

When it is necessary to infuse alkali as well as re-expand the ECF volume, e.g. in patients with cholera whose stool losses contain significant amounts of bicarbonate:
• Ringer-Lactate

Volumes infused must be based on the estimated deficit in the ECF volume (see above) and an assessment of ongoing losses.

Note:
Some glucose-containing fluids like rehydration fluid are initially “isotonic” but once the dextrose is metabolised it is really hypotonic (sodium chloride 0.45%). If glucose is needed, use:
• sodium chloride 0.9% with dextrose 5%

If there is hypernatraemia due to water deficit and therefore “shrunken cells”, hypotonic fluids, e.g.:
• sodium chloride 0.45%
  OR
dextrose 5%
Avoid over-correction by quantifying the deficit as stated above.
21.7 MALIGNANCIES

The aim of this section is to ensure a seamless drug availability of oncostatic chemotherapy at secondary level.

- bleomycin
- busulfan
- chlorambucil
- cyclophosphamide
- dacarbazine
- doxorubicin
- epirubicin
- fludarabine
- 5-fluorouracil
- folinic acid
- hydroxyurea
- mechlorethamine
- mitoxantrone
- procarbazine
- tamoxifen
- vinblastine
- vincristine
GUIDELINE ON EDL REVIEW PROCESS AND SUBMISSION FOR AMENDMENTS

The National Essential Drugs selection process is based upon a well-developed network of provincial, district and institutional Pharmacy and Therapeutics committees.

Motivations for inclusion in the list will only be considered if:
- The prescribed form has been fully completed.
- The motivators’ contact details are complete.
- The drug name has been stated.
- The submission has been evaluated and approved by the provincial Pharmacy and Therapeutics Committee (PTC).
- The indication has been clearly stated.
- All relevant comparator drug/s have been listed.
- There is sufficient evidence to support the proposed amendment.

Motivations may address major or minor amendments.

Major amendments include:
- new indications
- new therapeutic entities
- new therapeutic classes

All major amendments must be supported by evidence reflecting safety, efficacy and cost of the medicine compared to an already listed drug for the same indication.

A major amendment may also include motivations for drugs not listed and for conditions not addressed in the EDL. In such cases submissions must be supported by demographic data.

Minor amendments include:
- new formulations
- combination therapies of existing essential drugs

For minor amendments the supporting evidence should be relevant to the nature of amendment.

Screening
Motivations are screened by the Rational Selection Group (RSG) at the National Department of Health to ensure that:
- the submission has been approved by the provincial PTC
- the motivators’ contact details are included
- the drug can be identified in terms of the INN
- an indication has been included
- relevant comparator drug/s have been identified with their corresponding dosing regimens
- there are supporting references to substantiate the request
GUIDELINE ON EDL REVIEW PROCESS AND SUBMISSION FOR AMENDMENTS

RSG will compile a review of the prevailing cost of therapy.

Submissions that have been accepted by RSG are tabled at the relevant technical subcommittee for allocation to a suitably qualified reviewer who compiles a technical report. This technical report summarizes a review of the submitted data in terms of the following:
- relative safety
- relative efficacy
- practice environment - the focus here being efficacy relative to current EDL drugs
- pharmacoeconomic evaluation

The report is then presented to the technical subcommittee. The committee may request further information from the applicant through the province or commission a literature search and review.

The technical subcommittee will make recommendations to the National Essential Drug List Committee (NEDLC) for approval or rejection. Where the NEDLC is of the opinion that further review is required the decision will be sent back to the technical subcommittee for further review.

The data elements of the submission form

The motivation form is divided into 5 sections.

SECTION 1: PROPOSAL

The proposal consists of:
a) The International Nonproprietary Name (INN) of the medicine – this identifies a pharmaceutical substance or active pharmaceutical ingredient by a unique name that is globally recognized and is public property. A nonproprietary name is also known as a generic name.
b) Level of Care - indicate whether the proposed medicine should be listed for use at primary care (PHC) or hospital level (Note drugs at PHC level are automatically included at the hospital level).
c) Prescriber level - indicate the level of competency required to prescribe the drug.

