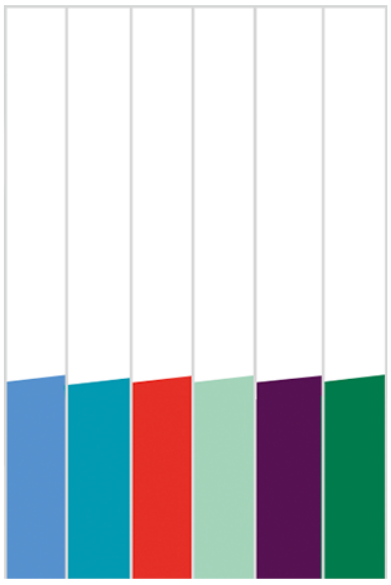
Clinical guidelines



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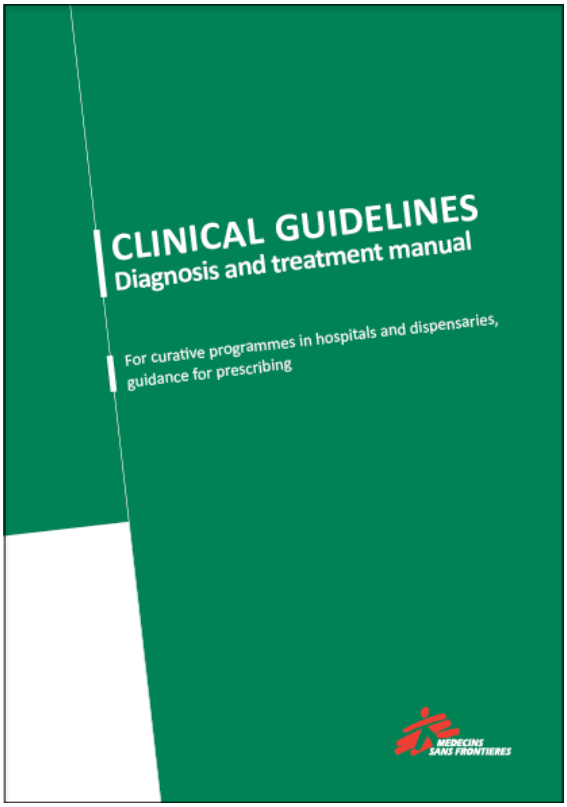
Clinical guidelines - Diagnosis and treatment manual

For curative programmes in hospitals and dispensaries
Guidance for prescribing



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Preface

This guide is designed for use by medical professionals involved in curative care at the dispensary and primary hospital.

We have tried to respond in the simplest and most practical way possible to the questions and problems faced by field medical staff, using the accumulated field experience of Médecins Sans Frontières, the recommendations of reference organizations such as the World Health Organization (WHO) and specialized works in each field.

This edition touches on the curative and, to a lesser extent, the preventive aspects of the main diseases encountered in the field. The list is incomplete, but covers the essential needs.

This guide is used not only in programmes supported by Médecins Sans Frontières, but also in other programmes and in other contexts. It is notably an integral part of the WHO Emergency Health Kit.

Médecins Sans Frontières has also issued French and Spanish editions. Editions in other languages have also been produced in the field.

This guide is a collaborative effort of medical professionals from many disciplines, all with field experience.

Despite all efforts, it is possible that certain errors may have been overlooked in this guide. Please inform the authors of any errors detected. It is important to remember, that if in doubt, it is the responsibility of the prescribing medical professional to ensure that the doses indicated in this manual conform to the manufacturer ’s specifications.

To ensure that this guide continues to evolve while remaining adapted to field realities, please send any comments or suggestions.

As treatment protocols are regularly revised, please check the monthly updates.

Abbreviations and acronyms

ACE	angiotensin converting enzyme
ACT	artemisinin-based combination therapy
AFB	acid-fast bacillus
ALT	alanine aminotransferase
ARV	antiretroviral
AST	aspartate aminotransferase
BCG	bacillus Calmette-Guérin
BMI	body mass index
BP	blood pressure
°C	degree Celsius
co-amoxiclav	amoxicillin + clavulanic acid
co-trimoxazole	sulfamethoxazole + trimethoprim
CRT	capillary refill time
CSF	cerebrospinal fluid
CMV	cytomegalovirus
D1 (D2, D3, etc.)	Day 1 or first day (Day 2 or 2nd day, Day 3 or 3rd day, etc.)
dl	decilitre
g	gram
HBP	high blood pressure (hypertension)
HF	heart failure
HIV	human immunodeficiency virus
HR	heart rate
IM	intramuscular
IO	intraosseous
IU	international unit
IV	intravenous
kcal	kilocalorie
kg	kilogram

LP	lumbar puncture
M	million
mg	milligram
ml	millilitre
mmHg	millimetre of mercury
mmol	millimole
MSF	Médecins Sans Frontières
NSAID	nonsteroidal anti-inflammatory drug
ORS	oral rehydration solution or salts
PCP	pneumocystosis
PO	per os – oral administration
RR	respiratory rate
SAM	severe acute malnutrition
SC	subcutaneous
SMX	sulfamethoxazole
SMX + TMP	sulfamethoxazole + trimethoprim = co-trimoxazole
SpO_2	arterial blood oxygen saturation measured by pulse oximetry
tab	tablet
TB	tuberculosis
TMP	trimethoprim
TT	tetanus toxoid
WHO	World Health Organization

Chapter 1: A few symptoms and syndromes

- Shock(see page 10)
- Seizures(see page 16)
- Hypoglycaemia(see page 20)
- Fever(see page 21)
- Pain(see page 23)
- Anaemia(see page 30)
- Dehydration(see page 34)
- Severe acute malnutrition(see page 38)

Shock

Acute circulatory failure leading to inadequate tissue perfusion which, if prolonged, results in irreversible organ failure. Mortality is high without early diagnosis and treatment.

- Aetiology and pathophysiology(see page 10)
  - Hypovolaemic shock(see page 10)
  - Septic shock(see page 11)
  - Cardiogenic shock(see page 11)
- Clinical features(see page 11)
  - Signs common to most forms of shock(see page 11)
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    - Hypovolaemic shock(see page 11)
    - Anaphylactic shock(see page 11)
    - Septic shock(see page 11)
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- Management(see page 12)
  - In all cases(see page 12)
  - Management according to the cause(see page 12)
    - Haemorrhage(see page 12)
    - Severe acute dehydration due to bacterial/viral gastroenteritis(see page 12)
    - Severe anaphylactic reaction(see page 13)
    - Septic shock(see page 13)
    - Cardiogenic shock(see page 14)

Aetiology and pathophysiology

Hypovolaemic shock

Absolute hypovolaemia due to significant intravascular fluid depletion:
– Internal or external haemorrhage: post-traumatic, peri or postoperative, obstetrical (ectopic pregnancy, uterine rupture, etc.), blood loss due to an underlying condition (gastrointestinal ulcer, etc.). A loss of greater than 30% of blood volume in adults will lead to haemorrhagic shock.
– Dehydration: severe diarrhoea and vomiting, intestinal obstruction, diabetic ketoacidosis or hyperosmolar coma, etc.
– Plasma leaks: extensive burns, crushed limbs, etc.

Relative hypovolaemia due to vasodilation without concomitant increase in intravascular volume:
– Anaphylactic reaction: allergic reaction to insect bites or stings; drugs, mainly neuromuscular blockers, antibiotics, acetylsalicylic acid, colloid solutions (dextran, modified gelatin fluid); equine sera; vaccines containing egg protein; food, etc.
– Acute haemolysis: severe malaria, drug poisoning (rare).

Septic shock

By a complex mechanism, often including vasodilation, heart failure and absolute hypovolaemia.

Cardiogenic shock

By decrease of cardiac output:
– Direct injury to the myocardium: infarction, contusion, trauma, poisoning.
– Indirect mechanism: arrhythmia, constrictive pericarditis, haemopericardium, pulmonary embolism, tension pneumothorax, valvular disease, severe anaemia, beri beri, etc.

Clinical features

Signs common to most forms of shock

– Pallor, mottled skin, cold extremities, sweating and thirst.
– Rapid and weak pulse often only detected on major arteries (femoral or carotid).
– Low blood pressure (BP), narrow pulse pressure, BP sometimes undetectable.
– Capillary refill time (CRT) > 3 seconds.
– Cyanosis, dyspnoea, tachypnoea are often present in varying degrees depending on the mechanism.
– Consciousness usually maintained, but anxiety, confusion, agitation or apathy are common.
– Oliguria or anuria.

Signs specific to the mechanism of shock

Hypovolaemic shock

The common signs of shock listed above are typical of hypovolaemic shock.
Do not underestimate hypovolaemia. Signs of shock may not become evident until a 50% loss of blood volume in adults.

Anaphylactic shock

– Significant and sudden drop in BP
– Tachycardia
– Frequent cutaneous signs: rash, urticaria, angioedema
– Respiratory signs: dyspnoea, bronchospasm

Septic shock

– High fever or hypothermia (< 36 °C), rigors, confusion
– BP may be initially maintained, but rapidly, same pattern as for hypovolaemic shock.

Cardiogenic shock

– Respiratory signs of left ventricular failure (acute pulmonary oedema) are dominant: tachypnoea, crepitations on auscultation.

– Signs of right ventricular failure: raised jugular venous pressure, hepatojugular reflux, sometimes alone, more often associated with signs of left ventricular failure.

The aetiological diagnosis is oriented by:
– The context: trauma, insect bite, ongoing medical treatment, etc.
– The clinical examination:
• fever
• skin pinch consistent with dehydration
• thoracic pain from a myocardial infarction or pulmonary embolus
• abdominal pain or rigidity of the abdominal wall from peritonitis, abdominal distension from intestinal obstruction
• blood in stools, vomiting blood in intestinal haemorrhage
• subcutaneous crepitations, likely anaerobic infection

Management

Symptomatic and aetiological treatment must take place simultaneously.

In all cases

– Emergency: immediate attention to the patient.
– Warm the patient, lay him flat, elevate legs (except in respiratory distress, acute pulmonary oedema).
– Insert a peripheral IV line using a large calibre catheter (16G in adults). If no IV access, use intraosseous route.
– Oxygen therapy, assisted ventilation in the event of respiratory distress.
– Assisted ventilation and external cardiac compression in the event of cardiac arrest.
– Intensive monitoring: consciousness, heart rate, BP, CRT, respiratory rate, hourly urinary output (insert a urinary catheter) and skin mottling.

Management according to the cause

Haemorrhage

– Control bleeding (compression, tourniquet, surgical haemostasis).
– Determine blood group.
– Priority: restore vascular volume as quickly as possible:

> Insert 2 peripheral IV lines (2 catheters 16G in adults).
> **Ringer lactate** or **0.9% sodium chloride**: replace 3 times the estimated losses
> and/or **plasma substitute**: replace 1.5 times the estimated losses

– Transfuse: classically once estimated blood loss represents approximately 30 to 40% of blood volume (25% in children). The blood must be tested (HIV, hepatitis B and C, syphilis, malaria in endemic areas, etc.)

Severe acute dehydration due to bacterial/viral gastroenteritis

– Urgently restore circulating volume using IV therapy with **Ringer lactate**:
Children under 5 years: 20 ml/kg over 15 minutes (to be repeated 2 times if necessary) then 70 ml/kg over 3 hours
Children 5 years and over and adults: 30 ml/kg over 30 minutes (to be repeated once if necessary) then 70 ml/kg over 3 hours
– As soon as the patient is able to drink (often within 2 hours), provide oral rehydration solution (ORS) as the patient tolerates.

– Closely monitor the patient; be careful to avoid fluid overload in young children and elderly patients.
– For aetiological treatment, see Acute diarrhoea(see page 79), Chapter 3.

Note: in severely malnourished children the IV rate is different than those for healthy children (see Severe acute malnutrition(see page 38), Chapter 1).

Severe anaphylactic reaction

– Determine the causal agent and remove it, e.g. stop ongoing injections or infusions, but if in place, maintain the IV line.

– Administer **epinephrine** (**adrenaline**) IM, into the anterolateral part of the thigh, in the event of hypotension, pharyngolaryngeal oedema, or breathing difficulties:

Use *undiluted* solution (1:1000 = 1 mg/ml) and a 1 ml syringe graduated in 0.01 ml:
Children under 6 years: 0.15 ml
Children from 6 to 12 years: 0.3 ml
Children over 12 years and adults: 0.5 ml

In children, if 1 ml syringe is not available, use a *diluted* solution, i.e. add 1 mg epinephrine to 9 ml of 0.9% sodium chloride to obtain a 0.1 mg/ml solution (1:10 000):
Children under 6 years: 1.5 ml
Children from 6 to 12 years: 3 ml

At the same time, administer rapidly **Ringer lactate** or **0.9% sodium chloride**: 1 litre in adults (maximum rate); 20 ml/kg in children, to be repeated if necessary.
If there is no clinical improvement, repeat IM epinephrine every 5 to 15 minutes.

In shock persists after 3 IM injections, administration of IV epinephrine at a constant rate by a syringe pump is necessary:
Use a *diluted* solution, i.e. add 1 mg epinephrine (1:1000) to 9 ml of 0.9% sodium chloride to obtain a 0.1 mg/ml solution (1:10 000):
Children: 0.1 to 1 microgram/kg/minute
Adults: 0.05 to 0.5 microgram/kg/minute
If syringe pump is not available, see box(see page 15).

– In patients with bronchospasm, epinephrine is usually effective. If the spasm persists give 10 puffs of inhaled **salbutamol**.

Note: corticosteroids are not indicated in the initial treatment of anaphylaxis. They may be administered once the patient is stabilised to prevent recurrence in the short term (**prednisolone** PO: 0.5 to 1 mg/kg once daily for 1 to 2 days).

Septic shock

– Vascular fluid replacement with **Ringer lactate** or **0.9% sodium chloride** or **plasma substitute**.

– Use of vasoconstrictors:

dopamine IV at a constant rate by syringe pump (see box(see page 15)): 10 to 20 micrograms/kg/minute
or, if not available
epinephrine IV at a constant rate by syringe pump:
Use a *diluted* solution, i.e. add 1 mg epinephrine (1:1000) to 9 ml of 0.9% sodium chloride to obtain a 0.1 mg/ml solution (1:10 000). Start with 0.1 microgram/kg/minute. Increase the dose progressively until a clinical improvement is seen.
If syringe pump is not available, see box(see page 15).

– Look for the origin of the infection (abscess; ENT, pulmonary, digestive, gynaecological or urological infection etc.). Antibiotic therapy according to the origin of infection:

Origin	Antibiotic therapy	Alternative
Cutaneous staphylococci, streptococci	cloxacillin + gentamicin	
Pulmonary pneumococci, *Haemophilus influenzae*	ampicillin or ceftriaxone +/- gentamicin	co-amoxiclav or ceftriaxone + ciprofloxacin
Intestinal or biliary enterobacteria, anaerobic bacteria, enterococci	co-amoxiclav + gentamicin	ceftriaxone + gentamicin + metronidazole
Gynaecological streptococci, gonococci, anaerobic bacteria, *E. coli*	co-amoxiclav + gentamicin	ceftriaxone + gentamicin + metronidazole
Urinary enterobacteria, enterococci	ampicillin + gentamicin	ceftriaxone + ciprofloxacin
Other or undetermined	ampicillin + gentamicin	ceftriaxone + ciprofloxacin

ampicillin IV
Children over 1 month: 50 mg/kg every 6 to 8 hours
Adults: 1 to 2 g every 6 to 8 hours

cloxacillin IV infusion (60 minutes)
Children over 1 month: 50 mg/kg every 6 hours (max. 8 g daily)
Adults: 3 g every 6 hours

amoxicillin/clavulanic acid (**co-amoxiclav**) slow IV injection (3 minutes) or IV infusion (30 minutes)
Doses are expressed in amoxicillin:
Children less than 3 months: 50 mg/kg every 12 hours
Children ≥ 3 months and < 40 kg: 50 mg/kg every 8 hours (max. 6 g daily)
Children 40 kg and adults: 2 g every 8 hours

ceftriaxone slow IV (see page 0) (3 minutes)
Children: 100 mg/kg once daily
Adults: 2 g once daily

ciprofloxacin PO (by nasogastric tube)
Children: 15 mg/kg 2 times daily
Adults: 500 mg 2 times daily

gentamicin IM or slow IV (3 minutes)
Children ≥ 1 month and adults: 6 mg/kg once daily

metronidazole IV infusion (30 minutes)
Children over 1 month: 10 mg/kg every 8 hours (max. 1500 mg daily)
Adults: 500 mg every 8 hours

– Corticosteroids: not recommended, the adverse effects outweigh the benefits.

Cardiogenic shock

The objective is to restore efficient cardiac output. The treatment of cardiogenic shock depends on its mechanism.

– *Acute left heart failure with pulmonary oedema*

Acute pulmonary oedema (for treatment, see Heart failure in adults(see page 300), Chapter 12).

In the event of worsening signs with vascular collapse, use a strong cardiotonic:
dopamine IV at a constant rate by syringe pump (see box(see page 15)): 3 to 10 micrograms/kg/minute

Once the haemodynamic situation allows (normal BP, reduction in the signs of peripheral circulatory failure), nitrates or morphine may be cautiously introduced.

Digoxin should no longer be used for cardiogenic shock, except in the rare cases when a supraventricular tachycardia has been diagnosed by ECG. Correct hypoxia before using digoxin.
digoxin slow IV
Children: one injection of 0.010 mg/kg (10 micrograms/kg), to be repeated up to 4 times per 24 hours if necessary
Adults: one injection of 0.25 to 0.5 mg, then 0.25 mg 3 or 4 times per 24 hours if necessary

– *Cardiac tamponade*: restricted cardiac filling as a result of haemopericardium or pericarditis. Requires immediate pericardial tap after restoration of circulating volume.

– *Tension pneumothorax*: drainage of the pneumothorax.

– *Symptomatic pulmonary embolism*: treat with an anticoagulant in a hospital setting.

Administration of **dopamine** or **epinephrine** at a constant rate requires the following conditions:
– close medical supervision in a hospital setting;
– use of a dedicated vein (no other infusion/injection in this vein), avoid the antecubital fossa if possible;
– use of an electric syringe pump;
– progressive increase and adaptation of doses according to clinical response;
– intensive monitoring of drug administration, particularly during syringe changes.
Example:
dopamine: 10 micrograms/kg/minute in a patient weighing 60 kg
Hourly dose: 10 (micrograms) x 60 (kg) x 60 (min) = 36 000 micrograms/hour = 36 mg/hour
In a 50 ml syringe, dilute one 200 mg-ampoule of dopamine with 0.9% sodium chloride to obtain 50 ml of solution containing 4 mg of dopamine per ml.
For a dose of 36 mg/hour, administer the solution (4 mg/ml) at 9 ml/hour.

If there is no electric syringe pump, dilution in an infusion bag may be considered. However, it is important to consider the risks related to this type of administration (accidental bolus or insufficient dose). The infusion must be constantly monitored to prevent any, even small, change from the prescribed rate of administration.
Example for **epinephrine**:
– In adults:
Dilute 10 ampoules of 1 mg epinephrine (10 000 micrograms) in 1 litre of 5% glucose or 0.9% sodium chloride to obtain a solution containing 10 micrograms of epinephrine per ml.
Knowing that 1 ml = 20 drops, *in an adult weighing 50 kg*:
• 0.1 microgram/kg/minute = 5 micrograms/minute = 10 drops/minute
• 1 microgram/kg/minute = 50 micrograms/minute = 100 drops/minute, etc.
– In children:
Dilute 1 ampoule of 1 mg epinephrine (1000 micrograms) in 100 ml of 5% glucose or 0.9% sodium chloride to obtain a solution containing 10 micrograms of epinephrine per ml.
For administration, use a **paediatric infusion set**; knowing that 1 ml = 60 drops, *in a child weighing 10 kg*:
• 0.1 microgram/kg/minute = 1 microgram/minute = 6 drops/minute
• 0.2 microgram/kg/minute = 2 micrograms/minute = 12 drops/minute, etc.

Note: account for all infused volumes when recording ins and outs.

1 (see page 0) The solvent of ceftriaxone for IM injection contains lidocaine. Ceftriaxone reconstituted using this solvent must never be administered by IV route. For IV administration, water for injection must always be used.

Seizures

- Initial treatment (see page 17)
  - During a seizure (see page 17)
  - The patient is no longer seizing (see page 17)
  - Status epilepticus (see page 17)
- Further treatment (see page 18)
  - Febrile seizures (see page 18)
  - Infectious causes (see page 18)
  - Metabolic causes (see page 19)
  - Iatrogenic causes (see page 19)

- Epilepsy(see page 19)

– Involuntary movements of cerebral origin (stiffness followed by clonic movements), accompanied by a loss of consciousness, and often urinary incontinence (generalized tonic-clonic seizures).

– In pregnant women, eclamptic seizures require specific medical and obstetrical care. Refer to the guide Essential obstetric and newborn care, MSF.

Initial treatment

During a seizure

– Protect from trauma, maintain airway, place patient in 'recovery position', loosen clothing.

– Most seizures are quickly self-limited. Immediate administration of an anticonvulsant is not systematic. If generalized seizure lasts more than 5 minutes, use diazepam to stop it:
diazepam
Children: 0.5 mg/kg preferably rectally 1(see page 0) without exceeding 10 mg
IV administration is possible (0.3 mg/kg over 2 or 3 minutes), only if means of ventilation are available (Ambu bag and mask).
Adults: 10 mg rectally or by slow IV

In all cases:
• If seizure continues, repeat dose once after 10 minutes.
• In infants and elderly patients, monitor respiratory rate and blood pressure.
• If seizure continues after the second dose, treat as status epilepticus.

The patient is no longer seizing

– Look for the cause of the seizure and evaluate the risk of recurrence.

– Keep diazepam and glucose available in case the patient starts seizing again.

Status epilepticus

Several distinct seizures without complete restoration of consciousness in between or an uninterrupted seizure lasting more than 30 minutes.

– Protect from trauma, loosen clothing, maintain airway and administer oxygen as required.

– Insert an intravenous or intraosseus line.

– Treat for hypoglycaemia (see Hypoglycaemia(see page 20), Chapter 1).

– If 2 doses of diazepam have not stopped the seizures, use phenytoin or phenobarbital if phenytoin is not available or if seizures persist despite phenytoin.

⚠ There is a high risk of hypotension, bradycardia and respiratory depression, especially in children and elderly patients. Never administer these drugs by rapid IV injection. Monitor heart rate, blood pressure and respiratory rate every 15 minutes during and after administration. Reduce the infusion rate in the event of a drop in blood pressure or bradycardia. Ensure that respiratory support (Ambu bag via face mask or intubation, etc.) and IV solutions for fluid replacement are ready at hand.

phenytoin slow IV infusion 250 mg in 5 ml ampoule (50 mg/ml)	– Children 1 month and over and adults: one dose of 15 to 20 mg/kg administered over 20 minutes minimum and 60 minutes maximum – The concentration of the diluted solution should be between 5 and 10 mg/ml. The infusion rate should not exceed 1 mg/kg/minute or 50 mg/minute (25 mg/minute in elderly patients or patients with cardiac disorders). For example: Child weighing 8 kg: 160 mg (20 mg x 8 kg), i.e. 3.2 ml of phenytoin in 17 ml of 0.9% sodium chloride over 30 minutes Adult weighing 50 kg: 1 g (20 mg x 50 kg), i.e. 20 ml of phenytoin in a bag of 100 ml of 0.9% sodium chloride over 30 minutes ⚠ Do not dilute phenytoin in glucose. Do not administer via a line used for glucose solution administration. Use a large catheter. Check the insertion site and for blood backflow (risk of necrosis in the event of extravasation). After each infusion, rinse with 0.9% sodium chloride to limit local venous irritation.
phenobarbital slow IV infusion 200 mg in 1 ml ampoule (200 mg/ml)	– Children 1 month to < 12 years: one dose of 15 to 20 mg/kg (max. 1 g) administered over 20 minutes minimum If necessary, a second dose of 10 mg/kg may be administered 15 to 30 minutes after the first dose. – Children ≥ 12 years and adults: one dose of 10 mg/kg (max. 1 g) administered over 20 minutes minimum If necessary, a second dose of 5 to 10 mg/kg may be administered 15 to 30 minutes after the first dose. – Do not administer more than 1 mg/kg/minute. For example: Child weighing 8 kg: 120 mg (15 mg x 8 kg), i.e. 0.6 ml of phenobarbital in 20 ml of 0.9% sodium chloride over 20 minutes Adult weighing 50 kg: 500 mg (10 mg x 50 kg), i.e. 2.5 ml of phenobarbital in a bag of 100 ml of 0.9% sodium chloride over 20 minutes ⚠ For doses less than 1 ml, use a 1 ml syringe graduated 0.01 ml to draw the phenobarbital.

Further treatment

Febrile seizures

– Determine the cause of the fever. Give paracetamol (see Fever(see page 21), Chapter 1).
– In children under 3 years, there is usually no risk of later complications after simple febrile seizures and no treatment is required after the crisis. For further febrile episodes, give paracetamol PO.

Infectious causes

Severe malaria(see page 123) (Chapter 6), meningitis(see page 157) (Chapter 7), meningo-encephalitis, cerebral toxoplasmosis (HIV infection and AIDS(see page 206), Chapter 8), cysticercosis (Cestodes(see page 144), Chapter 6), etc.

Metabolic causes

– Hypoglycaemia: administer glucose by slow IV injection to all patients who do not regain consciousness, to patients with severe malaria and to newborns and malnourished children. When possible, confirm hypoglycaemia (reagent strip test).

Iatrogenic causes

– Withdrawal of antiepileptic therapy in a patient being treated for epilepsy should be managed over a period of 4-6 months with progressive reduction of the doses. An abrupt stop of treatment may provoke severe recurrent seizures.

Epilepsy

– A first brief seizure does not need further protective treatment. Only patients with chronic repetitive seizures require further regular protective treatment with an antiepileptic drug, usually over several years.

– Once a diagnosis is made, abstention from treatment may be recommended due to the risks associated with treatment. However, these risks must be balanced with the risks of aggravation of the epilepsy, ensuing seizure-induced cerebral damage and other injury if the patient is not treated.

– It is always preferable to start with monotherapy. The effective dose must be reached progressively and symptoms and drug tolerance evaluated every 15 to 20 days.

– An abrupt interruption of treatment may provoke status epilepticus. The rate of dose reduction varies according to the length of treatment; the longer the treatment period, the longer the reduction period (see Iatrogenic causes(see page 19)). In the same way, a change from one antiepileptic drug to another must be made progressively with an overlap period of a few weeks.

– First line treatments for generalised tonic-clonic seizures in children under 2 years are carbamazepine or phenobarbital, in older children and adults sodium valproate or carbamazepine.
For information:

sodium valproate PO
Children over 20 kg: initial dose of 200 mg 2 times daily irrespective of weight; increase the dose progressively if necessary until the optimal dose has been reached (usually 10 to 15 mg/kg 2 times daily).
Adults: initial dose of 300 mg 2 times daily; increase by 200 mg every 3 days if necessary until the optimal dose has been reached (usually 500 mg to 1 g 2 times daily).

carbamazepine PO
Children 1 month and over: initial dose of 5 mg/kg once daily or 2.5 mg/kg 2 times daily; increase the dose every week by 2.5 to 5 mg/kg, up to 5 mg/kg 2 to 3 times daily (max. 20 mg/kg daily)
Adults: initial dose of 100 to 200 mg once or 2 times daily; increase the dose every week by 100 to 200 mg, up to 400 mg 2 to 3 times daily (max. 1600 mg daily)

phenobarbital PO
Children: initial dose of 3 to 4 mg/kg once daily at bedtime; increase the dose progressively up to 8 mg/kg daily if necessary
Adults: initial dose of 2 mg/kg once daily (max. 100 mg); increase the dose progressively up to 6 mg/kg daily if necessary

(see page 0)
For rectal administration, use a syringe without a needle, or cut a nasogastric tube, CH8, to a length of 2-3 cm and attach it to the tip of the syringe.

Hypoglycaemia

- Clinical features(see page 20)
- Diagnosis(see page 20)
- Symptomatic treatment(see page 20)
- Aetiological treatment(see page 21)
- References(see page 21)

– Hypoglycaemia is an abnormally low concentration of blood glucose. Severe hypoglycaemia can be fatal or lead to irreversible neurological damage.

– Blood glucose levels should be measured whenever possible in patients presenting symptoms of hypoglycaemia. If hypoglycaemia is suspected but blood glucose measurement is not available, glucose (or another available sugar) should be given empirically.

– Always consider hypoglycaemia in patients presenting impaired consciousness (lethargy, coma) or seizures.

– For diagnosis and treatment of hypoglycaemia in neonates, refer to the guide Essential obstetric and newborn care, MSF.

Clinical features

Rapid onset of non-specific signs, mild to severe depending on the degree of the hypoglycaemia: sensation of hunger and fatigue, tremors, tachycardia, pallor, sweats, anxiety, blurred vision, difficulty speaking, confusion, convulsions, lethargy, coma.

Diagnosis

Capillary blood glucose concentration (reagent strip test):

– Non-diabetic patients:
• Hypoglycaemia: < 3.3 mmol/litre (< 60 mg/dl)
• Severe hypoglycaemia: < 2.2 mmol/litre (< 40 mg/dl)

– Diabetic patients on home treatment: < 3.9 mmol/litre (< 70 mg/dl)[1](see page 21)

If blood glucose measurement is not available, diagnosis is confirmed when symptoms resolve after the administration of sugar or glucose.

Symptomatic treatment

– Conscious patients:
Children: a teaspoon of powdered sugar in a few ml of water or 50 ml of fruit juice, maternal or therapeutic milk or 10 ml/kg of 10% glucose by oral route or nasogastric tube.
Adults: 15 to 20 g of sugar (3 or 4 cubes) or sugar water, fruit juice, soda, etc.
Symptoms improve approximately 15 minutes after taking sugar by oral route.

– Patients with impaired consciousness or prolonged convulsions:
Children: 2 ml/kg of **10% glucose** by slow IV (2 to 3 minutes)
Adults: 1 ml/kg of **50% glucose** by slow IV (3 to 5 minutes)
Neurological symptoms improve a few minutes after the injection.

Check blood glucose after 15 minutes. If it is still low, re-administer glucose by IV route or sugar by oral route according to the patient's clinical condition.

If there is no clinical improvement, differential diagnoses should be considered: e.g. serious infection (severe malaria, meningitis, etc.), epilepsy, unintentional alcohol intoxication or adrenal insufficiency in children.

In all cases, after stabilisation, give a meal or snack rich in complex carbohydrates and monitor the patients for a few hours.

If patient does not return to full alertness after an episode of severe hypoglycaemia, monitor blood glucose levels regularly.

Aetiological treatment

– Other than diabetes:
• Treat severe malnutrition, neonatal sepsis, severe malaria, acute alcohol intoxication, etc.
• End prolonged fast.
• Replace drugs inducing hypoglycaemia (e.g. quinine IV, pentamidine, ciprofloxacin, enalapril, beta-blockers, high-dose aspirin, tramadol), or anticipate hypoglycaemia (e.g. administer quinine IV in a glucose infusion).

– In diabetic patients:
• Avoid missing meals, increase intake of carbohydrates if necessary.
• Adjust dosage of insulin according to blood glucose levels and physical activity.
• Adjust dosage of oral antidiabetics, taking into account possible drug interactions.

References

1. American Diabetes Association Standards of Medical Care in Diabetes, 2017. http://care.diabetesjournals.org/content/diacare/suppl/2016/12/15/40.Supplement_1.DC1/DC_40_S1_final.pdf [Accessed 24 May 2018]

Fever

- Signs of severity(see page 21)
- Infectious causes of fever according to localizing symptoms(see page 22)
- Laboratory and other examinations(see page 22)
- Aetiological treatment(see page 23)
- Symptomatic treatment(see page 23)
- Prevention of complications(see page 23)

– Fever is defined as an axillary temperature higher than or equal to 37.5 °C.
– Fever is frequently due to infection. In a febrile patient, first look for signs of serious illness then, try to establish a diagnosis.

Signs of severity

– Severe tachycardia, tachypnoea, respiratory distress, $SpO_2 \leq 90\%$.

– Shock, altered mental status, petechial or purpuric rash, meningeal signs, seizures, heart murmur, severe abdominal pain, dehydration, critically ill appearance (see page 0) ; a bulging fontanel in young children.

Infectious causes of fever according to localizing symptoms

Signs or symptoms	Possible aetiology
Meningeal signs, seizures	Meningitis/meningoencephalitis/severe malaria
Abdominal pain or peritoneal signs	Appendicitis/peritonitis/typhoid fever
Diarrhoea, vomiting	Gastroenteritis/typhoid fever
Jaundice, enlarged liver	Viral hepatitis
Cough	Pneumonia/measles/tuberculosis if persistent
Ear pain, red tympanic membrane	Otitis media
Sore throat, enlarged lymph nodes	Streptococcal pharyngitis, diphtheria
Dysuria, urinary frequency, back pain	Urinary tract infection
Red, warm, painful skin	Erysipelas, cellulitis, abscess
Limp, difficulty walking	Osteomyelitis/septic arthritis
Rash	Measles/dengue/haemorrhagic fever/chikungunya
Bleeding (petechiae, epistaxis, etc.)	Dengue/haemorrhagic fever
Joint pain	Rheumatic fever/chikungunya/dengue

– In endemic area, always consider malaria.

– If the patient is ill appearing (see page 0) and has a persistent fever, consider HIV infection and tuberculosis, according to clinical presentation.

Laboratory and other examinations

– Children less than 2 months with a temperature higher than or equal to 37.5 °C without a focus:
• Urinary dipstick;
• Lumbar puncture (LP) if child less than 1 month or if any of the following: meningeal signs, coma, seizures, critically ill appearance (see page 0) , failure of prior antibiotic therapy, suspicion of staphylococcal infection;
• Chest X-Ray (if available) in case of signs of respiratory disease.

– Children 2 months to 3 years with a temperature higher than or equal to 38 °C without a focus:
• Urine dipstick;
• White blood cell count (WBC) if available;
• LP if meningeal signs.

– Children over 3 years and adults with a temperature higher than or equal to 39 °C:
According to clinical presentation.

Aetiological treatment

– Antibiotherapy according to the cause of fever.

– For patients with sickle cell disease, see Sickle cell disease(see page 287), Chapter 12.

– If no source of infection is found, hospitalise and treat the following children with empiric antibiotics:
• Children less than 1 month;
• Children 1 month to 3 years with WBC ≥ 15000 or ≤ 5000 cells/mm^3;
• All critically ill appearing[1](see page 0) patients or those with signs of serious illness;
For antibiotic doses according to age, see Acute pneumonia(see page 65), Chapter 2.

Symptomatic treatment

– Undress the patient. Do not wrap children in wet towels or cloths (not effective, increases discomfort, risk of hypothermia).

– Antipyretics may increase the patient's comfort but they do not prevent febrile convulsions. Do not treat for more than 3 days with antipyretics.
paracetamol PO
Children less than 1 month: 10 mg/kg 3 to 4 times daily (max. 40 mg/kg daily)
Children 1 month and over: 15 mg/kg 3 to 4 times daily (max. 60 mg/kg daily)
Adults: 1 g 3 to 4 times daily (max. 4 g daily)
or
ibuprofen PO
Children over 3 months and < 12 years: 5 to 10 mg/kg 3 to 4 times daily (max. 30 mg/kg daily)
Children 12 years and over and adults: 200 to 400 mg 3 to 4 times daily (max. 1200 mg daily)
or
acetylsalicylic acid (**ASA**) PO
Children over 16 years and adults: 500 mg to 1 g 3 to 4 times daily (max. 4 g daily)

Prevention of complications

– Encourage oral hydration. Continue frequent breastfeeding in infants.
– Look for signs of dehydration.
– Monitor urine output.

Notes:
– In pregnant or breast-feeding women use paracetamol only.
– In case of haemorrhagic fever and dengue: acetylsalicylic acid and ibuprofen are contraindicated; use paracetamol with caution in the presence of hepatic dysfunction.

[1](see page 0) Critically ill appearing child: weak grunting or crying, drowsiness, difficult to arrouse, does not smile, unconjugate or anxious gaze, pallor or cyanosis, general hypotonia. [a(see page 0) b(see page 0) c(see page 0) d(see page 0)]

Pain

- Clinical features(see page 24)

- Pain assessment(see page 24)
- Clinical examination(see page 24)
- Synthesis(see page 24)
- Pain evaluation scales(see page 25)
  - Self-evaluation scale - Children over 5 years and adults(see page 25)
  - Observational evaluation scale - Children 2 months-5 years(see page 25)
  - Observational evaluation scale - Children under 2 months(see page 25)
- Treatment(see page 26)
  - Nociceptive pain(see page 26)
    - Treatment of acute pain(see page 26)
    - Treatment of nociceptive pain in pregnant and breast-feeding women(see page 29)
  - Neuropathic pain(see page 30)
  - Mixed pain(see page 30)
  - Chronic pain(see page 30)
  - Co-analgesics(see page 30)

Pain results from a variety of pathological processes. It is expressed differently by each patient depending on cultural background, age, etc. It is a subjective experience meaning that only the individual is able to assess his/her level of pain. Regular assessment of the intensity of pain is indispensable in establishing effective treatment.

Clinical features

Pain assessment

– Intensity: use a simple verbal scale in children over 5 years and adults, and NFCS or FLACC scales in children less than 5 years (see Pain evaluation scales(see page 25)).
– Pattern: sudden, intermittent, chronic; at rest, at night, on movement, during care procedures, etc.
– Character: burning, cramping, spasmodic, radiating, etc.
– Aggravating or relieving factors, etc.

Clinical examination

– Of the organ or area where the pain is located.
– Specific signs of underlying disease (e.g. bone or osteoarticular pain may be caused by a vitamin C deficiency) and review of all systems.
– Associated signs (fever, weight loss, etc.).

Synthesis

The synthesis of information gathered during history taking and clinical examination allows aetiological diagnosis and orients treatment. It is important to distinguish:

– *Nociceptive pain*: it presents most often as acute pain and the cause-effect relationship is usually obvious (e.g. acute post-operative pain, burns, trauma, renal colic, etc.). The pain may be present in different forms, but neurological exam is normal. Treatment is relatively well standardized.

– *Neuropathic pain*, due to a nerve lesion (section, stretching, ischaemia): most often chronic pain. On a background of constant, more or less localized pain, such as paraesthesia or burning, there are recurrent acute attacks such as electric shock-like pain, frequently associated with disordered sensation (anaesthesia, hypo or hyperaesthesia). This type of pain is linked to viral infections directly affecting the CNS (herpes simplex, herpes zoster), neural compression by tumors, post- amputation pain, paraplegia, etc.

– *Mixed pain* (cancer, HIV) for which management requires a broader approach.

Pain evaluation scales

Self-evaluation scale - Children over 5 years and adults

Simple verbal scale (SVS)

Intensity of pain	No pain	Mild pain	Moderate pain	Severe pain
Scoring	0	1	2	3
Write down	0	+	++	+++

Observational evaluation scale - Children 2 months-5 years

FLACC scale (Face Limb Activity Cry Consolability)

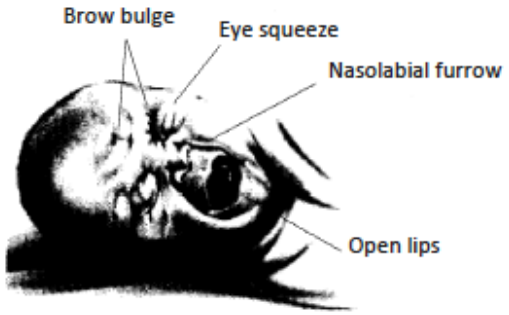
Items	Scoring		
	0	1	2
Face	No particular expression or smile	Occasional grimace or frown, withdrawn, disinterested	Frequent to constant frown, clenched jaw, quivering chin
Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking, or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid or jerking
Cry	No cry (awake or asleep)	Moans or whimpers, occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching, hugging or being talked to, distractible	Difficult to console or comfort

Each category is scored from 0 to 2, giving a final score between 0 and 10.
0 to 3: mild pain, 4 to 7: moderate pain, 7 to 10: severe pain

Observational evaluation scale - Children under 2 months

NFCS scale (Neonatal Facial Coding System)

Items	Scoring	
	0	1
Brow bulge	no	yes
Eye squeeze	no	yes
Nasolabial furrow	no	yes
Open lips	no	yes



A score of 2 or more signifies significant pain, requiring analgesic treatment.

Treatment

Treatment depends on the type and intensity of the pain. It may be both aetiological and symptomatic if a treatable cause is identified. Treatment is symptomatic only in other cases (no cause found, non-curable disease).

Nociceptive pain

The WHO classifies analgesics used for this type of pain on a three-step ladder:
– *Step 1*: non-opioid analgesics such as paracetamol and nonsteroidal anti-inflammatory drugs (NSAIDs).
– *Step 2*: weak opioid analgesics such as codeine and tramadol. Their combination with one or two Step 1 analgesics is recommended.
– *Step 3*: strong opioid analgesics, first and foremost morphine. Their combination with one or two Step 1 analgesics is recommended.

The treatment of pain is based on a few fundamental concepts:
– Pain can only be treated correctly if it is correctly evaluated. The only person who can evaluate the intensity of pain is the patient himself. The use of pain assessment scales is invaluable.
– The pain evaluation observations should be recorded in the patient chart in the same fashion as other vital signs.
– Treatment of pain should be as prompt as possible.
– It is recommended to administer analgesics in advance when appropriate (e.g. before painful care procedures).
– Analgesics should be prescribed and administered at fixed time intervals (not on demand).
– Oral forms should be used whenever possible.
– The combination of different analgesic drugs (multimodal analgesia) is advantageous.
– Start with an analgesic from the level presumed most effective: e.g., in the event of a fractured femur, start with a Step 3 analgesic.
– The treatment and dose chosen are guided by the assessment of pain intensity, but also by the patient's response which may vary significantly from one person to another.