SECTION 2: MOTIVATORS’ DETAILS

The NEDLC will acknowledge all submissions and communicate decisions with supporting arguments where appropriate. This section therefore forms a vital link between the motivator and the decision making process.
SECTION 3: PROPOSED INDICATIONS

a) Indication

Points to consider:
• The EDL targets those conditions that are the most prevalent in South Africa. Where the motivator suggests an indication not currently reflected in the EDL, a brief motivation based upon South African epidemiological data must be included as an annexure.
• The indication allows for the identification of the appropriate comparator in the current EDL.
• Many drugs have multiple indications. However, not all are equally cost effective.

b) Proposed Regimen

This data will be used for cost comparison and is very important for pharmacoeconomic evaluation.

c) Cost assessment

The information is necessary for the determination of affordability. It is expected that the provincial PTC will deliberate about the affordability during their review prior to submission to NEDLC. For this reason, this data is considered mandatory at the national level.

SECTION 4: DRUGS ON THE CURRENT EDL FOR THE SAME INDICATION

As a principle, the addition of an EDL item should replace an existing item. This is of particular importance when safety and economic implications are taken into account.

Evidence

Evidence is a vital component of the submission and review process. Evidence does not constitute a drug decision and merely informs the strength of the argument. It forms the basis upon which the decision is made and allows for transparent scrutiny of the decision as well as facilitating the review.

Evidence is required in support of:
• relative efficacy
• relative safety
• pharmacoeconomic benefits

Note

Evidence needs to be relevant to the South African context. Multinational or foreign studies must be supported by a motivation of the relevance of both the outcome measures as well as socio-economic facets to the South African context.

The inclusion of at least one relevant reference is mandatory. A copy of the full journal article should be included in order to expedite the review process.

SECTION 5: FOR USE AT NATIONAL LEVEL ONLY

This section is intended to ensure that the submissions have followed the proper process.
# Motivation Form for the Inclusion of a Drug on the National Essential Drugs List

**Please complete Sections 1 to 4 in full.**

**NB - Only use INN (International Nonproprietary Name/Generic names) on this form.**

## SECTION 1

**Proposed Drug**

<table>
<thead>
<tr>
<th>For Inclusion on the Essential Drug List for</th>
<th>PHC Hospital</th>
<th>Check all appropriate blocks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescriber Level</td>
<td>Primary Health Care - 1</td>
<td>Medical Officer - 2</td>
</tr>
<tr>
<td></td>
<td>Specialist - 3</td>
<td>Designated Specialist - 4</td>
</tr>
</tbody>
</table>

**Submission Date**

**PTC Title**

## SECTION 3

**Proposed Indication**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Proposed Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dose</td>
</tr>
<tr>
<td></td>
<td>hour</td>
</tr>
</tbody>
</table>

**Level Of Evidence**

<table>
<thead>
<tr>
<th>Ia Meta-analysis</th>
<th>Ib Randomized Controlled Trial</th>
<th>Ic Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iv Expert committee</td>
<td>V Clinical experience</td>
<td></td>
</tr>
</tbody>
</table>

## SECTION 4

**Drugs on the Current EDL for the Same Indication**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
<th>Dose</th>
<th>Route</th>
<th>Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>as per list above</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## SECTION 5

**FOR NATIONAL USE ONLY**

**Correspondence**

Date received: / /  Acknowledged: / /

**Evidence**

No of articles submitted: 

**For National Evaluation**

- Yes
- No
- Further evidence

**Decision**

- Accepted /
- Rejected /
### SECTION 2

#### Motivator's Details

<table>
<thead>
<tr>
<th>Title</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tel No Code</td>
<td>Number</td>
</tr>
<tr>
<td>Fax No Code</td>
<td>Number</td>
</tr>
<tr>
<td>Postal Address</td>
<td></td>
</tr>
<tr>
<td>E Mail</td>
<td>Code</td>
</tr>
</tbody>
</table>

#### Cost Assessment

<table>
<thead>
<tr>
<th>Duration</th>
<th>Cost/Unit</th>
<th>Cost per Day</th>
<th>Cost per Course / Month</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>hourly</td>
<td>Days R / R</td>
<td>R R</td>
<td>R R R R</td>
<td></td>
</tr>
<tr>
<td>hourly</td>
<td>Days R / R</td>
<td>R R</td>
<td>R R R R</td>
<td></td>
</tr>
<tr>
<td>hourly</td>
<td>Days R / R</td>
<td>R R</td>
<td>R R R R</td>
<td></td>
</tr>
</tbody>
</table>

II Controlled study with no randomization  
III Comparative, correlation or case control

NB The literature review on the reverse side must support this

#### Request for more evidence

<table>
<thead>
<tr>
<th>Route</th>
<th>Interval</th>
<th>Duration</th>
<th>Cost/Unit</th>
<th>Cost per Day</th>
<th>Cost Per course /month</th>
<th>Can Be Replaced by Proposed Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>hourly</td>
<td></td>
<td>Days R /</td>
<td>R</td>
<td>R R</td>
<td>R R R R</td>
<td>Yes / No</td>
</tr>
<tr>
<td>hourly</td>
<td></td>
<td>Days R /</td>
<td>R</td>
<td>R R</td>
<td>R R R R</td>
<td>Yes / No</td>
</tr>
<tr>
<td>hourly</td>
<td></td>
<td>Days R /</td>
<td>R</td>
<td>R R</td>
<td>R R R R</td>
<td>Yes / No</td>
</tr>
</tbody>
</table>

New Drug  
Standard Therapeutic Guideline New/Change  
Prescriber level
Source of Information

- Literature Review by Yourself
  - Submit with copies of original articles
    - Randomised controlled trial
      - Submit
    - Comparative correlative trial
      - Watch the literature
- Published Systematic Review
- Single Article
  - ? Type of Article
- Information from an opinion leader
  - Request references
    - Supplied
      - Include with Submission
    - None
      - Watch the literature for evidence
- Industry Recommendation
### Levels of Evidence

Ia Meta-analysis  Ib Randomized Controlled Trial  Ii Controlled study with no randomization.  Iii Comparative correlation or case study  Iv Expert committee  V Clinical experience

#### Evidences (articles or abstracts) included with your submission

<table>
<thead>
<tr>
<th>Heading</th>
<th>Journal name</th>
<th>Vol.</th>
<th>Date</th>
<th>Pages</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Included**

- Full article
- Abstract

**Comments**

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DISEASE NOTIFICATION PROCEDURES

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.
DISEASE NOTIFICATION PROCEDURES

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

Diagnosis
can be any health worker, not necessarily a Doctor

GW 17/5
immediately

Local authority / Hospital / District
whoever is responsible for disease containment

GW17/3 (cases)
GW 17/4 (deaths)
weekly

Regional office
Health Information Unit
if data entry is done at regional level -
province specific

computer disks
e-mail
weekly

Provincial office
Health Information Unit
if data entry is done at provincial level -
province specific

computer disks
e-mail
weekly

National Department
Directorate HSR & Epidemiology
Private Bag X828, Pretoria 0001
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 (rattle-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
GUIDELINES FOR ADVERSE DRUG REACTION REPORTING

National Pharmacovigilance Programme
The Medicines Control Council (MCC) has a responsibility to ensure the safety, efficacy and quality of all medicines used by the South African public. The National Pharmacovigilance Programme is coordinated by the MCC and has two dedicated Units responsible for the monitoring of the safety of medicines. The National Adverse Drug Event Monitoring Centre (NADEMC) in Cape Town monitors the safety of all registered medicines in South Africa. In addition, a focused surveillance unit at MEDUNSA is responsible for monitoring the safety of anti-retroviral (ARV) medicines and complementary medicines. The unit at MEDUNSA is also responsible for monitoring the safety of unregistered medicines used during clinical trials.