Treatment of acute pain

Mild pain	Paracetamol + /- NSAID
Moderate pain	Paracetamol + /- NSAID + tramadol or codeine
Severe pain	Paracetamol + /- NSAID + morphine

	Analgesics	Children	Adults (except pregnant/breast-feeding women)	Remarks
Level 1	**paracetamol** PO	< 1 month: 10 mg/kg every 6 to 8 hours (max. 40 mg/kg daily) ≥ 1 month: 15 mg/kg every 6 to 8 hours (max. 60 mg/kg daily)	1 g every 6 to 8 hours (max. 4 g daily)	The efficacy of IV paracetamol is not superior to the efficacy of oral paracetamol; the IV route is restricted to situations where oral administration is impossible.
	paracetamol IV	< 1 month: 7.5 mg/kg every 6 hours (max. 30 mg/kg daily) ≥ 1 month and < 10 kg: 10 mg/kg every 6 hours (max. 30 mg/kg daily) ≥ 10 kg: 15 mg/kg every 6 hours (max. 60 mg/kg daily)	< 50 kg: 15 mg/kg every 6 hours (max. 60 mg/kg daily) ≥ 50 kg: 1 g every 6 hours (max. 4 g daily)	
	acetylsalicylic acid (**aspirin**) PO	–	300 mg to 1 g every 4 to 6 hours (max. 4 g daily)	Avoid in children less than 16 years.
	diclofenac IM	–	75 mg once daily	Treatment must be as short as possible. Respect contra-indications.
	ibuprofen PO	> 3 months: 5 to 10 mg/kg every 6 to 8 hours (max. 30 mg/kg daily) > 12 years: as for adults	200 to 400 mg every 6 to 8 hours (max. 1200 mg daily)	
Level 2	**codeine** PO	> 12 years: 30 to 60 mg every 4 to 6 hours (max. 240 mg daily)	30 to 60 mg every 4 to 6 hours (max. 240 mg daily)	Add a laxative if treatment > 48 hours.
	tramadol PO	> 12 years: 50 to 100 mg every 4 to 6 hours (max. 400 mg daily)	50 to 100 mg every 4 to 6 hours (max. 400 mg daily)	25 to 50 mg every 12 hours in elderly patients and in patients with severe renal or hepatic impairment.
	tramadol IM, slow IV or infusion	> 12 years: 50 to 100 mg every 4 to 6 hours (max. 600 mg daily)	50 to 100 mg every 4 to 6 hours (max. 600 mg daily)	

	Analgesics	Children	Adults (except pregnant/breast-feeding women)	Remarks
Level 3	**morphine** PO immediate release (MIR)	> 6 months: 0.15 mg/kg every 4 hours, to be ajusted in relation to pain intensity	10 mg every 4 hours, to be ajusted in relation to pain intensity	• Reduce the dose by half in elderly patients and patients with renal or hepatic impairment. • Add a laxative if treatment > 48 hours.
	morphine PO sustained release (MSR)	The daily dose is determined during the initial treatment with immediate release morphine (MIR). If treatment is initiated directly with MSR: > 6 months: 0.5 mg/kg every 12 hours, to be ajusted in relation to pain intensity	The daily dose is determined during the initial treatment with immediate release morphine (MIR). If treatment is initiated directly with MSR: 30 mg every 12 hours, to be ajusted in relation to pain intensity	• Do not initiate treatment with the MSR in elderly patients and patients with renal or hepatic impairment. Begin treatment with MIR. • Add a laxative if treatment > 48 hours.
	morphine SC, IM	> 6 months: 0.1 to 0.2 mg/kg every 4 hours	0.1 to 0.2 mg/kg every 4 hours	• Reduce doses by half and administer less frequently, according to clinical response, in elderly patients and patients with severe renal or hepatic impairment. • Add a laxative if treatment > 48 hours.
	morphine IV	> 6 months: 0.1 mg/kg administered in fractionated doses (0.05 mg/kg every 10 minutes) every 4 hours if necessary	0.1 mg/kg administered in fractionated doses (0.05 mg/kg every 10 minutes) every 4 hours if necessary	

Notes on the use of morphine and derivatives:

– Morphine is an effective treatment for many types of severe pain. Its analgesic effect is dosedependent. Its adverse effects have often been exaggerated and should not be an obstacle to its use.

– The most serious adverse effect of morphine is respiratory depression, which may be fatal. This adverse effect results from overdose. It is, therefore, important to increase doses gradually. Respiratory depression is preceded by drowsiness, which is a warning to monitor respiratory rate (RR).
The RR should remain equal to or greater than the thresholds indicated below:

Children 1 to 12 months	RR ≥ 25 respirations/minute
Children 1 to 2 years	RR ≥ 20 respirations/minute
Children 2 to 5 years	RR ≥ 15 respirations/minute
Children > 5 years and adults	RR ≥ 10 respirations/minute

Respiratory depression must be identified and treated quickly: verbal and physical stimulation of the patient; administration of oxygen; respiratory support (bag and mask) if necessary. If no improvement, administer **naloxone** (antagonist of morphine) in bolus to be repeated every minute until RR normalises and the excessive drowsiness resolves: 5 micrograms/kg in children and 1 to 3 micrograms/kg in adults.

– Morphine and codeine always cause constipation. A laxative should be prescribed if the opioid treatment continues more than 48 hours. **Lactulose** PO is the drug of choice: children < 1 year: 5 ml daily; children 1-6 years: 5 to 10 ml daily; children 7-14 years: 10 to 15 ml daily; adults: 15 to 45 ml daily.
If the patient's stools are soft, a stimulant laxative (**bisacodyl** PO: children > 3 years: 5 to 10 mg once daily; adults: 10 to 15 mg once daily) is preferred.

– Nausea and vomiting are common at the beginning of treatment.
Children:
ondansetron PO: 0.15 mg/kg (max. 4 mg per dose) up to 3 times daily
Do not use metoclopramide in children.
Adults:
haloperidol PO (2 mg/ml oral solution): 1 to 2 mg up to 6 times daily or **metoclopramide** PO: 5 to 10 mg 3 times daily with an interval of at least 6 hours between each dose
Do not combine haloperidol and metoclopramide.

– For chronic pain in late stage disease (cancer, AIDS etc.), morphine PO is the drug of choice. It may be necessary to increase doses over time according to pain assessment. Do not hesitate to give sufficient and effective doses.

– Morphine, tramadol and codeine have similar modes of action and should not be combined.

– Buprenorphine, nalbuphine and pentazocine must not be combined with morphine, pethidine, tramadol or codeine because they have competitive action.

Treatment of nociceptive pain in pregnant and breast-feeding women

Analgesics		Pregnancy		Breast-feeding
		0-5 months	From 6th month	
Level 1	paracetamol	first choice	first choice	first choice
	aspirin	avoid	contra-indicated	avoid
	ibuprofen	avoid	contra-indicated	possible
Level 2	codeine	possible	The neonate may develop withdrawal symptoms, respiratory depression and drowsiness in the event of prolonged administration of large doses at the end of the thirdtrimester. Closely monitor the neonate.	Use with caution, for a short period (2-3 days), at the lowest effective dose. Monitor the mother and the child: in the event of excessive drowsiness, stop treatment.
	tramadol	possible	The child may develop drowsiness when the mother receives tramadol at the end of the thirdtrimester and during breast-feeding. Administer with caution, for a short period, at the lowest effective dose, and monitor the child.	

Level 3	**morphine**	possible	The child may develop withdrawal symptoms, respiratory depression and drowsiness when the mother receives morphine at the end of the third trimester and during breast-feeding. Administer with caution, for a short period, at the lowest effective dose, and monitor the child.

Neuropathic pain

Commonly used analgesics are often ineffective in treating this type of pain.

Treatment of neuropathic pain is based on a combination of two centrally acting drugs:

amitriptyline PO
Adults: 25 mg once daily at bedtime (Week 1); 50 mg once daily at bedtime (Week 2); 75 mg once daily at bedtime (as of Week 3); max.150 mg daily. Reduce the dose by half in elderly patients.

carbamazepine PO
Adults: 200 mg once daily at bedtime (Week 1); 200 mg 2 times daily (Week 2); 200 mg 3 times daily (as of Week 3)
Given its teratogenic risk, carbamazepine should only be used in women of childbearing age when covered by effective contraception (intrauterine device or injectable progestogen). It is not recommended in pregnant women.

Mixed pain

In mixed pain with a significant component of nociceptive pain, such as in cancer or AIDS, morphine is combined with antidepressants and antiepileptics.

Chronic pain

In contrast to acute pain, medical treatment alone is not always sufficient in controlling chronic pain. A multidisciplinary approach including medical treatment, physiotherapy, psychotherapy and nursing is often necessary to allow good pain relief and encourage patient selfmanagement.

Co-analgesics

The combination of certain drugs may be useful or even essential in the treatment of pain: antispasmodics, muscle relaxants, anxiolytics, corticosteroids, local anaesthesia, etc.

Anaemia

- Clinical features(see page 31)
- Laboratory(see page 31)
- Aetiological treatment(see page 31)
- Blood transfusion(see page 32)
  - Indications(see page 32)
  - Volume to be transfused(see page 32)
  - Monitoring(see page 33)
- Prevention(see page 33)

Anaemia is defined as a haemoglobin (Hb) level below reference values, which vary depending on sex, age and pregnancy status (see Table 2(see page 33)).

Anaemia may be caused by:
− Decreased production of red blood cells: iron deficiency, nutritional deficiencies (folic acid, vitamin B_{12}, vitamin A), depressed bone marrow function, certain infections (HIV, visceral leishmaniasis), renal failure;
− Loss of red blood cells: acute or chronic haemorrhage (ancylostomiasis, schistosomiasis, etc.);
− Increased destruction of red blood cells (haemolysis): parasitic (malaria), bacterial and viral (HIV) infections; haemoglobinopathies (sickle cell disease, thalassaemia); intolerance to certain drugs (primaquine, dapsone, co-trimoxazole, etc.) in patients with G6PD deficiency.

In tropical settings, the causes of anaemia are often interlinked.

Clinical features

– Common signs: pallor of the conjunctivae, mucous membranes, palms of hands and soles of feet; fatigue, dizziness, dyspnoea, tachycardia, heart murmur.
– Signs that anaemia may be immediately life threatening: sweating, thirst, cold extremities, oedema in the lower limbs, respiratory distress, angina, shock.
– Significant signs: cheilosis and glossitis (nutritional deficiency), jaundice, hepatosplenomegaly, dark coloured urine (haemolysis), bleeding (maelena, haematuria, etc.), signs of malaria(see page 123).

Laboratory

– Hb levels
– Rapid test or systematic thick and thin blood films in areas where malaria is endemic.
– Urinary dipstick: check for haemoglobinuria or haematuria.
– Emmel test if sickle cell disease is suspected.
– Blood cell count if available to guide diagnosis.

Table 1 - Possible diagnoses with blood cell count

Characteristics	Possible diagnoses
Macrocytic	Deficiency (folic acid, vitamin B_{12}), chronic alcoholism
Microcytic	Iron deficiency (malnutrition, chronic haemorrhage), chronic inflammation (HIV infection, cancer), thalassaemia
Normocytic	Acute haemorrhage, renal failure, haemolysis
Reduced number of reticulocytes	Deficiency (iron, folic acid, vitamin B_{12}), spinal tumour, renal failure
Increased or normal number of reticulocytes	Haemolysis, sickle cell disease, thalassaemia
Eosinophilia	Ancylostomiasis, trichuriasis, schistosomiasis, HIV infection, malignant haemopathies

Aetiological treatment

Anaemia in itself is not an indication for transfusion. Most anaemias are well tolerated and can be corrected with simple aetiological treatment.
Aetiological treatment may be given alone or together with transfusion.

– Iron deficiency

elemental iron PO for 3 months. Doses are expressed in elemental iron[1](see page 0):
Neonates: 1 to 2 mg/kg 2 times daily
Children 1 month to < 6 years: 1.5 to 3 mg/kg 2 times daily
Children 6 to < 12 years: 65 mg 2 times daily
Children ≥ 12 years and adults: 65 mg 2 to 3 times daily

Age	Weight	Treatment	
		45 mg/5 ml syrup	65 mg tablet
< 1 month	< 4 kg	0.5 ml x 2	–
1 month to < 1 year	4 to < 10 kg	1.5 ml x 2	–
1 to < 6 years	10 to < 20 kg	2.5 ml x 2	–
6 to < 12 years	20 to < 40 kg	–	1 tab x 2
≥ 12 years and adults	≥ 40 kg	–	1 tab x 2 or 3

or preferably,
elemental iron + **folic acid** PO based on elemental iron dosages.

– Helminthic infections: see Schistosomiasis(see page 142) and Nematode infections(see page 147) (Chapter 6).

– Folic acid deficiency (rarely isolated)
folic acid PO for 4 months
Children < 1 year: 0.5 mg/kg once daily
Children ≥ 1 year and adults: 5 mg once daily

– Malaria: see Malaria(see page 123) (Chapter 6). In the event of associated iron deficiency, wait 4 weeks after malaria treatment before prescribing iron supplements.

– Suspected haemolytic anaemia: stop any drug that causes haemolysis in patients with (or that may possibly have) G6PD deficiency.

Blood transfusion

Indications

To decide whether to transfuse, several parameters should be taken into account:
– Clinical tolerance of anaemia
– Underlying conditions (cardiovascular disease, infection, etc.)
– Rate at which anaemia develops.
– Hb levels

If transfusion is indicated, it should be carried out without delay[2](see page 0). For transfusion thresholds, see Table 2(see page 33).

Volume to be transfused

In the absence of hypovolaemia or shock:
Children < 20 kg: 15 ml/kg of red cell concentrate in 3 hours or 20 ml/kg of whole blood in 4 hours
Children ≥ 20 kg and adults: start with an adult unit of whole blood or red cell concentrate; do not exceed a transfusion rate of 5 ml/kg/hour
Repeat if necessary, depending on clinical condition.

Monitoring

Monitor the patient's condition and vital signs (heart rate, blood pressure, respiratory rate, temperature):
– During the transfusion: 5 minutes after the start of transfusion, then every 15 minutes during the first hour, then every 30 minutes until the end of the transfusion.
– After the transfusion: 4 to 6 hours after the end of the transfusion.

If signs of circulatory overload appear:
– Stop temporarily the transfusion.
– Sit the patient in an upright position.
– Administer oxygen.
– Administer **furosemide** by slow IV:
Children: 0.5 to 1 mg/kg
Adults: 20 to 40 mg
Repeat the injection (same dose) after 2 hours if necessary.
Once the patient has been stabilised, start the transfusion again after 30 minutes.

Prevention

– Iron (and folic acid) deficiency:
• *Drug supplements*
elemental iron PO as long as the risk of deficiency persists (e.g. pregnancy, malnutrition)
Neonates: 4.5 mg once daily
Children 1 month to < 12 years: 1 to 2 mg/kg once daily (max. 65 mg daily)
Children ≥ 12 years and adults: 65 mg once daily

Age	Weight	Prevention	
		45 mg/5 ml syrup	65 mg tablet
< 1 month	< 4 kg	0.5 ml	–
1 month to < 1 year	4 to < 10 kg	1 ml	–
1 to < 6 years	10 to < 20 kg	2.5 ml	–
6 to < 12 years	20 to < 40 kg	5 ml	–
≥ 12 years and adults	≥ 40 kg	–	1 tab

or preferably,
elemental iron + **folic acid** PO based on elemental iron dosages.

• *Nutritional supplements* (if the basic diet is insufficient)

– In the event of sickle cell anaemia: see Sickle cell disease(see page 287) (Chapter 12).

– Early treatment of malaria, helminthic infections, etc.

Table 2 - Definition of anaemia and transfusion thresholds

Patients	Hb levels defining anaemia	Transfusion threshold

Children 2-6 months	< 9.5 g/dl	Hb < 4 g/dl, even if there are no signs of decompensation Hb ≥ 4 g/dl and < 6 g/dl if there are signs of decompensation or sickle cell disease or severe malaria or serious bacterial infection or pre-existing heart disease
Children 6 months-5 years	< 11 g/dl	
Children 6-11 years	< 11.5 g/dl	
Children 12-14 years	< 12 g/dl	
Men	< 12 g/dl	Hb < 7 g/dl if there are signs of decompensation or sickle cell disease or severe malaria or serious bacterial infection or pre-existing heart disease
Women	< 13 g/dl	
Pregnant women	< 11 g/dl (1^{st} and 3^{rd} trimester) < 10.5 g/dl (2^{nd} trimester)	**< 36 weeks** Hb ≤ 5 g/dl, even if there are no signs of decompensation Hb > 5 g/dl and < 7 g/dl if there are signs of decompensation or sickle cell disease or severe malaria or serious bacterial infection or pre-existing heart disease
		≥ 36 weeks Hb ≤ 6 g/dl, even if there are no signs of decompensation Hb > 6 g/dl and < 8 g/dl if there are signs of decompensation or sickle cell disease or severe malaria or serious bacterial infection or pre-existing heart disease

1 (see page 0) Available in 140 mg/5 ml syrup of ferrous fumarate containing approximately 45 mg/5 ml of elemental iron and 200 mg ferrous sulfate tablets or ferrous sulfate + folic acid tablets containing 65 mg of elemental iron. Tablets of 185 or 200 mg ferrous fumurate or sulfate + folic acid (60 or 65 mg of elemental iron) contain 400 micrograms folic acid.

2 (see page 0) Before transfusing: determine the recipient's and potential donors' blood groups/rhesus and carry out screening tests on the donor's blood for HIV-1 and 2, syphilis and, in endemic areas, malaria and Chagas disease.

Dehydration

- Clinical features and assessment (see page 35)
- Treatment of dehydration (see page 35)
  - Severe dehydration (see page 35)
  - Some dehydration (see page 36)
  - No dehydration (see page 37)
- Treatment of diarrhoea (see page 37)
- References (see page 37)

– Dehydration results from excessive loss of water and electrolytes from the body. If prolonged, dehydration can compromise organ perfusion, resulting in shock.
– It is principally caused by diarrhoea, vomiting and severe burns.

− Children are particularly susceptible to dehydration due to frequent episodes of gastroenteritis, high surface area to volume ratio and inability to fully communicate, or independently meet their fluid needs.

The protocols below are focused on treatment of dehydration caused by diarrhoea and vomiting. Alternative treatment protocols should be used for children with malnutrition (see Severe acute malnutrition(see page 38), Chapter 1) or in patients with severe burns (see Burns(see page 258), Chapter 10).

Clinical features and assessment

− History of diarrhoea and/or vomiting and concomitant reduced urine output.
− Clinical features depend on the degree of dehydration (see table below). Features such as dry mouth, absence of tears may also be noted.
− Patients with severe dehydration should be assessed for shock (tachycardia, low blood pressure and delayed capillary refill time etc.).
− Electrolyte disorders may cause tachypnoea, muscle cramps or weakness, cardiac arrhythmia (irregular heart rate, palpitation), confusion and/or seizures.

Classification of degree of dehydration (adapted from the WHO)[1(see page 37),2(see page 37)]

	Severe dehydration At least 2 of the following signs:	**Some dehydration** At least 2 of the following signs:	**No dehydration** No signs of "severe" or "some" dehydration.
Mental status	Lethargic or unconscious	Restless or irritable	Normal
Radial pulse	Weak or absent	Palpable	Easily palpable
Eyes[(a)]	Sunken	Sunken	Normal
Skin pinch[(b)]	Goes back very slowly (> 2 seconds)	Goes back slowly (< 2 seconds)	Goes back quickly (< 1 second)
Thirst	Drinks poorly or not able to drink	Thirst, drinks quickly	No thirst, drinks normally

[(a)] Sunken eyes may be a normal feature in some children. Ask the mother if the child's eyes are the same as usual or if they are more sunken than usual.
[(b)] Skin pinch is assessed by pinching the skin of the abdomen between the thumb and forefinger without twisting. In older people this sign is not reliable as normal aging diminishes skin elasticity.

Treatment of dehydration

Severe dehydration

– Treat shock if present (see Shock(see page 10), Chapter 1).
– If able to drink, administer oral rehydration solution (ORS) PO whilst obtaining IV access.
– Insert peripheral IV line using large caliber catheter (22-24G in children or 18G in adults) or intraosseous needle.
– Administer **Ringer lactate** (RL)[1(see page 0)] according to WHO Treatment Plan C, monitoring infusion rate closely:

WHO Treatment Plan C[1(see page 37),2(see page 37)]

Age	First, give 30 ml/kg over[a]:	Then, give 70 ml/kg over:
Children < 1 year	1 hour	5 hours
Children ≥ 1 year and adults	30 minutes	2 ½ hours

[a] Repeat once if radial pulse remains weak or absent after first bolus.

– In case of suspected severe anaemia, measure haemoglobin and treat accordingly (see Anaemia(see page 30), Chapter 1).2(see page 0)
– As soon as the patient is able to drink safely (often within 2 hours), provide ORS as the patient tolerates. ORS contains glucose and electrolytes which prevent development of complications.
– Monitor ongoing losses closely. Assess clinical condition and degree of dehydration at regular intervals to ensure continuation of appropriate treatment.

If over the course of treatment the patient:

• remains or becomes lethargic: measure blood glucose level and/or treat hypoglycaemia (see Hypoglycaemia(see page 20), Chapter 1).

• develops muscle cramps/weakness and abdominal distention: treat for moderate hypokalaemia with **7.5% potassium chloride** syrup (1 mmol of K^+/ml) PO for 2 days:
Children under 45 kg: 2 mmol/kg (2 ml/kg) daily (according to weight, the daily dose is divided into 2 or 3 doses)
Children 45 kg and over and adults: 30 mmol (30 ml) 3 times daily
This treatment should only be given as an inpatient3(see page 0) .

• develops peri-orbital or peripheral oedema: reduce the infusion rate to a minimum, auscultate the lungs, re-evaluate the stage of dehydration and the necessity of continuing IV rehydration. If IV rehydration is still required, continue the infusion at a slower rate and observe the patient closely. If IV rehydration is no longer required, change to oral treatment with ORS.

• develops dyspnoea, cough and bibasal crepitations are heard on auscultation of the lungs: sit the patient up, reduce the infusion rate to a minimum and administer one dose of **furosemide** IV (1 mg/kg in children; 40 mg in adults). Monitor the patient closely over 30 minutes and assess for underlying cardiorespiratory or renal disease. Once the patient is stabilised, reassess the degree of dehydration and the necessity of continuing IV rehydration. If IV rehydration is still required, re-start at half the previous infusion rate and monitor closely. If IV rehydration is no longer required, change to oral treatment with ORS.

Some dehydration

– Administer ORS according to WHO Treatment Plan B which equates to 75 ml/kg ORS given over 4 hours.

WHO Treatment Plan B1(see page 37), 4(see page 0)

Age	< 4 months	4 to 11 months	12 to 23 months	2 to 4 years	5 to 14 years	≥ 15 years
Weight	< 5 kg	5 to 7.9 kg	8 to 10.9 kg	11 to 15.9 kg	16 to 29.9 kg	≥ 30 kg
Quantity of ORS over 4 hours	200 to 400 ml	400 to 600 ml	600 to 800 ml	800 to 1200 ml	1200 to 2200 ml	2200 to 4000 ml

– Encourage additional age-appropriate fluid intake, including breastfeeding in young children. Give additional ORS after each loose stool (see below).
– Monitor ongoing losses closely. Assess clinical condition and degree of dehydration at regular intervals to ensure continuation of appropriate treatment.

No dehydration

Prevent dehydration:
– Encourage age-appropriate fluid intake, including breastfeeding in young children.
– Administer ORS according to WHO Treatment Plan A after any loose stool.

WHO Treatment Plan A[1](see page 37),[2](see page 37)

Age	Quantity of ORS
Children < 2 years	50 to 100 ml *(10 to 20 teaspoons)*
Children 2 to 10 years	100 to 200 ml *(½ to 1 glass)*
Children > 10 years and adults	at least 250 ml (*at least 1 glass)*

Treatment of diarrhoea

In addition to the WHO treatment plan corresponding to patient's degree of dehydration:
– Administer aetiologic treatment if required.
– Administer zinc sulfate to children under 5 years (see Acute diarrhoea(see page 79), Chapter 3).

1(see page 0) If RL not available, 0.9% sodium chloride can be used.
2(see page 0) If transfusion is required, it should be provided in parallel to IV fluids, using a separate IV line. The blood volume administered should be deducted from the total volume of Plan C.
3(see page 0) If available, take blood tests to monitor urea and electrolyte levels.
4(see page 0) For more detailed information on ORS recommendations by age and weight, refer to the guide Management of a cholera epidemic, MSF.

References

1. World Health Organization. The treatment of diarrhoea : a manual for physicians and other senior health workers, 4th rev. World Health Organization. 2005. https://apps.who.int/iris/handle/10665/43209

2. World Health Organization. Pocket book of Hospital Care for children. Guidelines for the Management of Common Childhood Illnesses. 2013. https://apps.who.int/iris/bitstream/handle/10665/81170/9789241548373_eng.pdf?sequence=1

Severe acute malnutrition

- Children over 6 months of age(see page 38)
  - Treatment(see page 39)
    - 1) Nutritional treatment(see page 39)
    - 2) Routine medical treatment(see page 39)
    - 3) Management of common complications(see page 39)
- Adolescents and adults(see page 41)

Severe acute malnutrition (SAM) is caused by a significant imbalance between nutritional intake and individual needs. It is most often caused by both quantitative (number of kilocalories/day) and qualitative (vitamins and minerals, etc.) deficiencies.

Children over 6 months of age

The two principal forms of SAM are:
– *Marasmus*: significant loss of muscle mass and subcutaneous fat, resulting in a skeletal appearance.
– *Kwashiorkor*: bilateral oedema of the lower limbs/oedema of the face, often associated with cutaneous signs (shiny or cracked skin, burn-like appearance; discoloured and brittle hair).

The two forms may be associated (marasmic-kwashiorkor).

In addition to these characteristic signs, SAM is accompanied by significant physiopathological disorders (metabolic disturbances, anaemia, compromised immunity, leading to susceptibility to infections often difficult to diagnose, etc.).
Complications are frequent and potentially life-threatening.
Mortality rates may be elevated in the absence of appropriate medical management.

Admission and discharge criteria for treatment programmes for SAM are both anthropometric and clinical:
– Mid-upper arm circumference (MUAC) is the circumference, measured in mid-position, of the relaxed left upper arm, taken in children of 6 to 59 months (65 to 110 cm in height). MUAC measures the degree of muscle wasting. A MUAC of < 115 mm indicates SAM and significant mortality risk.
– Weight for height (W/H) index assesses the degree of weight loss by comparing the weight of the SAM child with non-malnourished children of the same height. Severe malnutrition is defined as a W/H index of < – 3 Z-score with reference to the new WHO child growth standards[1](see page 0) .
– The presence of bilateral oedema of the lower limbs (when other causes of oedema have been ruled out) indicates SAM, regardless of the MUAC and W/H.

Usual admission criteria are: MUAC < 115 mm (MUAC is not used as an admission criterion in children older than 59 months or taller than 110 cm) or W/H < – 3 Z-score[1](see page 0) or presence of bilateral oedema of the lower limbs.

Usual discharge (cure) criteria are: W/H > – 2 Z-score[1](see page 0) and absence of bilateral oedema (2 consecutive assessments, one week apart) and absence of acute medical problems.

Medical management (hospitalisation or ambulatory care) is based on the presence or absence of associated serious complications:
– Children exhibiting anorexia, or significant medical complications, such as severe anaemia, severe dehydration or severe infection (complicated acute malnutrition) should be hospitalised[2](see page 0) .
– Children without significant medical complications (uncomplicated acute malnutrition) may undergo treatment on an ambulatory basis, with weekly medical follow-up.

Treatment

1) Nutritional treatment

Nutritional treatment is based on the use of therapeutic foods enriched with vitamins and minerals:

– Therapeutic milks (for use exclusively in hospitalised patients):
• F-75 therapeutic milk, low in protein, sodium and calories (0.9 g of protein and 75 kcal per 100 ml) is used in the initial phase of treatment for patients suffering from complicated SAM. It is used to cover basic needs while complications are being treated. It is given in 8 daily meals.
• F-100 therapeutic milk, in which the concentration of protein and calories is higher (2.9 g of protein and 100 kcal per 100 ml), replaces F-75 after several days, once the patient is stabilised (return of appetite, clinical improvement; disappearance or reduction of oedema). The objective is to facilitate rapid weight gain. It can be given with, or be replaced by, RUTF.

– RUTF (ready-to-use therapeutic food), i.e. foods which are ready for consumption (for example, peanut paste enriched with milk solids, such as Plumpy'nut®), are used in children treated in both hospital or ambulatory settings. The nutritional composition of RUTF is similar to F-100, but the iron content is higher. It is designed to promote rapid weight gain (approximately 500 kcal per 100 g). RUTF are the only therapeutic foods which can be used in ambulatory treatment.

Furthermore, it is important to give drinking water, in addition to meals, especially if the ambient temperature is high or the child has a fever.

Breastfeeding should continue in children of the appropriate age.

2) Routine medical treatment

In the absence of specific medical complications, the following routine treatments should be implemented in both ambulatory and hospital settings:

Infections

– Measles vaccination on admission.
– Broad spectrum antibiotherapy starting on D1 (**amoxicillin** PO: 50 mg/kg 2 times daily for 5 days)[3](see page 0).
– In endemic malaria areas: rapid test on D1, with treatment in accordance with results. If testing is not available, give malaria treatment (Malaria(see page 123), Chapter 6).
– Treatment for intestinal worms on D8:
albendazole PO
Children > 6 months: 400 mg single dose (200 mg in children > 6 months but < 10 kg)

Micronutrient deficiencies

Therapeutic foods correct most of these deficiencies.

3) Management of common complications

Diarrhoea and dehydration

Diarrhoea is common in malnourished children. Therapeutic foods facilitate the recovery of gastrointestinal mucosa and restore the production of gastric acid, digestive enzymes and bile. Amoxicillin, administered as part of routine treatment, is effective in reducing bacterial load. Diarrhoea generally resolves without any additional treatment.

Watery diarrhoea is sometimes related to another pathology (otitis, pneumonia, malaria, etc.), which should be considered.

If an aetiological treatment is necessary, see Acute diarrhoea(see page 79), Chapter 3.

If a child has a significant diarrhoea (very frequent or abundant stools) but is not dehydrated, administer specific oral rehydration solution (ReSoMal, see below), after each watery stool, to avoid dehydration, according to the WHO Treatment Plan A (see Dehydration(see page 34), Chapter 1).

However, if the child has no profuse diarrhoea, give plain water (not ReSoMal) after each loose stool.

Dehydration is more difficult to assess in malnourished than healthy children (e.g., delay in return of skin pinch and sunken eyes are present even without dehydration in children with marasmus).

The diagnosis is made on the basis of a history of watery diarrhoea of recent onset accompanied by weight loss, corresponding to fluid losses since the onset of diarrhoea. Chronic and persistent diarrhoea does not require rapid rehydration.

In the event of dehydration:

– *If there is no hypovolaemic shock*, rehydration is made by the oral route (if necessary using a nasogastric tube), with specific oral rehydration solution (ReSoMal) 4(see page 0), containing less sodium and more potassium than standard solutions.
ReSoMal is administered under medical supervision (clinical evaluation and weight every hour). The dose is 20 ml/kg/hour for the first 2 hours, then 10 ml/kg/hour until the weight loss (known or estimated) has been corrected. Give ReSoMal after each watery stool according to the WHO Treatment Plan A (see Dehydration(see page 34), Chapter 1).
In practice, it is useful to determine the target weight before starting rehydration. The target weight is the weight before the onset of diarrhoea. If the child is improving and showing no signs of fluid overload, rehydration is continued until the previous weight is attained.
If the weight loss cannot be measured (e.g. in newly admitted child), it can be estimated at 2 to 5% of the child's current weight. The target weight should not exceed 5% of the current weight (e.g., if the child weighs 5 kg before starting rehydration, the target weight should not exceed 5.250 kg). Regardless of the target weight, rehydration should be stopped if signs of fluid overload appear.

– *In case of hypovolaemic shock* (weak and rapid or absent radial pulse, cold extremities, CRT ≥ 3 seconds, whether or not consciousness is altered) in a child with diarrhoea or dehydration:

- Place an IV line and administer 10 ml/kg of **0.9% sodium chloride** over 30 minutes, under close medical supervision.
  Simultaneously:
- Start broad spectrum antibiotic therapy: **ceftriaxone** IV 100 mg/kg once daily + **cloxacillin** IV 50 mg/kg every 6 hours
- Administer oxygen (2 litres minimum).
- Check blood glucose level or, if not available, treat for hypoglycaemia (see Hypoglycaemia(see page 20), Chapter 1).
  Every 5 minutes, evaluate clinical response (recovery of consciousness, strong pulse, CTR < 3 seconds) and check for signs of over-hydration.
  - If the clinical condition has improved after 30 minutes, switch to the oral route with **ReSoMal**: 5 ml/kg every 30 minutes for 2 hours.
  - If the clinical condition has not improved, administer again 10 ml/kg of **0.9% sodium chloride** over 30 minutes then, when the clinical condition has improved, switch to the oral route as above.
  When switching to the oral route, stop the infusion but leave the catheter (capped) in place to keep a venous access, for IV antibiotherapy.

Bacterial infections

Lower respiratory infections, otitis, skin and urinary infections are common, but sometimes difficult to identify (absence of fever and specific symptoms).
Infection should be suspected in a drowsy or apathetic child.
Severe infection should be suspected in the event of shock, hypothermia or hypoglycaemia. Since the infectious focus may be difficult to determine, a broad spectrum antibiotic therapy (cloxacilline + ceftriaxone) is recommended.

Fever

Avoid antipyretics. If absolutely necessary, **paracetamol** PO: 10 mg/kg 3 times daily maximum
Do not wrap children in wet towels or cloths: not effective, increases disconfort, risk of hypothermia.

Hypothermia and hypoglycaemia

Hypothermia (axillary temperature < 35 °C) is a frequent cause of death in the first days of hospitalisation.
Prevention measures include keeping the child close to the mother 's body (kangaroo method) and provision of blankets.
In case of hypothermia, warm the child as above, monitor the temperature, treat hypoglycaemia (see Hypoglycaemia(see page 20), Chapter 1). Severe infection should be suspected in the event of hypothermia (see above).

Oral candidiasis

Look routinely for oral candidiadis as it interferes with feeding; see Stomatitis(see page 87), Chapter 3.

If the child fails to recover despite appropriate nutritional and medical treatment, consider another pathology: tuberculosis, HIV infection, etc.

Adolescents and adults

Clinical examination of the patient (sudden weight loss, loss of mobility from muscle wasting, cachexia, bilateral lower limb oedema in the absence of other causes of oedema) is indispensable for the diagnosis and adapted medical, nutritional and even social care of the patient.

Admission and discharge criteria, as a rough guide, are:

– Admission criteria:
Adolescents: W/H according to NCHS-CDC-WHO 1982 reference table or bilateral lower limb oedema (Grade 3 or more, having excluded other causes of oedema).
Adults: MUAC < 160 mm or bilateral lower limb oedema or MUAC < 185 mm in poor general condition (for example, inability to stand, evident dehydration).
As in children, any malnourished patient presenting with significant complications should initially be hospitalised, regardless of the anthropometric criteria above.

– Discharge criteria:
Adolescents: as in children.
Adults: weight gain of 10-15% over admission weight and oedema below Grade 2 and good general condition.

Nutritional treatment follows the same principles as in children, but the calorie intake in relation to body weight is lower.

Routine treatment is similar to that in children, with the following exceptions:
– Measles vaccine is only administered to adolescents (up to age 15).
– Antibiotics are not routinely given, but infections should be considered, and treated or excluded, in the assessment of the patient.

1 (see page 0) Some national programmes define anthropometric admission and discharge criteria with reference to NCHS growth standards, with thresholds expressed in percentage of the median.

[a (see page 0) b (see page 0) c (see page 0)]

2 (see page 0) As a rule, any malnourished child presenting with medical complications should initially be hospitalised, even if s/he suffers from moderate, rather than severe, malnutrition (W/H > – 3 Z-score).

3 (see page 0) If specific signs of infection are present, the choice of treatment should be directed by the suspected focus.

4 (see page 0) Except for cholera, in which case standard oral rehydration solutions are used.

Chapter 2: Respiratory diseases

- Acute upper airway obstruction(see page 43)
- Rhinitis and rhinopharyngitis (common cold)(see page 45)
- Acute sinusitis(see page 46)
- Acute pharyngitis(see page 48)
- Diphtheria(see page 50)
- Other upper respiratory tract infections(see page 53)
    - Laryngotracheitis and laryngotracheobronchitis (croup)(see page 53)
    - Epiglottitis(see page 55)
    - Bacterial tracheitis(see page 56)
- Otitis(see page 57)
    - Acute otitis externa(see page 57)
    - Acute otitis media (AOM)(see page 57)
    - Chronic suppurative otitis media (CSOM)(see page 59)
- Whooping cough (pertussis)(see page 60)
- Bronchitis(see page 62)
    - Acute bronchitis(see page 62)
    - Chronic bronchitis(see page 62)
- Bronchiolitis(see page 63)
- Acute pneumonia(see page 65)
    - Pneumonia in children under 5 years of age(see page 65)
    - Pneumonia in children over 5 years and adults(see page 68)
    - Persistent pneumonia(see page 70)
- Staphylococcal pneumonia(see page 70)
- Asthma(see page 72)
    - Asthma attack (acute asthma)(see page 72)
    - Chronic asthma(see page 75)
- Pulmonary tuberculosis(see page 76)

Acute upper airway obstruction

- Clinical features(see page 43)
- Management in all cases(see page 44)
- Management of foreign body aspiration(see page 44)
- Differential diagnosis and management of airway obstructions of infectious origin(see page 45)
- Management of other causes(see page 45)

Acute upper airway obstruction can be caused by foreign body aspiration, viral or bacterial infections (croup, epiglottitis, tracheitis), anaphylaxis, burns or trauma.
Initially stable and partial obstruction may worsen and develop into a life-threatening emergency, especially in young children.

Clinical features

Clinical signs of the severity of obstruction:

Obstruction	Signs	Danger signs
Complete	• Respiratory distress followed by cardiac arrest	Yes
Imminent complete	• Severe respiratory distress with cyanosis or SpO_2 < 90% • Agitation or lethargy • Tachycardia, capillary refill time > 3 seconds	

Severe	• Stridor (abnormal high pitched sound on inspiration) at rest
	• Severe respiratory distress:
	  • Severe intercostal and subcostal retractions
	  • Nasal flaring
	  • Substernal retractions (inward movement of the breastbone during inspiration)
	  • Severe tachypnoea	

Moderate	• Stridor with agitation
	• Moderate respiratory distress:
	  • Mild intercostal and subcostal retractions
	  • Moderate tachypnoea
		No

Mild	• Cough, hoarse voice, no respiratory distress	

Management in all cases

– Examine children in the position in which they are the most comfortable.
– Evaluate the severity of the obstruction according to the table above.
– Monitor SpO_2, except in mild obstruction.
– Administer oxygen continuously:
• to maintain the SpO_2 between 94 and 98% if it is ≤ 90%1(see page 0) or if the patient has cyanosis or respiratory distress;
• if pulse oxymeter is not available: at least 5 litres/minute or to relieve the hypoxia and improve respiration.
– Hospitalize (except if obstruction is mild), in intensive care if danger signs.
– Monitor mental status, heart and respiratory rate, SpO_2 and severity of obstruction.
– Maintain adequate hydration by mouth if possible, by IV if patient unable to drink.

Management of foreign body aspiration

Acute airway obstruction (the foreign body either completely obstructs the pharynx or acts as a valve on the laryngeal inlet), no warning signs, most frequently in a child 6 months-5 years playing with a small object or eating. Conscience is initially maintained.

Perform maneuvers to relieve obstruction only if the patient cannot speak or cough or emit any sound:
– Children over 1 year and adults:
Heimlich manoeuvre: stand behind the patient. Place a closed fist in the pit of the stomach, above the navel and below the ribs. Place the other hand over fist and press hard into the abdomen with a quick, upward thrust. Perform one to five abdominal thrusts in order to compress the lungs from the below and dislodge the foreign body.
– Children under 1 year:
Place the infant face down across the forearm (resting the forearm on the leg) and support the infant's head with the hand. With the heel of the other hand, perform one to five slaps on the back, between

shoulder plates.
If unsuccessful, turn the infant on their back. Perform five forceful sternal compressions as in cardiopulmonary resuscitation: use 2 or 3 fingers in the center of the chest just below the nipples. Press down approximately one-third the depth of the chest (about 3 to 4 cm).

Repeat until the foreign body is expelled and the patient resumes spontaneous breathing (coughing, crying, talking). If the patient loses consciousness ventilate and perform cardiopulmonary rescucitation. Tracheostomy if unable to ventilate.

Differential diagnosis and management of airway obstructions of infectious origin

Infections	Symptoms	Appearance	Timing of symptoms
Viral croup	Stridor, cough and moderate respiratory difficulty	Prefers to sit	Progressive
Epiglottitis	Stridor, high fever and severe respiratory distress	Prefers to sit, drooling (cannot swallow their own saliva)	Rapid
Bacterial tracheitis	Stridor, fever, purulent secretions and severe respiratory distress	Prefers to lie flat	Progressive
Retropharyngeal or tonsillar abscess	Fever, sore throat and painful swallowing, earache, trismus and hot potato voice	Prefers to sit, drooling	Progressive

– Croup, epiglottitis, and tracheitis: see Other upper respiratory tract infections(see page 53).
– Abscess: refer for surgical drainage.

Management of other causes

– Anaphylactic reaction (angioedema): see Anaphylactic shock(see page 13) (Chapter 1)
– Burns to the face or neck, smoke inhalation with airway oedema: see Burns(see page 258) (Chapter 10).

1(see page 0) If possible it is better to treat all patients with a SpO_2 < 95% with oxygen.

Rhinitis and rhinopharyngitis (common cold)

- Clinical features(see page 46)
- Treatment(see page 46)

Rhinitis (inflammation of the nasal mucosa) and rhinopharyngitis (inflammation of the nasal and pharyngeal mucosa) are generally benign, self-limited and most often of viral origin. However, they may be an early sign of another infection (e.g. measles or influenza) or may be complicated by a bacterial infection (e.g. otitis media or sinusitis).

Clinical features

– Nasal discharge or obstruction, which may be accompanied by sore throat, fever, cough, lacrimation, and diarrhoea in infants. Purulent nasal discharge is not indicative of a secondary bacterial infection.
– In children under 5 years, routinely check the tympanic membranes to look for an associated otitis media.

Treatment

– Antibiotherapy is not recommended: it does not promote recovery nor prevent complications.

– Treatment is symptomatic:
• Clear the nose with 0.9% sodium chloride[1](see page 0) .
• Fever, throat soreness: paracetamol PO for 2 to 3 days (Fever(see page 21), Chapter 1).

[1](see page 0) For a child: place him on his back, head turned to the side, and instil 0.9% sodium chloride into each nostril.

Acute sinusitis

- Clinical features(see page 46)
  - Sinusitis in adults(see page 46)
  - Sinusitis in children(see page 47)
- Treatment(see page 47)
  - Symptomatic treatment(see page 47)
  - Antibiotherapy(see page 47)
  - Other treatments(see page 47)

Acute sinusitis is an inflammation of one or more of the sinus cavities, caused by an infection or allergy. Most acute sinus infections are viral and resolve spontaneously in less than 10 days. Treatment is symptomatic.
Acute bacterial sinusitis may be a primary infection, a complication of viral sinusitis or of dental origin. The principal causative organisms are *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis*.
It is essential to distinguish between bacterial sinusitis and common rhinopharyngitis (see Rhinitis and rhinopharyngitis(see page 45)). Antibiotic therapy is required in case of bacterial sinusitis only.
Without treatment, severe sinusitis in children may cause serious complications due to the spread of infection to the neighbouring bony structures, orbits or the meninges.

Clinical features

Sinusitis in adults

– Purulent unilateral or bilateral discharge, nasal obstruction
and
– Facial unilateral or bilateral pain that increases when bending over; painful pressure in maxillary area

or behind the forehead.
– Fever is usually mild or absent.

Sinusitis is likely if symptoms persist for longer than 10 to 14 days or worsen after 5 to 7 days or are severe (severe pain, high fever, deterioration of the general condition).

Sinusitis in children

– Same symptoms; in addition, irritability or lethargy or cough or vomiting may be present.
– In the event of severe infection: deterioration of the general condition, fever over 39 °C, periorbital or facial oedema.

Treatment

Symptomatic treatment

– Fever(see page 21) and pain(see page 23) (Chapter 1).
– Clear the nose with 0.9% sodium chloride[1](see page 0) .

Antibiotherapy

– In adults:

Antibiotherapy is indicated if the patient meets the criteria of duration or severity of symptoms. Oral amoxicillin is the first-line treatment.
If the diagnosis is uncertain (moderate symptoms < 10 days) and the patient can be reexamined in the next few days, start with a symptomatic treatment, as for rhinopharyngitis or viral sinusitis.

– In children:

Antibiotic therapy is indicated if the child has severe symptoms or mild symptoms associated with risk factors (e.g. immunosuppression, sickle cell disease, asthma). Oral amoxicillin is the first-line treatment.
amoxicillin PO for 7 to 10 days:
Children: 30 mg/kg 3 times daily (max. 3 g daily)
Adults: 1 g 3 times daily

In the event of failure to respond within 48 hours of therapy:
amoxicillin/clavulanic acid PO for 7 to 10 days. Use formulations in a ratio of 8:1 or 7:1 exclusively. The dose is expressed in amoxicillin:
Children < 40 kg: 25 mg/kg 2 times daily
Children ≥ 40 kg and adults:
Ratio 8:1: 2000 mg daily (2 tablets of 500/62.5 mg 2 times daily)
Ratio 7:1: 1750 mg daily (1 tablet of 875/125 mg 2 times daily)

In penicillin-allergic patients:
erythromycin PO for 7 to 10 days:
Children: 30 to 50 mg/kg daily[2](see page 0)
Adults: 1 g 2 to 3 times daily

– In infants with ethmoiditis, see Periorbital and orbital cellulitis(see page 119) (Chapter 5).

Other treatments

– For sinusitis secondary to dental infection: dental extraction while under antibiotic treatment.
– In the event of ophthalmologic complications (ophthalmoplegia, mydriasis, reduced visual acuity, corneal anesthesia), refer for surgical drainage.

1(see page 0) For a child: place him on his back, head turned to the side, and instil 0.9% sodium chloride into each nostril.
2(see page 0) For dosage according to age or weight, see erythromycin in the guide Essential drugs, MSF.

Acute pharyngitis

Last updated: November 2020

- Clinical features(see page 48)
- Treatment(see page 49)
- References(see page 50)

– Acute inflammation of the tonsils and pharynx. The majority of cases are of viral origin and do not require antibiotic treatment. Group A streptococcus (GAS) is the main bacterial cause, and mainly affects children aged 3 to 14 years.
– Acute rheumatic fever (ARF), a serious late complication of GAS pharyngitis, can be prevented with antibiotic treatment.
– One of the main objectives of assessing acute pharyngitis is to identify patients requiring antibiotic treatment.

Clinical features

– Features common to all types of pharyngitis: throat pain, dysphagia (difficulty swallowing), inflammation of the tonsils and pharynx, tender anterior cervical lymph nodes, with or without fever.

– Specific features, depending on the cause:

Common forms:

• *Erythematous* (red throat) or *exudative* (red throat and whitish exudate) pharyngitis: this appearance is common to both viral and GAS pharyngitis. Centor criteria help assessment and decrease the empirical use of antibiotics in settings where rapid testing for GAS is not available. A Centor score of less than 2 rules out GAS infection[1(see page 50),2(see page 50)]. Nevertheless, in patients with risk factors (immunosuppression, personal or family history of ARF) for poststreptococcal complications, or for local or general complications, do not use Centor score and prescribe empirical antibiotic treatment.

Centor criteria

Criteria	Score
Temperature > 38 °C	1
Absence of cough	1
Tender anterior cervical lymph node(s)	1
Tonsillar swelling or exudate	1

In patients over 14 years, the probability of GAS pharyngitis is low. Infectious mononucleosis (IM) due to the Epstein-Barr virus should be suspected in adolescents and young adults with extreme fatigue, generalized adenopathy and often splenomegaly.

Erythematous or exudative pharyngitis may also be associated with gonococcal or primary HIV infection. In these cases, the diagnosis is mainly prompted by the patient's history.

• *Pseudomembranous pharyngitis* (red tonsils/pharynx covered with an adherent greyish white false membrane): see Diphtheria(see page 50), Chapter 2.
• *Vesicular pharyngitis* (clusters of tiny blisters or ulcers on the tonsils): always viral (coxsackie virus or primary herpetic infection).
• *Ulcero-necrotic pharyngitis*: hard and painless syphilitic chancre of the tonsil; tonsillar ulcer soft on palpation in a patient with poor oral hygiene and malodorous breath (Vincent tonsillitis).

Other forms of pharyngitis:
• *Spots on oral mucosa (Koplik's spots) accompanied by conjunctivitis and skin rash* (see Measles(see page 183), Chapter 8).
• *"Strawberry" (red and bumpy) tongue accompanied by a skin rash*: scarlet fever caused by GAS.

– Local complications:
Peritonsillar, retropharyngeal or lateral pharyngeal abscess: fever, intense pain, dysphagia, hoarse voice, trismus (limitation of mouth opening), unilateral deviation of the uvula.

– General complications:
• *Complications due to the toxin*: diphtheria (see Diphtheria(see page 50), Chapter 2).
• *Poststreptococcal complications*: ARF, acute glomerulonephritis.
• *Signs of serious illness in children:* severe dehydration, severe difficulty swallowing, upper airway compromise, deterioration of general condition.

– Differential diagnosis: epiglottitis (see Epiglottitis(see page 55), Chapter 2).

Treatment

– Symptomatic treatment (fever and pain): paracetamol or ibuprofen PO (Fever(see page 21), Chapter 1).

– Centor score ≤ 1: viral pharyngitis, which typically resolves within a few days (or weeks, for IM): no antibiotic treatment.

– Centor score ≥ 2 or scarlet fever: antibiotic treatment for GAS infections[3](see page 50):

• If single-use injection equipment is available, benzathine benzylpenicillin is the drug of choice as streptococcus A resistance to penicillin remains rare; it is the only antibiotic proven effective in reducing the incidence of rheumatic fever; and the treatment is administered as a single dose.
benzathine benzylpenicillin IM
Children under 30 kg (or under 10 years): 600 000 IU single dose
Children 30 kg and over (or 10 years and over) and adults: 1.2 MIU single dose

• Penicillin V is the oral reference treatment, but poor adherence is predictable due to the length of treatment.
phenoxymethylpenicillin (penicillin V) PO for 10 days
Children under 1 year: 125 mg 2 times daily
Children 1 to < 6 years: 250 mg 2 times daily
Children 6 to < 12 years: 500 mg 2 times daily
Children 12 years and over and adults: 1 g 2 times daily

• Amoxicillin is an alternative and the treatment has the advantage of being relatively short. However, it can cause adverse skin reactions in patients with undiagnosed IM and thus should be avoided when IM has not been excluded.
amoxicillin PO for 6 days
Children: 25 mg/kg 2 times daily
Adults: 1 g 2 times daily

• Macrolides should be reserved for penicillin allergic patients as resistance to macrolides is frequent and their efficacy in the prevention of rheumatic fever has not been studied.
azithromycin PO for 3 days
Children: 20 mg/kg once daily (max. 500 mg daily)
Adults: 500 mg once daily

– Gonococcal or syphilitic pharyngitis: as for genital gonorrhoea(see page 232) (Chapter 9) and syphilis(see page 237) (Chapter 9).

– Diphtherial pharyngitis: see Diphtheria(see page 50) (Chapter 2).

– Vincent tonsillitis: metronidazole or amoxicillin.

– Peritonsillar retropharyngeal or lateral pharyngeal abscess: refer for surgical drainage.

– If signs of serious illness or epiglottitis are present in children: hospitalise.

References

1. Fine AM, Nizet V, Mandl KD. Large-scale validation of the Centor and McIsaac scores to predict group A streptococcal pharyngitis. *Arch Intern Med*. 2012;172(11):847-852. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3627733/ [Accessed 20 October 2020]

2. National Institute for Health and Care Excellence. Sore throat (acute): antimicrobial prescribing. 2018. http://www.nice.org.uk/ng84 [Accessed 20 October 2020]

3. Group A Streptococcal Disease, Centers for Disease Control and Prevention. Atlanta (GA): CDC; 2020. https://www.cdc.gov/groupastrep/diseases-hcp/strep-throat.html[Accessed 20 October 2020]

Diphtheria

- Clinical features(see page 51)
- Laboratory(see page 51)
- Treatment(see page 51)
- Management of close contacts(see page 52)
- Prevention(see page 52)
- References(see page 53)

– Diphtheria is a bacterial infection due to *Corynebacterium diphtheriae*, characterized by proliferation of the bacteria in the upper respiratory tract and systemic diffusion of the diphtheria toxin through the body.
– The infection is spread by droplets (coughing, sneezing, speaking) from the upper respiratory tract of a patient or carrier.
– The disease does not confer sufficient immunity. Immunisation protects against the effects of the toxin but does not prevent individuals from becoming carriers.

Clinical features

– Signs related to the infection:
• Pseudomembranous tonsillitis (grey, tough and very sticky membranes) with dysphagia and cervical adenitis, at times progressing to massive swelling of the neck;
• Airway obstruction and possible suffocation when the infection extends to the nasal passages, the larynx, the trachea and the bronchi;
• Fever is generally low-grade.

– Generalised signs due to the toxin, they determine the prognosis:
• Cardiac dysfunction (gallop on auscultation, arrhythmias), myocarditis with severe heart failure at times leading to cardiogenic shock;
• Neuropathies 1 to 3 months after the onset of the disease leading to difficulty with: swallowing (paralysis of the soft palate), vision (ocular motor paralysis), breathing (paralysis of respiratory muscles) and ambulation (limb paralysis);
• Oliguria, anuria and renal failure.

Laboratory

Confirmation is made by culturing a toxigenic strain of *C. diphtheriae* from a throat swab.

Treatment

– Careful examination of the throat.
– Strict isolation of patients; contact and droplet precautions for medical staff (gloves, gown, masks and handwashing).
– Administration of **diphtheria antitoxin** derived from horse serum. Do not wait for bacteriological confirmation any delay can diminish efficacy. Administer according to the Besredka method to assess possibility of allergy.

⚠ Risk of an anaphylactic reaction, especially in patients with asthma. Close monitoring of the patient is essential, with immediate availability of equipment for manual ventilation (Ambu bag, face mask) and intubation, Ringer lactate and epinephrine.

Besredka method: inject 0.1 ml SC and wait 15 minutes. If there is no allergic reaction (no erythema at the injection site or a flat erythema of less than 0.5 in diameter, inject a further 0.25 ml SC. If there is no reaction after 15 minutes, inject the rest of the product IM or IV depending on the volume to be administered.

Doses are given as a function of the severity of illness, and the delay in treatment:

Clinical signs	Dose in units	Administration route
Laryngitis or pharyngitis or duration < 48 hours	20 to 40 000	IM or IV infusion in 250 ml of 0.9% sodium chloride in 2 to 4 hours for doses of more than 20 000 units.
Rhinopharyngitis	40 to 60 000	
Severe form, cervical oedema or duration ≥ 48 hours	80 to 100 000	

– Antibiotherapy for 14 days (or according to length of treatment recommended by the national protocol):

• If the patient can swallow:
azithromycin PO
Children: 20 mg/kg once daily (max. 500 mg daily)
Adults: 500 mg once daily
or
erythromycin PO
Children: 30 to 50 mg/kg daily[1](see page 0)
Adults: 1 g 2 times daily
or
phenoxymethylpenicillin (**penicillin V**) PO
Children under 1 year: 12.5 mg/kg 4 times daily (max. 500 mg daily)
Children from 1 to 6 years: 125 mg 4 times daily
Children over 6 years and adults: 250 mg 4 times daily

• If the patient cannot swallow, start with one of the treatments below and change as soon as possible to oral route with one of the oral treatments above to complete 14 days of treatment:
procaine benzylpenicillin IM[1](see page 53)
Children: 50 000 IU/kg (= 50 mg/kg) once daily (max. 1.2 g daily)
Adults: 1.2 MIU (1.2 g) once daily

⚠ Never administer procaine benzylpenicillin by IV injection.
or, if not available,
benzylpenicillin IM or slow IV (3 minutes)
Children: 50 000 IU/kg (= 30 mg/kg) every 6 hours (max. 4 MIU or 2.4 g daily)
Adults: 1 MIU (600 mg) every 6 hours
In penicillin-allergic patients, use erythromycin IV[2](see page 0) .

– Urgent intervention to secure an airway (intubation, tracheotomy) may be necessary in the event of laryngeal obstruction, cardiac or neurologic complications.

Management of close contacts

Close contacts include family members living under the same roof and people who were directly exposed to nasopharyngeal secretions of the patient on a regular basis (e.g. children in the same class, medical personnel).

– Throat culture; temperature and throat examination daily (7 days); exclusion from school or work until 48 hours of antibiotics have been completed.
– Antibiotherapy:
benzathine benzylpenicillin IM
Children under 30 kg (or under 10 years): 600 000 IU single dose
Children 30 kg and over (or 10 years and over) and adults: 1.2 MIU single dose

⚠ Benzathine benzylpenicillin should NEVER be administered by IV route.

In penicillin-allergic patients, use azithromycin or erythromycin PO as above for 7 days.

– Verify vaccination status:
• Less than 3 injections: complete with DTP, DT or Td according to age;
• 3 injections: if the last injection was given more than one year before, give a booster dose.
– Medical personnel in direct contact with patients: one dose of Td (booster).

Prevention

– Once the patient has recovered update their immunisations.
– Routine vaccination (EPI), for information: DTP: 3 doses at one month intervals before the age of 1 year, DTP booster one year later, and DT (diphtheria 30 IU/tetanus) at 6 years of age followed by 3 more Td

(diphtheria 3 IU/tetanus) boosters at 10 year intervals.
– Mass vaccination (epidemic): update routine immunisations with DTP for children under 3 years of age; DT for children from 3 to 6 years of age; Td for children over 7 years of age and adults.

[1](see page 0) For exact dosage according to age or weight, see erythromycin in the guide Essential drugs, MSF.
[2](see page 0) **erythromycin** IV infusion (60 minutes)
Children: 12.5 mg/kg every 6 hours (max. 2 g daily); adults: 500 mg every 6 hours
Erythromycin powder (1 g) should be reconstituted in 20 ml of water for injection only. Then, dilute each dose of erythromycin in 10 ml/kg of 0.9% sodium chloride in children less than 20 kg and in a bag of 250 ml of 0.9% sodium chloride in children over 20 kg and in adults. Do not dilute in glucose.

References

1. Word Health Organization. Pocket book for hospital care in children: guidelines for the management of common childhood illnesses, 2013. http://apps.who.int/iris/bitstream/handle/10665/81170/9789241548373_eng.pdf;jsessionid=CE5C46916607EF413AA9FCA89B84163F?sequence=1 [Accessed 2 September 2018]

Other upper respiratory tract infections

- Laryngotracheitis and laryngotracheobronchitis (croup)(see page 53)
- Epiglottitis(see page 55)
- Bacterial tracheitis(see page 56)

Laryngotracheitis and laryngotracheobronchitis (croup)

- Clinical features(see page 53)
- Treatment(see page 54)

Viral infection in children aged 3 months to 4 years.

Clinical features

– Typical barking cough, hoarse voice or cry.

– Inspiratory stridor (abnormal high pitched sound on inspiration):
• Croup is considered mild or moderate if the stridor only occurs with agitation;
• Croup is considered severe if there is stridor at rest, especially when it is accompanied by respiratory distress.

– Wheezing may also be present if the bronchi are involved.

Treatment

– In the absence of inspiratory stridor or retractions, treat symptomatically: ensure adequate hydration, seek medical attention if symptoms worsen (e.g. respiratory difficulty, noisy breathing and inability to tolerate oral fluids).

– If stridor is only present with agitation (moderate croup):
• Hospitalize for treatment and observation (risk of worsening).
• Assure adequate hydration.
• **dexamethasone** [1](see page 0) PO (use IV preparation flavoured with sugar water, 10% or 50% glucose or juice) or IM if child is vomiting: 0.6 mg/kg single dose (see table(see page 54)).

– If danger signs are present (stridor at rest, respiratory distress), admit in intensive care:
• Oxygen continuously: at least 5 litres/minute or to maintain the SpO_2 between 94 and 98%.
• Insert a peripheral IV line and provide IV hydration.
• **epinephrine (adrenaline)** via nebulizer (1 mg/ml, 1 ml ampoule): 0.5 mg/kg (max. 5 mg) to be repeated every 20 minutes if danger signs persist.
Monitor heart rate during nebulization (if heart rate greater than 200, stop the nebulization).

Age	**3 months**	**4-6 months**	**7-9 months**	**10-11 months**	**1-4 years**
Weight	**6 kg**	**7 kg**	**8 kg**	**9 kg**	**10-17 kg**
Dose in mg	3 mg	3.5 mg	4 mg	4.5 mg	5 mg
Dose in ml	3 ml	3.5 ml	4 ml	4.5 ml	5 ml
NaCl 0.9%*	1 ml	1 ml	–	–	–

* Add sufficient NaCl 0.9% to obtain a total volume of 4 to 4.5 ml in the nebulizing chamber.

⚠ Epinephrine is intended exclusively for nebulized administration and should not be given IV or IM in croup.

• **dexamethasone** [1](see page 0) (4 mg/ml, 1 ml ampoule) IM or IV: 0.6 mg/kg single dose

Age	**3-11 months**	**1-2 years**	**3-4 years**
Weight	**6-9 kg**	**10-13 kg**	**14-17 kg**
Dose in mg	4 mg	8 mg	10 mg
Dose in ml	1 ml	2 ml	2.5 ml

Suspect bacterial tracheitis in a critically ill appearing child [2](see page 0) with croup who does not improve with the above treatment.

– If wheezing is present:
salbutamol aerosol (using a spacer): 2 to 3 puffs every 20 to 30 minutes as needed

– If the patient has a complete airway obstruction, intubation if possible or emergency tracheotomy.

[1](see page 0) Administer orally if possible in order to avoid causing agitation in the child as this may worsen symptoms. [a(see page 0) b(see page 0)]
[2](see page 0) Critically ill appearing child: weak grunting or crying, drowsiness, difficult to arrouse, does not smile, unconjugate or anxious gaze, pallor or cyanosis, general hypotonia.

Epiglottitis

- Clinical features(see page 55)
- Treatment(see page 55)

Bacterial infection of the epiglottis in young children caused by *Haemophilus influenzae* (Hib), it is rare when Hib vaccine coverage is high. It can be caused by other bacteria and occur in adults.

Clinical features

– Rapid (less than 12-24 hours) onset of high fever.
– Typical “tripod or sniffing” position, preferring to sit, leaning forward with an open mouth, anxious appearing.
– Difficulty swallowing, drooling, and respiratory distress.
– Stridor may be present (as opposed to croup, hoarse voice and cough are usually absent).
– Critically ill appearing[1](see page 0) .

⚠ Allow the child to sit in a comfortable position or on the parent’s lap. Do not force them to lie down (may precipitate airway obstruction). Avoid any examination that will upset the child including examination of the mouth and throat.

Treatment

– In case of imminent airway obstruction, emergency intubation or tracheotomy is indicated. The intubation is technically difficult and should be performed under anaesthesia by a physician familiar with the procedure. Be prepared to perform a tracheotomy if intubation is unsuccessful.
– In all cases:
• Insert a peripheral IV line and provide IV hydration.
• Antibiotherapy:
ceftriaxone slow IV (3 minutes) or IV infusion (30 minutes)[2](see page 0) . Avoid IM route (may agitate the child and precipitate a respiratory arrest).
Children: 50 mg/kg once daily
Adults: 1 g once daily
The IV treatment is administered for at least 5 days then, if the clinical condition has improved[3](see page 0) and oral treatment can be tolerated, change to:
amoxicillin/clavulanic acid (**co-amoxiclav**) PO to complete a total of 7 to 10 days of treatment. Use formulations in a ratio of 8:1 or 7:1 exclusively. The dose is expressed in amoxicillin:
Children < 40 kg: 50 mg/kg 2 times daily
Children ≥ 40 kg and adult:
Ratio 8:1: 3000 mg daily (2 tablets of 500/62.5 mg 3 times daily)
Ratio 7:1: 2625 mg daily (1 tablet of 875/125 mg 3 times daily)

[1](see page 0) Critically ill appearing child: weak grunting or crying, drowsiness, difficult to arrouse, does not smile, unconjugate or anxious gaze, pallor or cyanosis, general hypotonia.

[2](see page 0) For administration by IV route, ceftriaxone powder should to be reconstituted in water for injection only. For administration by IV infusion, dilute each dose of ceftriaxone in 5 ml/kg of 0.9% sodium chloride or 5% glucose in children less than 20 kg and in a bag of 100 ml of 0.9% sodium chloride or 5% glucose in children over 20 kg and in adults.

[3](see page 0) Improvement criteria include: fever reduction, diminished respiratory distress, improved SpO_2, improved appetite and/or activity.

Bacterial tracheitis

- Clinical features(see page 56)
- Treatment(see page 56)

Bacterial infection of the trachea in children, occurring as a complication of a previous viral infection (croup, influenza, measles, etc.).

Clinical features

– Fever in a critically ill appearing child[1](see page 0) .
– Stridor, cough and respiratory distress.
– Copious purulent secretions.
– As opposed to epiglottitis the onset of symptoms is gradual and the child prefers to lie flat.
– In severe cases there is a risk of complete airway obstruction, especially in very young children.

Treatment

– Suction purulent secretions.

– Insert a peripheral IV line and provide IV hydration.

– Antibiotherapy:
ceftriaxone slow IV[2](see page 0) (3 minutes) or IV infusion (30 minutes). Do not administer by IM route (may agitate the child and precipitate a respiratory arrest).
Children: 50 mg/kg once daily
Adults: 1 g once daily
+
cloxacillin IV infusion (60 minutes)
Children less than 12 years: 25 to 50 mg/kg every 6 hours
Children 12 years and over and adults: 2 g every 6 hours
The IV treatment is administered for at least 5 days then, if the clinical condition has improved[3](see page 0) and oral treatment can be tolerated, change to :
amoxicillin/clavulanic acid (**co-amoxiclav**) PO to complete 7 to 10 days of treatment, as in epiglottitis.

– If the event of complete airway obstruction, intubation if possible or emergency tracheotomy.

[1](see page 0) Critically ill appearing child: weak grunting or crying, drowsiness, difficult to arrouse, does not smile, unconjugate or anxious gaze, pallor or cyanosis, general hypotonia.

[2](see page 0) For administration by IV route, ceftriaxone powder should to be reconstituted in water for injection only. For administration by IV infusion, dilute each dose of ceftriaxone in 5 ml/kg of 0.9% sodium chloride or 5% glucose in children less than 20 kg and in a bag of 100 ml of 0.9% sodium chloride or 5% glucose in children over 20 kg and in adults.

(see page 0)
Improvement criteria include: fever reduction, diminished respiratory distress, improved SpO_2, improved appetite and/or activity.

Otitis

- Acute otitis externa(see page 57)
- Acute otitis media (AOM)(see page 57)
- Chronic suppurative otitis media (CSOM)(see page 59)

Acute otitis externa

- Clinical features(see page 57)
- Treatment(see page 57)

Diffuse inflammation of the external ear canal, due to bacterial or fungal infection. Common precipitants of otitis externa are maceration, trauma of the ear canal or presence of a foreign body or dermatologic diseases (such as eczema, psoriasis).

Clinical features

– Ear canal pruritus or ear pain, often severe and exacerbated by motion of the pinna; feeling of fullness in the ear; clear or purulent ear discharge or no discharge

– Otoscopy (remove skin debris and secretions from the auditory canal by gentle dry mopping (use a dry cotton bud or a small piece of dry cotton wool):
• diffuse erythema and edema, or infected eczema, of the ear canal
• look for a foreign body
• if visible, the tympanic membrane is normal (swelling and pain very often prevent adequate visualization of the tympanic membrane)

Treatment

– Remove a foreign body, if present.

– Treatment of pain: paracetamol PO (Chapter 1, Pain(see page 23)).

– Local treatment:
• Remove secretions from the auditory canal by gentle dry mopping (use a dry cotton bud or a small piece of dry cotton wool). Consider ear irrigation (0.9% sodium chloride, using a syringe) only if the tympanic membrane can be fully visualised and is intact (no perforation). Otherwise, ear irrigation is contra-indicated.
• Apply **ciprofloxacin** ear drops in the affected ear(s) for 7 days:
Children ≥ 1 year: 3 drops 2 times daily
Adults: 4 drops 2 times daily

Acute otitis media (AOM)

- Clinical features(see page 58)
- Treatment(see page 58)

Acute inflammation of the middle ear, due to viral or bacterial infection, very common in children under 3 years, but uncommon in adults.
The principal causative organisms of bacterial otitis media are *Streptococcus pneumoniae, Haemophilus influenzae, Moraxella catarrhalis* and in older children, *Streptococcus pyogenes*.

Clinical features

– Rapid onset of ear pain (in infants: crying, irritability, sleeplessness, reluctance to nurse) and ear discharge (otorrhoea) or fever.

– Other signs such as rhinorrhoea, cough, diarrhoea or vomiting are frequently associated, and may confuse the diagnosis, hence the necessity of examining the tympanic membranes.

– Otoscopy: bright red tympanic membrane (or yellowish if rupture is imminent) and presence of pus, either externalised (drainage in ear canal if the tympanic membrane is ruptured) or internalised (opaque or bulging tympanic membrane). The combination of these signs with ear pain or fever confirms the diagnosis of AOM.
Note:
The following otoscopic findings are not sufficient to make the diagnosis of AOM:
• A red tympanic membrane alone, with no evidence of bulging or perforation, is suggestive of viral otitis in a context of upper respiratory tract infection, or may be due to prolonged crying in children or high fever.
• The presence of air bubbles or fluid behind an intact tympanic membrane, in the absence of signs and symptoms of acute infection, is suggestive of otitis media with effusion (OME).

– Complications, particularly in high-risk children (malnutrition, immunodeficiency, ear malformation) include chronic suppurative otitis media, and rarely, mastoiditis, brain abscess or meningitis.

Treatment

– In all cases:
• Treatment of fever(see page 21) and pain(see page 23): paracetamol PO (Chapter 1).
• Ear irrigation is contra-indicated if the tympanic membrane is ruptured, or when the tympanic membrane cannot be fully visualised. Ear drops are not indicated.

– Indications for antibiotic therapy:
• Antibiotics are prescribed in children less than 2 years, children whose assessment suggests severe infection (vomiting, fever > 39 °C, severe pain) and children at risk of unfavourable outcome (malnutrition, immunodeficiency, ear malformation).
• For other children:

1. If the child can be re-examined within 48 to 72 hours: it is preferable to delay antibiotic prescription. Spontaneous resolution is probable and a short symptomatic treatment of fever and pain may be sufficient. Antibiotics are prescribed if there is no improvement or worsening of symptoms after 48 to 72 hours.
2. If the child cannot be re-examined: antibiotics are prescribed.

• For children treated with antibiotics: advise the mother to bring the child back if fever and pain persist after 48 hours.

– Choice of antibiotherapy:

• Amoxicillin is the first-line treatment:
amoxicillin PO for 5 days
Children: 30 mg/kg 3 times daily (max. 3 g daily)
Adults: 1 g 3 times daily

• Amoxicillin/clavulanic acid is used as second-line treatment, in the case of treatment failure. Treatment failure is defined as persistence of fever and/or ear pain after 48 hours of antibiotic treatment.
amoxicillin/clavulanic acid (**co-amoxiclav**) PO for 5 days
Use formulations in a ratio of 8:1 or 7:1. The dose is expressed in amoxicillin:
Children < 40 kg: 25 mg/kg 2 times daily
Children ≥ 40 kg and adult:
Ratio 8:1: 2000 mg daily (2 tablets of 500/62.5 mg 2 times daily)
Ratio 7:1: 1750 mg daily (1 tablet of 875/125 mg 2 times daily)

Persistence of a ear drainage alone, without fever and pain, in a child who has otherwise improved (reduction in systemic symptoms and local inflammation) does not warrant a change in antibiotic therapy. Clean ear canal by gentle dry mopping until no more drainage is obtained.

• Macrolides should be reserved for very rare penicillin-allergic patients, as treatment failure (resistance to macrolides) is frequent.
azithromycin PO
Children over 6 months: 10 mg/kg once daily for 3 days

Chronic suppurative otitis media (CSOM)

- Clinical features(see page 59)
- Treatment(see page 59)

Chronic bacterial infection of the middle ear with persistent purulent discharge through a perforated tympanic membrane.
The principal causative organisms are *Pseudomonas aeruginosa, Proteus* sp, staphylococcus, other Gram negative and anaerobic bacteria.

Clinical features

– Purulent discharge for more than 2 weeks, often associated with hearing loss or even deafness; absence of pain and fever

– Otoscopy: perforation of the tympanic membrane and purulent exudate

– Complications:
• Consider a superinfection (AOM) in the case of new onset of fever with ear pain, and treat accordingly.
• Consider mastoiditis in the case of new onset of high fever, severe ear pain and/or tender swelling behind the ear, in a patient who appears significantly unwell.
• Consider brain abscess or meningitis in the case of impaired consciousness, neck stiffness and focal neurological signs (e.g. facial nerve paralysis).

Treatment

– Remove secretions from the auditory canal by gentle dry mopping (use a dry cotton bud or a small piece of dry cotton wool).

– Apply **ciprofloxacin** ear drops until no more drainage is obtained (approximately 2 weeks, max. 4 weeks):
Children 1 year and over: 3 drops 2 times daily
Adults: 4 drops 2 times daily

– Complications:
• Chronic mastoiditis is a medical emergency that requires prompt hospitalisation, prolonged antibiotherapy that covers the causative organisms of CSOM (**ceftriaxone** IM for 10 days
+ **ciprofloxacin** PO for 14 days), atraumatic cleaning of the ear canal; surgical treatment may be

required. Before transfer to hospital, if the patient needs to be transferred, administer the first dose of antibiotics.
• Meningitis(see page 157) (Chapter 7).

Whooping cough (pertussis)

- Clinical features(see page 60)
- Management and treatment(see page 60)
  - Suspect cases(see page 60)
  - Post-exposure prophylaxis(see page 61)
- Prevention(see page 61)

Whooping cough is a highly contagious bacterial infection of the lower respiratory tract, of prolonged duration, due to *Bordetella pertussis*.
B. pertussis is transmitted through inhalation of droplets spread by infected individuals (coughing, sneezing).
The majority of cases arise in non-vaccinated or incompletely vaccinated individuals. Whooping cough affects all age groups. Signs and symptoms are usually minor in adolescents and adults. As a result the infection may be ignored, thus contributing to the spread of *B. pertussis* and infection in infants and young children, in whom the illness is severe.

Clinical features

After an incubation period of 7 to 10 days, the illness evolves in 3 phases:

– Catarrhal phase (1 to 2 weeks): coryza and cough. At this stage, the illness is indistinguishable from a minor upper respiratory infection.

– Paroxysmal phase (1 to 6 weeks):

- Typical presentation: cough of at least 2 weeks duration, occurring in characteristic bouts (paroxysms), followed by a laboured inspiration causing a distinctive sound (whoop), or vomiting. Fever is absent or moderate, and the clinical exam is normal between coughing bouts; however, the patient becomes more and more fatigued.
- Atypical presentations:
  - Infants under 6 months: paroxysms are poorly tolerated, with apnoea, cyanosis; coughing bouts and whoop may be absent.
  - Adults: prolonged cough, often without other symptoms.
- Complications:
  - Major: in infants, secondary bacterial pneumonia (new-onset fever is an indicator); malnutrition and dehydration triggered by poor feeding due to cough and vomiting; rarely, seizures, encephalopathy; sudden death.
  - Minor: subconjunctival haemorrhage, petechiae, hernias, rectal prolapse.

– Convalescent phase: symptoms gradually resolve over weeks or months.

Management and treatment

Suspect cases

– Routinely hospitalise infants less than 3 months, as well as children with severe cases. Infants under 3 months must be monitored 24 hours per day due to the risk of apnoea.

– When children are treated as outpatients, educate the parents about signs that should lead to re-consultation (fever, deterioration in general condition, dehydration, malutrition, apnoea, cyanosis).

– Respiratory isolation (until the patient has received 5 days of antibiotic treatment):
• at home: avoid contact with non-vaccinated or incompletely vaccinated infants;
• in congregate settings: exclusion of suspect cases;
• in hospital: single room or grouping together of cases away from other patients (cohorting).

– Hydration and nutrition: ensure children < 5 years are well hydrated; breastfeeding should continue. Advise mothers to feed the child frequently in small quantities after coughing bouts and the vomiting which follows. Monitor the weight of the child during the course of the illness, and consider food supplements for several weeks after recovery.

– Antibiotherapy:
Antibiotic treatment is indicated in the first 3 weeks after onset of cough. Infectivity is virtually nil after 5 days of antibiotherapy.

	Antibiotic	Children	Adults
First line	**azithromycin** PO for 5 days	10 mg/kg once daily (max. 500 mg daily)	D1 500 mg D2 to D5 250 mg once daily
Alternative [1](see page 0)	**co-trimoxazole** PO for 14 days (if macrolides contra-indicated or not tolerated)	20 mg/kg SMX + 4 mg/kg TMP 2 times daily (avoid in infant < 1 month, and in the last month of pregnancy)	800 mg SMX + 160 mg TMP 2 times daily

– For hospitalised children:
• Place the child in a semi-reclining position (± 30°).
• Oro-pharyngeal suction if needed.

Post-exposure prophylaxis

– Antibiotic prophylaxis (same treatment as for suspect cases) is recommended for unvaccinated or incompletely vaccinated infants of less than 6 months, who have had contact with a suspect case.
– Isolation of contacts is not necessary.

Note: pertussis vaccination should be updated in all cases (suspects and contacts). If the primary series has been interrupted, it should be completed, rather than restarted from the beginning.

Prevention

Routine vaccination with polyvalent vaccines containing pertussis antigens (e.g. DTP, or DTP + Hep B, or DTP + Hib + Hep B) from the age of 6 weeks or according to national protocol.
Neither vaccination nor natural disease confers lasting immunity. Booster doses are necessary to reinforce immunity and reduce the risk of developing disease and transmitting it to young children.

[1](see page 0) Erythromycin (7 days) is a possible alternative but azithromycin is better tolerated and simpler to administrate (shorter treatment duration, fewer daily doses). For dosage according to age or weight, see erythromycin in the guide Essential drugs, MSF.

Bronchitis

- Acute bronchitis(see page 62)
- Chronic bronchitis(see page 62)

Acute bronchitis

- Clinical features(see page 62)
- Treatment(see page 62)

An acute inflammation of the bronchial mucosa, most commonly of viral origin. In older children it can be caused by *Mycoplasma pneumoniae*. In children over 2 years of age with repetitive acute bronchitis or 'wheezing' bronchitis, consider asthma (see Asthma(see page 72)). In children under 2 years of age, consider bronchiolitis (see Bronchiolitis(see page 63)).

Clinical features

Often begins with a rhinopharyngitis that descends progressively: pharyngitis, laryngitis, tracheitis.
– Heavy cough, dry at the beginning then becoming productive
– Low-grade fever
– No tachypnoea, no dyspnoea
– On pulmonary auscultation: bronchial wheezing

Treatment

– Fever(see page 21): paracetamol PO (Chapter 1).

– Keep the patient hydrated, humidify air (with a bowl of water or a wet towel).

– Children: nasal irrigation with 0.9% sodium chloride or Ringer lactate, 4 to 6 times daily to clear the airway.

– Antibiotherapy is not useful for patients in good overall condition with rhinopharyngitis or influenza.

– Antibiotherapy is indicated only if:
• the patient is in poor general condition: malnutrition, measles, rickets, severe anaemia, cardiac disease, elderly patient etc.
• if the patient has dyspnoea, fever greater than 38.5 °C and purulent expectorations: a secondary infection with *Haemophilus influenzae* or with pneumococcus is probable.
amoxicillin PO
Children: 30 mg/kg 3 times daily (max. 3 g daily) for 5 days
Adults: 1 g 3 times daily for 5 days

Chronic bronchitis

- Clinical features(see page 63)
- Treatment(see page 63)

A chronic inflammation of the bronchial mucosa due to irritation (tobacco, pollution), allergy (asthma) or infection (repetitive acute bronchitis). It may develop into chronic obstructive pulmonary disease.

Clinical features

– Productive cough for 3 consecutive months per year for 2 successive years.
– No dyspnoea at onset. Dyspnoea develops after several years, first on exertion, then becoming persistent.
– On pulmonary auscultation: bronchial wheeze (always exclude tuberculosis).

A patient with an acute exacerbation of chronic bronchitis presents with:
– Onset or increase of dyspnoea.
– Increased volume of sputum.
– Purulent sputum.

Treatment

– Antibiotic treatment is not useful in treating simple chronic bronchitis.
– Antibiotic treatment may be useful, for patients in a poor general condition only, for acute exacerbations of chronic bronchitis (see Acute bronchitis(see page 62)).
– Discourage smoking and other irritating factors.

Bronchiolitis

- Clinical features(see page 63)
- Treatment(see page 64)
  - Outpatient treatment(see page 64)
  - Hospitalisation(see page 64)
- Prevention and control(see page 65)

Bronchiolitis is an epidemic and seasonal viral infection of the lower respiratory tract in children less than 2 years of age, characterised by bronchiolar obstruction.
Respiratory syncytial virus (RSV) is responsible for 70% of cases of bronchiolitis. Transmission of RSV is direct, through inhalation of droplets (coughing, sneezing), and indirect, through contact with hands or materials contaminated by infected secretions.
In the majority of cases, bronchiolitis is benign, resolves spontaneously (relapses are possible), and can be treated on an outpatient basis.
Severe cases may occur, which put the child at risk due to exhaustion or secondary bacterial infection. Hospitalisation is necessary when signs/criteria of severity are present (10 to 20% of cases).

Clinical features

– Tachypnoea, dyspnoea, wheezing, cough; profuse, frothy, obstructive secretions.
– On auscultation: prolonged expiration with diffuse, bilateral wheezes; sometimes diffuse fine, end-inspiratory crackles.
Rhinopharyngitis, with dry cough, precedes these features by 24 to 72 hours; fever is absent or moderate.

– Signs of severity:
• Significant deterioration in general condition, toxic appearance (pallor, greyish colouration)
• Apnoea, cyanosis (check lips, buccal mucosa, fingernails)
• Respiratory distress (nasal flaring, sternal and chest wall indrawing)
• Anxiety and agitation (hypoxia), altered level of consciousness
• Respiratory rate > 60/minute
• Decreased respiratory distress and slow respirations (< 30/minute below the age of 1 year and < 20/

minute below the age of 3 years, exhaustion). Exercise caution in interpreting these signs as indicators of clinical improvement.
• Sweats, tachycardia at rest and in the absence of fever
• Silence on auscultation (severe bronchospasm)
• Difficulty drinking or sucking (reduced tolerance for exertion)

Treatment

Treatment is symptomatic. Obstructive signs and symptoms last for about 10 days; cough may persist for 2 weeks longer.

Hospitalise children with one of the following criteria:
– Presence of any sign of severity
– Pre-existing pathology (cardiac or pulmonary disease, malnutrition, HIV, etc.)

Consider hospitalisation on a case-by-case basis in the following situations:
– Associated acute pathology (viral gastro-enteritis, bacterial infection, etc.)
– Age less than 3 months

In all other cases, the child may be treated at home, provided the parents are taught how to carry out treatment, and what signs of severity should lead to re-consultation.

Outpatient treatment

– Nasal irrigation with 0.9% NaCl before each feeding (demonstrate the technique to the mother) 1(see page 0).
– Small, frequent feedings to reduce vomiting triggered by bouts of coughing.
– Increased fluids if fever and/or significant secretions are present.
– Treat fever(see page 21) (Chapter 1).
– Handle the patient the patient as little as possible and avoid unnecessary procedures.

Hospitalisation

– In all cases:
• Place the infant in a semi-reclining position (± 30°).
• Nasal irrigation, small, frequent feeds, treatment of fever: as for outpatient treatment.
• Gentle oro-pharyngeal suction if needed.
• Monitor fluid intake: normal requirements are 80 to 100 ml/kg/day + 20 to 25 ml/kg/day with high fever or very profuse secretions.