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) or adverse 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.
GUIDELINES FOR ADVERSE DRUG REACTION REPORTING

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 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 it 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)
GUIDELINES FOR ADVERSE DRUG REACTION REPORTING

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 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) 312 0295; Fax: (021) 3123106

2. The National Adverse Drug Event Monitoring Centre (NADEMC)
   C/o Division of Pharmacology, University of Cape Town,
   Observatory, 7925
   Tel: (021) 447 1618; Fax: (021) 448 6181

3. MEDUNSA Pharmacovigilance Unit
   Fax (012) 521 4335
ADVERSE DRUG REACTION AND PRODUCT QUALITY PROBLEM REPORT FORM

(Identities of reporter and patient will remain strictly confidential)

NATIONAL ADVERSE DRUG EVENT MONITORING CENTRE

Medicines Control Council,
The Registrar of Medicines,
Department of Health

In collaboration with the WHO International Drug Monitoring Programme

PATIENT INFORMATION

Name (or initials): _______________________________  Age: _______________  Weight (kg): _______________

Sex:  M  F  DOB: __/__/____  Height (cm): _______________

ADVERSE REACTION/PRODUCT QUALITY PROBLEM

Adverse reaction¹  □  and/or Product Quality problem²  □  Date of onset of reaction: __/__/____

Time of onset of reaction: ______h:______min

Description of reaction or problem (Include relevant tests/lab data, including dates):

1. MEDICINES/VACCINES/DEVICES (include all concomitant medicines)

<table>
<thead>
<tr>
<th>Trade Name &amp; Batch No. (Asterisk Suspected Product)</th>
<th>Daily Dosage</th>
<th>Route</th>
<th>Date Started</th>
<th>Date Stopped</th>
<th>Reasons for use</th>
</tr>
</thead>
</table>

ADVERSE REACTION OUTCOME (Check all that apply)

- death
- disability
- congenital anomaly
- required intervention to prevent permanent impairment/damage
- life-threatening hospitalisation
- other

Event reappeared on rechallenge:  Y  N  [Rechallenge not done]

Treatment (of reaction)………………………………………………………………………………………………

Recovered:  Y  N  [Sequelea:  Y  N]

Describe Sequelae:……………………………………………………………………………………………………

COMMENTS:  (e.g. Relevant history, Allergies, Previous exposure, Baseline test results/lab data)

2. PRODUCT QUALITY PROBLEM:

| Trade Name | Batch No | Registration No | Dosage form & strength | Expiry Date | Size/Type of container |

Product available for evaluation?:  Y  N

REPORTING DOCTOR/PHARMACIST Etc:

NAME: ___________________________________________  QUALIFICATIONS: ___________________________________________

ADDRESS: ___________________________________________  Signature: _________________________________________

……………………………………………………………………………………………………………………………………

TEL: (______)………………

This report does not constitute an admission that medical personnel or the product caused or contributed to the event.

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ADVICE ABOUT VOLUNTARY REPORTING

Report adverse experiences with:
• medications (drugs, vaccines and biologicals)
• medical devices (including in-vitro diagnostics)
• traditional and herbal remedies
• For Adverse Events Following Immunisation (AEFI), please follow the reporting procedure recommended by the Expanded Programme in Immunisation (EPI)

Please report:
• adverse drug reactions to recently marketed products
• serious reactions and interactions with all products
• adverse drug reactions which are not clearly reflected in the package insert.

Report even if:
• you’re not certain the product caused the event
• you don’t have all the details

Report Product Quality Problems such as:
• suspected contamination
• questionable stability
• defective components
• poor packaging or labelling
• therapeutic failures

Important numbers:
Investigational Products and Product Quality Problems:
• (012) 326-4344 to fax a report
• (012) 312-0000 to report by phone
Registered Medicines and Traditional and Herbal remedies:
• (021) 448-6181 to fax a report
• (021) 447-1618 to report by phone
Adverse Events Following Immunisation:
• (012) 312 0110 to phone for information
• (012) 321 9882 to fax a report

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 drug safety and therapy in South Africa.

PLEASE USE ADDRESS PROVIDED BELOW- JUST FOLD IN THIRDS, TAPE and MAIL

BUSINESS REPLY SERVICE
BESIGHEIDSANTWOORDDIENS
Free Mail Number: Vryposnommer: BNT 178

DEPARTMENT OF HEALTH
DEPARTEMENT VAN GESONDHEID
REGISTRAR OF MEDICINES
REGISTRATEUR VAN MEDISYNE
PRIVATE BAG/ PRIVAATSAK X828
PRETORIA
0001
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<td>glucose-6-phosphate dehydrogenase</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Full Form</td>
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<tr>
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</tr>
<tr>
<td>GFR</td>
<td>glomerular filtration rate</td>
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<tr>
<td>GIT</td>
<td>gastro-intestinal tract</td>
</tr>
<tr>
<td>H</td>
<td>isoniazid</td>
</tr>
<tr>
<td>H₂O</td>
<td>water</td>
</tr>
<tr>
<td>HAART</td>
<td>highly active antiretroviral therapy</td>
</tr>
<tr>
<td>Hb</td>
<td>haemoglobin</td>
</tr>
<tr>
<td>HbA₁C</td>
<td>glycosylated haemoglobin</td>
</tr>
<tr>
<td>HbS</td>
<td>sickle haemoglobin</td>
</tr>
<tr>
<td>HbsAb</td>
<td>hepatitis B surface antibody</td>
</tr>
<tr>
<td>HbsAg</td>
<td>hepatitis B surface antigen</td>
</tr>
<tr>
<td>HbSS</td>
<td>sickle cell haemoglobin</td>
</tr>
<tr>
<td>HCl</td>
<td>hydrochloric acid</td>
</tr>
<tr>
<td>HCO₃</td>
<td>bicarbonate</td>
</tr>
<tr>
<td>HDCV</td>
<td>human diploid cell</td>
</tr>
<tr>
<td>HGT</td>
<td>haemoglucotest</td>
</tr>
<tr>
<td>HIV</td>
<td>human immunodeficiency virus</td>
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<tr>
<td>HMGCoA</td>
<td>3-hydroxy-3-methylglutaryl coenzyme</td>
</tr>
<tr>
<td>HRT</td>
<td>hormone replacement therapy</td>
</tr>
<tr>
<td>HSV</td>
<td>herpes simplex virus</td>
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<tr>
<td>IgE</td>
<td>immunoglobulin</td>
</tr>
<tr>
<td>IgG</td>
<td>immunoglobulin Gamma</td>
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<tr>
<td>IM</td>
<td>intramuscular</td>
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<tr>
<td>INR</td>
<td>international normalised ratio</td>
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<tr>
<td>IUCD</td>
<td>intrauterine contraceptive device</td>
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<tr>
<td>IV</td>
<td>intravenous</td>
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<tr>
<td>JVP</td>
<td>jugular venous pressure</td>
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<tr>
<td>K</td>
<td>potassium</td>
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<tr>
<td>kg</td>
<td>kilogram</td>
</tr>
<tr>
<td>l</td>
<td>litre</td>
</tr>
<tr>
<td>LBBB</td>
<td>left bundle branch block</td>
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<tr>
<td>LDH</td>
<td>lactate dehydrogenase</td>
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<tr>
<td>LDL</td>
<td>low-density lipoprotein</td>
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<tr>
<td>LH</td>
<td>luteinising hormone</td>
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<tr>
<td>LV</td>
<td>left ventricular</td>
</tr>
<tr>
<td>mcg</td>
<td>microgram</td>
</tr>
<tr>
<td>MCS</td>
<td>microscopy, culture and sensitivity</td>
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<tr>
<td>MDI</td>
<td>metered dose inhaler</td>
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<tr>
<td>MEq</td>
<td>milliequivalent</td>
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<tr>
<td>mg</td>
<td>milligram</td>
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<tr>
<td>MI</td>
<td>myocardial infarction</td>
</tr>
<tr>
<td>MIBG</td>
<td>Meta-IodoBenzylGuadinine</td>