– According to symptoms:
• Humidified nasal oxygen (1 to 2 litres/minute).
• When there is vomiting or significant fatigue when sucking, fluid requirements may be administered by nasogastric tube (small volumes on a frequent basis) or the IV route, for the shortest possible time. Avoid breastfeeding or oral feeds in children with severe tachypnoea, but do not prolong NG feeds (respiratory compromise) or IV infusions any longer than necessary.
• Bronchodilator therapy: this therapy may be considered after a trial treatment has been given (**salbutamol** inhaler, 100 micrograms/puff: 2 to 3 puffs with spacer, repeated twice at an interval of 30 minutes). If inhaled salbutamol appears effective in relieving symptoms, the treatment is continued (2 to 3 puffs every 6 hours in the acute phase, then gradual reduction as recovery takes place). If the trial is ineffective, the treatment is discontinued.
• Antibiotics are not indicated unless there is concern about complications such as secondary bacterial pneumonia.

Prevention and control

The risk of transmission of the virus is increased in hospital settings:
– Children with bronchiolitis should be grouped together, away from other children (cohorting).
– As infection is most commonly transmitted by the hands, the most important prevention measure is hand-washing after any contact with patients, and objects or surfaces in contact with patients on which the virus may survive for several hours.
– In addition, staff should wear gowns, gloves and surgical masks when in contact with patients.

Lie the child on his back, head turned to the side and instil 0.9% NaCl into the nose, one nostril at a time.

Acute pneumonia

- Pneumonia in children under 5 years of age(see page 65)
- Pneumonia in children over 5 years and adults(see page 68)
- Persistent pneumonia(see page 70)

Acute pneumonia is a viral, bacterial (pneumococcus, *Haemophilus influenzae*, staphylococcus, atypical bacteria) or parasitic (pneumocystosis) infection of the pulmonary alveoli.

Pneumonia in children under 5 years of age

- Clinical features(see page 65)
- Treatment(see page 66)
  - Severe pneumonia (inpatient treatment)(see page 66)
  - Pneumonia with no signs of serious illness(see page 68)

The most common causes are viruses, pneumococcus and *Haemophilus influenzae*.

Clinical features

– Cough or difficulty breathing
– Fever often high (> 39 °C), but the child may present with low-grade fever or may have no fever (often a sign of serious illness)

Clinical examination must be done on a calm child in order to correctly count the respiratory rate and look for signs of serious illness.

– A child has tachypnoea (increased respiratory rate) if:
RR ≥ 60 breaths/minute in children under 1 months
RR ≥ 50 breaths/minute in children from 1 to 11 months
RR ≥ 40 breaths/minute in children from 12 months to 5 years

– On pulmonary auscultation: dullness with diminished vesicular breath sounds, crepitations and sometimes bronchial breathing or normal pulmonary auscultation.

– Signs of serious illness (severe pneumonia):
• Chest indrawing: the inferior thoracic wall depresses on inspiration as the superior abdomen expands
• Cyanosis (lips, oral mucosa, fingernails) or SpO_2 < 90%
• Nasal flaring

• Altered consciousness (child is abnormally sleepy or difficult to wake)
• Stridor (hoarse noise on inspiration)
• Grunting (a short repetitive noise produced by a partial closure of the vocal cords) on expiration
• Refusal to drink or feed
• Children under 2 months
• Severe malnutrition

Notes:
– In malnourished children, the RR thresholds should be decreased by 5 breaths/minute from those listed above.
– Chest indrawing is significant if it is clearly visible and present at all times. If it is observed when a child is upset or feeding and is not visible when the child is resting, there is no chest indrawing.
– In children under 2 months of age, moderate chest indrawing is normal as the thoracic wall is flexible.
– If only the soft tissues between the ribs or above the clavicles depress, there is no chest indrawing.

Consider also:
– Malaria in endemic areas, as it may also cause cough and tachypnoea.
– Staphylococcal pneumonia(see page 70) in patients with empyema or painful abdominal swelling and diarrhoea.
– Pneumocystosis in children with confirmed or suspected HIV infection (see HIV infection and AIDS(see page 206), Chapter 8).
– Tuberculosis:
• in a child with cough, fever and poor weight gain and a history of close contact with a tuberculous patient[1](see page 0) . For the diagnosis, refer to the MSF handbook, Tuberculosis.
• in the event of pneumonia complicated with empyema (pus in the pleural space).

Treatment

Severe pneumonia (inpatient treatment)

Children under 2 months

The first line treatment is the combination **ampicillin** slow IV (3 minutes) for 10 days + **gentamicin** slow IV (3 minutes) or IM for 5 days:

Children 0 - 7 days	< 2 kg	**ampicillin** 50 mg/kg every 12 hours + **gentamicin** 3 mg/kg once daily
	≥ 2 kg	**ampicillin** 50 mg/kg every 8 hours + **gentamicin** 5 mg/kg once daily
Children 8 days - < 1 month		**ampicillin** 50 mg/kg every 8 hours + **gentamicin** 5 mg/kg once daily
Children 1 month - < 2 months		**ampicillin** 50 mg/kg every 6 hours + **gentamicin** 6 mg/kg once daily

For ampicillin, IV route is preferred but IM route may be an alternative.

If ampicillin is not available, alternatives may be **cefotaxime** slow IV (3 minutes) or infusion (20 minutes) or IM for 10 days (for doses, see Meningitis(see page 157), Chapter 7), or, as a last resort: **ceftriaxone** slow IV[2](see page 0) (3 minutes) or infusion (30 minutes; 60 minutes in neonates) or IM: 50 mg/kg once daily for 10 days.

If the child's condition does not improve[3](see page 0) after 48 hours of well administered treatment, add **cloxacillin** IV for 10 to 14 days:

Children 0 - 7 days	< 2 kg	**cloxacillin** 50 mg/kg every 12 hours
	≥ 2 kg	**cloxacillin** 50 mg/kg every 8 hours
Children > 7 days	< 2 kg	**cloxacillin** 50 mg/kg every 8 hours
	≥ 2 kg	**cloxacillin** 50 mg/kg every 6 hours

Children from 2 months to 5 years

The first line treatment is:
ceftriaxone IM or slow IV[2](see page 0) (3 minutes): 50 mg/kg once daily
or
ampicillin slow IV (3 minutes) or IM: 50 mg/kg every 6 hours
+ **gentamicin** slow IV (3 minutes) or IM: 6 mg/kg once daily
Ampicillin is preferably administered in 4 divided doses. If the context does not permit it, the daily dose must be divided in at least 3 doses.

The treatment is administered by parenteral route for at least 3 days then, if the clinical condition has improved[3](see page 0) and oral treatment can be tolerated, switch to **amoxicillin** PO: 30 mg/kg 3 times daily to complete 10 days of treatment.

If the child's condition deteriorates or does not improve after 48 hours of correct administration, add **cloxacillin** IV: 25 to 50 mg/kg every 6 hours. After clinical improvement and 3 days with no fever, switch to **amoxicillin/clavulanic acid** (**co-amoxiclav**) PO to complete 10 to 14 days of treatment. Use formulations in a ratio of 8:1 or 7:1 exclusively. The dose is expressed in amoxicillin: 50 mg/kg 2 times daily.

If the child's condition does not improve after 48 hours with ceftriaxone + cloxacillin, consider tuberculosis. For the diagnosis, refer to the guide Tuberculosis, MSF.

If tuberculosis is unlikely, continue with ceftriaxone + cloxacillin and add azithromycin (see Atypical pneumonia(see page 70)).

Notes:
– For malnourished children, refer to specific protocol.
– In the event of moderate-large empyema, assess if drainage is required. Administer antibiotics active against pneumococci and staphylococci (see Staphylococcal pneumonia(see page 70)).

Adjuvant therapy

– Fever(see page 21): paracetamol PO (Chapter 1).
– Infants: keep warm.
– Install on an incline (head elevated) or in semi-sitting position.
– Clear the airway (nasal irrigation with 0.9% sodium chloride if needed).
– Oxygen at the flow rate required to maintain SpO_2 ≥ 90% or, if pulse oxymeter is not available, minimum 1 litre/minute.

– Maintain adequate hydration and nutrition:
• In children with severe respiratory difficulty: place an IV line and give 70% of normal maintenance fluids. Resume oral feeding as soon as possible (no severe respiratory difficulty, ability to eat normally). Use a nasogastric tube only if an IV line cannot be established: children under 12 months: 5 ml/kg/hour; children over 12 months: 3 to 4 ml/kg/hour; alternate milk and water. Resume normal oral feeding as soon as possible.

• In the absence of severe respiratory difficulty: breastfeed on demand; milk/food and water by spoon on demand.
• ORS when required (Dehydration(see page 34), Chapter 1).

Pneumonia with no signs of serious illness

Children under 2 months

Admit the child for inpatient care and treat for severe pneumonia(see page 66).

Children from 2 months to 5 years

Treat as outpatient, except infants.
amoxicillin PO: 30 mg/kg 3 times daily for 5 days
Follow-up in 48 to 72 hours or sooner if the child's condition deteriorates:
– If the condition is improving[3](see page 0): continue with the same antibiotic to complete treatment.
– If there is no improvement after 3 days of correct administration: add azithromycin (see Atypical pneumonia(see page 70)).
– If the condition is deteriorating: hospitalise and treat as severe pneumonia.

[1](see page 0) Contact is defined as living in the same household, or in close and regular contact with any known or suspected tuberculous case within the last 12 months.
[2](see page 0) The solvent of ceftriaxone for IM injection contains lidocaine. Ceftriaxone reconstituted using this solvent must never be administered by IV route. For IV administration, water for injection must always be used. [a(see page 0) b(see page 0)]
[3](see page 0) Improvement criteria include: fever reduction, diminished respiratory distress, improved SpO_2, improved appetite and/or activity. [a(see page 0) b(see page 0) c(see page 0)]

Pneumonia in children over 5 years and adults

- Clinical features(see page 68)
- Treatment(see page 69)
  - Severe pneumonia (inpatient treatment)(see page 69)
  - Pneumonia without signs of serious illness (outpatient treatment)(see page 70)

The most common causes are viruses, pneumococcus, and *Mycoplasma pneumoniae*.

Clinical features

– Cough, with or without purulent sputum, fever, thoracic pain, tachypnoea
– On pulmonary auscultation: decreased vesicular breath sounds, dullness, localised foci of crepitations, sometimes bronchial wheeze.

Sudden onset with high fever (higher than 39 °C), thoracic pain and oral herpes are suggestive of pneumococcal infection. Symptoms may be confusing, particularly in children with abdominal pain, meningeal syndrome, etc.

Signs of serious illness (severe pneumonia) include:
– Cyanosis (lips, oral mucosa, fingernails)
– Nasal flaring

– Intercostal or subclavial indrawing
– RR > 30 breaths/minute
– Heart rate > 125 beats/minute
– Altered level of consciousness (drowsiness, confusion)

Patients at risk include the elderly, patients suffering from heart failure, sickle cell disease or severe chronic bronchitis; immunocompromised patients (severe malnutrition, HIV infection with CD4 < 200).

Treatment

Severe pneumonia (inpatient treatment)

ceftriaxone IM or slow IV[1](see page 0) (3 minutes)
Children: 50 mg/kg once daily
Adults: 1 g once daily
The treatment is given by parenteral route for at least 3 days then, if the clinical condition has improved[2](see page 0) and oral treatment can be tolerated, switch to **amoxicillin** PO to complete 7 to 10 days of treatment:
Children: 30 mg/kg 3 times daily (max. 3 g daily)
Adults: 1 g 3 times daily
or
ampicillin slow IV (3 minutes) or IM
Children: 50 mg/kg every 6 hours
Adults: 1 g every 6 to 8 hours
Ampicillin is preferably administered in 4 divided doses. If the context does not permit it, the daily dose must be divided in at least 3 doses.
The treatment is given by parenteral route for at least 3 days then, if the clinical condition has improved[2](see page 0) and oral treatment can be tolerated, switch to the oral route with amoxicillin PO as above, to complete 7 to 10 days of treatment.

If the clinical condition deteriorates or does not improve after 48 hours of correct administration, administer ceftriaxone as above + **cloxacillin** IV infusion:
Children: 25 to 50 mg/kg every 6 hours
Adults: 2 g every 6 hours

After clinical improvement and 3 days with no fever, switch to **amoxicillin/clavulanic acid** (**co-amoxiclav**) PO to complete 10 to 14 days of treatment. Use formulations in a ratio of 8:1 or 7:1 exclusively. The dose is expressed in amoxicillin:
Children < 40 kg: 50 mg/kg 2 times daily
Children ≥ 40 kg and adults:
Ratio 8:1: 3000 mg daily (2 tablets of 500/62.5 mg 3 times daily)
Ratio 7:1: 2625 mg daily (1 tablet of 875/125 mg 3 times daily)

If the clinical condition does not improve after 48 hours with ceftriaxone + cloxacillin, consider tuberculosis. For the diagnosis, refer to the guide Tuberculosis, MSF.

If tuberculosis is unlikely, continue with ceftriaxone + cloxacillin and add azithromycin (see Atypical pneumonia(see page 70)).

Adjuvant therapy

– Fever(see page 21): paracetamol PO (Chapter 1).
– Clear the airway (nasal irrigation with 0.9% sodium chloride if needed).
– Oxygen at the flow rate required to maintain SpO_2 ≥ 90% or, if pulse oxymeter is not available, minimum 1 litre/minute.
– Maintain adequate hydration and nutrition.

Pneumonia without signs of serious illness (outpatient treatment)

amoxicillin PO
Children: 30 mg/kg 3 times daily (max. 3 g daily) for 5 days
Adults: 1 g 3 times daily for 5 days

Follow-up in 48 to 72 hours or sooner if the child's condition deteriorates:
– If the condition is improving[2](see page 0): continue with the same antibiotic to complete treatment.
– If there is no improvement after 3 days of correct administration: add azithromycin (see Atypical pneumonia(see page 70)).
– If the condition is deteriorating: hospitalise and treat as severe pneumonia.

[1](see page 0) The solvent of ceftriaxone for IM injection contains lidocaine. Ceftriaxone reconstituted using this solvent must never be administered by IV route. For IV administration, water for injection must always be used.
[2](see page 0) Improvement criteria include: fever reduction, diminished respiratory distress, improved SpO_2, improved appetite and/or activity. [a(see page 0) b(see page 0) c(see page 0)]

Persistent pneumonia

In patients not responding to therapy, consider atypical pneumonia, tuberculosis, pneumocystosis (HIV infection and AIDS(see page 206), Chapter 8).

Bacteria responsible for atypical pneumonia are mainly *Mycoplasma pneumoniae* and *Chlamydophila pneumoniae*. If suspected, one of the following antibiotics may be used:

First choice, **azithromycin** PO
Children: 10 mg/kg once daily (max. 500 mg daily) for 5 days
Adults: 500 mg on D1 then, 250 mg once daily from D2 to D5

If not available,
erythromycin PO
Children: 10 mg/kg 4 times daily for 10 to 14 days
Adults: 500 mg 4 times daily for 10 to 14 days
or
doxycycline PO (except in children under 8 years and pregnant or lactating women)
Children 8 years and over: 2 mg/kg 2 times daily (max. 200 mg daily) for 10 to 14 days
Adults: 100 mg 2 times daily for 10 to 14 days

Staphylococcal pneumonia

- Clinical features(see page 71)
- Paraclinical investigations(see page 71)
- Treatment(see page 71)
- Clinical evolution(see page 71)

Pneumonia due to *Staphylococcus aureus* affecting young children, often those in a poor general condition (malnutrition, skin lesions, etc.). Staphylococcal pneumonia is a classic complication of measles.

Clinical features

– General signs: change in overall condition, pallor, high fever or hypothermia, frequently signs of shock; presence of skin lesions (point of bacterial entry), however, skin lesions may be absent.
– Gastrointestinal signs: nausea, vomiting, diarrhoea, painful abdominal distention.
– Respiratory signs: dry cough, tachypnoea, signs of distress (nasal flaring, chest indrawing). Pulmonary auscultation is often normal; sometimes dullness indicating pleural effusion.

Paraclinical investigations

– Chest x-ray (if available): may show multilobar consolidation, cavitation, pneumatoceles, spontaneous pneumothorax.

Treatment

Treatment is urgent as patients deteriorate quickly: hospitalise.

– Antibiotic treatment: if staphylococcal aetiology cannot be confirmed or while waiting for confirmation, a broad spectrum antibiotic therapy is recommended:
ceftriaxone IM or slow IV[1](see page 0) (at least 3 minutes): 50 mg/kg once daily
+ **cloxacillin** IV infusion (60 minutes)[2](see page 0)
Neonates 0 to 7 days (< 2 kg): 50 mg/kg every 12 hours
Neonates 0 to 7 days (≥ 2 kg): 50 mg/kg every 8 hours
Neonates 8 days to < 1 month (< 2 kg): 50 mg/kg every 8 hours
Neonates 8 days to < 1 month (≥ 2 kg): 50 mg/kg every 6 hours
Children 1 month and over: 25 to 50 mg/kg every 6 hours (max. 8 g daily)

After clinical improvement[3](see page 0), 3 days with no fever, and drain removal if any, switch to **amoxicillin/clavulanic acid** PO to complete 10 to 14 days. Use formulations in a ratio of 8:1 or 7:1 exclusively. The dose is expressed in amoxicillin: 50 mg/kg 2 times daily

In the event of large empyema: same treatment but switch to the oral route after 7 days with no fever and treat for 3 weeks.

Clindamycin IV may be an alternative to cloxacillin: 10 mg/kg every 8 hours then switch to clindamycin PO at the same dose, according to the criteria above.

– Fever(see page 21): paracetamol (Chapter 1).

– Hydration(see page 67) by oral route or infusion or nasogastric tube depending on clinical condition.

– Oxygen at the flow rate required to maintain SpO_2 ≥ 90% or, if pulse oxymeter is not available, minimum 1 litre/minute.

– Local disinfection of skin lesions.

– If there is significant pleural effusion: pleural tap with drainage (for pyopneumothorax; insert 2 drains, one anterior and one posterior) or without drainage (for suppurative pleurisy, make repetitive taps with an IV catheter).

Clinical evolution

– There is a serious risk of decompensation from pneumothorax or suppurative pleurisy or pyopneumothorax.

– On a paediatric ward, adequate equipment for urgent pleural drainage should always be available.

1 (see page 0) The solvent of ceftriaxone for IM injection contains lidocaine. Ceftriaxone reconstituted using this solvent must never be administered by IV route. For IV administration, water for injection must always be used.

2 (see page 0) Cloxacillin powder for injection should be reconstituted in 4 ml of water for injection. Then dilute each dose of cloxacillin in 5 ml/kg of 0.9% sodium chloride or 5 % glucose in children less than 20 kg and in a bag of 100 ml of 0.9% sodium chloride or 5% glucose in children 20 kg and over and in adults.

3 (see page 0) Improvement criteria include: fever reduction, diminished respiratory distress, improved SpO_2, improved appetite and/or activity.

Asthma

- Asthma attack (acute asthma) (see page 72)
- Chronic asthma (see page 75)

Asthma is a chronic inflammatory disorder of the airways associated with airway hyperresponsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness and coughing. These episodes are usually associated with airflow obstruction within the lung, often reversible, either spontaneously or with treatment.

Factors that precipitate/aggravate asthma include: allergens, infection, exercise, drugs (aspirin), tobacco, etc.

In young children, most initial episodes of asthma-like symptoms are associated with a respiratory tract infection, with no symptoms between infections. Wheezing episodes usually become less frequent with time; most of these children do not develop asthma.

Asthma attack (acute asthma)

- Assessment of the severity of asthma attack (see page 72)
- Treatment (see page 73)
  - Mild to moderate attack (see page 73)
  - Severe attack (see page 73)
  - Life-threatening attack (intensive care) (see page 74)

Asthma attack is a substantial worsening of asthma symptoms. The severity and duration of attacks are variable and unpredictable.

Assessment of the severity of asthma attack

The severity of the asthma attack must be rapidly evaluated by the following clinical criteria. Not all signs are necessarily present.

Assessment of severity in children over 2 years and adults

Mild to moderate attack	Severe attack	Life threatening attack
Able to talk in sentences **Respiratory rate (RR)** Children 2-5 years ≤ 40/minute Children > 5 years ≤ 30/minute **Heart rate** Children 2-5 years ≤ 140/minute Children > 5 years ≤ 125/minute and **No criteria of severity**	**Cannot complete sentences in one breath** or **Too breathless to talk or feed** **RR** Children 2-5 years > 40/minute Children > 5 years > 30/minute Adults ≥ 25/minute **Heart rate** Children 2-5 years > 140/minute Children > 5 years > 125/minute Adults ≥ 110/minute **SpO_2 ≥ 92%**	**Altered level of consciousness** (drowsiness, confusion, coma) **Exhaustion** **Silent chest** **Paradoxical thoracoabdominal movement** **Cyanosis** **Collapse** **Bradycardia in children or arrhythmia/hypotension in adults** **SpO_2 < 92%**

Treatment

Treatment and follow-up depend on the severity of the attack and the patient's response:

Mild to moderate attack

– Reassure the patient; place him in a 1/2 sitting position.

– Administer:
• **salbutamol** (aerosol): 2 to 4 puffs every 20 to 30 minutes, up to 10 puffs if necessary during the first hour. In children, use a spacer 1(see page 0) to ease administration (use face mask in children under 3 years). Single puffs should be given one at a time, let the child breathe 4 to 5 times from the spacer before repeating the procedure.
• **prednisolone** PO: one dose of 1 to 2 mg/kg

– If the attack is completely resolved: observe the patient for 1 hour (4 hours if he lives far from the health centre) then give outpatient treatment: **salbutamol** for 24 to 48 hours (2 to 4 puffs every 4 to 6 hours depending on clinical evolution) and **prednisolone** PO (1 to 2 mg/kg once daily) to complete 3 days of treatment.

– If the attack is only partially resolved, continue with **salbutamo**l 2 to 4 puffs every 3 to 4 hours if the attack is mild; 6 puffs every 1 to 2 hours if the attack is moderate, until symptoms subside, then when the attack is completely resolved, proceed as above.

– If symptoms worsen or do not improve, treat as severe attack(see page 73).

Severe attack

– Hospitalise the patient; place him in a 1/2 sitting position.

– Administer:
• **oxygen** continuously, at least 5 litres/minute or maintain the SpO_2 between 94 and 98%.
• **salbutamol** (aerosol): 2 to 4 puffs every 20 to 30 minutes, up to 10 puffs if necessary in children under 5 years, up to 20 puffs in children over 5 years and adults. Use a spacer to increase effectiveness,

irrespective of age.
or **salbutamol** (solution for nebulisation), see Life-threatening attack(see page 74).
• **prednisolone** PO: one dose of 1 to 2 mg/kg
In the case of vomiting, until the patient can tolerate oral prednisolone, use **hydrocortisone** IV:
Children 1 month to < 5 years: 4 mg/kg every 6 hours (max. 100 mg per dose)
Children 5 years and over and adults: 100 mg every 6 hours

– If the attack is completely resolved, observe the patient for at least 4 hours. Continue the treatment with **salbutamol** for 24 to 48 hours (2 to 4 puffs every 4 hours) and **prednisolone** PO (1 to 2 mg/kg once daily) to complete 3 days of treatment.
Reassess after 10 days: consider long-term treatment if the asthma attacks have been occurring for several months. If the patient is already receiving long-term treatment, reassess the severity of the asthma (see table(see page 75)) and review compliance and correct use of medication and adjust treatment if necessary.

– If symptoms worsen or do not improve, see Life-threatening attack(see page 74).

Life-threatening attack (intensive care)

– Insert an IV line.

– Administer:
• **oxygen** continuously, at least 5 litres/minute or maintain the SpO_2 between 94 and 98%.
• **salbutamol** + **ipratropium** nebuliser solutions using a nebuliser:

Children 1 month to < 5 years	**salbutamol** 2.5 mg + **ipratropium** 0.25 mg every 20 to 30 minutes
Children 5 to < 12 years	**salbutamol** 2.5 to 5 mg + **ipratropium** 0.25 mg every 20 to 30 minutes
Children 12 years and over and adults	**salbutamol** 5 mg + **ipratropium** 0.5 mg every 20 to 30 minutes

The two solutions can be mixed in the nebuliser reservoir.
• corticosteriods (prednisolone PO or hydrocortisone IV) as for severe attack(see page 73).

– If the attack is resolved after one hour: switch to salbutamol aerosol and continue prednisolone PO as for severe attack(see page 73).

– If symptoms do not improve after one hour:
• administer a single dose of **magnesium sulfate** by IV infusion in 0.9% sodium chloride over 20 minutes, monitoring blood pressure:
Children over 2 years: 40 mg/kg
Adults: 1 to 2 g
• continue salbutamol by nebulisation and corticosteriods, as above.

Notes:
– In pregnant women, treatment is the same as for adults. In mild or moderate asthma attacks, administering oxygen reduces the risk of foetal hypoxia.
– For all patients, irrespective of the severity of the asthma attack, look for underlying lung infection and treat accordingly.

1(see page 0) If a conventional spacer is not available, use a 500 ml plastic bottle: insert the mouthpiece of the inhaler into a hole made in the bottom of the bottle (the seal should be as tight as possible). The child breathes from the mouth of the bottle in the same way as he would with a spacer. The use of a plastic cup instead of a spacer is not recommended (ineffective).

Chronic asthma

- Clinical features(see page 75)
- Treatment(see page 75)

Clinical features

– Asthma should be suspected in patients with episodic respiratory symptoms (wheezing, chest tightness, shortness of breath and/or cough) of variable frequency, severity and duration, disturbing sleep, and causing the patient to sit up to breathe. These symptoms may appear during or after exercise.

– Chest auscultation may be normal or demonstrate diffuse sibilant wheezes.

– Atopic disorders or a personal or family history of atopy (eczema, allergic rhinitis/conjunctivitis) or a family history of asthma increases probability of asthma but their absence does not exclude asthma.

Patients with typical symptoms of asthma and a history of disease that is characteristic of asthma should be considered as having asthma after exclusion of other diagnoses.

The assessment of the frequency of daytime and nigthtime symptoms and limitations of physical activity determines whether asthma is *intermittent* or *persistent*.

Treatment

Only patients with persistent asthma need long-term treatment. The mainstay of treatment is inhaled corticosteroids. Treatment is started at the step most appropriate to initial severity then, re-evaluated and adjusted according to clinical response. It aims to abolish symptoms with the lowest possible dose of inhaled corticosteroids. An intervening severe exacerbation or loss of control necessitates reassessment to re-evaluate treatment.

Long-term treatment does not mean treatment for life. Asthma attacks may occur over months or years, with intervening asymptomatic intervals when long-term treatment is not required.

Long-term treatment of asthma according to severity

Categories	Treatment
Intermittent asthma • Day time symptoms < once weekly • Night time symptoms < 2 times monthly • Normal physical activity	No long term treatment Inhaled **salbutamol** when symptomatic
Mild persistent asthma • Day time symptoms > once weekly, but < once daily • Night time symptoms > 2 times monthly • Symptoms may affect activity	Continuous treatment with inhaled **beclometasone** + Inhaled **salbutamol** when symptomatic

Categories	Treatment
Moderate persistent asthma • Daily symptoms • Symptoms affect activity • Night time symptoms > once weekly • Daily use of salbutamol	Continuous treatment with inhaled **beclometasone** + Inhaled **salbutamol** (1 puff 4 times daily)
Severe persistent asthma • Daily symptoms • Frequent night time symptoms • Physical activity limited by symptoms	Continuous treatment with inhaled **beclometasone** + Inhaled **salbutamol** (1-2 puff/s 4 to 6 times daily)

Inhaled corticosteroid treatment: **beclometasone** dose varies according to the severity of asthma. Find the minimum dose necessary to both control the symptoms and avoid local and systemic adverse effects:
Children: 50 to 100 micrograms 2 times daily depending on the severity; increase to 200 micrograms 2 times daily if necessary (max. 800 micrograms daily)
Adults: 100 to 250 micrograms 2 times daily depending on the severity; increase to 500 micrograms 2 times daily if necessary (max. 1500 micrograms daily)

⚠ The number of puffs of beclometasone depends on its concentration in the inhaled aerosol: 50, 100 or 250 micrograms per puff.

Do not restrict exercise. If exercise is a trigger for asthma attacks, administer 1 or 2 puffs of salbutamol 10 minutes beforehand.

In pregnant women, poorly controlled asthma increases the risk of pre-eclampsia, eclampsia, haemorrhage, in utero growth retardation, premature delivery, neonatal hypoxia and perinatal mortality. Long-term treatment remains inhaled salbutamol and beclometasone at the usual dosage for adults. Whenever possible, avoid oral corticosteroids.

If symptoms are not well controlled during a period of at least 3 months, check the inhalation technique and adherence before changing to a stronger treatment.

If symptoms are well controlled for a period of at least 3 months (the patient is asymptomatic or the asthma has become *intermittent*): try a step-wise reduction in medication, finally discontinuing treatment, if it seems possible. Provide patients with a salbutamol inhaler for any possible attacks. Evaluate after 2 weeks. If the results are satisfactory, continue for 3 months and then re-evaluate. If the patient has redeveloped chronic asthma, restart long-term treatment, adjusting doses, as required.

Pulmonary tuberculosis

- Clinical features(see page 77)
- Laboratory(see page 77)
- Treatment(see page 77)
- Prevention(see page 77)
- References(see page 78)

– Pulmonary tuberculosis is a bacterial infection due to *Mycobacterium tuberculosis*, spread from person to person through inhalation of infected respiratory droplets.
– After infection, *M. tuberculosis* multiplies slowly in the lungs and is usually eliminated spontaneously or lies dormant.

– Only 10% of cases develop active tuberculosis. The risk of progressing to active tuberculosis is higher in immunocompromised patients. In certain countries, half of newly diagnosed tuberculosis patients are co-infected with HIV.[1](see page 78)

For more information on tuberculosis, refer to the guide Tuberculosis, MSF.

Clinical features

– Prolonged cough (> 2 weeks) with or without sputum production and/or haemoptysis, prolonged fever, night sweats, anorexia, weight loss, chest pain and fatigue.
– Differential diagnosis includes pneumonia, chronic obstructive pulmonary disease (COPD), lung cancer, pulmonary distomatosis (Flukes(see page 140), Chapter 6) and melioidosis (Southeast Asia).

In an endemic area, the diagnosis of tuberculosis is to be considered, in any patient consulting for respiratory symptoms for over 2 weeks who does not respond to non-specific antibacterial treatment.

Laboratory

– In the general population: Xpert® MTB/RIF test which simultaneously detects *M. tuberculosis* (MTB) in sputum and resistance to rifampicin (RIF). If not available perform sputum smear microscopy.[2](see page 78)
– If HIV co-infection suspected or diagnosed: Xpert® MTB/RIF test and point-of-care, urine LF-LAM (lateral flow urine lipoarabinomannan assay).[2](see page 78)

Treatment

For pulmonary tuberculosis, the standard treatment is a combination of four antituberculosis drugs (isoniazid, rifampicin, pyrazinamide, ethambutol). The regimen is organised into 2 phases (initial phase and continuation phase) and lasts 6 months.

If the strain is drug-resistant, the treatment is longer and different drug combinations are used.

It takes significant investment to cure tuberculosis, both from the patient and the medical team. Only uninterrupted treatment will lead to cure and prevent the development of resistance. It is essential that the patient understands the importance of treatment adherence and has access to correct case management until treatment is completed.

Prevention

– BCG vaccination in neonates: provides 59% protection against pulmonary tuberculosis.[3](see page 78)
– Infection control in healthcare settings: standard precautions and airborne precautions for confirmed or suspected cases.
– Close contacts: isoniazid preventive therapy for 6 months.

References

1. World Health Organization. Global tuberculosis report 2018. https://apps.who.int/iris/handle/10665/274453 [Accessed 21 October 2019]

2. Global Laboratory Initiative. GLI model TB diagnostic algorithms. 2018. http://www.stoptb.org/wg/gli/assets/documents/GLI_algorithms.pdf [Accessed 21 October 2019]

3. World Health Organization. Weekly epidemiological record/Relevé épidémiologique hebdomadaire 23rd February 2018, 93rd year/23 Février 2018, 93e année. No 8, 2018, 93, 73–96. https://www.who.int/immunization/policy/position_papers/bcg/en/ [Accessed 21 October 2019]

Chapter 3: Gastrointestinal disorders

- Acute diarrhoea(see page 79)
- Shigellosis(see page 81)
- Amoebiasis(see page 83)
- Disorders of the stomach and duodenum(see page 84)
    - Gastro-oesophageal reflux(see page 84)
    - Gastric and duodenal ulcers in adults(see page 85)
    - Dyspepsia(see page 87)
- Stomatitis(see page 87)
    - Oral and oropharyngeal candidiasis(see page 87)
    - Oral herpes(see page 88)
    - Other infectious causes(see page 89)
    - Stomatitis from scurvy (vitamin C deficiency)(see page 89)
    - Other lesions resulting from a nutritional deficiency(see page 89)

Acute diarrhoea

- Clinical features(see page 79)
- Treatment(see page 80)
    - Prevention and treatment of dehydration (see page 80)
    - Prevention of malnutrition(see page 80)
    - Zinc supplementation(see page 80)
    - Antimicrobial treatment(see page 80)
- Prevention(see page 81)
- References(see page 81)

– Acute diarrhoea is defined as at least 3 liquid stools per day for less than 2 weeks.
– There are 2 clinical types of acute diarrhoea:
• **Diarrhoea without blood**, caused by viruses in 60% of cases (rotavirus, enterovirus), bacteria (*Vibrio cholerae*, enterotoxigenic *Escherichia coli*, non Typhi *Salmonella*, *Yersinia enterocolitica*) or parasites (giardiasis). Diseases, such as malaria, acute otitis media, respiratory tract infections, etc. can be accompanied by this type of diarrhoea.
• **Diarrhoea with blood**, caused by bacteria (*Shigella* in 50% of cases, *Campylobacter jejuni*, enteroinvasive or enterohaemorrhagic *Escherichia coli*, *Salmonella*) or parasites (intestinal amoebiasis).
– Infectious diarrhoeas are transmitted by direct (dirty hands) or indirect (ingestion of contaminated water or food) contact.
– The high mortality rate from diarrhoeal diseases, even benign, is due to acute dehydration and malnutrition. This can be prevented by adequate rehydration and nutrition.

Clinical features

– First assess for signs of dehydration (see Dehydration(see page 34), Chapter 1).
– Then look for other signs:
• profuse watery diarrhoea (cholera, enterotoxigenic *E. coli*),
• repeated vomiting (cholera),
• fever (salmonellosis, viral diarrhoea),
• presence of red blood in stools: see also Shigellosis(see page 81) and Amoebiasis(see page 83) (Chapter 3).
– In a patient over 5 years with severe and rapid onset of dehydration, suspect cholera.

Treatment

General principles:
– Prevent or treat dehydration: rehydration consists of prompt replacement of fluid and electrolyte losses as required, until the diarrhoea stops.
– Administer zinc sulfate to children under 5 years.
– Prevent malnutrition.
– Do not systematically administer antimicrobials: only certain diarrhoeas require antibiotics (see Antimicrobial treatment(see page 80)).
– Do not administer anti-diarrhoeal drugs or antiemetics.
– Treat the underlying condition if any (malaria, otitis, respiratory infection, etc.).

Prevention and treatment of dehydration

See Dehydration(see page 34), Chapter 1.
Adapted treatment protocols are recommended for children with malnutrition (see Severe acute malnutrition(see page 38), Chapter 1).

Prevention of malnutrition

Continue unrestricted normal diet. In breastfed children, increase the frequency of feeds. Breast milk does not replace ORS. ORS should be given between feeds.

Zinc supplementation

Zinc sulfate is given in combination with oral rehydration solution in order to reduce the duration and severity of diarrhoea, as well as to prevent further occurrences in the 2 to 3 months after treatment:
zinc sulfate PO
Children under 6 months: 10 mg (½ tablet) once daily for 10 days
Children from 6 months to 5 years: 20 mg (1 tablet) once daily for 10 days

Place the half-tablet or full tablet in a teaspoon, add a bit of water to dissolve it, and give the entire spoonful to the child.

Antimicrobial treatment

Diarrhoea without blood

Most acute diarrhoeas are caused by viruses unresponsive to antimicrobials. Antimicrobials can be beneficial in the event of cholera or giardiasis.
– *Cholera*: the most important part of treatment is rehydration. In the absence of resistance (perform antibiotic-sensitivity testing at the beginning of an outbreak), antibiotic treatment shortens the duration of diarrhoea. See the guide Management of a cholera epidemic, MSF.
– *Giardiasis*: see Intestinal protozoan infections(see page 139), Chapter 6.

Diarrhoea with blood

– *Shigellosis* is the most frequent cause of bloody diarrhoea (amoebiasis is much less common). If there is no laboratory diagnosis to confirm the presence of amoebae, first line treatment is for shigellosis(see page 81) (Chapter 3).
– *Amoebiasis*: antiparasitic treatment only if motile *Entamoeba histolytica amoebae* are found in stools or if a correct shigellosis treatment has been ineffective (see Amoebiasis(see page 83), Chapter 3).

Prevention

– Breastfeeding reduces infant morbidity and mortality from diarrhoea and the severity of diarrhoea episodes.
– When the child is weaned preparation and storage of food are associated with the risk of contamination by faecal micro-organisms: discourage bottle-feeding; food must be cooked well; milk or porridge must never be stored at room temperature.
– Access to sufficient amounts of clean water and personal hygiene (washing hands with soap and water before food preparation and before eating, after defecation etc.) are effective methods of reducing the spread of diarrhoea.
– In countries with a high rotavirus diarrhoea fatality rate, the WHO recommends routine rotavirus vaccination in children between 6 weeks and 24 months of age.[1](see page 81)

References

1. Weekly epidemiological record/Relevé épidémiologique hebdomadaire 1st February 2013, 88th year/1er Février 2013, 88e année No. 5, 2013, 88, 49–64. https://www.who.int/wer/2013/wer8805.pdf [Accessed 02 January 2019]

Shigellosis

- Clinical features(see page 81)
- Laboratory(see page 82)
- Treatment(see page 82)
- Shigellosis in an epidemic context (see page 83)
- References(see page 83)

– Shigellosis is a highly contagious bacterial infection resulting in bloody diarrhoea. There are 4 serogroups of shigella: *S. dysenteriae*, *S. sonnei*, *S. flexneri*, *S. boydii*.
– *S. dysenteriae* type 1 (Sd1) is the only strain that causes large scale outbreaks. It has the highest case fatality rate (up to 10%).
– Patients at risk of death are children under 5 years, malnourished patients, children after measles, adults over 50 years.

Clinical features

– Diarrhoea with bright red blood visible in stool[1](see page 0), with or without fever
– Abdominal and rectal pain frequent
– Signs of serious illness: fever above 39 °C; severe dehydration; seizures, altered mental status
– Complications (more frequent with Sd1): febrile seizures (5 to 30% of children), rectal prolapse (3%), septicaemia, intestinal obstruction or perforation, moderate to severe haemolytic uraemic syndrome

Laboratory

Shigellosis in an epidemic context:
– Confirm the causal agent (stool culture) and perform antibiotic sensitivity tests.
– Perform monthly culture and sensitivity tests (antibiotic resistance can develop rapidly, sometimes during the course of an outbreak).

Treatment

– Patients with signs of serious illness or with life-threatening risk factors must be admitted as inpatients.
– Treat patients with neither signs of serious illness nor risk factors as outpatients.
– Antibiotherapy:

First-line treatment	
ciprofloxacin PO for 3 days Children: 15 mg/kg 2 times daily (max. 1 g daily) Adults: 500 mg 2 times daily	• if the strain is sensitive • if there is no antibiotic sensitivity test • if oral administration is possible
ceftriaxone IM for 3 days Children: 50 to 100 mg/kg once daily (max. 1 g daily) Adults: 1 to 2 g once daily	• in patients with severe infection and/or oral administration is not possible • in pregnant women[2](see page 0)

If resistance or contra-indication to ciprofloxacin or if no improvement within 48 hours of starting first-line treatment:
azithromycin PO for 5 days
Children: one dose of 12 mg/kg on D1 then 6 mg/kg once daily from D2 to D5
Adults: one dose of 500 mg on D1 then 250 mg once daily from D2 to D5
or
cefixime PO for 5 days
Children: 8 mg/kg once daily (max. 400 mg daily)
Adults: 400 mg once daily
If there is no improvement 48 hours after starting second-line treatment, treat for amoebiasis(see page 83).[1](see page 83),[2](see page 83)

– For pain and/or fever:
paracetamol PO (see Pain(see page 23), Chapter 1). All opioid analgesics are contra-indicated as they slow peristalsis.

– Supportive therapy:
• nutrition: nutritional supplement with frequent meals
+ 2500 kcal daily during hospitalisation
+ 1000 kcal daily as outpatients
• rehydration: administration of ORS according to WHO protocols (see Dehydration(see page 34), Chapter 1).
• zinc supplement in children under 5 years (see Acute diarrhoea(see page 79), Chapitre 3).

– Never give loperamide or any other antidiarrhoeal.

– Management of complications: rectal prolapse reduction, septicaemia (see Septic shock(see page 13), Chapter 1), etc.

Shigellosis in an epidemic context

– Isolation of hospitalised patients; school exclusion of children treated as outpatients.
– Hygiene (handwashing, hygienic preparation and storage of food, home hygiene, etc.).
– Management if signs worsen or bloody diarrhoea in entourage (seek medical attention).

1 (see page 0) This definition excludes: blood detected on microscope examination; stool containing digested blood (melaena); streaks of blood on the surface of normal stool (haemorrhoids, anal or rectal lesion, etc.).
2 (see page 0) Ciprofloxacin should be avoided in pregnant women. Nevertheless, if ceftriaxone is not available, the other antibiotics can be used, including ciprofloxacin if necessary.

References

1. Karen L. Kotloff et al. Seminar: Shigellosis. The Lancet, Volume 391, ISSUE 10122, P801-812, February 24, 2018.

2. Word Health Organization. Pocket book for hospital care in children: guidelines for the management of common childhood illnesses, 2013. http://apps.who.int/iris/bitstream/handle/10665/81170/9789241548373_eng.pdf;jsessionid=CE5C46916607EF413AA9FCA89B84163F?sequence=1 [Accessed 20 September 2018]

Amoebiasis

- Clinical features (see page 83)
- Laboratory (see page 84)
- Treatment (see page 84)

Amoebiasis is a parasitic infection due to the intestinal protozoa *Entamoeba histolytica*. Transmission is faecal-oral, by ingestion of amoebic cysts from food or water contaminated with faeces. Usually, ingested cysts release non-pathogenic amoebae and 90% of carriers are asymptomatic.
In 10% of infected patients, pathogenic amoebae penetrate the mucous of the colon: this is the intestinal amoebiasis (amoebic dysentery). The clinical picture is similar to that of shigellosis, which is the principal cause of dysentery.
Occasionally, the pathogenic amoebae migrate via the blood stream and form peripheral abscesses. Amoebic liver abscess is the most common form of extra-intestinal amoebiasis.

Clinical features

– *Amoebic dysentery*
• diarrhoea containing red blood and mucus
• abdominal pain, tenesmus
• no fever or moderate fever
• possibly signs of dehydration

– *Amoebic liver abscess*
• painful hepatomegaly; mild jaundice may be present
• anorexia, weight loss, nausea, vomiting
• intermittent fever, sweating, chills; change in overall condition

Laboratory

– Amoebic dysentery: identification of mobile trophozoites (*E. histolytica histolytica*) in fresh stool samples
– Amoebic liver abscess: indirect haemoagglutination and ELISA

Treatment

– *Amoebic* dysentery
• The presence of cysts alone should not lead to the treatment of amoebiasis.
• Amoebiasis confirmed with a parasitological stool examination:
tinidazole PO
Children: 50 mg/kg once daily for 3 days (max. 2 g daily)
Adults: 2 g once daily for 3 days
or **metronidazole** PO
Children: 15 mg/kg 3 times daily for 5 days
Adults: 500 mg 3 times daily for 5 days
• If there is no laboratory, first line treatment for dysentery is for shigellosis(see page 81). Treat for amoebiasis if correct treatment for shigellosis has been ineffective.
• Oral rehydration salts (**ORS**) if there is risk of, or if there are signs of dehydration (see Dehydration(see page 34), Chapter 1).

– *Amoebic liver abscess*
• **tinidazole** PO: same treatment for 5 days
• **metronidazole** PO: same treatment for 5 to 10 days

Disorders of the stomach and duodenum

- Gastro-oesophageal reflux(see page 84)
- Gastric and duodenal ulcers in adults(see page 85)
- Dyspepsia(see page 87)

Gastro-oesophageal reflux

- Clinical features(see page 84)
- Treatment(see page 85)

Clinical features

Burning stomachache or heartburn, generally relieved by antacids; acid regurgitation (often postural: while sitting forward or lying down). In the absence of dysphagia (oesophageal stenosis), these signs are benign.

Treatment

– First instance, encourage the patient to avoid alcohol and tobacco use.
Give **aluminium hydroxide/magnesium hydroxide** PO (400 mg/400 mg tablet)[1](see page 0) : 1 to 2 tablets 3 times daily 20 minutes to one hour after meals, or 1 tablet during painful attacks.

– If antacids are insufficient:
omeprazole PO: 20 mg once daily in the morning for 3 days

– In young children: no drug treatment, rest and sleep on an incline (30° to 45°).

[1](see page 0) Aluminium hydroxide/magnesium hydroxide may decrease intestinal absorption of drugs taken at the same time:
• atazanavir, chloroquine, digoxin, doxycycline, iron salts, gabapentin, itraconazole, levothyroxine (take at least 2 hours apart).
• ciprofloxacin (take ciprofloxacin 2 hours before or 4 hours after antacids), dolutegravir (take dolutegravir 2 hours before or 6 hours after antacids), velpatasvir (take 4 hours apart).

Gastric and duodenal ulcers in adults

- Clinical features(see page 85)
- Treatment of non-complicated ulcers(see page 85)
- Treatment of complicated ulcers(see page 85)
  - Perforation(see page 85)
  - Gastrointestinal bleeding(see page 86)
  - Eradication of Helicobacter pylori(see page 86)

Clinical features

Burning epigastric pain or epigastric cramps between meals, that wake the patient at night. Recurrent episodes characteristically last a few days and are often accompanied by nausea and even vomiting. The most common complications are perforation and bleeding.

Treatment of non-complicated ulcers

– For an isolated episode:
• identify patients taking NSAID or acetylsalicylic acid; stop treatment;
• encourage patients to avoid alcohol and tobacco use;
• **omeprazole** PO: 20 mg once daily in the morning for 7 to 10 days. In severe or recurrent cases, dose can be increased to 40 mg once daily and the treatment can be prolonged for up to 8 weeks.

– If the patient has frequent recurrences, unrelated to NSAID use, that require repeated treatment with antiulcer drugs: see eradication of *Helicobacter pylori*(see page 86).

Treatment of complicated ulcers

Perforation

Perforation should be considered in patients presenting with sudden onset intense epigastric pain, particularly if there is rigidity of the abdominal wall. The risk of peritonitis is increased if the perforation occurs on a full stomach.

– To start:
• place the patient on a strict fast (NPO); insert a nasogastric tube and aspirate if possible;
• insert an intravenous line and hydrate (Ringer lactate);
• treat acute pain (see Pain(see page 23), Chapter 1);
• **omeprazole** IV infusion: 40 mg once daily over 20 to 30 minutes

– Refer to a surgeon.

– If referral not possible, risk of mortality is high. Continue conservative management including maintenance fluid (alternate 5% glucose and Ringer lactate). Start IV antibiotics (see Shock(see page 10), Chapter 1). If after 3 days, the patient's clinical condition has improved, cautiously restart oral feeding, remove the nasogastric tube and start PO treatment to eradicate *Helicobacter pylori* (see eradication of *Helicobacter pylori*(see page 86)).

Gastrointestinal bleeding

Passing of black stool (maelena) and/or vomiting blood (haematemesis). In 80% of cases the bleeding stops spontaneously.

– Insert a nasogastric tube for aspiration and insert an IV line (16G).

If the haemodynamic state is stable (pulse and blood pressure are normal):
– Hydrate (Ringer lactate), monitor, keep NPO for 12 hours.
– If there is no active haemorrhage, restart oral feeding after 12 hours.
Gastric lavage with cold water is not essential, but may help evaluate persistence of bleeding.

If the haemorrhage continues (haematemesis) and/or *if the haemodynamic state deteriorates* (pulse increases, BP drops):
– Intensive care and transfusion according to the severity of the bleeding (see haemorrhagic shock(see page 12), Chapter 1).
– Emergency surgical intervention.

Eradication of *Helicobacter pylori*

Most peptic ulcers are caused by *Helicobacter pylori* infection. If a diagnosis of ulcer is probable, treatment to eradicate *H. pylori* should be considered if the patient has frequent attacks requiring repeated and/or prolonged treatments with antiulcer drugs over 8 weeks or in cases of complicated ulcers (perforation or gastrointestinal bleeding). Infection should be confirmed with a test where possible.

H. pylori resistance to antibiotics varies globally, follow national recommendations where available. If not, for information, administer a triple therapy for 7 days:
omeprazole PO 20 mg 2 times daily + **clarithromycin** PO 500 mg 2 times daily + **amoxicillin** PO 1 g 2 times daily[1](see page 0)

In immunocompromised patients, consider mycobacterium avium complex (MAC) infection or other nontuberculous mycobacterium (NTM) infection prior to starting a clarithromycin-containing triple therapy.

If symptoms continue despite treatment, consider the differential diagnosis of gastric cancer. Refer for investigations if possible.

Notes:
– Acetylsalicylic acid (aspirin) and NSAID (ibuprofen, diclofenac, etc.) are contra-indicated in patients suffering from or with a history of ulcers.
– Omeprazole is as effective PO as IV.

1(see page 0) In penicillin-allergic patients, amoxicillin PO can be substituted with **metronidazole** PO 500 mg 2 times daily.

Dyspepsia

- Clinical features(see page 87)
- Treatment(see page 87)

Clinical features

Epigastric pain or discomfort following meals, often accompanied by bloating, sensation of fullness and nausea. Dyspepsia is most commonly functional, linked with stress and not linked to the quantity of gastric acid (antiacids and antisecretory drugs are ineffective). Resolution is usually spontaneous.

Treatment

If the symptoms persist, short term symptomatic treatment may be considered.

In adults:
– **metoclopramide** PO, 10 mg 3 times daily, with an interval of at least 6 hours between each dose, ½ hour before meals, for 2 to 3 days may be helpful in the event of nausea, vomiting, bloating.
– **hyoscine butylbromide** PO, 10 mg 3 times daily, ½ hour before meals, for 2 to 3 days, may be helpful in the event of spasmodic pain.

Note: consider and treat possible intestinal parasites (taeniasis, ascariasis, ancylostomiasis, giardiasis, amoebiasis).

Stomatitis

- Oral and oropharyngeal candidiasis(see page 87)
- Oral herpes(see page 88)
- Other infectious causes(see page 89)
- Stomatitis from scurvy (vitamin C deficiency)(see page 89)
- Other lesions resulting from a nutritional deficiency(see page 89)

Stomatitis is an inflammation of the mucous membranes of the mouth caused by a fungal, viral or bacterial infection, a vitamin deficiency, an injury, etc.
Prolonged or painful stomatitis may contribute to dehydration or may cause loss of appetite with denutrition, particularly in children.
In infants, examine routinely the mouth in the event of breast refusal or difficulties in sucking.

In all cases:
– Maintain adequate hydration and feeding; offer foods that will not irritate the mucosa (soft, non-acidic). Use a nasogastric tube for a few days if pain is preventing the patient from eating.
– Keep the mouth clean to prevent complications and recurrence.

Oral and oropharyngeal candidiasis

- Clinical features(see page 88)
- Treatment(see page 88)

Infection due to *Candida albicans*, common in infants, immunocompromised or diabetic patients. Other risk factors include treatment with oral antibiotics or high-dose inhaled corticosteroids.

Clinical features

White patches on the tongue, inside the cheeks, that may spread to the pharynx.

In patients with frequent recurrences or extensive forms invading the esophagus (swallowing difficulty and pain), consider HIV infection.

Treatment

nystatin oral suspension for 7 days
Children and adults: 400 000 IU daily, i.e. 1 ml of the oral suspension (100 000 IU) 4 times daily
or
miconazole oral gel for 7 days
Children 6 months to 2 years: 1.25 ml 4 times daily
Children over 2 years and adults: 2.5 ml 4 times daily

Apply the oral suspension of nystatin or the oral gel of miconazole between meals; keep in the mouth for 2 to 3 minutes, then swallow. In young children, apply to the tongue and inside of each cheek.

Show the mother how to treat since, in most cases, candidiasis will be treated at home.

In immunocompromised patients: see HIV infection and AIDS(see page 206), Chapter 8.

Oral herpes

- Clinical features(see page 88)
- Treatment(see page 88)

Infection due to the *herpes simplex* virus. Primary infection typically occurs in children aged 6 months to 5 years and may cause acute gingivostomatitis, sometimes severe. After primary infection, the virus remains in the body and causes in some individuals periodic recurrences which are usually benign (herpes labialis).

Clinical features

– *Primary herpetic gingivostomatitis*
Multiple vesicles on the oral mucosa and lips which rupture to form painful, yellowish, at times extensive ulcers. Local lesions are usually associated with general malaise, regional lymphadenopathy and fever.

– *Recurrent herpes labialis*
Clusters of vesicles at the junction between the lip and the skin.

In patients with frequent recurrences or extensive forms, consider HIV infection (see HIV infection and AIDS(see page 206), Chapter 8).

Treatment

Primary herpetic gingivostomatitis

– Treat pain(see page 23): paracetamol or ibuprofen PO (Chapter 1)

– In the event of severe lesions, inability to drink and significant pain:
• Admit the child to hospital (high risk of dehydration).

• If the child presents within the first 96 hours of symptoms onset, **aciclovir** PO for 5 to 7 days:
Children under 2 years: 200 mg 5 times daily
Children 2 years and over and adults: 400 mg 5 times daily

– In the event of secondary bacterial infection: amoxicillin PO 7 days.

In immunocompromised patients: see HIV infection and AIDS(see page 206), Chapter 8.

Recurrent herpes labialis

Spontaneous resolution within 7 to 10 days. An antiseptic (chlorhexidine or povidone iodine) may be applied; paracetamol PO if necessary.

Both forms of herpes are contagious: do not touch lesions (or wash hands afterwards); avoid oral contact.

Other infectious causes

See Pharyngitis(see page 48) (Chapter 2), Diphtheria(see page 50) (Chapter 2), Measles(see page 183) (Chapter 8).

Stomatitis from scurvy (vitamin C deficiency)

- Clinical features(see page 89)
- Treatment(see page 89)

Clinical features

Bleeding gums, associated in infants with lower limb pain caused by subperiosteal haemorrhage. It is common in contexts of poor food quality or in populations completely dependent on food aid (refugee camps).

Treatment

ascorbic acid (**vitamin C**) PO
The optimal dose has not been established. For information:
Children 1 month to 11 years: 100 mg 3 times daily
Children 12 years and over and adults: 250 mg 3 times daily
or
Children 1 month to 3 years: 100 mg 2 times daily
Children 4 to 11 years: 250 mg 2 times daily
Children 12 years and over and adults: 500 mg 2 times daily

Treatment is administred at least 2 weeks or longer (until symptoms resolve), then preventive treatment is given (children and adults: 50 mg daily as long as the situation requires).

Other lesions resulting from a nutritional deficiency

Other vitamin deficiencies may provoke mouth lesions: angular stomatitis of the lips and glossitis from vitamin B_2 (riboflavin), niacin (see Pellagra(see page 112), Chapter 4) or vitamin B_6 (pyridoxine) deficiencies.

Iron deficiency may also provoke angular stomatitis (see Anaemia(see page 30), Chapter 1).

Give the corresponding vitamins at curative doses. Multivitamins are insufficient to treat true vitamin deficiencies.

Chapter 4: Skin diseases

- Dermatology(see page 91)
- Scabies(see page 92)
- Lice (pediculosis)(see page 95)
- Superficial fungal infections(see page 96)
- Bacterial skin infections(see page 98)
    - Impetigo(see page 98)
    - Furuncles and carbuncles(see page 99)
    - Erysipelas and cellulitis(see page 100)
- Cutaneous anthrax(see page 102)
- Endemic treponematoses(see page 104)
- Leprosy(see page 107)
- Herpes simplex and herpes zoster(see page 110)
    - Herpes simplex(see page 110)
    - Herpes zoster (shingles)(see page 110)
- Other skin disorders(see page 111)
    - Eczema(see page 111)
    - Seborrheic dermatitis(see page 112)
    - Urticaria(see page 112)
    - Pellagra(see page 112)

Dermatology

Skin diseases, particularly infectious skin diseases, are very common. They must be treated individually or collectively, but must also be considered as indicators of the sanitary condition of a population. A high prevalence of infectious skin diseases may reflect a problem of insufficient water quantity and lack of hygiene in a population.

Dermatological examination

– Observe the type of lesion:

- *Macule*: flat, non palpable lesion that is different in colour than the surrounding skin
- *Papule*: small (< 1 cm) slightly elevated, circumscribed, solid lesion
- *Vesicle* (< 1 cm), *bulla* (> 1 cm): clear fluid-filled blisters
- *Pustule*: vesicle containing pus
- *Nodule*: firm, elevated palpable lesion (> 1 cm) that extend into the dermis or subcutaneous tissue
- *Erosion*: loss of the epidermis that heals without leaving a scar
- *Excoriation*: erosion caused by scratching
- *Ulcer*: loss of the epidermis and at least part of the dermis that leaves a scar
- *Scale*: flake of epidermis that detaches from the skin surface
- *Crust*: dried serum, blood, or pus on the skin surface
- *Atrophy*: thinning of the skin
- *Lichenification*: thickening of the skin with accentuation of normal skin markings

– Look at the distribution of the lesions over the body; observe their arrangement: isolated, clustered, linear, annular (in a ring). Ask if the lesions are itchy.

– Look for a possible cause: insect bites; scabies, lice, other parasitic skin infections; contact with plants, animals, jewellery, detergents, etc.

– Ask about any past or ongoing treatment: topical, oral or parenteral.

– Look for local or regional signs (secondary infection, lymphangitis, adenopathy, erysipelas) and/or systemic signs (fever, septicaemia, secondary focus).

– Consider the sanitary conditions of the family, particularly for contagious skin diseases (scabies, scalp ringworm, lice).

– Check tetanus vaccination status.

Patients with skin disease often present late. At this stage, primary lesions and specific signs may be masked by secondary infection. In these cases, it is necessary to re-examine the patient, after treating the secondary infection, in order to identify and treat the underlying skin disease.

Scabies

- Clinical features(see page 92)
  - Ordinary scabies(see page 92)
  - Crusted (Norwegian) scabies(see page 93)
- Treatment(see page 93)
  - In all cases(see page 93)
  - Ordinary scabies(see page 93)
  - Crusted scabies(see page 94)

– Scabies is a cutaneous parasitosis due to the presence of the mite *Sarcoptes scabiei hominis* within the epidermis. It exists in two forms: ordinary scabies, relatively benign and moderately contagious; and crusted scabies, favoured by immune deficiency, extremely contagious and refractory to conventional treatment.
– Person to person transmission takes place chiefly through direct skin contact, and sometimes by indirect contact (sharing clothing, bedding). The challenge in management is that it must include simultaneous treatment of both the patient and close contacts, and at the same time, decontamination of clothing and bedding of all persons undergoing treatment, in order to break the transmission cycle.

Clinical features

Ordinary scabies

In older children and adults

– Itching, worse at night, very suggestive of scabies if close contacts have the same symptom
and
– Typical skin lesions:
• Scabies burrows (common): fine wavy lines of 5 to 15 mm, corresponding to the tunnels made by the parasite within the skin. Burrows are most often seen in the interdigital spaces of the hand and flexor aspect of the wrist, but may be present on the areolae, buttocks, elbows, axillae. The back and the face are spared. Burrows may be associated with vesicles, corresponding to the entry point of the parasite in the skin.
• Scabies nodules (less common): reddish-brown nodules, measuring 2 to 20 mm, on the genitals in men, persisting after effective treatment (they are not necessarily indicative of active infection).

and/or
– Secondary skin lesions: resulting from scratching (excoriations, crusts) or super-infection (impetigo).

Typical lesions and secondary lesions may co-exist, or specific lesions may be entirely masked by secondary lesions.

In infants and young children

– Vesicular eruption; often involving palms and soles, back, face, and limbs. Secondary infection or eczematisation is frequent. Isolated scabies nodules in the axillae may be the only manifestation.
– Examination of the mother's hands may support the diagnosis.

Crusted (Norwegian) scabies

Thick, scaly, erythematous plaques, generalised or localised, resembling psoriasis, with or without itching (50% of cases). Delay in diagnosis may lead to a scabies epidemic.

Treatment

In all cases

– Close contacts of the patient are treated simultaneously, even in the absence of symptoms.
– Clothing and bedding (including that of contacts) are changed after each treatment. They are washed at ≥ 60 °C then dried in the sun, or exposed to sunlight for 72 hours, or sealed in a plastic bag for 72 hours.

Ordinary scabies

Topical treatment

Topical scabicides are applied over the entire body (including the scalp, post-auricular areas, umbilicus, palms and soles), avoiding mucous membranes and face, and the breasts in breastfeeding women. Particular attention should be paid to common infestation sites. The recommended contact time should not be shortened or exceeded; the patient must not wash his hands while the product is in use (or the product should be reapplied if the hands are washed). In children under 2 years, the hands must be wrapped to prevent accidental ingestion of the product and contact with eyes. Topical scabicides should not be applied to broken or inflamed skin. Treatment of secondary bacterial infection, if present, should be initiated 24 to 48 hours before use of topical scabicides (see Impetigo(see page 98)).

The preferred treatment is **5% permethrin** cream:
Children 2 months and over and adults: one application, with a contact time of 8 hours, then rinse thoroughly. Repeat the application after 7 days.

or, if not available, **25% benzyl benzoate** lotion:
See the table below for dilution (depending on age), contact time and number of applications.

	Children < 2 years	Children 2 to 12 years	Children > 12 years and adults	Pregnant women
Dilution	Lotion must be diluted before use: 1 part 25% lotion + 3 parts water	Lotion must be diluted before use: 1 part 25% lotion + 1 part water	Use undiluted 25% lotion	Use undiluted 25% lotion

Contact time	12 hours (6 hours for infants < 6 months) then rinse thoroughly	24 hours then rinse thoroughly	24 hours then rinse thoroughly	12 hours then rinse thoroughly
Number of applications	One application	Two applications (e.g. 24 hours apart, with a rinse between the 2 applications; or 2 successive applications, 10 minutes apart, when the first application has dried with a rinse after 24 hours)		One application

Oral treatment

Treatment with ivermectin PO (200 micrograms/kg single dose) is an alternative: it is more practical than topical treatment (e.g. in the case of an epidemic or for treating contacts) and can be started right away in the case of secondary infection. A single dose may be sufficient; a second dose 7 days later reduces the risk of treatment failure.

Ivermectin is not recommended for children < 15 kg or pregnant women (safety not established)[1](see page 0)
.
Administration of ivermectin to patients with loiasis carries a risk of severe neurological complications when significant *Loa loa* microfilaraemia is present (see Filariasis(see page 151), Chapter 6)[2](see page 0) .

ivermectin PO single dose:

Weight	15 to 24 kg	25 to 35 kg	36 to 50 kg	51 to 65 kg
Ivermectin 3 mg tab	1 tab	2 tab	3 tab	4 tab

Treatment effectiveness is judged on clinical grounds. Itching may persist for 1 to 3 weeks after elimination of the parasite.

Persistence of typical burrows beyond 4 weeks should lead to suspicion of treatment failure (insufficient treatment, e.g. the scalp was not included in topical treatment or the patient washed his hands during the treatment period), or early re-infestation (contacts and environment not treated). In these cases, patient and contacts should be retreated.

Persistent itching may be due to another condition, initially masked by scabies.

Crusted scabies

Treatment combines simultaneous administration of oral ivermectin and topical scabicide at regular intervals, e.g. every week for 2 to 3 weeks or more, according to severity and clinical response.

Crusts should be softened (salicylic acid ointment) and removed before applying local treatment (otherwise, local treatment is ineffective).

As exfoliated skin scales may spread the parasite, the patient should be isolated during the treatment, staff should use protection (gloves, gowns and hand washing after contact), and environment (bedding, floors and surfaces) should be decontaminated.

[1](see page 0) Treatment with ivermectin in these patients is reserved for severe cases for which no alternative exists (see Crusted scabies(see page 94)).

2(see page 0) In areas where loiasis is endemic, certain precautions are recommended before administering ivermectin: e.g. measure the *Loa loa* microfilaraemia, if possible, or ensure that the patient has no history of loiasis (migration of an adult worm under the conjunctiva or transient « Calabar » swellings), nor history of severe adverse reactions following a previous treatment with ivermectin, or if in doubt, use topical treatment in preference to oral.

Lice (pediculosis)

- Clinical features(see page 95)
- Treatment(see page 95)
  - Head lice(see page 95)
  - Body lice(see page 96)
  - Pubic lice(see page 96)

Pediculosis is a benign contagious parasitic infection due to 3 species of lice specific to humans: head lice, body lice and pubic lice. Transmission from person to person occurs through direct or indirect contact.
Body lice are potential vectors of relapsing fever(see page 178) (Chapter 7), typhus (Eruptive rickettsioses(see page 180), Chapter 7) and trench fever.

Clinical features

– Head lice mainly affect children: itching and scratch marks (nape of neck and around the ears), which may become secondarily infected (impetigo) in prolonged infestation; presence of live lice and/or live (shiny, grey) nits attached to the hair shaft within 5 mm of the scalp.
– Body lice mainly affect populations living under poor conditions (refugees, prisoners, the homeless): itching and scratch marks (back, belt line and armpits), often inflamed and infected; presence of lice and nits in the clothing (parasites are not found on the body).
– Pubic lice are considered to be a sexually transmitted infection (STI): itching and scratch marks (pubic and perianal area), but other hairy areas may also be affected (armpits, thighs, eyelashes); lice and nits at the base of the hair shaft, rarely visible.
– Examine contacts; check for associated systemic infection (body lice) or STI (pubic lice).

Treatment

Head lice

– Apply lotion to scalp and dry hair, paying particular attention to the areas behind the ears and around the nape of the neck. Do not reduce or exceed the recommended duration of application.
4% dimeticone lotion
Children 6 months and over and adults: leave on hair for 8 hours, then rinse thoroughly.
Keep away from flames and/or intense heat sources (including cigarettes) during application and until rinsing (risk of ignition).
or, if dimeticone is not available or in children 2 to 6 months:
1% permethrin lotion
Children 2 months and over and adults: leave on hair for 10 minutes, then rinse thoroughly.

– Repeat application of either treatment after 7 days.
– Decontaminate combs, headwear and bedding (wash ≥ 60 °C/30 minutes, iron or dry in the sun or, if not feasible, seal in a plastic bag for 2 weeks).
– Treat as above contacts with live lice and/or live nits. Do not treat those with dead nits alone (dull, white, > 1 cm from scalp).

Body lice

Mass treatment (outbreak)

Apply 30 to 60 g (2 to 4 heaped soup spoons) of **0.5% permethrin** powder to the inside of the clothes and underclothes in contact with the skin (front and back, neck and waistline, sleeves and socks) in a fully clothed patient, then rub in the powder by hand. Leave for 12 to 24 hours.
Treat other clothing (including headwear) and bedding in a plastic bag with **0.5% permethrin** powder.
Repeat in 8 to 10 days if the infestation persists.

Individual treatment

Disinfection of clothing and bedding as above or as for head lice.

Pubic lice

Shave and/or apply **1% permethrin** lotion to hairy areas (as for head lice). Treat the partner at the same time. Decontaminate clothing and bedding (as for head lice). Repeat the application after 7 days.

Treatment of secondary bacterial infection, if present, should begin 24 to 48 hours before local antiparasitic treatment (see Impetigo(see page 98)); local treatment is applied later when tolerated.

Superficial fungal infections

- Clinical features and treatment(see page 96)
  - Candidiasis(see page 96)
  - Dermatophytoses(see page 97)

Superficial fungal infections are benign infections of the skin, scalp and nails caused by *Candida albicans* or dermatophytes.

Clinical features and treatment

Candidiasis

Candidal diaper dermatitis

Erythema of the perianal area with peripheral desquamation and sometimes pustules. Secondary infection may develop.

– Buttocks must be kept clean (ordinary soap and water) and dry.
– Avoid humidity: according to the context, expose the buttocks to air or change diapers more frequently; remove plastic pants.
– Protect the skin with **zinc oxide ointment** if diarrhoea is present.
– If diaper dermatitis is severe and persistent despite these measures, consider an intestinal infection (**nystatin** PO: 100 000 IU 4 times daily for 20 days).

Other candidiasis

– Candidiasis of skin folds: **miconazole 2%** cream, one application 2 times daily for 2 to 4 weeks
– Oral candidiasis: see Stomatitis(see page 87), Chapter 3.
– Vulvovaginal candidiasis: see Abnormal vaginal discharge(see page 233), Chapter 9.

Dermatophytoses

Dermatophytes cause various clinical lesions, depending on the anatomic site involved: scalp, glabrous (hairless) skin, folds or nails.

Anatomic site[1](see page 0)	**Clinical features**	**Treatment**
Scalp Scalp ringworm *Tinea capitis*	Common in children. Depending on the species: • One or more round, scaly, erythematous plaques with the ends of broken hairs. • Inflammation, suppuration, crusting and peripheral lymphadenopathy (kerion). • Permanent hair loss (favus). Some scalp ringworms are contagious: simultaneously examine (and treat) symptomatic contacts.	• Shave or cut hair short on and around the lesions. • Local treatment: 2 times daily, clean with soap and water, dry and apply **miconazole 2%** cream or **Whitfield's ointment** for 2 weeks or longer if necessary. • Administer systemic treatment as local treatment alone does not cure scalp ringworm: **griseofulvin** PO for 6 weeks minimum (up to 8 to 12 weeks) Children 1 to 12 years: 10 to 20 mg/kg once daily (max. 500 mg daily) Children ≥ 12 years and adults: 500 mg to 1 g once daily, depending on severity or **itraconazole** PO Children: 3 to 5 mg/kg once daily for 4 to 6 weeks (max. 200 mg daily) Adults: 200 mg once daily for 2 to 4 weeks • Suppurative lesions: treat superinfection (see Impetigo(see page 98)) before applying local antifungal treatment. • For painful kerion: paracetamol PO. *In pregnant lactating/breastfeeding women*: oral antifungals are contraindicated. Apply a topical treatment (miconazole 2% cream or Whitfield's ointment) to limit the spread of infection until it is possible to treat orally.
Glabrous skin Ringworm of the body *Tinea corporis*	Erythematous, scaly, pruritic macule with a well-demarcated, raised, vesicular border and central healing.	• For non widespread, localised tinea: Local treatment: 2 times daily, clean with soap and water, dry and apply **miconazole 2%** cream or **Whitfield's ointment** for 2 to 4 weeks or for 2 weeks after clinical resolution. • Reserve oral antifungals for particularly extensive lesions: griseofulvin PO for 4 to 6 weeks or itraconazole for 2 weeks.

Folds *Tinea pedis* (athlete's foot) *Tinea cruris*	• Interdigital spaces *(Tinea pedis):* Pruritus, fissure and whitish scales in the 3rd and/or 4th interdigital spaces[2](see page 0) . • Groin *(Tinea cruris):* Circumscribed, pruritic, erythematous plaque, with a pale centre surrounded by vesiculo-pustules, extending outward from the groin.	Topical treatment as above. If oozing lesions, use **miconazole 2%** cream only (do not use Whitfield's ointment).

[1](see page 0) Dermatophytosis may affect the nails (*Tinea unguium*, onychomycosis). Treatment is prolonged (12 to 18 months with griseofulvin) thus, in practice, difficult. Failures and relapses are frequent.

[2](see page 0) In candidal intertrigo, lesions are usually located in the 1st and 2nd interdigital spaces.

Bacterial skin infections

- Impetigo(see page 98)
- Furuncles and carbuncles(see page 99)
- Erysipelas and cellulitis(see page 100)

Impetigo

- Clinical features(see page 98)
- Treatment(see page 99)

– Impetigo is a benign, contagious infection of the epidermis due to group A ß-haemolytic streptococcus and *Staphylococcus aureus*. Co-infection is common. Transmission is by direct contact. Lack of water, and poor hygiene, increase spread.
– Primary infections are most common in children. Secondary infections complicating preexisting pruritic dermatoses (lice, scabies, eczema, herpes, chickenpox, etc.) are more common in adults.

Clinical features

– Non bullous impetigo (classic form): flaccid vesicle on erythematous skin which becomes pustular and forms a yellowish crust. Different stages o the infection may be present simultaneously. The lesion does not leave a scar. The most common sites of infection are around the nose and mouth, on the limbs or on the scalp.

– Bullous impetigo: large flaccid bullae and erosions of the skin in the ano-genital region in newborns and infants.

– Ecthyma: an ulcerative form of impetigo that leaves scars. This form is most common in the immunocompromised (e.g. HIV infection, malnutrition), diabetics and alcoholics.

– Regardless of the type of impetigo: absence of fever or systemic signs.

– Possible complications:
• abscess, pyodermitis, cellulitis, lymphangitis, osteomyelitis, septicaemia;
• acute glomerulonephritis (routinely look for signs of glomerulonephritis).

Treatment

– *Localised non bullous impetigo* (max. 5 lesions in a single skin area):
• Clean with soap and water and dry before applying mupirocin.
• **2% mupirocin** ointment: one application 3 times daily for 7 days. Reassess after 3 days. If there is no response, switch to oral antibiotic therapy (see below).
• Keep fingernails short. Avoid touching the lesions, keep them covered with gauze if possible.

– *Extensive non bullous impetigo* (more than 5 lesions or impetigo involving more than one skin area), bullous impetigo, ecthyma, impetigo with abscess; immunocompromised patient; topical treatment failure:
• Clean with soap and water and dry 2 to 3 times daily.
• Keep fingernails short. Avoid touching the lesions, keep them covered with gauze if possible.
• Incise abscesses if present.
• Administer oral antibiotic therapy[1](see page 0) :
cefalexin PO for 7 days
Neonates under 7 days: 25 mg/kg 2 times daily
Neonates 7 to 28 days: 25 mg/kg 3 times daily
Children 1 month to 12 years: 25 mg/kg 2 times daily
Children 12 years and over and adults: 1 g 2 times daily
or
cloxacillin PO for 7 days
Children over 10 years: 15 mg/kg 3 times daily (max. 3 g daily)
Adults: 1 g 3 times daily

Note: in newborns with lesions located around the umbilicus(see page 159), administer cloxacilllin IV.

– For all patients:
• Quarantine from school (children can return to school after 24 to 48 hours of antibiotic therapy).
• Look for and treat any underlying dermatosis: lice(see page 95), scabies(see page 92), eczema(see page 111), herpes(see page 110), scalp ringworm(see page 97), or an ENT infection.
• Trace and treat contacts.
• Check for proteinuria (use urine dipstick) 3 weeks after the infection.

[1](see page 0) In penicillin-allergic patients only (resistance to macrolides is common), **azithromycin** PO for 3 days (children: 10 mg/kg once daily; adults: 500 mg once daily).

Furuncles and carbuncles

- Clinical features(see page 100)
- Treatment(see page 100)

Necrotising perifollicular infection, usually due to *Staphylococcus aureus*. Risk factors include: nasal carriage of *S. aureus*, maceration, breaks in the skin, poor hygiene; diabetes mellitus, malnutrition, iron deficiency or immunodeficiency.

Clinical features

– Furuncle: red, warm, painful nodule with a central pustule, usually around a hair follicle. It becomes fluctuant, discharges a core of purulent exudate, and leaves a depressed scar. It occurs most frequently on the thighs, groin, buttocks, armpits, neck and back. There is no fever.

– Carbuncle: a cluster of interconnected furuncles, sometimes with fever and peripheral lymphadenopathy. It leaves a depressed scar.

Treatment

– Single furuncle:
• Clean with soap and water 2 times daily and cover with a dry dressing.
• Apply warm moist compresses to the furuncle in order to encourage it to drain.
• After drainage, clean and apply a dry dressing until the lesion has healed.

– Furuncle on the face, multiple furuncles, carbuncles or in immunocompromised patients:
• Same local care.
• Add systematically an antibiotic for 7 days[1](see page 0) :
cefalexin PO
Neonates under 7 days: 25 mg/kg 2 times daily
Neonates 7 to 28 days: 25 mg/kg 3 times daily
Children 1 month to 12 years: 25 mg/kg 2 times daily
Children 12 years and over and adults: 1 g 2 times daily
or
amoxicillin/clavulanic acid (**co-amoxiclav**) PO
Use formulations in a ratio of 8:1 or 7:1. The dose is expressed in amoxicillin:
Children < 40 kg: 25 mg/kg 2 times daily
Children ≥ 40 kg and adults:
Ratio 8:1: 2000 mg daily (2 tablets of 500/62.5 mg 2 times daily)
Ratio 7:1: 1750 mg daily (1 tablet of 875/125 mg 2 times daily)

– In all cases: wash hand frequently, wash bedding.

[1](see page 0) For penicillin-allergic patients:
clindamycin PO (children: 10 mg/kg 3 times daily; adults: 600 mg 3 times daily)

Erysipelas and cellulitis

Last updated: October 2020

- Clinical signs(see page 101)
- Paraclinical investigations(see page 101)
- Treatment(see page 101)

– Acute skin infections, due to bacteria (usually Group A beta-haemolytic streptococcus and sometimes *Staphylococcus aureus*, including methicillin resistant *S. aureus*–MRSA) that enter through a break in the skin.
– The main risk factors are: venous insufficiency, obesity, oedema or lymphoedema, history of erysipelas or cellulitis, immunosuppression and cutaneous inflammation (e.g. dermatosis, wound).
– Erysipelas is a superficial infection (affecting the dermis and superficial lymph vessels), while cellulitis

affects the deeper tissues (deep dermis layers and subcutaneous fat).
– Generally, these infections affect the lower extremities and sometimes the face. If the orbital and periorbital tissues are infected, see Periorbital and orbital cellulitis(see page 119), Chapter 5. If the infection is perifollicular, see Furuncles and carbuncles(see page 99), Chapter 4.

Clinical signs

– Warm, tender, swollen well–demarcated erythematous plaque.
– Fever, lymphadenopathy and lymphangitis.
– Look for a portal of entry (bite, ulcer, wound, intertrigo, eczema, fungal infection, etc.).
– In case of intense pain disproportionate to the skin lesion, hypoesthesia, rapidly progressing local signs, crepitation, skin necrosis or critically ill appearing patient, consider necrotising fasciitis that is a surgical emergency (see Necrotising infections of the skin and soft tissues(see page 271), Chapter 10).
– Other complications: septicaemia (see Septic shock(see page 10), Chapter 1), acute glomerulonephritis, osteomyelitis, septic arthritis.
– The main differential diagnoses include: contact dermatitis, stasis dermatitis due to venous insufficiency, venous thrombosis and erythema migrans characteristic of Lyme disease.

Paraclinical investigations

– Ultrasound: can detect signs of cellulitis and rule out an underlying abscess, deep vein thrombosis or a foreign body.
– Radiography: can detect a foreign body, underlying osteomyelitis (or gas in the subcutaneous tissue in case of a necrotising infection, nevertheless the absence of gas does not rule out this diagnosis).
– Test for proteinuria with urine dipstick 3 weeks after infection to look for glomerulonephritis.

Treatment

– In all cases:
• Outline the area of erythema with a pen in order to follow the infection[1](see page 0) .
• Bed rest, elevation of affected area (e.g. leg).
• Treatment of pain(see page 23) (Chapter 1). Avoid NSAIDs that may increase the risk of necrotising fasciitis.
• Administer antibiotics: either orally or IV depending on severity.
• Treat portal of entry and comorbidities.
• Check and/or catch up tetanus vaccination (see Tetanus(see page 162), Chapter 7).
• In case of necrotising fasciitis, septic arthritis or osteomyelitis: urgent transfer to a surgical centre, initiate IV antibiotic treatment while awaiting transfer.

– Hospitalize for the following: children younger than 3 months, critically ill appearing patient[2](see page 0) , local complications, debilitated patient (chronic conditions, the elderly) or if there is a risk of non-compliance with or failure of outpatient treatment. Treat other patients as outpatients.

– Outpatient antibiotherapy[3](see page 0) :
cefalexin PO for 7 to 10 days
Children 1 month to under 12 years: 25 mg/kg 2 times daily
Children 12 years and over and adults: 1 g 2 times daily
or
amoxicillin/clavulanic acid (**co-amoxiclav**) PO for 7 to 10 days
Use formulations in a ratio of 8:1 or 7:1. The dose is expressed in amoxicillin:
Children < 40 kg: 25 mg/kg 2 times daily
Children ≥ 40 kg and adults:
Ratio 8:1: 2000 mg daily (2 tablets of 500/62.5 mg 2 times daily)
Ratio 7:1: 1750 mg daily (1 tablet of 875/125 mg 2 times daily)

In the event of worsening clinical signs after 48 hours of antibiotic treatment, consider IV route.

– Inpatient antibiotherapy[4](see page 0) :

• First line therapy:
cloxacillin IV infusion over 60 minutes[5](see page 0)
Children 1 month to under 12 years: 12.5 to 25 mg/kg every 6 hours
Children 12 years and over and adults: 1 g every 6 hours
or
amoxicillin/clavulanic acid (**co-amoxiclav**) by slow IV injection (3 minutes) or IV infusion (30 minutes).
The dose is expressed in amoxicillin:
Children under 3 months: 30 mg/kg every 12 hours
Children 3 months and over: 20 to 30 mg/kg every 8 hours (max. 3 g daily)
Adults: 1 g every 8 hours
If there is clinical improvement after 48 hours (afebrile and erythema and oedema have improved) switch to cefalexin or amoxicillin/clavulanic acid PO at the doses indicated above to complete 7 to 10 days of treatment.

• If there is no clinical improvement after 48 hours, consider MRSA:
clindamycin IV infusion over 30 minutes[6](see page 0)
Children 1 month and over: 10 mg/kg every 8 hours
Adults: 600 mg every 8 hours
After 48 hours, change to clindamycin PO at the doses indicated above to complete 7 to 10 days of treatment.

[1](see page 0) The erythema will regress if the treatment is effective. If the erythema spreads consider a treatment failure (MRSA or a necrotising infection).
[2](see page 0) Critically ill appearing child: weak grunting or crying, drowsy and difficult to arouse, does not smile, disconjugate or anxious gaze, pallor or cyanosis, general hypotonia.
[3](see page 0) For penicillin-allergic patients, **clindamycin** PO for 7 to 10 days (children: 10 mg/kg 3 times daily; adults: 600 mg 3 times daily).
[4](see page 0) For penicillin-allergic patients, **clindamycin** IV infusion (children: 10 mg/kg 3 times daily; adults: 600 mg 3 times daily).
[5](see page 0) Cloxacillin powder for injection should be reconstituted in 4 ml of water for injection. Then dilute each dose of cloxacillin in 5 ml/kg of 0.9% sodium chloride or 5% glucose in children less than 20 kg and in a bag of 100 ml of 0.9% sodium chloride or 5% glucose in children 20 kg and over and in adults.
[6](see page 0) Dilute each dose of clindamycin in 5 ml/kg of 0.9% sodium chloride or 5% glucose in children less than 20 kg and in a bag of 100 ml of 0.9% sodium chloride or 5% glucose in children 20 kg and over and in adults.

Cutaneous anthrax

- Clinical features(see page 103)
- Laboratory(see page 103)
- Treatment(see page 103)
  - Uncomplicated cutaneous anthrax (see page 103)
  - Severe cutaneous anthrax(see page 103)
- Prevention(see page 104)

– Anthrax is caused by the bacterium *Bacillus anthracis* that primarily affects herbivores (sheep, goats, cows, camels, horses, etc.). Humans may become infected through contact of broken skin with a dead or sick animal. People at risk include livestock farmers and those that manipulate skins, wool or carcasses of infected animals.
– The disease is found in Eastern Europe, Central Asia, the Mediterranean Basin, Africa and South America.
– Pulmonary (acquired by inhalation) and intestinal (acquired by eating infected meat) forms also exist.