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<tr>
<td>MI</td>
<td>myocardial infarction</td>
</tr>
<tr>
<td>mL</td>
<td>millilitre</td>
</tr>
<tr>
<td>mm³</td>
<td>cubic millimetre</td>
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<tr>
<td>mmHg</td>
<td>millimetre mercury</td>
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### ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>mmol</td>
<td>millimole</td>
</tr>
<tr>
<td>mOsm</td>
<td>milliosmole</td>
</tr>
<tr>
<td>MSU</td>
<td>midstream urine specimen</td>
</tr>
<tr>
<td>Na</td>
<td>sodium</td>
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<tr>
<td>ng</td>
<td>nanograms</td>
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<tr>
<td>nmol</td>
<td>nanomoles</td>
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<tr>
<td>NSAID</td>
<td>non-steroidal anti-inflammatory drug</td>
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<tr>
<td>NYHA</td>
<td>New York Heart Association</td>
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<tr>
<td>PaO₂</td>
<td>partial pressure of oxygen in arterial blood</td>
</tr>
<tr>
<td>PCR</td>
<td>polymerase chain reaction</td>
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<tr>
<td>pH</td>
<td>acidity (partial pressure of hydrogen)</td>
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<tr>
<td>PID</td>
<td>pelvic inflammatory disease</td>
</tr>
<tr>
<td>PO₂</td>
<td>oxygen partial pressure</td>
</tr>
<tr>
<td>PO₄</td>
<td>phosphate</td>
</tr>
<tr>
<td>PPI</td>
<td>proton pump inhibitors</td>
</tr>
<tr>
<td>PSA</td>
<td>prostate specific antigen</td>
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<tr>
<td>PTH</td>
<td>parathyroid hormone</td>
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<tr>
<td>PV</td>
<td>vaginally</td>
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<tr>
<td>R</td>
<td>rifampicin</td>
</tr>
<tr>
<td>RBC</td>
<td>red blood cell</td>
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<tr>
<td>RDA</td>
<td>recommended dietary allowance</td>
</tr>
<tr>
<td>RH</td>
<td>rifampicin/isoniazid combination</td>
</tr>
<tr>
<td>RHZE</td>
<td>rifampicin/isoniazid/pyrazinamide/ethambutol combination</td>
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<tr>
<td>RPR</td>
<td>rapid plasma reagent test</td>
</tr>
<tr>
<td>SBP</td>
<td>systolic blood pressure</td>
</tr>
<tr>
<td>SC</td>
<td>subcutaneous</td>
</tr>
<tr>
<td>SL</td>
<td>sublingual</td>
</tr>
<tr>
<td>SLE</td>
<td>systemic lupus erythematosus</td>
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<tr>
<td>T₃</td>
<td>triiodothyronine</td>
</tr>
<tr>
<td>T₄</td>
<td>thyroxine</td>
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<tr>
<td>TB</td>
<td>tuberculosis</td>
</tr>
<tr>
<td>TCO₂</td>
<td>total carbon dioxide</td>
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<tr>
<td>TIA</td>
<td>transient ischemic attack</td>
</tr>
<tr>
<td>TOD</td>
<td>target organ damage</td>
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<tr>
<td>TSH</td>
<td>thyroid stimulating hormone</td>
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<tr>
<td>VSD</td>
<td>ventricular septal defect</td>
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<td>WBC</td>
<td>white blood cell</td>
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<tr>
<td>WHO</td>
<td>World Health Organisation</td>
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<tr>
<td>Z</td>
<td>pyrazinamide</td>
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<tr>
<td>ZN</td>
<td>Ziehl-Nielsen</td>
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