Clinical features

– Papule, then pruritic vesicle on uncovered skin surfaces (face, neck, arms, legs). The vesicle ulcerates and becomes a painless black eschar surrounded by oedema, often associated with with lymphangitis and regional lymphadenopathy.

– The following are criteria of severity:
• lesion located on the head or neck, or
• presence of systemic symptoms (fever, malaise, headache, tachycardia, tachypnoea, hypotension, hyper/hypothermia), or
• presence of extensive oedema, or
• multiple, extensive or bullous lesions.

Laboratory

– From vesicular fluid 1 (see page 0) : culture and susceptibility testing (rarely available) or Gram stain for microscopic examination.
– PCR testing (reference laboratory).

Treatment

Uncomplicated cutaneous anthrax

– Do not excise the eschar; daily dry dressings.
– Antibiotherapy for 7 to 10 days:
• If drug susceptibility is not known:
ciprofloxacin PO is first-line treatment for all patients including pregnant women and children:
Children: 15 mg/kg 2 times daily (max. 1 g daily)
Adults: 500 mg 2 times daily
Alternatives include:
doxycycline PO (except in children under 8 years and pregnant or lactating women)
Children 8 to 12 years: 50 mg 2 times daily
Children over 12 years and adults: 100 mg 2 times daily
or
clindamycin PO (e.g. in pregnant or lactating women and children less than 8 years)
Children: 10 mg/kg 3 times daily (max. 1800 mg daily)
Adults: 600 mg 3 times daily

• If penicillins are effective (documented susceptibility):
amoxicillin PO
Children: 30 mg/kg 3 times daily
Adults: 1 g 3 times daily

Severe cutaneous anthrax

– Combination antibiotherapy for 14 days:

⚠ Whatever the protocol used, do not mix the two drugs in the same infusion bag (incompatibility).

• If drug susceptibility is not known:
ciprofloxacin IV infusion over 60 minutes[2](see page 0)
Children: 10 mg/kg every 8 hours
Adults: 400 mg every 8 hours
+
clindamycin IV infusion over 30 minutes[2](see page 0)
Children 1 month and over: 10 to 13 mg/kg every 8 hours (max. 2700 mg daily)
Adults: 900 mg every 8 hours

• If penicillins are effective (documented susceptibility):
ampicillin IV
Children 1 month and over: 50 mg/kg every 6 to 8 hours
Adults: 4 g every 8 hours
+
clindamycin IV infusion as above.

Change to oral treatment as soon as possible to complete 14 days of treatment with ciprofloxacin + clindamycin or amoxicillin + clindamycin as for cutaneous anthrax without severity criteria.

– Intensive care: symptomatic treatment of shock (see Shock(see page 10), Chapter 1); tracheostomy and ventilatory support may be necessary.

Prevention

– Antibiotic prophylaxis in case of known skin exposure: treat for 10 days PO as for cutaneous anthrax without severity criteria.
– Livestock vaccination; burial or burning of animal carcasses.

[1](see page 0) Samples can be stored (including transport time) for 7 days max. in cold chain (if not available, at a temperature < 30 °C).
[2](see page 0) Dilute each dose of ciprofloxacin or clindamycin in 5 ml/kg of 0.9% sodium chloride or 5% glucose in children less than 20 kg and in a bag of 100 ml of 0.9% sodium chloride or 5% glucose in children above 20 kg and in adults. Administer ciprofloxacin more slowly than clindamycin. [a(see page 0) b(see page 0)]

Endemic treponematoses

- Clinical features(see page 105)
- Treatment(see page 106)
  - Yaws(see page 106)
  - Pinta and bejel(see page 106)
  - Treatment of contacts and latent cases(see page 106)
- References(see page 107)

– Endemic treponematoses are bacterial infections caused by 3 different types of treponema (other than *Treponema pallidum*). Human-to-human transmission may be direct or indirect.

– The 3 endemic treponematoses result in positive syphilis serology (TPHA-VDRL), but these tests are not necessary as diagnosis is clinical. There is no laboratory test that can distinguish between the different treponematoses.

– For the diagnosis and treatment of syphilis, see Genital infections(see page 229), Chapter 9.

Clinical features

	Yaws	Pinta	Bejel
Pathogen	*Treponema pertenue*	*Treponema carateum*	*Treponema pallidum* type M
Geographic distribution	Tropical and humid forests	Tropical zones of Latin America	Arid areas, semi-desert of the Middle East and Africa
Population	Children between 4 and 14 years	Children and adults	Nomadic populations, particularly children
First stage	Yaws chancre: skin coloured lesion, non-indurated, itchy, on the lower limbs in 95% of cases, with peripheral adenopathy. Spontaneous healing or development of a large yaw surrounded by smaller yaws.	Annular, erythematous, scaly plaques, usually on uncovered body parts (face, extremities), resemble dermatophytes. Lesions heal sponta-neously leaving scars.	Discrete chancre: moist papule, most commonly on the mucous membranes or in dermal folds, with peripheral adenopathy.
Second stage	Lesions appear 3 weeks after the initial chancre, occur in crops and heal spontaneously: • Frambesioma (papillomatous lesion, vegetal, very contagious) • Isolated or associated with yaws (round, squamous papules, not very contagious) • Osteoperiostitis of the long bones (phalanges, nasal process of the maxilla, tibia)	Pintids: plaques of various colours (bluish, reddish, whitish). May occur anywhere on the body.	• Mucous patches of the mouth common: very contagious ulcerated, round in form, indurated, with white coating, bleed easily, usually occur on the inside of the lips, cheek and tongue or labial folds • Condyloma in the anogenital region (rare) • Cutaneous lesions are rare: vegetal aspect, in dermal folds • Bone destruction identical to that of yaws, in the legs and forearms

	Yaws	Pinta	Bejel
Late stage	After some years of latency: • Periostitis; painful, debilitating osteitis • Ulcerating and disfiguring rhinopharyngitis • Juxta-articular nodules	Symmetrical white patches on the limbs. The depigmentation is permanent, remaining after treatment.	After several years of latency: • Gummatous lesions of skin and long bones • Plantar and palmar keratosis • Juxta-articular nodules • Hyper- and hypo-pigmented patches (as in pinta)

Treatment

Yaws

azithromycin PO[1](see page 107)
Children and adults: 30 mg/kg single dose (max. 2 g)
or, if not available,
benzathine benzylpenicillin IM[2](see page 107),[3](see page 107)
Children under 10 years: 1.2 MIU single dose
Children 10 years and over and adults: 2.4 MIU single dose

Pinta and bejel

benzathine benzylpenicillin IM
As for yaws.

For patients allergic to penicillin:
doxycycline PO (except in children under 8 years and pregnant or lactating women)
Children 8 years and over: 50 mg 2 times daily for 14 days
Adults: 100 mg 2 times daily for 14 days

Notes:
– Antibiotic treatment will cure early stage cases and may relieve the pain of osteitis. It may be ineffective for late stage infections.
– Syphilis serology will remain positive despite clinical cure.

Treatment of contacts and latent cases

The same treatment should be administered to all symptomatic and asymptomatic contacts and to all latent cases (asymptomatic individuals with positive serologic test for syphilis) in endemic zones.

References

1. World Health Organization (2012). Yaws: recognition booklet for communities. Reprinted with changes, 2014.
http://www.who.int/iris/handle/10665/75360 [Accessed 15 May 2018]

2. Oriol Mitjà, David Mabey. Yaws, bejel, and pinta (last updated. May 07, 2018). UpToDate [1Accessed 15 May 2018].

3. Michael Marks, Anthony W Solomon, David C Mabey. Endemic treponemal diseases. Transactions of The Royal Society of Tropical Medicine and Hygiene, Volume 108, Issue 10, 1 October 2014, Pages 601–607.
https://doi.org/10.1093/trstmh/tru128 [2Accessed 15 May 2018]

Leprosy

- Clinical features(see page 107)
- Laboratory(see page 108)
- Treatment(see page 108)
- Leprosy reactions(see page 109)
- References(see page 110)

– Leprosy is a chronic bacterial infection due to *Mycobacterium leprae.*
– It is transmitted by frequent close contact, mainly between household members.
– It mainly affects young adults. 94% of reported cases globally were in Bangladesh, Brazil, Democratic Republic of Congo, Ethiopia, India, Indonesia, Madagascar, Myanmar, Nepal, Nigeria, the Philippines, Sri Lanka and the United Republic of Tanzania.[1](see page 110)

Clinical features

Leprosy should be considered in any patient presenting with:
– Hypopigmented or erythematous skin lesion(s) with partial or complete loss of sensation to touch, pain, heat;
– Infiltrated pigmented nodules, initially with no sensory loss, on the face, ear lobes and the upper and lower limbs;
– Tender, infiltrated and hypertrophied peripheral nerve (ulnar, radial, median, popliteal, tibial etc.) with possible paraesthesia of the extremities, trophic changes (perforating ulcer of the foot) or paralysis (steppage gait, deformaties of hands and feet, facial nerve paralysis).

There are different clinical forms and classification systems of leprosy.

Ridley-Jopling classification
This classification differentiates 5 forms based on the bacteriological index. These forms correlate with the immunological response to *M. leprae.* Patients with tuberculoid leprosy (TT) are resistant to the bacillus and infection is localised. Patients with lepromatous leprosy (LL) are extremely sensitive to the

1 https://www.uptodate.com/contents/yaws-bejel-and-pinta/contributors
2 https://www.uptodate.com/contents/yaws-bejel-and-pinta/contributors

bacillus and the infection is disseminated. Borderline forms (BT, BB, BL) are between the two ends of the spectrum (TT and LL).

Paucibacillary forms (least contagious forms)		**Multibacillary forms** (most contagious forms)		
Tuberculoid	Borderline Tuberculoid	Borderline	Borderline Lepromatous	Lepromatous
T.T.	B.T.	B.B.	B.L.	L.L.

WHO classification

In order to simplify diagnosis and to promote rapid implementation of treatment, the WHO has simplified clinical classification of leprosy and differentiates only 2 forms:

– Multibacillary leprosy: more than 5 skin lesions

– Paucibacillary leprosy: 1 to 5 skin lesions

Multibacillary leprosy includes LL, BL and BB forms and paucibacillary leprosy includes the TT and BT forms of the Ridley-Jopling classification system.

Laboratory

– Laboratory diagnosis is based on the detection of acid-fast bacilli in a Ziehl-Neelsen stained nasal smear and skin-split smear taken from the ear lobe or from a skin lesion. In TT leprosy bacilli are not found.

– In practice, in most endemic countries diagnosis is based on the WHO clinical classification (number of lesions).

Treatment

Countries where leprosy is endemic have a control programme. Check national recommendations.

First-line treatment regimens recommended by the WHO

Age	**Multibacillary leprosy** (more than 5 skin lesions)	**Paucibacillary leprosy** (1 to 5 skin lesions)
Children 10 to 14 years	**rifampicin** PO: 450 mg once monthly + **clofazimine** PO: 150 mg once monthly and 50 mg on alternate days + **dapsone** PO: 50 mg once daily	**rifampicin** PO: 450 mg once monthly + **clofazimine** PO: 150 mg once monthly and 50 mg on alternate days + **dapsone** PO: 50 mg once daily
Children 15 years and over and adults	**rifampicin** PO: 600 mg once monthly + **clofazimine** PO: 300 mg once monthly and 50 mg once daily + **dapsone** PO: 100 mg once daily	**rifampicin** PO: 600 mg once monthly + **clofazimine** PO: 300 mg once monthly and 50 mg once daily + **dapsone** PO: 100 mg once daily
Duration	**12 months**	**6 months**

Note: the monthly doses of rifampicin and clofazimine are administered under direct observation by medical staff whereas the daily doses of clofazimine and dapsone are taken by the patient at home. Rifampicin should be taken on an empty stomach to improve absorption.

Teach the patient to recognise and quickly report a lepra reaction or relapse in order to modify or restart treatment.

Leprosy reactions

These reactions usually occur during the course of treatment in patients with multibacillary leprosy (BL and LL). They are associated with the immunological response to *M. leprae* antigens. Urgent treatment is required to avoid irreversible disability. Do not interrupt ongoing leprosy treatment.

Clinical features

– Reversal reactions:
• Exacerbation of the skin lesions that become erythematous and oedematous and risk or ulceration. Onset or worsening of numbness of skin lesions;
• Onset of acute painful hypertrophic neuritis.

– Erythema nodosum leprosum:
• Fever, asthenia, alteration of the general state;
• Crops of purplish-red, tender subcutaneous nodules, warmer than the surrounding skin.

Treatment

– Reversal reactions:
prednisolone (or **prednisone**) PO: 0.5 to 1 mg/kg once daily for 2 weeks. Re-examine the patient every 2 weeks and decrease the dosage if the neurological signs recede. According to clinical response, treatment may last 3 to 6 months.[2](see page 110)

For example, for an adult:[3](see page 110)
Week 1 and 2: 40 mg once daily
Week 3 and 4: 30 mg once daily
Week 5 and 6: 20 mg once daily
Week 7 and 8: 15 mg once daily
Week 9 and 10: 10 mg once daily
Week 11 and 12: 5 mg once daily

– Erythema nodosum leprosum:
• **prednisolone** (or **prednisone**) PO as for reversal reactions, for 3 months.[2](see page 110)
• Fever: paracetamol PO (see Fever(see page 21), Chapter 1).

References

1. World Health Organization. Global Leprosy Programme. Global leprosy strategy 2016-2020. Accelerating towards a leprosy-free world, 2016. http://apps.who.int/iris/bitstream/handle/10665/208824/9789290225096_en.pdf?sequence=14&isAllowed=y [Accessed 17 October 2018]

2. World Health Organization. WHO Expert Committee on Leprosy. Eighth report. WHO technical report series, n° 968. Geneva, 2012. http://www.searo.who.int/entity/global_leprosy_programme/publications/8th_expert_comm_2012.pdf [Accessed 17 October 2018]

3. World Health Organization. A guide to eliminating leprosy as a public health problem. Leprosy Elimination Group, 2000. http://apps.who.int/iris/bitstream/handle/10665/66612/WHO_CDS_CPE_CEE_2000.14.pdf?sequence=1 [Accessed 17 October 2018]

Herpes simplex and herpes zoster

- Herpes simplex(see page 110)
- Herpes zoster (shingles)(see page 110)

Herpes simplex

- Clinical features(see page 110)
- Treatment(see page 110)

Recurrent viral infection of the skin and mucous membranes due to the *Herpes simplex* virus. Recurrent lesions have a different presentation than primary infection.

Clinical features

– Recurrent herpes labialis: tingling feeling followed by an eruption of vesicles on an erythematous base, located on the lips ('fever blisters') and around the mouth, they may extend onto the face. Recurrence corresponds to a reactivation of the latent virus after a primary infection. No associated malaise, adenopathy or fever.
– Carefully consider other sites: buccal (Stomatitis(see page 87), Chapter 3), genital (Genital ulcers(see page 235), Chapter 9), ophthalmic, and secondary bacterial infections.

Treatment

– Clean with soap and water 2 times daily until the lesions have healed.
– For patients with secondary bacterial infections: antibiotic treatment as for impetigo(see page 98).

Herpes zoster (shingles)

- Clinical features(see page 111)
- Treatment(see page 111)

Acute viral infection due to the varicella-zoster virus. Chickenpox is the primary infection and herpes zoster the reactivation of the latent virus.

Clinical features

– Unilateral neuralgic pain followed by an eruption of vesicles on a erythematous base, that follow the distribution of a nerve pathway.
– Lesions most commonly occur on the thorax, but herpes zoster may also develop on the face with a risk of ophthalmic complications.
– Herpes zoster is more common in adults than in children.

Treatment

– Similar to that of herpes simplex, with the addition of systematic analgesics: paracetamol PO (see Pain(see page 23), Chapter 1).
– Aciclovir PO given within the first 48 hours after the eruption of lesions is only indicated for severe forms: necrotic or extensive lesions or lesion on the face which may spread to the eyes (see HIV infection and AIDS(see page 206), Chapter 8).

Other skin disorders

- Eczema(see page 111)
- Seborrheic dermatitis(see page 112)
- Urticaria(see page 112)
- Pellagra(see page 112)

Eczema

– Acute eczema: erythematous plaque, pruritic, vesicular, oozing, with poorly demarcated and crumbly borders.
– Chronic eczema: erythematous plaque, scaly, dry, poorly demarcated and pruritic.
– Look for a cause (contact allergic dermatitis, fungal or bacterial infection with a distant focus, malnutrition) and ask about family history.

Treatment

– Clean with soap and water 2 times daily.

– Then:
• for acute eczema: **calamine** lotion, one application 2 times daily
• for chronic eczema: **zinc oxide** ointment, one application 2 times daily

– Look for and treat any pre-existing condition (scabies, lice etc.).

– For patients with secondary infections: treat as impetigo(see page 98).

– For patients with intense pruritus, antihistamines for a few days (see Urticaria(see page 112)).

Seborrheic dermatitis

- Clinical features(see page 112)
- Treatment(see page 112)

Seborrheic dermatitis is an inflammatory chronic dermatosis that can be localized on areas rich with sebaceous glands. This dermatosis is more common in infected patients with HIV.

Clinical features

– Erythematous plaques covered by greasy yellow scales that can be localized on the scalp, the face (nose wings, eyebrows, edge of the eyelids), sternum, spine, perineum, and skin folds.

Treatment

– Clean with soap and water 2 times daily; shampooing the scalp.

– **Hydrocortisone 1%** cream: one application once daily or 2 times daily to the affected area only, in thin layer, for 7 days maximum

– Do not apply if pre-existing bacterial infection; treat first the infection (see Impetigo(see page 98)).

Urticaria

– Papules: transient, erythematous, oedematous, pruritic, resembling nettle stings.
– Look for a cause: food or drug (particularly antibiotic) allergy, insect bites; the invasive stage of a bacterial or parasitic infection (ascariasis, strongylodiasis, ancylostomiasis, schistosomiasis, loiasis), viral infection (hepatitis B or C); generalised disease (cancer, lupus, dysthyroidism, vasculitis).

Treatment

– If the pruritus is intense, antihistamines for a few days:
loratadine PO
Children over 2 years and under 30 kg: 5 mg (5 ml) once daily
Children over 30 kg and adults: 10 mg (1 tab) once daily
or
chlorphenamine PO
Children 1 to < 2 years: 1 mg 2 times daily
Children 2 to < 6 years: 1 mg 4 to 6 times daily (max. 6 mg daily)
Children 6 to < 12 years: 2 mg 4 to 6 times daily (max. 12 mg daily)
Children ≥ 12 years and adults: 4 mg 4 to 6 times daily (max. 24 mg daily; 12 mg daily in elderly patients)

– In the event of anaphylactic reaction, see Shock(see page 13) (Chapter 1).

Pellagra

- Clinical features(see page 113)
- Treatment(see page 113)
- References(see page 113)

Pellagra is a dermatitis resulting from niacin and/or tryptophane deficiency (in persons whose staple food is sorghum; patients with malabsorption, or during famine).

Clinical features

Classically, disease of the 'three Ds': dermatitis, diarrhoea and dementia.
– Dark red plaques, well demarcated, symmetric, located on exposed areas of the body (forehead, neck, forearms, legs). The skin becomes very scaly, pigmented, sometimes with haemorrhagic bullae.
– Gastrointestinal (glossitis, stomatitis and diarrhoea) and neuropsychiatric symptoms are seen in more serious forms.

Treatment

– **nicotinamide** (**vitamin PP**) PO[1](see page 113)
Children and adults: 100 mg 3 times daily, give with a diet rich in protein until the patient is fully cured.

– In the event of an epidemic of pellagra, for example in a refugee camp, it is vital that the food ration be modified (add groundnuts or dry vegetables) in order to meet the daily requirements (approximately 15 mg daily for adults).

References

1. World Health Organization, United Nations High Commissions for Refugees. Pellagra and its prevention and control in major emergencies. World Health Organization, 2000. http://www.who.int/nutrition/publications/en/pellagra_prevention_control.pdf [[3]Accessed 23 May 2018]

3 https://www.uptodate.com/contents/yaws-bejel-and-pinta/contributors

Chapter 5: Eye diseases

- Xerophthalmia (vitamin A deficiency)(see page 114)
- Conjunctivitis(see page 116)
    - Neonatal conjunctivitis(see page 116)
    - Viral epidemic keratoconjunctivitis(see page 117)
- Trachoma(see page 118)
- Periorbital and orbital cellulitis(see page 119)
- Other pathologies(see page 121)
    - Onchocerciasis(see page 121)
    - Loiasis(see page 121)
    - Pterygium(see page 122)
    - Cataract(see page 122)

Xerophthalmia (vitamin A deficiency)

- Clinical features(see page 114)
- Treatment(see page 114)
- Prevention(see page 115)

The term xerophthalmia covers all the ocular manifestations of vitamin A deficiency. Xerophthalmia can progress to irreversible blindness if left untreated.

In endemic areas, vitamin A deficiency and xerophthalmia affect mainly children (particularly those suffering from malnutrition or measles) and pregnant women.

Disorders due to vitamin A deficiency can be prevented by the routine administration of retinol.

Clinical features

– The first sign is hemeralopia (crepuscular blindness): the child cannot see in dim light, may bump into objects and/or show decreased mobility.

– Then, other signs appear gradually:
• Conjunctival xerosis: bulbar conjunctiva appears dry, dull, thick, wrinkled and insensitive
• Bitot's spots: greyish foamy patches on the bulbar conjunctiva, usually in both eyes (specific sign, however not always present)
• Corneal xerosis: cornea appears dry and dull
• Corneal ulcerations
• Keratomalacia (the last and most severe sign of xerophthalmia): softening of the cornea, followed by perforation of the eyeball and blindness (extreme care must be taken during ophthalmic examination due to risk of rupturing cornea)

Treatment

Treat early symptoms to avoid the development of severe complications. Vision can be saved provided that ulcerations affect less than a third of the cornea and the pupil is spared. Even if deficiency has already led to keratomalacia and irreversible loss of sight, it is imperative to administer treatment, in order to save the other eye and the life of the patient.

– **Retinol** (**vitamin A**) PO
Treatment is the same regardless of the clinical stage, except in pregnant women.

Age	200 000 IU capsule[(a)]
Children < 6 months[(b)]	50 000 IU (2 drops) once daily on D1, D2 and D8
Children 6 months to < 1 year	100 000 IU (4 drops) once daily on D1, D2 and D8
Children ≥ 1 year and adults	200 000 IU (one capsule) once daily on D1, D2 and D8

[(a)] Capsules must not be swallowed whole. Cut the end of the capsule and deliver the dose directly into the mouth.
[(b)] Vitamin A deficiency is rare in breastfed infants under 6 months.

In pregnant women, treatment varies according to the stage of illness:
• Hemeralopia or Bitot's spots: 10 000 IU once daily or 25 000 IU once weekly for at least 4 weeks. Do not exceed indicated doses (risk of foetal malformations).
• If the cornea is affected, risk of blindness outweighs teratogenic risk. Administer 200 000 IU once daily on D1, D2 and D8.

– Corneal lesions are a medical emergency. In addition to the immediate administration of retinol, treat or prevent secondary bacterial infections with **1% tetracycline eye ointment**, one application 2 times daily (do not apply eye drops containing corticosteroids) and protect the eye with an eye-pad after each application.

Prevention

– Systematically administer retinol PO to children suffering from measles (one dose on D1 and D2).

– In areas where vitamin A deficiency is endemic[1](see page 0), routine supplementation of **retinol** PO:

Age	200 000 IU capsule[(a)]
Children < 6 months	50 000 IU (2 drops) single dose
Children 6 months to < 1 year	100 000 IU (4 drops) every 4 to 6 months
Children 1 to < 5 years	200 000 IU (one capsule) every 4 to 6 months
Women after delivery	200 000 IU (one capsule) single dose

[(a)] Capsules must not be swallowed whole. Cut the end of the capsule and deliver the dose directly into the mouth.

To avoid excessive dosage, record any doses administered on the health/immunisation card and do not exceed indicated doses. Vitamin A overdose may cause raised intracranial pressure (bulging fontanelle in infants; headache, nausea, vomiting) and, in severe cases, impaired consciousness and convulsions. These adverse effects are transient; they require medical surveillance and symptomatic treatment if needed.

[1](see page 0) For more information country-specific prevalence of vitamin A deficiency, see https://www.thelancet.com/action/showPdf?pii=S2214-109X%2815%2900039-X

Conjunctivitis

- Neonatal conjunctivitis(see page 116)
- Viral epidemic keratoconjunctivitis(see page 117)

Conjunctivitis is an acute inflammation of the conjunctiva due to a bacterial or viral infection, allergy, or irritation.
Conjunctivitis may be associated with measles or rhinopharyngitis in children.
In the absence of hygiene and effective treatment, secondary bacterial infections may develop, affecting the cornea (keratitis).

Clinical features

– Clinical signs of all conjuctivites include: redness of the eye and irritation. Visual acuity is not affected.

– Depending on the cause:
• abundant and purulent secretions, eyelids stuck together on waking, unilateral infection at onset: bacterial conjunctivitis;
• watery (serous) secretions, no itching: viral conjunctivitis;
• excessive lacrimation, eyelid oedema, intense itching: allergic conjunctivitis.

– In endemic areas, turn both upper eyelids up to check for signs of trachoma (see Trachoma(see page 118)).

– Suspect keratitis if patient reports intense pain (more than is usually associated with conjunctivitis) and photophobia. Instill one drop of **0.5% fluorescein** to check for possible ulcerations.

– Always check for foreign bodies (subconjunctival or corneal) and remove after administering **0.4% oxybuprocaine** anaesthetic eye drops. Never give bottle of eye drops to the patient.

Treatment

Bacterial conjunctivitis
– Clean eyes 4 times daily with boiled water or 0.9% sodium chloride.
– Apply into both eyes **1% tetracycline eye ointment**: one application 2 times daily for 7 days
– Never use corticosteroid drops or ointment.

Viral conjunctivitis
– Clean eyes 4 times daily with boiled water or 0.9% sodium chloride.
– Apply local antibiotics if there is a (risk of) secondary bacterial infection (see above).

Allergic conjunctivitis
– Local treatment as for viral conjunctivitis.
– Antihistamines PO for one to 3 days (see Urticaria(see page 112), Chapter 4).

Note: in the event of a foreign body, check tetanus immunisation status.

Neonatal conjunctivitis

- Clinical features(see page 117)
- Treatment(see page 117)
- Prevention(see page 117)

– Conjunctivitis due to *Neisseria gonorrhoeae* and/or *Chlamydia trachomatis* in neonates born to mothers with genital gonococcal and/or chlamydial infections at the time of delivery.
– Neonatal conjunctivitis is a medical emergency. Without prompt treatment, risk of corneal lesions and visual impairment.

Clinical features

– Unilateral or bilateral purulent conjunctivitis in the first 28 days of life.

Treatment

– Clean eyes with isotonic sterile solution (0.9% sodium chloride or Ringer lactate) 4 times daily to remove secretions.
– Antibiotherapy:
• for all neonates with conjunctivitis in the first 28 days of life
• for all neonates born to mothers with a genital infection (purulent cervical discharge) at the time of delivery

	0 to 7 days	**8 to 28 days**
First line	**ceftriaxone** IM: 50 mg/kg single dose (max. 125 mg)	**ceftriaxone** IM: 50 mg/kg single dose (max. 125 mg) + **azithromycin** PO: 20 mg/kg once daily for 3 days
Alternatives	If ceftriaxone contra-indicated: **cefotaxime** IM: 100 mg/kg single dose	If azithromycin unavailable: **erythromycin** PO: 12.5 mg/kg 4 times daily for 14 days

If symptoms persist 48 hours after parenteral treatment alone, administer **azithromycin** PO (or **erythromycin** PO as above).

Notes:
– When systemic treatment is not immediately available, clean both eyes and apply **1% tetracycline eye ointment** every hour, until systemic treatment is available.
– In all cases, treat the genital infection of the mother and partner (see Genital infections(see page 229), Chapter 9).

Prevention

Apply as soon as possible and preferably within one hour after birth:
1% tetracycline eye ointment: application of 1 cm in each eye.

Viral epidemic keratoconjunctivitis

Corneal and conjunctival lesions

– Treat as viral conjunctivitis. If possible, refer to an ophthalmologist.

– Protect the eye with a compress as long as photophobia lasts. Remove as soon as possible.

– If necessary, administer a preventive dose of vitamin A(see page 115).

Trachoma

- Clinical features(see page 118)
- Treatment(see page 118)
- Prevention(see page 119)

Trachoma is a highly contagious keratoconjunctivitis due to *Chlamydia trachomatis*. The disease is endemic in the poorest rural areas of Africa, Asia, Central and South America and the Middle East.

Infection is usually first contracted early in childhood by direct or indirect contact (dirty hands, contaminated towels, flies). In the absence of hygiene and effective treatment, the inflammation intensifies with successive infections, causing scars and deformities on the upper tarsal conjunctiva. The resulting ingrowing eyelashes (trichiasis) cause corneal lesions followed by permanent blindness, usually in adulthood.

The WHO classifies trachoma into 5 stages. Early diagnosis and treatment of first stages is essential to avoid the development of trichiasis and associated complications.

Clinical features

Several stages can occur simultaneously:

– Stage I: trachomatous inflammation - follicular (TF)
Presence of five or more follicles in the upper tarsal conjunctiva. Follicles are whitish, grey or yellow elevations, paler than the surrounding conjunctiva.

– Stage II: trachomatous inflammation - intense (TI)
The upper tarsal conjunctiva is red, rough and thickened. The blood vessels, normally visible, are masked by a diffuse inflammatory infiltration or follicles.

– Stage III: trachomatous scarring (TS)
Follicles disappear, leaving scars: scars are white lines, bands or patches in the tarsal conjunctiva.

– Stage IV: trachomatous trichiasis (TT)
Due to multiple scars, the margin of the eyelid turns inwards (entropion); the eyelashes rub the cornea and cause ulcerations and chronic inflammation.

– Stage V: corneal opacity (CO)
Cornea gradually loses its transparency, leading to visual impairment and blindness.

Treatment

– Stages I and II:
• Clean eyes and face several times per day.
• Antibiotic therapy:
The treatment of choice is **azithromycin** PO:
Children over 6 months or over 6 kg: 20 mg/kg single dose
Adults: 1 g single dose
Failing the above, **1% tetracycline eye ointment**: one application 2 times daily for 6 weeks
In children under 6 months or 6 kg: **erythromycin** PO (20 mg/kg 2 times daily for 14 days)

– Stage III: no treatment

– Stage IV: surgical treatment
While waiting for surgery, if regular patient follow-up is possible, taping eyelashes to the eyelid is a palliative measure that can help protect the cornea. In certain cases, this may lead to permanent

correction of the trichiasis within a few months.
The method consists in sticking the ingrowing eyelashes to the external eyelid with thin strip of sticking-plaster, making sure that the eyelid can open and close perfectly. Replace the plaster when it starts to peel off (usually once a week); continue treatment for 3 months.
Note: epilation of ingrowing eyelashes is not recommended since it offers only temporary relief and regrowing eyelashes are more abrasive to the cornea.

– Stage V: no treatment

Prevention

Cleaning of the eyes, face and hands with clean water reduces direct transmission and the development of secondary bacterial infections.

Periorbital and orbital cellulitis

- Clinical features(see page 119)
- Treatment(see page 119)

– Periorbital cellulitis is a common, usually benign, bacterial infection of the eyelids. It arises principally following trauma to the eyelids (insect bite or abrasion).
– Orbital cellulitis is a serious infection involving the contents of the orbit (fat and ocular muscles) that may lead to loss of vision or a brain abscess. It usually arises secondary to spread from sinusitis (e.g. as a complication of ethmoid sinusitis).
– Periorbital and orbital cellulitis are more common in children than in adults.
– The most common organisms causing periorbital and orbital cellulitis are *Staphylococcus aureus, Streptococcus pneumoniae* and other streptococci, as well as *Haemophilus influenzae type b* (Hib) in children living in countries where rates of immunisation with Hib remain low.

Clinical features

– Signs common to both periorbital and orbital cellulitis: acute eyelid erythema and oedema; the oedema has a violaceous hue if secondary to *H. influenzae*.

– In case of orbital cellulitis only:
• Pain with eye movements;
• Ophthalmoplegia (paralysis of eye movements) often with diplopia (double vision);
• Protrusion of the eye (eye bulges out of the socket);
• High fever, systemic signs.

Treatment

– Hospitalize for the following: orbital cellulitis, children younger than 3 months, critically ill appearing patient[1](see page 0) , local complications, debilitated patient (chronic conditions, the elderly), if there is a risk of non-compliance with or failure of outpatient treatment. Treat the other patients as outpatients.

– Outpatient antibiotic therapy[2](see page 0) :
cefalexin PO for 7 to 10 days
Neonates 0 to 7 days: 25 mg/kg 2 times daily
Neonates 8 days to 1 month: 25 mg/kg 3 times daily
Children over 1 month: 25 mg/kg 2 times daily (max. 2 g daily)
Children ≥ 40 kg and adults: 1 g 2 times daily

or
amoxicillin/clavulanic acid (**co-amoxiclav**) PO for 7 to 10 days
Use formulations in a ratio of 8:1 or 7:1 exclusively. The dose is expressed in amoxicillin:
Children < 40 kg: 50 mg/kg 2 times daily
Children ≥ 40 kg and adults:
Ratio 8:1: 3000 mg daily (2 tab of 500/62.5 mg 3 times daily)
Ratio 7:1: 2625 mg daily (1 tab of 875/125 mg 3 times daily)

– Inpatient antibiotic therapy[3] :
ceftriaxone slow IV[4] (3 minutes) or IV infusion (30 minutes; 60 minutes in neonates) for at least 5 days
Children: one dose of 100 mg/kg on the first day, then 50 mg/kg 2 times daily
Adults: 1 to 2 g once daily
+
cloxacillin IV infusion (60 minutes)[5]
Neonates 0 to 7 days (< 2 kg): 50 mg/kg every 12 hours
Neonates 0 to 7 days (≥ 2 kg): 50 mg/kg every 8 hours
Neonates 8 days to < 1 month (< 2 kg): 50 mg/kg every 8 hours
Neonates 8 days to < 1 month (≥ 2 kg): 50 mg/kg every 6 hours
Children 1 month and over: 25 to 50 mg/kg every 6 hours (max. 8 g daily)
Children ≥ 40 kg and adults: 2 g every 6 hours
If there is clinical improvement (patient afebrile and erythema and oedema have improved) after 5 days, change to amoxicillin/clavulanic acid PO at the doses indicated above to complete 7 to 10 days of treatment.

If there is no improvement in the first 48 hours (suspicion of methicillin resistant *S. aureus*), replace cloxacillin with:
clindamycin IV infusion (30 minutes)[6]
Neonates 0 to 7 days (< 2 kg): 5 mg/kg every 12 hours
Neonates 0 to 7 days (≥ 2 kg): 5 mg/kg every 8 hours
Neonates 8 days to < 1 month (< 2 kg): 5 mg/kg every 8 hours
Neonates 8 days to < 1 month (≥ 2 kg): 10 mg/kg every 8 hours
Children 1 month and over: 10 mg/kg every 8 hours (max. 1800 mg daily)
Adults: 600 mg every 8 hours
After 5 days, change to clindamycin PO at the same doses to complete 7 to 10 days of treatment.

– If orbital cellulitis is unresponsive to IV antibiotics, consider an abscess. Transfer patient to a surgical centre for drainage.

[1] Critically ill appearing child: weak grunting or crying, drowsy and difficult to arrouse, does not smile, disconjugate or anxious gaze, pallor or cyanosis, general hypotonia.
[2] For penicillin-allergic patients, **clindamycin** PO for 7 to 10 days:
Children: 10 mg/kg 3 times daily; adults: 600 mg 3 times daily
[3] For penicillin-allergic patients, **clindamycin** IV infusion (doses as above).
[4] For administration by IV route, ceftriaxone powder should to be reconstituted in water for injection only. For administration by IV infusion, dilute each dose of ceftriaxone in 5 ml/kg of 0.9% sodium chloride or 5% glucose in children less than 20 kg and in a bag of 100 ml of 0.9% sodium chloride or 5% glucose in children over 20 kg and in adults.
[5] Cloxacillin powder for injection should be reconstituted in 4 ml of water for injection. Then dilute each dose of cloxacillin in 5 ml/kg of 0.9% sodium chloride or 5 % glucose in children less than 20 kg and in a bag of 100 ml of 0.9% sodium chloride or 5% glucose in children over 20 kg and in adults.

6(see page 0) Dilute each dose of clindamycin in 5 ml/kg of 0.9% sodium chloride or 5% glucose in children less than 20 kg and in a bag of 100 ml of 0.9% sodium chloride or 5% glucose in children over 20 kg and in adults.

Other pathologies

- Onchocerciasis(see page 121)
- Loiasis(see page 121)
- Pterygium(see page 122)
- Cataract(see page 122)

Onchocerciasis

River blindness

Ocular lesions result from the invasion of the eye by microfilariae. They generally develop in adults and progress to blindness in the absence of early treatment.

Clinical features and treatment

Ocular lesions are always associated with onchocercal skin lesions (see Onchocerciasis(see page 151), Chapter 6).

– Pruritus, hemeralopia (crepuscular blindness), decrease in visual acuity, narrowing of the visual field, awareness of microfilariae in the visual field (the patient sees “little wiggling worms before his eyes”).

– Lesions of the cornea (punctuate, then sclerosing, keratitis), iris (iridocyclitis) or posterior segment (chorioretinopathy and optic atrophy); microfilariae within the anterior chamber or vitreous humor (slit lamp).

For treatment, see Onchocerciasis(see page 151), Chapter 6. Ivermectin treatment may improve anterior segment lesions (sclerosing keratitis, iridocyclitis) and visual acuity. Severe lesions (chorioretinal lesions, optic atrophy) continue to progress despite treatment.

Loiasis

Clinical features and treatment

Migration of an adult worm under the palpebral or bulbar conjunctiva (white, filiform worm, measuring 4 to 7 cm in length, mobile) and ocular pruritus, lacrimation, photophobia or eyelid oedema.

For treatment, see Loiais(see page 153), Chapter 6. The migration of the worm is often of very brief duration. Do not attempt to extract it, or administer anaesthetic drops; simply reassure the patient, the event is harmless. Surgical removal is likewise futile if the worm is dead/calcified.

Pterygium

A whitish, triangular growth of fibrovascular tissue extending slowly from the conjunctiva to the cornea. It occurs most frequently in patients who are exposed to wind, dust, or arid climates and never disappears spontaneously.

Clinical features and treatment

Two stages:

– Benign pterygium develops slowly, does not reach the pupil: no treatment.

– Progressive vascularized pterygium: red and inflamed growth covers the pupil and may impair vision:
• Clean eye with sterile water or 0.9% sodium chloride.
• Surgical removal if facilities are available.

Cataract

Opacity of the lens that causes a progressive loss of visual acuity. Cataract is common in the tropics and can occur at a younger age than in Europe. The presence of cataract in both eyes leads to blindness. Surgery is the only treatment.

Chapter 6: Parasitic diseases

- Malaria(see page 123)
- Human African trypanosomiasis (sleeping sickness)(see page 130)
- American trypanosomiasis (Chagas disease)(see page 133)
- Leishmaniases(see page 136)
- Intestinal protozoan infections (parasitic diarrhoea)(see page 139)
- Flukes(see page 140)
- Schistosomiases(see page 142)
- Cestodes(see page 144)
- Nematode infections(see page 147)
- Filariasis(see page 151)
    - Onchocerciasis (river blindness)(see page 151)
    - Loiasis.(see page 153)
    - Lymphatic filariasis (LF)(see page 155)

Malaria

- Clinical features(see page 124)
    - Uncomplicated malaria(see page 124)
    - Severe malaria(see page 124)
- Laboratory(see page 124)
    - Parasitological diagnosis2(see page 124)
    - Additional examinations(see page 124)
- Treatment of malaria due to P. vivax, P. ovale, P. malariae, P. knowlesi(see page 125)
- Treatment of uncomplicated falciparum malaria(see page 125)
    - Antimalarial treatment(see page 125)
    - Symptomatic treatment(see page 127)
- Treatment of severe malaria(see page 127)
    - Antimalarial treatment(see page 127)
    - Symptomatic treatment and management of complications(see page 128)
- Antimalarial treatment in pregnant women(see page 129)
    - Uncomplicated P. vivax, P. ovale, P. malariae, P. knowlesi malaria(see page 129)
    - Uncomplicated falciparum malaria(see page 129)
    - Severe malaria(see page 129)
- Prevention(see page 129)
- References(see page 130)

– Malaria is a parasitic infection due to protozoa of the genus *Plasmodium*, transmitted to humans by the bite of *Anopheles* mosquitoes. Transmission by transfusion of parasite infected blood and transplacental transmission are also possible.
– 5 species of *Plasmodium* cause malaria in humans: *P. falciparum, P. vivax, P. ovale, P. malariae* and *P. knowlesi*. All species may cause uncomplicated malaria. Severe malaria (defined by the presence of complications) is almost always due to *P. falciparum*, and, less frequently, *P. vivax* and *P. knowlesi*.
– Uncomplicated malaria can rapidly progress to severe malaria, and severe malaria may cause death within a few hours if left untreated.

Clinical features

Malaria should always be considered in patients living in or coming from, an endemic area, who presents with fever (or history of fever in the previous 48 hours).

Uncomplicated malaria

Fever is frequently associated with chills, sweating, headache, muscular ache, malaise, anorexia or nausea. In children, fever may be associated with abdominal pain, diarrhoea and vomiting. Mild to moderate anaemia is frequent in children and pregnant women.

Severe malaria

In addition to the above, patients presenting with one or more of the following complications[1](see page 130) should be hospitalised immediately:
– Impaired consciousness, including coma.
– Seizures: more than 2 episodes of generalised or focal (e.g. abnormal eye movements) seizures within 24 hours.
– Prostration: extreme weakness; in children: inability to sit or drink/suck.
– Respiratory distress: rapid, laboured breathing or slow, deep breathing.
– Shock: cold extremities, weak or absent pulse, capillary refill time ≥ 3 seconds, cyanosis.
– Jaundice: yellow discolouration of mucosal surfaces of the mouth, conjunctivae and palms.
– Haemoglobinuria: dark red urine.
– Abnormal bleeding: skin (petechiae), conjunctivae, nose, gums; blood in stools.
– Acute renal failure: oliguria (urine output < 12 ml/kg/day in children and < 400 ml/day in adults) despite adequate hydration.

Laboratory

Parasitological diagnosis[2]

Diagnosis of malaria should be confirmed, whenever possible. If testing is not available, treatment of suspected malaria should not be delayed.

Rapid diagnostic tests (RDTs)[1](see page 0)

Rapid tests detect parasite antigens. They give only a qualitative result (positive or negative) and may remain positive several days or weeks following elimination of parasites.

Microscopy

Thin and thick blood films enable parasite detection, species identification, quantification and monitoring of parasitaemia.
Blood films may be negative due to sequestration of the parasitized erythrocytes in peripheral capillaries in severe malaria, as well as in placental vessels in pregnant women.

Note: even with positive diagnostic results, rule out other causes of fever.

Additional examinations

Haemoglobin (Hb) level

To be measured routinely in all patients with clinical anaemia, and in all patients with severe malaria.

Blood glucose level

To be measured routinely to detect hypoglycaemia in patients with severe malaria and those with malnutrition (see Hypoglycaemia(see page 20), Chapter 1).

Treatment of malaria due to *P. vivax, P. ovale, P. malariae, P. knowlesi*

chloroquine (**CQ**) PO [2](see page 0)
Children and adults:
Day 1: 10 mg base/kg
Day 2: 10 mg base/kg
Day 3: 5 mg base/kg

In general *P. vivax* remains sensitive to CQ but resistance is found in several countries. Where such resistance is high (>10%), or in countries which have de-registered CQ due to *P. falciparum* resistance, an artemisinin-based combination therapy (ACT) [3](see page 0) should be used instead.[1](see page 130) For dosing information, see Treatment of uncomplicated falciparum malaria(see page 125).

Relapses can occur with *P. vivax* and *P. ovale* due to activation of dormant parasites in the liver. **Primaquine** PO for 14 days (0.25 to 0.5 mg/kg once daily in children ≥ 15 kg; 15 mg once daily in adults) can be given to eliminate these parasites, after the initial treatment with CQ or an ACT. However, this treatment is only recommended for patients living in areas where reinfection is unlikely, i.e. non-endemic, low transmission areas or in countries aiming for elimination of malaria. This treatment is contra-indicated in individuals with G6PD deficiency. If G6PD deficiency cannot be tested individually, the decision to prescribe primaquine must take into account the prevalence of deficiency in the population.

Treatment of uncomplicated falciparum malaria

Antimalarial treatment

During pregnancy, see Antimalarial treatment in pregnant women(see page 129).

Treatment is an artemisinin-based combination therapy (ACT) [3](see page 0) given by the oral route for 3 days.[1](see page 130) The first-line ACT is chosen according to therapeutic efficacy in the area where the patient is living. If the first line ACT is unavailable, contra-indicated or has failed despite being correctly administered, use another ACT. For dosing information, see table below.

Treatment of uncomplicated falciparum malaria [2](see page 0)

ACT	Presentation	Dosage
artemether/lumefantrine (AL)	**Coformulated tablets** of 20 mg artemether/120 mg lumefantrine	On D1, the first dose is given at 0 hour and the 2nd dose at 8-12 hours. Subsequent doses on D2 and D3 are given 2 times daily (morning and evening).
	Blister child 5 to < 15 kg, 6 tab/blister	==> 1 tab 2 times daily on D1, D2, D3
	Blister child 15 to < 25 kg, 12 tab/blister	==> 2 tab 2 times daily on D1, D2, D3
	Blister child 25 to < 35 kg, 18 tab/blister	==> 3 tab 2 times daily on D1, D2, D3
	Blister child ≥ 35 kg and adult, 24 tab/blister	==> 4 tab 2 times daily on D1, D2, D3
	Coformulated tablets of 80 mg artemether/ 480 mg lumefantrine	
	Blister child ≥ 35 kg and adult, 6 tab/blister	==> 1 tab 2 times daily on D1, D2, D3
artesunate/amodiaquine (AS/AQ)	**Coformulated tablets**	
	Blister child 4.5 to < 9 kg, tab of AS 25 mg/AQ base 67.5 mg, 3 tab/blister	==> 1 tab once daily on D1, D2, D3
	Blister child 9 to < 18 kg, tab of AS 50 mg/AQ base 135 mg, 3 tab/blister	==> 1 tab once daily on D1, D2, D3
	Blister child 18 to < 36 kg, tab of AS 100 mg/AQ base 270 mg, 3 tab/blister	==> 1 tab once daily on D1, D2, D3
	Blister child ≥ 36 kg and adult, tab of AS 100 mg/AQ base 270 mg, 6 tab/blister	==> 2 tab once daily on D1, D2, D3
dihydroartemisinin/piperaquine (DHA/PPQ)	**Coformulated tablets**	
	Blister child, tab of DHA 20 mg/PPQ 160 mg, 3 tab/blister	5 to < 8 kg: 1 tab 20/160 mg once daily on D1, D2, D3
	Blister child, tab of DHA 40 mg/PPQ 320 mg, 3 tab/blister	8 to < 11 kg: 1½ tab 20/160 mg once daily on D1, D2, D3 11 to < 17 kg: 1 tab 40/320 mg once daily on D1, D2, D3
	Blister child, tab of DHA 40 mg/PPQ 320 mg, 6 tab/blister	17 to < 25 kg: 1½ tab 40/320 mg once daily on D1, D2, D3 25 to < 36 kg: 2 tab 40/320 mg once daily on D1, D2, D3
	Blister adolescent-adult, tab of DHA 40 mg/PPQ 320 mg, 9 tab/blister	36 to < 60 kg: 3 tab 40/320 mg once daily on D1, D2, D3
	Blister adolescent-adult, tab of DHA 40 mg/PPQ 320 mg, 12 tab/blister	60 to < 80 kg: 4 tab 40/320 mg once daily on D1, D2, D3 ≥ 80 kg: 5 tab 40/320 mg once daily on D1, D2, D3

In low malaria endemic areas, in addition to ACT, all individuals (except in children < 30 kg, pregnant women or breastfeeding women of infants aged < 6 months) diagnosed with *P. falciparum* malaria, should be given a single dose of 0.25 mg/kg **primaquine** to reduce the risk of transmission.[3](see page 130)

Notes:
– In infants below the age/weight mentioned in the table above, there is little data on efficacy and safety of ACTs.
– The combinations AL, AS/AQ and DHA/PPQ can be used. The dose should be calculated so as to correspond to 10-16 mg/kg/dose of lumefantrine; 10 mg/kg daily of amodiaquine; 20 mg/kg daily of piperaquine.
– Clinical condition of young children can deteriorate rapidly; it may be preferable to start parenteral treatment straight away (see below).

Quinine PO is not recommended as standard treatment, however still remains in some national protocols:

quinine PO for 7 days [2](see page 0)
Children and adults under 50 kg: 10 mg/kg 3 times daily
Adults 50 kg and over: 600 mg 3 times daily

Symptomatic treatment

Paracetamol PO in the event of high fever only (Fever(see page 21), Chapter 1).

Treatment of severe malaria

The patient must be hospitalised.

Antimalarial treatment

During pregnancy, see Antimalarial treatment in pregnant women(see page 129).

Pre-referral treatment

If the patient needs to be transferred, administer before transfer:
– At community level, for children under 6 years: one dose of rectal **artesunate**(see page 0) (10 mg/kg)
• Children 2 months to < 3 years (≤ 10 kg): 1 rectal capsule (100 mg)
• Children 3 to < 6 years (≤ 20 kg): 2 rectal capsules (200 mg)
or
– At dispensary level, for children and adults: the first dose of artesunate or, if unavailable, the first dose of artemether. For dosing information, see below.

In either case, provide patients, especially children, with some sugar prior to or during transfer.

Inpatient treatment

The drug of choice is artesunate, preferably IV, or if not possible IM.
For patients in shock: IM route is not appropriate, use artesunate IV only.

artesunate slow IV injection (3 to 5 minutes) or, if not possible, slow IM injection, into the anterior thigh:
Children under 20 kg: 3 mg/kg/dose
Children 20 kg and over and adults: 2.4 mg/kg/dose
– One dose on admission (H0)
– One dose 12 hours after admission (H12)
– One dose 24 hours after admission (H24)
– Then one dose once daily
Treat parenterally for at least 24 hours (3 doses), then, if the patient can tolerate the oral route, change to a complete 3-day course of an ACT. If not, continue parenteral treatment once daily until the patient can change to oral route (without exceeding 7 days of parenteral treatment).

If artesunate is not unavailable, artemether may be an alternative:
artemether IM into the anterior thigh (never administer by IV route)
Children and adults: 3.2 mg/kg on admission (D1) then 1.6 mg/kg once daily
Treat parenterally for at least 24 hours (2 doses), then, if the patient can tolerate the oral route, change to a complete 3-day course of an ACT. If not, continue parenteral treatment once daily until the patient can change to oral route (without exceeding 7 days of parenteral treatment).

Note: if patient is still on parenteral treatment on Day 5, continue on the same treatment until Day 7. In this case it is not necessary to start an ACT.

Quinine IV is still recommended in some national protocols. It may be used in treatment of malaria with shock if artesunate IV is not available. The dose is expressed in quinine salt:
– Loading dose: 20 mg/kg to be administered over 4 hours, then, keep the vein open with an infusion of 5% glucose over 4 hours; then
– Maintenance dose: 8 hours after the start of the loading dose, 10 mg/kg every 8 hours (alternate quinine over 4 hours and 5% glucose over 4 hours).
For adults, administer each dose of quinine in 250 ml of glucose. For children under 20 kg, administer

each dose of quinine in a volume of 10 ml/kg of glucose.
Do not administer a loading dose to patients who have received oral quinine, or mefloquine within the previous 24 hours: start with maintenance dose.
Treat parenterally for at least 24 hours, then, if the patient can tolerate the oral route, change to a complete 3-day course of an ACT (or if not available, oral quinine to complete 7 days of quinine treatment). If not, continue parenteral treatment until the patient can change to oral route (without exceeding 7 days of parenteral treatment).

Symptomatic treatment and management of complications

Hydration

Maintain adequate hydration. As a guide, for volume to be administered per 24 hours by oral or IV route, see Appendix 1a(see page 307).
Adjust the volume according to clinical condition in order to avoid dehydration or fluid overload (risk of pulmonary oedema).

Fever

Paracetamol in the event of high fever only (Fever(see page 21), Chapter 1).

Severe anaemia

For treatment, see Anaemia(see page 30), Chapter 1.

Hypoglycaemia

For treatment, see Hypoglycaemia(see page 20), Chapter 1.

Notes:
– In an unconscious or prostrated patient, in case of emergency or when venous access is unavailable or awaited, use granulated sugar by the sublingual route to correct hypoglycaemia.[5](see page 0)
– The risk of hypoglycaemia is higher in patients receiving IV quinine.

Coma

Check/ensure the airway is clear, measure blood glucose level and assess level of consciousness.
In the event of hypoglycaemia or if blood glucose level cannot be measured, administer glucose.
If the patient does not respond to administration of glucose, or if hypoglycaemia is not detected:
– Insert a urinary catheter; place the patient in the recovery position.
– Monitor vital signs, blood glucose level, level of consciousness, fluid balance (urine output and fluid input) hourly until stable, then every 4 hours.
– Rule out meningitis (lumbar puncture) or proceed directly to administration of an antibiotic (see Meningitis(see page 157), Chapter 7).
– Reposition the patient every 2 hours; ensure eyes and mouth are kept clean and moist, etc.

Seizures

See Seizures(see page 16), Chapter 1. Address possible causes (e.g. hypoglycaemia; fever in children).

Respiratory distress

– Rapid laboured breathing:
Check for pulmonary oedema (crepitations on auscultation), which may occur with or without fluid overload: reduce IV infusion rate if the patient is receiving IV therapy, nurse semi-sitting, oxygen,

furosemide IV: 1 mg/kg in children, 40 mg in adults. Repeat after 1 to 2 hours if necessary.
Associated pneumonia should also be considered (see Acute pneumonia(see page 65), Chapter 2).

– Slow, deep breathing (suspected metabolic acidosis):
Look for dehydration (and correct if present), decompensated anaemia (and transfuse if present).

Oliguria and acute renal failure

Look first for dehydration (Dehydration(see page 34), Chapter 1), especially due to inadequate fluid intake or excessive fluid losses (high fever, vomiting, diarrhoea). Treat dehydration if present. Be aware of the risk of fluid overload and acute pulmonary oedema. Monitor for the return of urine output.

Acute renal failure (ARF) is found almost exclusively in adults and is more common in Asia than Africa. Insert a urinary catheter, measure output. Restrict fluids to 1 litre/day (30 ml/kg/day in children), plus additional volume equal to urine output. Renal dialysis is often necessary.

Antimalarial treatment in pregnant women

Uncomplicated *P. vivax, P. ovale, P. malariae, P. knowlesi* malaria

As other patients.
Primaquine should not be given in pregnancy.

Uncomplicated falciparum malaria

All ACT included in the table Treatment of uncomplicated falciparum malaria(see page 125) can be used in all trimesters.
If ACTs are not available, quinine PO (for dosing, see Treatment of uncomplicated falciparum malaria(see page 125)) combined with **clindamycin** PO if possible (10 mg/kg 2 times daily for 7 days) may be an alternative to ACT.
Primaquine should not be given in pregnancy.

Severe malaria

Artesunate, or if unavailable artemether, is recommended in all trimesters.
Quinine IV is not recommended as standard treatment, however it still remains in some national protocols.

Prevention

– For pregnant women in areas with high risk of infection with *P. falciparum*, refer to the guide Essential obstetric and newborn care, MSF.
– In areas with seasonal malaria transmission (in particular across the Sahel sub-region), seasonal malaria chemoprevention in children < 5 years reduces mortality: administer amodiaquine + SP at monthly intervals for 4 months during the transmission period.[4](see page 130)
– In malaria endemic areas and in epidemic-prone contexts, all in-patient facilities (including HIV treatment centres and feeding centres), should be furnished with long-lasting insecticidal nets (LLINs). For more information, refer to the guide Public health engineering, MSF.
– See specialised literature for information regarding anti-vector measures and prevention in travellers.

1 (see page 0) Most rapid tests detect the following antigens alone or in combination: HRP2 protein specific to *P. falciparum*; an enzyme (Pf pLDH) specific to *P. falciparum*; an enzyme (pan pLDH) common to all 4 plasmodium species. HRP2 may continue to be detectable for 6 weeks or more after parasite clearance; pLDH remains detectable for several days (up to 2 weeks) after parasite clearance.
Use pan pLDH tests as first choice in hyper and holo-endemic areas, as well as in areas of intense seasonal transmission and during outbreaks or complex emergencies. In other contexts, HRP2 tests (*P. falciparum* > 95%) or HRP2 + pLDH combination tests (*P. falciparum* < 95%) are preferred.

2 (see page 0) If the patient vomits within 30 minutes after administration: re-administer the full dose. If the patient vomits between 30 minutes and 1 hour after administration, re-administer half of the dose. If severe vomiting precludes oral therapy, manage as severe malaria, see Treatment of severe malaria (see page 127). [a (see page 0) b (see page 0) c (see page 0)]

3 (see page 0) ACT: a combination of artemisinin or one of its derivatives (e.g. artesunate, artemether) with another antimalarial of a different class. [a (see page 0) b (see page 0)]

4 (see page 0) If it is impossible to refer a patient to a center capable of providing parenteral treatment, rectal artesunate should be given according to the same schedule as artesunate slow IV injection (H0, H12, H24, then once daily).

5 (see page 0) Place a level teaspoon of sugar, moistened with a few drops of water, under the tongue, then place the patient in the recovery position. Repeat after 15 minutes if the patient has not regained consciousness. As with other methods for treating hypoglycaemia, maintain regular sugar intake, and monitor.

References

1. World Health Organization. Guidelines for the treatment of malaria, 3rd ed. World Health Organization. 2015. https://apps.who.int/iris/handle/10665/162441

2. World Health Organization. Compendium of WHO malaria guidance: prevention, diagnosis, treatment, surveillance and elimination. 2019. https://apps.who.int/iris/handle/10665/312082

3. World Health Organization. WHO policy brief on single-dose primaquine as gametocytocide in Plasmodium falciparum malaria. 2015. https://www.who.int/malaria/publications/atoz/who_htm_gmp_2015.1.pdf?ua=1

4. World Health Organization. WHO Policy Recommendation: Seasonal Malaria Chemoprevention (SMC) for P*lasmodium falciparum* malaria control in highly seasonal transmission areas of the Sahel sub-region in Africa. 2012. https://www.who.int/malaria/publications/atoz/smc_policy_recommendation_en_032012.pdf?ua=1

Human African trypanosomiasis (sleeping sickness)

- Clinical features (see page 131)
- Laboratory (see page 131)

- Treatment (except in pregnant women)(see page 132)
  - Haemolymphatic stage (Stage I)(see page 132)
  - Meningoencephalitic stage (Stage II)(see page 132)
- Treatment in pregnant women(see page 133)
- Prevention and control(see page 133)

Human African trypanosomiasis (HAT) is a zoonosis caused by protozoa (trypanosomes), transmitted to humans through the bite of a tsetse fly (*Glossina*). Transmission by contaminated blood transfusion and transplacental transmission are also possible.

The disease is found only in sub-Saharan Africa. There are two forms: *Trypanosoma brucei gambiense* HAT in western and central Africa and *Trypanosoma brucei rhodesiense* HAT in eastern and southern Africa.

Clinical features

Inoculation may be followed by an immediate local reaction (trypanosomal chancre). This chancre arises in about 50% of all rhodesiense but rarely in gambiense.

Gambiense HAT

– Incubation lasts from a few days to several years.
– The first stage (haemolymphatic stage) corresponds to the haematogenous and lymphatic dissemination of the parasite. Signs include intermittent fever, joint pain, lymphadenopathy (firm, mobile, painless lymph nodes, mainly cervical), hepatosplenomegaly and skin signs (facial oedema, pruritus).
– The second stage (meningoencephalitic stage) corresponds to the invasion of the central nervous system. Signs of the haemolymphatic stage recede or disappear and varying neurological signs progressively develop: sensory disturbances (deep hyperaesthesia), psychiatric disorders (apathy or agitation), disturbance of the sleep cycle (with daytime somnolence alternating with insomnia at night), impaired motor functions (paralysis, seizures, tics) and neuroendocrine disorders (amenorrhoea, impotence).
– In the absence of treatment: cachexia, lethargy, coma and death.

Rhodesiense HAT

The first stage is the same as above, but the incubation period is shorter (< 3 weeks), the disease evolves more rapidly and symptoms are more severe. Patients often die of myocarditis in 3 to 6 months without having developed signs of the meningo-encephalitic stage.

In practice, gambiense and rhodesiense HAT can be difficult to differentiate: e.g., there exist cases of acute gambiense infection and others of chronic rhodesiense infection.

Laboratory

– Diagnosis involves 3 steps for gambiense HAT (screening test, diagnostic confirmation and stage determination) and 2 steps for rhodesiense HAT (diagnostic confirmation and stage determination).

– The recommended screening test for *T.b. gambiense* infection is the CATT (Card Agglutination Test for Trypanosomiasis). It detects the presence of specific antibodies in the patient's blood or serum.

– Diagnostic confirmation: presence of trypanosomes in lymph node aspirates or in blood using concentration techniques: capillary tube centrifugation technique (Woo test), quantitative buffy coat (QBC), mini-anion exchange centrifugation technique (mAEC).

– Stage determination: detection of trypanosomes (after centrifugation) and white cell count in the cerebrospinal fluid (lumbar puncture):

• Haemolymphatic stage: no trypanosomes AND ≤ 5 white cells/mm^3

• Meningoencephalitic stage: evidence of trypanosomes OR > 5 white cells/mm^3

Treatment (except in pregnant women)

– Due to the toxicity of trypanocides, detection of the parasite is essential before initiating treatment. In the absence of parasitological confirmation, treatment may nevertheless be justified in certain cases: very strong clinical suspicion, patients in life-threatening condition, strong serological suspicion (CATT 1:16 positive) in a population where the disease is highly prevalent (> 2%).
– Several treatment regimens exist. Check national recommendations and local resistance levels.
– Treatment must be administered under close medical supervision. Patients receiving pentamidine can be treated as outpatients but those receiving suramin, eflornithine (with or without nifurtimox) or melarsoprol should be hospitalised.
– After treatment, patients should be checked every 6 months (clinical examination, lumbar puncture and examination for trypanosomes) over 24 months, to look for relapse.

Haemolymphatic stage (Stage I)

Gambiense HAT

pentamidine isetionate deep IM
Children and adults: 4 mg/kg once daily for 7 to 10 days
Patients should receive a source of glucose (meal, sweet tea) one hour before injection (risk of hypoglycaemia); they should remain supine during administration and one hour after injection (risk of hypotension).

Rhodesiense HAT

suramin slow IV
Children and adults:
D1: test dose of 4 to 5 mg/kg
D3, D10, D17, D24, D31: 20 mg/kg (max. 1 g per injection)
Suramin may cause anaphylactic reactions, a test dose is recommended prior to starting treatment. In the event of an anaphylactic reaction after the test dose, the patients must not be given suramin again.

Meningoencephalitic stage (Stage II)

Before administrating trypanocides, the priority is to improve the patient's general condition (rehydration, treatment of malaria, intestinal worms, malnutrition, bacterial infections). It is nonetheless recommended not to postpone the trypanocidal treatment for more than 10 days.

Gambiense HAT

– First choice: nifurtimox-eflornithine combination therapy (NECT)
nifurtimox PO
Children and adults: 5 mg/kg 3 times daily for 10 days
+ **eflornithine** IV infusion over 2 hours
Children and adults: 200 mg/kg every 12 hours for 7 days

The catheter must be handled with great attention to avoid local or general bacterial infections: thoroughly disinfect the insertion site, ensure secure catheter fixation, protect the insertion site with a sterile dressing, systematically change the catheter every 48 hours or earlier in case of signs of phlebitis.

– Second choice:
eflornithine IV infusion over 2 hours
Children under 12 years: 150 mg/kg every 6 hours for 14 days
Children 12 years and over and adults: 100 mg/kg every 6 hours for 14 days

– In the event of a relapse after NECT or eflornithine:
melarsoprol slow IV
Children and adults: 2.2 mg/kg once daily for 10 days
Melarsoprol is highly toxic: reactive encephalopathy (coma, or recurrent or prolonged seizures) in 5 to 10% of treated patients, fatal in around 50% of cases; peripheral neuropathy, invasive diarrhoea, severe skin rash, phlebitis, etc.
Prednisolone PO (1 mg/kg once daily) is frequently combined throughout the duration of treatment.

Rhodesiense HAT

melarsoprol slow IV
Children and adults: 2.2 mg/kg once daily for 10 days
Prednisolone PO (1 mg/kg once daily) is frequently combined throughout the duration of treatment.

Treatment in pregnant women

All trypanocides are potentially toxic for the mother and the foetus (risk of miscarriage, malformation, etc.). However, due to the life-threatening risk for the mother and the risk of mother-to-child transmission, treatment must be initiated as follows:

Haemolymphatic stage:
pentamidine for gambiense HAT as of the second trimester and suramin for rhodesiense HAT.

Meningoencephalitic stage:
Treatment depends on the mother's condition:
– If in immediately life-threatening condition: treatment with NECT or eflornithine cannot be deferred until after delivery.
– If not immediately life-threatening condition: pentamidine for gambiense HAT and suramin for rhodesiense HAT. Treatment with NECT or eflornithine is to be administered after delivery.

Prevention and control

– Individual protection against tsetse fly bites: long sleeves and trousers, repellents, keeping away from risk areas (e.g. near rivers).
– Disease control: mass screening and treatment of patients (*T.b. gambiense*), trypanocide treatment of cattle (*T.b. rhodesiense*), vector control using tsetse fly traps or insecticides.

American trypanosomiasis (Chagas disease)

- Clinical features(see page 134)
- Diagnosis(see page 134)
- Treatment(see page 135)
- Prevention(see page 135)
- References(see page 136)

– Chagas disease is a zoonosis caused by the protozoa *Trypanosoma cruzi.* It is transmitted to humans by contact of triatomine bug faeces with a break in the skin (often caused by a bite from the triatomine

bug), or with mucous membranes. Transmission by contaminated blood transfusion, accidental exposure to blood, mother-to-child (during pregnancy or childbirth) or consumption of contaminated food and water is also possible.
– Chagas disease has two phases: an acute phase, which lasts approximately 4 to 6 weeks, and a chronic phase, which is lifelong if left untreated.
– The disease is primarily found on the American continent.[1](see page 0) It is significantly underdiagnosed.[1](see page 136)

Clinical features

Acute phase

– Most cases are asymptomatic.
– If transmitted through a break in the skin: a red swelling on the skin (chagoma) or unilateral painless purplish periorbital oedema (Romaña's sign) with local lymphadenopathy, headache and fever.
– Rarely: multiple lymphadenopathies, hepatosplenomegaly, myocarditis (chest pain, dyspnoea), meningoencephalitis (seizures, paralysis).

Chronic phase

– Many cases remain asymptomatic (indeterminate phase).
– Up to 30% of cases develop organ damage:[2](see page 136)
• cardiac lesions (conduction disorders, dilated cardiomyopathy): arrhythmia, dyspnoea, chest pain, heart failure;
• gastrointestinal lesions (dilation of the oesophagus or colon i.e. megaoesophagus, megacolon): difficulty swallowing, severe constipation.
Individuals with immunosuppression have a higher risk of developing organ damage than the general population.

Diagnosis

Laboratory[1]

– Acute phase:
• Identification of *Trypanosoma cruzi* by direct microscopy of fresh blood or blood concentrated by microhematocrit method.
• In case of strong clinical suspicion despite no definitive diagnosis from direct microscopy, perform serologic tests after a delay of approximately 1 month (see "Chronic phase").

– Chronic phase:
• Identification of anti-*Trypanosoma cruzi* antibodies by serologic tests, e.g. enzyme-linked immunosorbent assay (ELISA), hemagglutination inhibition assay (HAI), indirect immunofluorescence (IIF) or rapid diagnostic test (RDT).
• For a definitive diagnosis, two different serological tests should be performed simultaneously; in case of conflicting results, a third test is recommended.[2](see page 0)

Other investigations

– ECG may demonstrate conduction disorders.
– Chest or abdominal x-ray may demonstrate cardiomegaly, megaoesophagus or megacolon.

Treatment

Aetiologic treatment

– Acute or chronic Chagas disease can be treated with either benznidazole or nifurtimox. However, treatment is not recommended if patient has already developed cardiac or digestive complications.
– Close clinical monitoring should be provided due to the frequent occurrence of adverse effects. Where available, blood tests (complete blood count, liver and renal function tests) should be performed before, during and after treatment.
– Protocols vary according to the country, follow national recommendations.

For information:

	Age	Dose and duration
benznidazole PO[(a)]	2 to 12 years[3](see page 136)	5 to 8 mg/kg daily in 2 divided doses for 60 days
	> 12 years and adults[4](see page 136)	5 to 7 mg/kg daily in 2 divided doses for 60 days
nifurtimox PO[(b)] 3(see page 136)	≤ 10 years	15 to 20 mg/kg daily in 3 to 4 divided doses for 90 days
	11 to 16 years	12.5 to 15 mg/kg daily in 3 to 4 divided doses for 90 days
	≥ 17 years and adults	8 to 10 mg/kg daily in 3 to 4 divided doses for 90 days

[(a)] Benznidazole is contra-indicated in pregnancy, breastfeeding and in patient with severe hepatic/renal impairment.
[(b)] Nifurtimox is contra-indicated in pregnancy, breastfeeding, patients with severe hepatic/renal impairment or history of severe mental disorders or seizures. Adverse effects (gastrointestinal disturbances, agitation, sleeping disorders, seizure) are frequent and reversible and should not necessarily result in discontinuation of treatment. Avoid alcohol and fatty meals during treatment.

Symptomatic treatment

See Seizures(see page 16) (Chapter 1), Pain(see page 23) (Chapter 1) and Heart failure(see page 300) (Chapter 12).

Prevention

– Individual protection against bite from triatomine bugs: use of long-lasting insecticidal net.
– In healthcare settings: standard precautions to avoid contamination with soiled materials or potentially infected body fluids.
– Blood transfusions: advise patients with Chagas disease not to donate blood. In endemic areas, screen donor blood for *Trypanosoma cruzi* antibodies.

1(see page 0) For more information on geographical distribution of cases of *T. cruzi* infection: http://gamapserver.who.int/mapLibrary/Files/Maps/Global_chagas_2009.png
2(see page 0) If resources are limited, ELISA alone can be performed. If the result is positive, a second serologic test should then be performed to confirm the diagnosis before starting treatment.

References

1. Pan American Health Organization. Guidelines for diagnosis and treatment of Chagas disease. Washington, D.C. 2019. http://iris.paho.org/xmlui/bitstream/handle/123456789/49653/9789275120439_eng.pdf?sequence=6&isAllowed=y

2. Rassi A, Marin-Neto J. Seminar: Chagas disease. The Lancet, Volume 375, ISSUE 9723, P1388-1402, April 17, 2010.

3. Centers for Disease Control and Prevention. Parasites - American Trypanosomiasis. https://www.cdc.gov/parasites/chagas/ [Accessed 17 February 2020]

4. World Health Organization. WHO Model Prescribing Information: Drugs Used in Parasitic Diseases - Second Edition. Geneva. 1995. https://apps.who.int/iris/handle/10665/41765 [Accessed 6 May 2020]

Leishmaniases

- Clinical features(see page 136)
  - Cutaneous and mucocutaneous leishmaniasis(see page 136)
  - Visceral leishmaniasis(see page 137)
  - Post-kala azar dermal leishmaniasis(see page 137)
- Laboratory(see page 137)
  - Cutaneous and mucocutaneous leishmaniasis(see page 137)
  - Visceral leishmaniasis(see page 137)
- Treatment(see page 137)
  - Cutaneous and mucocutaneous leishmaniasis(see page 137)
  - Visceral leishmaniasis(see page 138)
  - Post-kala azar dermal leishmaniasis (PKDL)(see page 138)
- Prevention(see page 139)

The leishmaniases are a group of parasitic diseases caused by protozoa of the genus *Leishmania*, transmitted by the bite of a sandfly. Over 20 species cause disease in man.
– *Cutaneous* leishmaniasis is endemic in more than 70 countries in South and Central America, Middle East, Central Asia, and Africa.
– *Mucocutaneous* leishmaniasis occurs in Latin America and, more rarely, in Africa (Ethiopia, Sudan).
– *Visceral* leishmaniasis occurs in more than 60 countries in East and North Africa, South and Central Asia, Southern Europe, and South and Central America.

Clinical features

Cutaneous and mucocutaneous leishmaniasis

– Single or multiple lesions on the uncovered parts of the body: an erythematous papule begins at the sandfly bite, enlarges to a nodule and extends in surface and depth to form a scabbed ulcer. Ulcers are painless, unless there is secondary bacterial or fungal infection.
Usually, lesions heal spontaneously, leaving a scar, and result in lifelong protection from disease.

– Lesions may also spread to the mucosa (mouth, nose, conjunctiva) giving rise to the mucocutaneous form, which may cause severe disfigurement.

Visceral leishmaniasis

Visceral leishmaniasis (kala azar) is a systemic disease, resulting in pancytopenia, immunosuppression, and death if left untreated.

– Prolonged (> 2 weeks) irregular fever, splenomegaly, and weight loss are the main signs.
– Other signs include: anaemia, diarrhoea, epistaxis, lymphadenopathy, moderate hepatomegaly.
– Bacterial diarrhoea, pneumonia, and tuberculosis may develop due to immunosuppression.

Post-kala azar dermal leishmaniasis

Macular, nodular or papular skin rash of unknown aetiology, particularly on the face, and typically occurring after apparent cure of visceral leishmaniasis.

Laboratory

Cutaneous and mucocutaneous leishmaniasis

– Parasitological diagnosis: identification of Giemsa-stained parasites in smears of tissue biopsy from the edge of the ulcer.
– No useful serological tests.

Visceral leishmaniasis

– Parasitological diagnosis: identification of Giemsa-stained parasites in smears of splenic, bone marrow, or lymph node aspiration-biopsy. Splenic aspiration is the most sensitive technique but carries a theoretical risk of potentially fatal haemorrhage.
– Serological diagnosis: rK39 dipstick test and direct agglutination test (DAT) can be used for diagnosis of primary visceral leishmaniasis in clinically suspect cases. Diagnosis of relapse is only by parasitological confirmation.

Treatment

The various species of *Leishmania* respond differently to drugs. Follow national recommendations.
For information:

Cutaneous and mucocutaneous leishmaniasis

– Cutaneous lesions generally heal spontaneously in 3 to 6 months. Treatment is only indicated if lesions are persistent (> 6 months), disfiguring, ulcerating, or disseminated.

– Forms with a single lesion or few lesions: start with local treatment with a pentavalent antimonial: **sodium stibogluconate** or **meglumine antimoniate**, 1 to 2 ml infiltrated into the lesion if it is a nodule and into the edges and base around the crust if it is an ulcer.
It should be repeated every 3 to 7 days for 2 to 4 weeks. Once healing begins, the treatment can be stopped and healing will continue.

– IM treatment with a pentavalant antimonial (20 mg/kg daily for 10 to 20 days) is restricted to severe cases and must be administered under close medical supervision.

– Miltefosine PO (as for visceral leishmaniasis) for 28 days is effective in many forms of cutaneous leishmaniasis.

– Ulcers are often secondarily infected with streptococci and staphylococci: administer suitable antibiotics.

– Mucocutaneous forms: as for visceral leishmaniasis.

Visceral leishmaniasis

Visceral leishmaniasis in East Africa

– First-line treatment:
a **pentavalent antimonial** IM or slow IV: 20 mg/kg daily for 17 days
+ **paromomycin** IM: 15 mg (11 mg base)/kg daily for 17 days

– Second-line treatment for relapse and for specific vulnerable groups: severe disease, pregnant women, patients over 45 years:
liposomal amphotericin B IV infusion: 3 to 5 mg/kg once daily for 6 to 10 days up to a total dose of 30 mg/kg

– Treatment in HIV co-infected patients:
liposomal amphotericin B IV infusion: 3 to 5 mg/kg once daily for 6 to 10 days up to a total dose of 30 mg/kg
+ **miltefosine** PO for 28 days:
Children 2 to 11 years: 2.5 mg/kg once daily
Children ≥ 12 years and < 25 kg: 50 mg once daily
Children ≥ 12 years and adults 25 to 50 kg: 50 mg 2 times daily
Adults > 50 kg: 50 mg 3 times daily

Visceral leishmaniasis in South Asia

– First-line treatment:
liposomal amphotericin B IV infusion: 3 to 5 mg/kg once daily for 3 to 5 days up to a total dose of 15 mg/kg
or
liposomal amphotericin B IV infusion: 10 mg/kg single dose

– Second-line treatment for relapse:
liposomal amphotericin B IV infusion: 3 to 5 mg/kg once daily for 5 to 8 days up to a total dose of 25 mg/kg

For all patients with visceral leishmaniasis, hydration, nutritional support and treatment of intercurrent infections (malaria, dysentery, pneumonia, etc.) are essential.
Tuberculosis and/or HIV infection may also be present and should be suspected if relapse occurs more than once or in the event of treatment failure.

Post-kala azar dermal leishmaniasis (PKDL)

Only patients with severe or disfiguring disease or with lesions remaining for > 6 months, and young children with oral lesions that interfere with feeding, are treated.

PKDL in East Africa

a **pentavalent antimonial** IM or slow IV: 20 mg/kg daily for 17 to 60 days
+ **paromomycin** IM: 15 mg (11 mg base)/kg daily for 17 days
or
liposomal amphotericin B IV infusion: 2.5 mg/kg once daily for 20 days
or
miltefosine PO for 28 days (as for visceral leishmaniasis) may be beneficial in HIV co-infected patients

PKDL in South Asia

liposomal amphotericin B IV infusion: 5 mg/kg 2 times weekly up to a total dose of 30 mg/kg

Prevention

– Insecticide-treated mosquito nets.
– Vector control and elimination of animal reservoir hosts.

Intestinal protozoan infections (parasitic diarrhoea)

- Clinical features(see page 139)
- Laboratory(see page 139)
- Treatment(see page 139)

The most important intestinal protozoan infections are amoebiasis (*Entamoeba histolytica*), giardiasis (*Giardia lamblia*), cryptosporidiosis (*Cryptosporidium sp*), cyclosporiasis (*Cyclospora cayetanensis*) and isosporiasis (*Isospora belli*).

Intestinal protozoa are transmitted by the faecal-oral route (soiled hands, ingestion of food or water contaminated with faeces) and may cause both individual cases of diarrhoea and epidemic diarrhoea outbreaks.

Clinical features

– Amoebiasis gives rise to bloody diarrhoea (see Amoebiasis(see page 83), Chapter 3).

– Clinical presentation of giardiasis, cryptosporidiosis, cyclosporiasis and isosporiasis is very similar:
• Diarrhoea is usually mild and self-limiting, except in children and patients with advanced HIV disease (CD4 < 200). These patients are likely to develop severe, intermittent or chronic diarrhoea that may be complicated by malabsorption with significant wasting (or failure to gain weight in children) or severe dehydration.
• Stools are usually watery, but steatorrhoea (pale, bulky, fatty stools) may be found in the event of secondary fat malabsorption; stools may contain mucus.
• Diarrhoea is usually associated with non-specific gastrointestinal symptoms (abdominal distension and cramps, flatulence, nausea, anorexia), but patients have low-grade fever or no fever.

Laboratory

Definitive diagnosis relies on parasite identification in stool specimens (trophozoites and cysts for giardia; oocysts for cryptosporidium, cyclospora, isospora). Two to three samples, collected 2 to 3 days apart are necessary, as pathogens are shed intermittently.

Treatment

– Correct dehydration if present (for clinical features and management, see Dehydration(see page 34), Chapter 1).

– If the causal agent has been identified in the stool:

Giardiasis	**tinidazole** PO single dose Children: 50 mg/kg (max. 2 g) Adults: 2 g or **metronidazole** PO for 3 days Children: 30 mg/kg once daily Adults: 2 g once daily
Cryptosporidiosis	In immunocompetent patients, no aetiological treatment; spontaneous resolution in 1 to 2 weeks.
Cyclosporiasis	**co-trimoxazole** PO for 7 days Children: 25 mg SMX + 5 mg TMP/kg 2 times daily Adults: 800 mg SMX + 160 mg TMP 2 times daily In immunocompetent patients, symptoms usually resolve spontaneous in 1 to 3 weeks. Treatment is given in case of severe or prolonged symptoms.
Isoporiasis	**co-trimoxazole** PO for 7 to 10 days Adults: 800 mg SMX + 160 mg TMP 2 times daily In immunocompetent patients, symptoms usually resolve spontaneous in 2 to 3 weeks. Treatment is given in case of severe or prolonged symptoms.

– If reliable stool examination cannot be carried out: parasitic diarrhoeas cannot be differentiated on clinical grounds, nor is it possible to distinguish these from non- parasitic diarrhoeas. An empirical treatment (using tinidazole or metronidazole and co-trimoxazole as above, together or in succession) may be tried in the case of prolonged diarrhoea or steatorrhoea. In patients with HIV infection, see empirical treatment (HIV infections and AIDS(see page 206), Chapter 8).

– In patients with advanced HIV disease, cryptosporidiosis, cyclosporiasis and isosporiasis are opportunistic infections; the most effective intervention is the treatment of the underlying HIV infection with antiretrovirals. Patients remain at high risk for dehydration/death until immunity is restored.

Flukes

Infection/ Epidemiology	Clinical features/Diagnosis	Treatment
Lung flukes *Paragonimus* sp *Distribution*: South-East Asia, China, parts of Cameroon, Nigeria, Gabon, Congo, Colombia, Peru *Transmission*: eating raw freshwater crustaceans	The two most prominent symptoms are prolonged (> 2 weeks) productive cough and intermittent haemoptysis (rusty-brown sputum). In endemic areas, paragonimosis should be considered whenever pulmonary tuberculosis is suspected as the clinical and radiological features overlap. Paragonimosis is confirmed when eggs are detected in sputum (or possibly in stools).	**praziquantel** PO Children 4 years and over and adults: 25 mg/kg 3 times daily for 2 days

Hepatobiliary flukes *Fasciola hepatica* and *gigantica* *Distribution*: worldwide, in areas where sheep and cattle are raised *Transmission*: eating uncooked aquatic plants	*During migration phase*: asthenia, prolonged fever, myalgia, right upper quadrant pain, mild hepatomegaly; sometimes, allergic signs (e.g. pruritus). At this stage, the diagnosis is rarely considered and can only be confirmed through serology; parasitological examination of stools is always negative. *Once adult flukes are present in the biliary tract*: presentation resembles cholelithiasis: right upper quadrant pain, recurrent episodes of obstructive jaundice/ febrile cholangitis. The diagnosis is confirmed when parasite eggs are detected in stools (or flukes are seen in the biliary tract with sonography).	**triclabendazole** PO Children and adults: 10 mg/kg single dose May repeat in 24 hours in the event of severe infection
Opisthorchis felineus (Asia, Eastern Europe) *Opisthorchis viverrini* (Cambodia, Laos, Vietnam, Thailand) *Clonorchis sinensis* (China, Koera, Vietnam) *Transmission*: eating raw/ undercooked freshwater fish	Abdominal pain and diarrhoea. With heavy infection, hepatobiliary symptoms: hepatomegaly, right upper quadrant pain, jaundice or episodes of febrile cholangitis. The diagnosis is confirmed when parasite eggs are detected in stools.	**praziquantel** PO Children 4 years and over and adults: 25 mg/kg 3 times daily for 2 days
Intestinal flukes *Fasciolopsis buski* (India, Bangladesh, South-East Asia) *Heterophyes heterophyes* (South-East Asia, Nile delta) *Metagonimus yokogawai* (Siberia, China, Korea) *Transmission*: eating uncooked aquatic plants (*F. buski*), raw/ undercooked fish (other species)	Symptoms are limited to diarrhoea and epigastric or abdominal pain. With massive infection, *F. buski* can cause oedematous allergic reactions (including ascites, anasarca). The diagnosis is confirmed when parasite eggs are detected in stools.	**praziquantel** PO Children 4 years and over and adults: 25 mg/kg 3 times daily, 1 day

Schistosomiases

– Schistosomiases are acute or chronic visceral parasitic diseases due to 5 species of trematodes (schistosomes). The three main species infecting humans are *Schistosoma haematobium, Schistosoma mansoni* and *Schistosoma japonicum*. *Schistosoma mekongi* and *Schistosoma intercalatum* have a more limited distribution.
– Humans are infected while wading/bathing in fresh water infested with schistosome larvae. Symptoms occurring during the phases of parasite invasion (transient localized itching as larvae penetrate the skin) and migration (allergic manifestations and gastrointestinal symptoms during migration of schistosomules) are frequently overlooked. In general, schistosomiasis is suspected when symptoms of established infection become evident. Each species gives rise to a specific clinical form: genito-urinary schistosomiasis due to *S. haematobium*, intestinal schistosomiasis due *S. mansoni, S. japonicum, S. mekongi* and *S. intercalatum*.
– The severity of the disease depends on the parasite load. Heavily infected patients are prone to visceral lesions with potentially irreversible sequelae. Children aged 5 to 15 years are particularly at risk: prevalence and parasite load are highest in this age group.
– An antiparasitic treatment should be administered to reduce the risk of severe lesions, even if there is a likelihood of re-infection.

Clinical features

	Parasite/ Epidemiology 1(see page 0)	**Clinical features/Diagnosis (established infection)**

Genito-urinary schistosomiasis	***S. haematobium***
	Distribution: Africa, Madagascar and the Arabian peninsula
		• Urinary manifestations:
		  • In endemic areas, urinary schistosomiasis should be suspected in any patients who complain of macroscopic haematuria (red coloured urine throughout, or at the end of, micturition). Haematuria is frequently associated with polyuria/ dysuria (frequent and painful micturition).
		  • In patients, especially children and adolescents, with urinary symptoms, visual inspection of the urine (and dipstick test for microscopic haematuria if the urine appears grossly normal) is indispensible.
		  • Presumptive treatment is recommended in the presence of macro- or microscopic haematuria, when parasitological confirmation (parasite eggs detected in urine) cannot be obtained.
		• Genital manifestations:
		In women, symptoms of genital infection (white-yellow or bloody vaginal discharge, itching, lower abdominal pain, dyspareunia) or vaginal lesions resembling genital warts or ulcerative lesions on the cervix; in men, haematospermia (blood in the semen).
		• If left untreated: risk of recurrent urinary tract infections, fibrosis/calcification of the bladder and ureters, bladder cancer; increased susceptibility to sexually transmitted infections and risk of infertility.
		• In endemic areas, genito-urinary schistosomiasis may be a differential diagnosis to the genito-urinary tuberculosis, and in women, to the sexually transmitted infections (especially in women with an history of haematuria).

Intestinal schistosomiasis	***S. mansoni*** *Distribution*: tropical Africa, Madagascar, the Arabian peninsula, South America (especially Brazil) ***S. japonicum*** *Distribution*: China, Indonesia, the Philippines ***S. mekongi*** *Distribution*: parts of Lao PDR, Cambodia (along the Mekong River) ***S. intercalatum*** *Distribution*: parts of DRC, Congo, Gabon, Cameroon, Chad	• Non-specific digestive symptoms (abdominal pain; diarrhoea, intermittent or chronic, with or without blood) and hepatomegaly. • For *S. intercalatum*: digestive symptoms only (rectal pain, tenesmus, rectal prolapse, bloody diarrhoea). • If left untreated: risk of hepatic fibrosis, portal hypertension, cirrhosis, gastrointestinal haemorrhage (hematemesis, melena, etc.), except with *S. intercalatum* (less pathogenic than other intestinal schistosomes, no severe hepatic lesions). • The diagnosis is confirmed when parasite eggs are detected in stools. • In the absence of reliable parasitological diagnosis: in areas where intestinal schistosomiasis is common, diarrhoea (especially bloody diarrhoea) with abdominal pain and/or hepatomegaly may be a basis for presumptive diagnosis and treatment.

Treatment

praziquantel PO[1](see page 144),[2](see page 144)

Children 4 years and over and adults[2](see page 0) :

• *S. haematobium, S. mansoni, S. intercalatum*: 40 mg/kg single dose or 2 doses of 20 mg/kg administered 4 hours apart

• *S. japonicum, S. mekongi*: 2 doses of 30 mg/kg or 3 doses of 20 mg/kg administered 4 hours apart

[1](see page 0) For more information on geographic distribution of schistosomiasis: https://www.who.int/schistosomiasis/Schistosomiasis_2012-01.png?ua=1

[2](see page 0) For the treatment of schistosomiasis, praziquantel may me administered to pregnant women.

References

1. Treatment Guidelines from The Medical Letter. Vol. 11 (Suppl). Drugs for Parasitic Infections. 2013. https://www.uab.edu/medicine/gorgas/images/docs/syllabus/2015/03_Parasites/RxParasitesMedicalLetter2013.pdf [Accessed 25 May 2020]

2. Centers for Disease Control and Prevention (CDC). Schistosomiasis. Resources for Health Professionals. 2018. https://www.cdc.gov/parasites/schistosomiasis/health_professionals/index.html#tx [Accessed 25 May 2020]

Cestodes

- Cestodes (adult forms)(see page 145)
- Cestodes (larvae)(see page 146)

Cestodes (adult forms)

Parasites	Clinical features/ Laboratory	Treatment	Transmission/ Prevention
Taeniasis *Taenia saginata* *Taenia solium* (worldwide)	Often asymptomatic Segments expelled in the stools, sometimes gastrointestinal disturbances (epigastric or abdominal pain, nausea, diarrhoea) Laboratory: eggs in stools or collected from perianal skin (scotch tape method), segments in stools	**praziquantel** PO (see page 0) Children 4 years and over and adults: 5 to 10 mg/kg single dose	**Transmission** by eating raw or under-cooked meat: • beef for *T. saginata* • pork for *T. solium* **Prevention**: • individual: cook meat thoroughly • collective: slaughterhouse monitoring
Diphyllobothriasis *Diphyllobothrium latum* (temperate or cold lake areas)	Often asymptomatic In the event of heavy infection: mild gastrointestinal disturbances, anaemia due to vitamin B_{12} deficiency associated with (rare) neurological sequelae Laboratory: eggs in stools	**praziquantel** PO (see page 0) Children 4 years and over and adults: 5 to 10 mg/kg single dose If anaemia: **vitamin B_{12} + folic acid**	**Transmission** by eating raw or under-cooked freshwater fish **Prevention**: • individual: cook fish thoroughly
Hymenolepiasis *Hymenolepis nana* (worldwide)	Often asymptomatic In the event of heavy infection: gastrointestinal disturbances (epigastric pain) Laboratory: eggs in stools	**praziquantel** PO (see page 0) Children 4 years and over and adults: 15 to 25 mg/kg single dose	**Transmission** by faecal-oral route or auto-infection **Prevention**: • individual: hand washing, nail cutting • collective: hygiene and sanitation (water, latrines, etc.)

Cestodes (larvae)

Parasites	Clinical features/ Laboratory	Treatment	Transmission/ Prevention
Cysticercosis *Taenia solium* (worldwide)	• Muscular: asymptomatic or myalgia • Subcutaneous: nodules • Neurological (neurocysticercosis): head ache, convulsions, coma, etc. • Ocular: exophthalmia, strabismus, iritis, etc. Laboratory: hypereosinophilia in blood and cerebrospinal fluid	Neurological and ocular cysticercosis should be managed in specialized facilities. Antiparasitic treatment without diagnosis of location by computerirsed tomography and/or magnetic resonance imaging can worsen the symptoms even threat the life. Neurosurgical treatment can be required.	**Transmission** by eating food contaminated with *T. solium* eggs or auto-infection **Prevention**: • individual: treat *T. solium* carriers, hygiene, cook meat thoroughly
Hydatid cyst *Echinococcus granulosus* (South America, North, East and South Africa, Western Europe)	Cysts located in the liver (60% of cases); lungs (30% of cases), and, less frequently, in other sites including the brain. Long asymptomatic period. The cyst becomes symptomatic when complications develop (biliary obstruction; anaphylactic shock in the event of rupture into peritoneal cavity, vessels or an organ; febrile painful jaundice in the event of rupture into the biliary tree, etc.).	First-line treatment: surgical excision **albendazole** PO [2](see page 0) is useful in addition to, or instead of, surgery: Children over 2 years and adults under 60 kg: 7.5 mg/kg 2 times daily Adults over 60 kg: 400 mg 2 times daily Treatment duration: In addition to surgery (pre-operatively or post- operatively): continuous course of minimum 2 months or at least two 28-day courses with a drug-free interval of 14 days. Inoperable cases: 28-day courses with drug-free intervals of 14 days, for 3 to 6 months (on average), possibly up to 1 year.	**Transmission**: • direct: contact with dogs • indirect: water and food contaminated by dog faeces **Prevention**: • individual: avoid contact with dogs • collective: eliminate stray dogs, monitor slaughterhouses

[1](see page 0) Praziquantel may be administered to pregnant women with *T. solium* taeniasis. For the other indications, treatment can usually be deferred until after delivery. [a(see page 0) b(see page 0) c(see page 0)]

[2](see page 0) Albendazole is contra-indicated during the first trimester of pregnancy.

Nematode infections

Infection/ Epidemiology	Clinical features/Diagnosis	Treatment
Ascariasis (roundworms) 1 (see page 0) *Ascaris lumbricoides* *Distribution*: worldwide, mainly in tropical and subtropical *Transmission*: ingestion of ascaris eggs	• *During larval migration* Loeffler 's syndrome: transient pulmonary symptoms (dry cough, dyspnoea, wheezing) and mild fever. • *Once adult worms are present in the intestine* Abdominal pain and distension. In general, the diagnosis is made when adult worms are expelled from the anus (or occasionally from the mouth). Ascaris are large (15-30 cm), cylindrical worms, pinkish-white, with slightly tapered ends. • *Complications* Ascariasis is usually benign, but massive infestation may cause intestinal obstruction (abdominal pain, vomiting, constipation), especially in children < 5 years. Worms may accidentally migrate to gall bladder, liver or peritoneum, causing jaundice, liver abscess, or peritonitis. • Ascaris eggs may be detected through parasitological examination of stools.	**albendazole** PO single dose Children > 6 months and adults: 400 mg (200 mg in children > 6 months but < 10 kg) or **mebendazole** PO for 3 days Children > 6 months and adults: 100 mg 2 times daily (50 mg 2 times daily in children > 6 months but < 10 kg)
Trichuriasis (whipworms) 1 (see page 0) *Trichuris trichiura* *Distribution and transmission*: as for *A. lumbricoides*	• In heavy infection: abdominal pain and diarrhoea. • In massive infection: chronic bloody diarrhea, tenesmus, rectal prolapse due to frequent attempts to defecate, especially in children. Worms may sometimes be seen on the rectal mucosa when prolapsed: these are grayish-white, 3-5 cm in length, in the shape of a whip, with a thickened body and a long, threadlike extremity. • Trichuris eggs may be detected through parasitological examination of stools.	**albendazole** PO for 3 days Children > 6 months and adults: 400 mg once daily (200 mg once daily in children > 6 months but < 10 kg) or **mebendazole** PO for 3 days, as for ascariasis. A single dose of albendazole or mebendazole is often insufficient.

Infection/ Epidemiology	Clinical features/Diagnosis	Treatment
Ankylostomiase 1 (see page 0) *Ancylostoma duodenale* *Necator americanus* *Distribution*: tropical and subtropical regions *Transmission*: larval skin penetration following contact (feet, hands) with contaminated soil	• *During larval penetration/migration* Cutaneous signs (pruritic papulo-vesicular rash at the site of penetration, usually the feet) and pulmonary symptoms (similar to ascariasis). • *Once adult worms are present in the intestine* Mild abdominal pain. Attachment of the parasite to the mucosa leads to chronic blood loss and anaemia (in endemic areas, antihelminthic treatment is recommended for patients with iron-deficiency anaemia). • Hookworm eggs may be detected through parasitological examination of stools.	**albendazole** single dose (as for ascariasis) is much more effective than mebendazole single dose. When using **mebendazole**, a 3-day treatment (as for ascariasis) is recommended. Treatment of anaemia (see page 30) (Chapter 1).

Infection/ Epidemiology	Clinical features/Diagnosis	Treatment

Strongyloidiasis
Strongyloides stercoralis
 	
Distribution: humid tropical regions
 	
Transmission: larval skin penetration and auto-infection
	• *Acute strongyloidiasis*
	  • During larval penetration/ migration: cutaneous signs (erythema and pruritus at the site of penetration, which may persist several weeks) and pulmonary symptoms (similar to ascariasis).
	  • Once larvae are present in the intestine: gastrointestinal symptoms (bloating, abdominal and epigastric pain, vomiting, diarrhoea).
	• *Chronic strongyloidiasis*
	Intestinal larvae may re-infect their host (auto-infection) by penetrating through the intestinal wall or by migrating transcutaneously from perianal skin. Chronic infections result in prolonged or recurrent pulmonary and gastrointestinal symptoms. Transcutaneous migration of intestinal larvae gives rise to a typical rash (larva currens), mainly in the anal region and on the trunk: sinuous, raised, linear, migrating lesion, intensely pruritic, moving rapidly (5 to 10 cm/hour) and lasting several hours or days.
	• *Complications*
	Hyperinfection (massive infestation) results in exacerbation of pulmonary and gastrointestinal symptoms, and possible dissemination of larvae to atypical locations, (CNS, heart, etc.). This form occurs mainly in patients receiving immunosuppressive therapy (e.g. corticosteroids).
	• Strongyloides larvae may be detected through parasitological examination of stools.
		First line treatment is:
		ivermectin PO 2 (see page 0) single dose
		Children > 15 kg and adults: 200 micrograms/kg, on an empty stomach
		
		While less effective, a 3-day treatment with **albendazole** PO (as for trichuriasis) may be an alternative.
		
		Hyperinfections are refractory to conventional therapy. Prolonged or intermittent multiple-dose regimens are required.

Infection/ Epidemiology	Clinical features/Diagnosis	Treatment
Enterobiasis (pinworms) *Enterobius vermicularis* *Distribution*: worldwide *Transmission*: faecal-oral route or auto-infection	• Anal pruritus, more intense at night, vulvovaginitis in girls (rare). In practice, the diagnosis is most often made when worms are seen on the perianal skin (or in the stool in heavy infestation). Pinworms are small (1 cm), mobile, white, cylindrical worms with slightly tapered ends. • Pinworm eggs may be collected from the anal area (scotch tape method) and detected under the microscope.	**albendazole** PO single dose, as for ascariasis or **mebendazole** PO single dose Children > 6 months and adults: 100 mg (50 mg in children > 6 months but < 10 kg) A second dose may be given after 2 to 4 weeks.
Trichinellosis *Trichinella* sp *Distribution*: worldwide, particularly frequent in Asia (Thailand, Laos, China, etc.) *Transmission*: consumption of raw or undercooked meat containing trichinella larvae (pork, wart-hog, bear, dog, etc.)	• *Enteric phase* (1 to 2 days after ingestion of infected meat) Self-limited episode of diarrhoea and abdominal pain lasting several days. • *Muscular phase* (about 1 week after ingestion) High fever; muscular pain (ocular [pain on eye movement], masseters [limitation of mouth opening], throat and neck [pain with swallowing and speech], trunk and limbs); facial or bilateral peri-orbital oedema; conjunctival haemorrhage, subungual haemorrhage; headache. Typical features are not always present and the patient may present with a non-specific flu-like syndrome. Other features, such as dietary habits (consuming pork/raw meat), suggestive symptoms (fever > 39 °C and myalgia and facial oedema) in several individuals who have shared the same meal (e.g. ceremony) or hypereosinophilia > 1000/mm3, reinforce the clinical suspicion. • Definitive diagnosis: muscle biopsy; serology (ELISA, Western Blot).	**albendazole** PO for 10 to 15 days Children > 2 years: 5 mg/kg 2 times daily Adults: 400 mg 2 times daily or **mebendazole** PO for 10 to 15 days Children > 2 years: 2.5 mg/kg 2 times daily Adults: 200 mg 2 times daily *plus, regardless of which anti-helminthic is chosen:* **prednisolone** PO 0.5 to 1 mg/kg once daily for the duration of treatment

[1] (see page 0) Roundworms, whipworms and hookworms frequently co-infect the same host. This should be taken into account when prescribing antihelminthic treatment. [a (see page 0) b (see page 0) c (see page 0)]

[2] (see page 0) The migrating larvae of *Ancylostoma braziliense* and *caninum* (hookworms of cats and dogs) also present as a pruritic, inflammatory, creeping eruption in humans (cutaneous larva migrans) but with a slower rate of progression and a longer duration (several weeks or months). Treatment is with **albendazole** (400 mg single dose or once daily for 3 days in children > 6 months and adults; 200 mg in children > 6 months but < 10 kg) or **ivermectin** (200 micrograms/kg single dose).

Filariasis

- Onchocerciasis (river blindness)(see page 151)
- Loiasis.(see page 153)
- Lymphatic filariasis (LF)(see page 155)

Filariases are helminthiases due to tissue-dwelling nematode worms (filariae). Human to human transmission takes place through the bite of an insect vector.

The most important pathogens are outlined in the table below. Mixed infections are common in co-endemic regions.

Each filarial species is found in 2 principal developmental stages: macrofilariae (adult worms) and microfilariae (larval offspring). The treatment depends on the pathogenic stage of the species considered and targets microfilariae for *O. volvulus* and macrofilariae for the other species.

Species/Infections	Location of macrofilariae	Location of microfilariae	Pathogenic stage	Presence of *Wolbachia*
Onchocerca volvulus (onchocerciasis)	Subcutaneous nodules	Skin and eye	Microfilariae	Yes
Loa loa (loiasis)	Subcutaneous tissue	Blood	Macrofilariae	No
Wuchereria bancrofti, ***Brugia malayi*** and ***Brugia timori*** (lymphatic filariasis)	Lymph vessels	Blood	Macrofilariae	Yes

Classical antifilarial agents include diethylcarbamazine (DEC), ivermectin and albendazole. Doxycycline is used solely in the treatment of *O. volvulus* and lymphatic filarial worms, which harbour an endosymbiotic bacterium (*Wolbachia*) sensitive to doxycycline.

Onchocerciasis (river blindness)

- Clinical features(see page 151)
- Laboratory(see page 152)
- Treatment(see page 152)
  - Antiparasitic treatment(see page 152)
  - Nodulectomy (surgical removal of onchocercomas)(see page 152)

The distribution of onchocerciasis is linked to that of its vector (*Simulium*), which reproduces near rapidly flowing rivers in intertropical Africa (99% of cases), Latin America (Guatemala, Mexico, Ecuador, Colombia, Venezuela, Brazil) and Yemen.

Clinical features

In endemic areas, the following signs, alone or in combination, are suggestive of onchocerciasis:

– Onchocercomas: painless subcutaneous nodules containing adult worms, usually found over a bony prominence (iliac crest, trochanters, sacrum, rib cage, skull, etc.), measuring several mm or cm in size, firm, smooth, round or oval, mobile or adherent to underlying tissue; single, or multiple and clustered.

– Acute papular onchodermatitis: papular rash, sometimes diffuse but often confined to the buttocks or lower extremities, intensely itchy, associated with scratch marks, often superinfected ("filarial scabies")[1](see page 0) . This arises from dermal invasion by microfilariae.

– Late chronic skin lesions: patchy depigmentation on the shins ("leopard skin"), skin atrophy or areas of dry, thickened, peeling skin (lichenification; "lizard skin").

– Visual disturbances and ocular lesions: see Onchocerciasis(see page 121), Chapter 5.

Laboratory

– Detection of the microfilariae in the skin (skin snip biopsy, iliac crest).
– If the skin biopsy is positive, look for loiasis in regions where loiasis is co-endemic (mainly in Central Africa).

Treatment

Antiparasitic treatment

– Diethylcarbamazine is contra-indicated (risk of severe ocular lesions).

– **Doxycycline** PO (200 mg once daily for 4 weeks; if possible 6 weeks) kills a significant percentage of adult worms and progressively reduces the number of *O. volvulus* microfilariae[2](see page 0) . It is contraindicated in children < 8 years and pregnant or breast-feeding women.

– **Ivermectin** PO is the drug of choice: 150 micrograms/kg single dose; a 2nd dose should be administered after 3 months if clinical signs persist. Repeat the treatment every 6 or 12 months to maintain the parasite load below the threshold at which clinical signs appear[3](see page 0) . Ivermectin is not recommended in children < 5 years or < 15 kg and pregnant women.

– In case of co-infection with *Loa loa* or in regions where loiasis is co-endemic, ivermectin should be administered with caution (risk of severe adverse reactions in patients with high *L. loa* microfilarial load):

- If it is possible to test for *Loa loa* (thick blood film):
  Confirm and quantify the microfilaraemia. Administer the appropriate treatment according to the microfilarial load (see Loiasis(see page 153)).

- If it is not possible to perform a thick film examination, take a history from the patient:
  If the patient has received a previous treatment with ivermectin without developing serious adverse reactions (see Loiasis(see page 153)), administer the treatment.
  If the patient has never received ivermectin nor developed signs of loiasis (migration of an adult worm under the conjunctiva, or « Calabar » swellings), administer the treatment.
  If the patient already has developed signs of loiaisis and if onchocerciasis has a significant clinical impact, administer ivermectin under close supervision (see Loiasis(see page 153)) or use an alternative (doxycycline, as above).

– In the case of concomitant lymphatic filariasis: administer ivermectin first then start treatment for lymphatic filariasis with doxycycline PO (see Lymphatic filariasis(see page 155)) one week later.

Nodulectomy (surgical removal of onchocercomas)

Nodules are benign, often deep, and their ablation does not treat onchocerciasis. Thus, nodulectomy is reserved for cranial nodules (their proximity to the eye is a risk factor for visual compromise) or nodules

which are cosmetically unacceptable. In other cases, refrain from nodulectomy. Nodulectomy is performed under local anaesthesia, in an appropriately equipped facility.

1(see page 0) Differential diagnosis is sarcoptic scabies (Scabies(see page 92), Chapter 4).
2(see page 0) Elimination of *Wolbachia* reduces the longevity and fertility of the macrofilariae, and thus the production of new microfilariae within the organism.
3(see page 0) Ivermectin kills microfilariae and disrupts production of microfilariae by adult worms. However the treatment must be administered at regular intervals since it does not kill adult worms.

Loiasis.

- Clinical features(see page 153)
- Laboratory(see page 153)
- Treatment(see page 153)
  - Antiparasitic treatment(see page 153)
  - Extraction of macrofilariae(see page 154)

The distribution of loiasis is linked to that of its vector (*Chrysops*) in forests or savannah with gallery forests in West or Central Africa (limits West: Benin; East: Uganda; North: Sudan and South: Angola).

Clinical features

– The subconjunctival migration of an adult worm is pathognomonic of *Loa loa* infection.

– Localised subcutaneous swellings, allergic in origin, transient (several hours or days), painless, non-pitting, appearing anywhere on the body, frequently the upper extremities and face, often associated with localised or generalised pruritus (« Calabar swellings »).

– Onset of pruritus, in the absence of other signs.

– Subcutaneous migration of an adult worm: pruritic, palpable red cord-like linear lesion, sinuous, advancing (1 cm/hour), disappearing rapidly with no trace1(see page 0) . Such migration generally arises following treatment with diethylcarbamazine, rarely spontaneously.

Laboratory

– Detection of microfilariae in the peripheral blood (thick film, stained with Giemsa). Blood specimens should be collected between 10 am and 5 pm. Quantify microfilaraemia even if the diagnosis is certain, since treatment is determined by the intensity of the parasite load.

– If the thick film is positive, look for onchocerciasis in regions where onchocerciasis is coendemic (mainly in Central Africa).

Treatment

Antiparasitic treatment

– Diethylcarbamazine (DEC) is the only macrofilaricide available but is contra-indicated in:
• Patients with microfilaraemia > 2000 mf/ml (risk of severe encephalopathy, with poor prognosis).

• Patients co-infected with *O. volvulus* (risk of severe eye lesions).
• Pregnant women, infants, and patients in poor general condition.

– Ivermectin (and possibly albendazole) is used to reduce microfilaraemia before administration of DEC; however, ivermectin administration may trigger encephalopathy in patients with very high *Loa loa* microfilaraemia (> 30 000 mf/ml).

– Doxycycline is not indicated since *Loa loa* does not harbour *Wolbachia*.

– Management:

1) *L. loa microfilaraemia is < 1,000-2,000 mf/ml*
A 28-day treatment of **DEC** may be started using a small dose: 6 mg on D1, i.e. 1/8 of a 50 mg tablet 2 times daily.
Double the dose every day up to 200 mg 2 times daily in adults (1.5 mg/kg 2 times daily in children).
If microfilaraemia or symptoms persist, a second treatment is given 4 weeks later.
If DEC is contra-indicated due to possible or confirmed co-infection with *O. volvulus*, **ivermectin** (150 microgams/kg single dose) treats onchocerciasis, and reduces pruritus and frequency of Calabar swellings.
The treatment may be repeated every month or every 3 months.

2) *L. loa microfilaraemia is between 2,000 and 8,000 mf/ml*
Reduce microfilaraemia with **ivermectin** (150 micrograms/kg single dose); repeat the treatment every month if necessary; administer DEC when the microfilaraemia is < 2000 mf/ml.

3) *L. loa microfilaraemia is between 8,000 and 30,000 mf/ml*
Treatment with **ivermectin** (150 micrograms/kg single dose) may cause marked functional impairment for several days. Close supervision and support from family member(s) are necessary[2](see page 0). Prescribe paracetamol as well for 7 days.

4) *L. loa microfilaraemia is > 30,000 mf/ml*

• If the loiasis is well tolerated, it is preferable to refrain from treatment: the disease is benign and treatment with ivermectin may cause very severe adverse reactions (encephalopathy), albeit rarely.

• If loiasis has a significant clinical impact and/or the patient presents with symptomatic onchocerciasis requiring treatment, **ivermectin** (150 micrograms/kg single dose) is administered for 5 days under supervision in hospital[3](see page 0). An attempt to first reduce *L. loa* microfilaraemia using **albendazole** (200 mg 2 times daily for 3 weeks) is an option. When *L. loa* microfilaraemia is < 30 000 mf/ml, treat with ivermectin under close supervision and support, then DEC when the microfilaraemia is < 2000 mf/ml.

Extraction of macrofilariae

Subcutaneous migration of a microfilaria usually results from treatment with DEC; the worm will die beneath the skin and extracting it serves no purpose.

Removal of an adult worm from the conjunctiva: see Loasis(see page 121), Chapter 5.

[1](see page 0) For differential diagnosis, see cutaneous larva migrans(see page 150).
[2](see page 0) Patients may present with various pain syndromes, be unable to move without help or unable to move at all. Monitoring is necessary to determine whether the patient can manage activities of daily living, and provide assistance if necessary. If the patient remains bedridden for several days, ensure pressure sores do not develop (mobilisation, repositioning).

3(see page 0) A severe reaction may occur on D2-D3. It is usually preceded by haemorrhages of the palpebral conjunctiva on D1-D2. Routinely check for this sign by turning back the eyelids. Symptoms of post ivermectin encephalopathy are reversible and the prognosis favourable, if the patient is correctly managed; the treatment is symptomatic until symptoms resolve. Avoid the use of steroids due to adverse effects.

Lymphatic filariasis (LF)

- Clinical features(see page 155)
- Laboratory(see page 155)
- Treatment(see page 156)
  - Antiparasitic treatment(see page 156)
  - Control/prevention of inflammatory manifestations and infectious complications(see page 156)
  - Surgery(see page 156)

The distribution of LF is linked to that of its mosquito vectors (Anopheles, Culex, Aedes, etc.):
– *W. bancrofti*: sub-Saharan Africa, Madagascar, Egypt, India, South East Asia, Pacific region, South America, The Caribbean
– *B. malayi*: South East Asia, China, India, Sri Lanka
– *B. timori*: Timor
90% of LF is due to *W. bancrofti* and 10% to *Brugia* spp.

Clinical features

– Acute recurrent inflammatory manifestations
• Adenolymphangitis: lymph node(s) and red, warm, tender oedema along the length of a lymphatic channel, with or without systemic signs (e.g. fever, nausea, vomiting). The inflammation may involve the lower limbs, external genitalia and breast.
• In men: acute inflammation of the spermatic cord (funiculitis), epididymis and testicle (epididymo-orchitis).
Attacks resolve spontaneously within a week and recur regularly in patients with chronic disease.

– Chronic manifestations
• Lymphoedema: oedema of the lower extremity or external genitalia or breast, secondary to obstruction of the lymphatics by macrofilariae. The oedema is reversible initially but then becomes chronic and increasingly severe: hypertrophy of the area affected, progressive thickening of the skin (fibrous thickening with formation of creases, initially superficial, but then deep, and verrucous lesions). The final stage of lymphoedema is elephantiasis.
• In men: increase in volume of fluid due to accumulation within the tunica vaginalis (hydrocoele, lymphocoele, chylocoele); chronic epididymo-orchitis.
• Chyluria: milky or rice-water urine (disruption of a lymphatic vessel in the urinary tract).
In patients parasitized by *Brugia* spp, genital lesions and chyluria are rare: lymphoedema is usually confined to below the knee.

Laboratory

– Detection of microfilariae in the peripheral blood (thick film)1(see page 0); blood specimens should be collected between 9 pm and 3 am.
– In regions where loiasis and/or onchocerciasis are co-endemic, check for co-infection if the LF diagnosis is positive.

Treatment

Antiparasitic treatment

– Treatment is not administered during an acute attack.

– **Doxycycline** PO, when administered as a prolonged treatment, eliminates the majority of macrofilariae and reduces lymphoedema: 200 mg once daily for 4 weeks minimum. It is contraindicated in children < 8 years and pregnant or breast-feeding women.

– **Diethylcarbamazine** PO single dose (400 mg in adults; 3 mg/kg in children) may be an alternative but eliminates a variable proportion of adult worms (up to 40%) and does not relieve symptoms; a prolonged treatment is no more effective than single dose therapy. In addition, DEC is contra-indicated in patients with onchocerciasis or *Loa loa* microfilarial load > 2000 mf/ml and in pregnant and breast-feeding women.

– Ivermectin (weak or absent macrofilaricidal effect) and albendazole should not be used for the treatment of individual cases (no effect on symptoms).

– In the case of confirmed or probable co-infection with *O. volvulus*: treat onchocerciasis(see page 151) first, then administer doxycycline.

Control/prevention of inflammatory manifestations and infectious complications

– Acute attacks: bed rest, elevation of the affected limb without bandaging, cooling of the affected limb (wet cloth, cold bath) and analgesics; antibacterial or antifungal cream if necessary; antipyretics if fever (paracetamol) and hydration.

– Prevention of episodes of lymphangitis and lymphoedema: hygiene of the affected extremity[2](see page 0) , comfortable footwear, immediate attention to secondary bacterial/fungal infections and wounds.

– Established lymphoedema: bandaging of the affected limb by day, elevation of the affected extremity (after removal of the bandage) when at rest, simple exercises (flexion-extension of the feet when recumbent or upright, rotation of the ankles); skin hygiene, as above.

Surgery

May be indicated in the treatment of chronic manifestations: advanced lymphoedema (diversion-reconstruction), hydrocoele and its complications, chyluria.

[1](see page 0) When test results are negative in a clinically suspect case, consider detection of antigens (ICT rapid test) and/or ultrasound of the inguinal area in search of the « filarial dance sign ».

[2](see page 0) Wash at least once daily (soap and water at room temperature), paying special attention to folds and interdigital areas; rinse thoroughly and dry with a clean cloth; nail care.

Chapter 7: Bacterial diseases

- Bacterial meningitis(see page 157)
- Tetanus(see page 162)
- Enteric (typhoid and paratyphoid) fevers(see page 168)
- Brucellosis(see page 171)
- Plague(see page 173)
- Leptospirosis(see page 175)
- Relapsing fever (borreliosis)(see page 178)
    - Louse-borne relapsing fever (LBRF)(see page 178)
    - Tick-borne relapsing fever (TBRF)(see page 179)
- Eruptive rickettsioses(see page 180)

Bacterial meningitis

- Clinical features(see page 158)
    - Children over 1 year and adults(see page 158)
    - Children under 1 year(see page 158)
- Laboratory(see page 158)
- Treatment in a non-epidemic context(see page 159)
    - Antibiotherapy(see page 159)
    - Additional treatment(see page 160)
- Treatment in an epidemic context(see page 161)
    - Antibiotherapy(see page 161)
    - Additional treatment(see page 161)
- References(see page 162)

– Meningitis is an acute bacterial infection of the meninges, which may affect the brain and lead to irreversible neurological damage and auditory impairment.
– Bacterial meningitis is a medical emergency. The treatment is based on early parenteral administration of antibiotics that penetrates well into the cerebrospinal fluid (CSF). Empiric antibiotic therapy is administered if the pathogen cannot be identified or while waiting for laboratory results.
– The main bacteria responsible vary depending on age and/or context:

Meningitis in a non-epidemic context:
• Children 0 to 3 months:
Children ≤ 7 days: Gram-negative bacilli (*Klebsiella spp*, *E. coli*, *S. marcescens*, *Pseudomona spp*, *Salmonella spp*) and group B streptococcus
Children > 7 days: *S. pneumoniae* accounts for 50% of all bacterial meningitis
L. monocytogenes is occasionally responsible for meningitis during this period.
• Children 3 months-5 years: *S. pneumoniae*, *H. influenza B* and *N. meningitidis*
• Children > 5 years and adults: *S. pneumoniae* and *N. meningitidis*
Special conditions:
• Immunodepressed patients (HIV, malnourished): high percentage of Gram- negative bacilli (specially *Salmonella spp*) and also *M. tuberculosis*.
• Sickle cell anaemia: *Salmonella spp* and *Staphylococcus aureus* are frequent causes.
• Meningitis may be related to *S. aureus* when associated with skin infection or skull fracture.

Meningitis in an epidemic context:
In the Sahelian region (but not exclusively, e.g. Rwanda, Angola, Brazil), during the dry season, epidemics

of meningococcal meningitis (*Neisseria meningitidis* A or C or W135) affect children from 6 months of age, adolescents and adults. In these regions, whether during epidemics or not, all the above pathogens can be found, especially in young children.

Clinical features

The clinical presentation depends on the patient's age.

Children over 1 year and adults

– Fever, severe headache, photophobia, neck stiffness
– Brudzinski's sign (neck flexion in a supine patient results in involuntary flexion of the knees) and Kernig's sign (attempts to extend the knee from the flexed-thigh position are met with strong passive resistance).
– Petechial or ecchymotic purpura (usually in meningococcal infections)
– In severe forms: coma, seizures, focal signs, purpura fulminans

Children under 1 year

The classic signs of meningitis are usually absent.
– The child is irritable, appears sick with fever or hypothermia, poor feeding or vomiting.
– Other features include: seizures, apnoea, altered consciousness, bulging fontanelle (when not crying); occasionally, neck stiffness and purpuric rash.

Laboratory

– Lumbar puncture (LP):
• Macroscopic examination of CSF: antibiotic therapy should be initiated immediately if the LP yields a turbid CSF.
• Microscopic examination: Gram stain (but a negative examination does not exclude the diagnosis) and white blood cell count (WBC).
• In an epidemic context, once the meningococcal aetiology has been confirmed, there is no need for routine LP for new cases.

	Pressure	**Aspect**	**WBC** (leucocytes/mm^3)	**Protein**	**Other tests**
Normal CSF		Clear	< 5	Pandy– < 40 mg/dl	–
Bacterial meningitis	++++	Cloudy, turbid	100-20 000 mainly neutrophiles In neonates: > 20 In immunocompromised, the WBC may be < 100	Pandy+ 100-500 mg/dl	Gram stain +
Viral meningitis	Normal to +	Clear	10-700 mainly lymphocytes	Pandy–	–

TB meningitis	+++	Clear or yellowish	< 500 mainly lymphocytes	Pandy+	AFB
Cryptococcal meningitis	++++	Clear	< 800 mainly lymphocytes	Pandy–	India ink

– Rapid test for detection of bacterial antigens.

Note: in an endemic area, it is essential to test for severe malaria (rapid test or thin/thick films).

Treatment in a non-epidemic context

Antibiotherapy

For the choice of antibiotic therapy and dosages according to age, see table below.

	No associated skin infection		**Associated skin infection (including umbilical cord infection)**	
	First line	**Alternative**	**First line**	**Alternative**
0 to 7 days < 2 kg	**ampicillin** IV 100 mg/kg every 12 hours + **cefotaxime** IV 50 mg/kg every 12 hours	**ampicillin** IV 100 mg/kg every 12 hours + **gentamicin** IV 3 mg/kg once daily	**cloxacillin** IV 50 mg/kg every 12 hours + **cefotaxime** IV 50 mg/kg every 12 hours	**cloxacillin** IV 50 mg/kg every 12 hours + **gentamicin** IV 3 mg/kg once daily
0 to 7 days ≥ 2 kg	**ampicillin** IV 100 mg/kg every 8 hours + **cefotaxime** IV 50 mg/kg every 8 hours	**ampicillin** IV 100 mg/kg every 8 hours + **gentamicin** IV 5 mg/kg once daily	**cloxacillin** IV 50 mg/kg every 8 hours + **cefotaxime** IV 50 mg/kg every 8 hours	**cloxacillin** IV 50 mg/kg every 8 hours + **gentamicin** IV 5 mg/kg once daily
8 days to < 1 month ≥ 2 kg	**ampicillin** IV 100 mg/kg every 8 hours + **cefotaxime** IV 50 mg/kg every 8 hours	**ampicillin** IV 100 mg/kg every 8 hours + **gentamicin** IV 5 mg/kg once daily	**cloxacillin** IV 50 mg/kg every 6 hours + **cefotaxime** IV 50 mg/kg every 8 hours	**cloxacillin** IV 50 mg/kg every 6 hours + **gentamicin** IV 5 mg/kg once daily

	No associated skin infection		Associated skin infection (including umbilical cord infection)	
	First line	**Alternative**	**First line**	**Alternative**
1 to 3 months	**ampicillin** IV 100 mg/kg every 8 hours + **ceftriaxone** IV 100 mg/kg on D1 then starting on D2: 100 mg/kg once daily or 50 mg/kg every 12 hours	**ampicillin** IV 100 mg/kg every 8 hours + **gentamicin** IV 2.5 mg/kg every 8 hours	**cloxacillin** IV 50 mg/kg every 6 hours + **ceftriaxone** IV 100 mg/kg on D1 then starting on D2: 100 mg/kg once daily or 50 mg/kg every 12 hours	**cloxacillin** IV 50 mg/kg every 6 hours + **gentamicin** IV 2.5 mg/kg every 8 hours
> 3 months	**ceftriaxone** IV Children: 100 mg/kg on D1 then starting on D2: 100 mg/kg once daily or 50 mg/kg every 12 hours (max. 4 g daily)		**cloxacillin** IV Children < 40 kg: 50 mg/kg every 6 hours Children ≥ 40 kg: 2 g every 6 hours + **ceftriaxone** IV Children: 100 mg/kg on D1 then starting on D2: 100 mg/kg once daily or 50 mg/kg every 12 hours (max. 4 g daily)	
Adults	**ceftriaxone** IV: 4 g once daily or 2 g every 12 hours		**cloxacillin** IV: 2 g every 6 hours + **ceftriaxone** IV: 4 g once daily or 2 g every 12 hours	

Duration of antibiotherapy:

1) According to the pathogen:
• *Haemophilus influenzae*: 7 days
• *Streptococcus pneumonia*: 10-14 days
• Group B streptococcus and *Listeria*: 14-21 days
• Gram-negative bacilli: 21 days
• *Neisseria meningitidis*: see antibiotherapy in an epidemic context

2) If the pathogen is unknown:
Children < 3 months: 2 weeks beyond the first sterile CSF culture or 21 days
Children > 3 months and adults: 10 days. Consider extending treatment or alternative diagnoses if fever persists beyond 10 days. On the other hand, a 7-day course of ceftriaxone is sufficient in patients who are making an uncomplicated recovery.

Additional treatment

– Dexamethasone reduces the risk of hearing loss in patients with *H. influenzae* or *S. pneumoniae*. Early administration is indicated in meningitis caused by these pathogens or when the pathogen is unknown, except in neonates (and in presumed meningococcal meningitis in an epidemic context).
dexamethasone IV[1](see page 162),[2](see page 162)
Children > 1 month: 0.15 mg/kg (max. 10 mg) every 6 hours for 2 to 4 days
Adults: 10 mg every 6 hours for 2 to 4 days

The treatment should be started before or with the first dose of antibiotic, otherwise, the treatment offers no benefit.

– Ensure that the patient is well fed and well hydrated (infusions or nasogastric tube if necessary).
– Seizures(see page 16) (Chapter 1).
– Coma: prevention of bed sores, care of the mouth and eyes, etc.

Treatment in an epidemic context

Antibiotherapy

In this context, *N. meningitidis* is the most likely pathogen.

Age	Treatment[3](see page 162)
Children < 2 months	**ceftriaxone** IV[1](see page 0) or IM[2](see page 0) for 7 days 100 mg/kg once daily
Children ≥ 2 months and adults	**ceftriaxone** IV[1](see page 0) or IM[2](see page 0) for 5 days Children 2 months to < 5 years: 100 mg/kg once daily (max. 2 g daily) Children ≥ 5 years and adults: 2 g once daily

Note:
A short treatment with a single dose of ceftriaxone IM can be used in children 2 years and older and in adults during a meningococcal meningitis epidemic if 1) confirmed by a reliable laboratory 2) the number of cases exceeds management capacities with the 5-day treatment. Check national recommendations. Nevertheless, it is essential to ensure a monitoring of cases after 24 hours.
ceftriaxone IM[2](see page 0)
Children 2 to < 12 years: 100 mg/kg single dose
Children ≥ 12 years and adults: 4 g single dose
If there is no clinical improvement (fever > 38.5 °C, repeated seizures, appearance or aggravation of a reduced level of consciousness or of neurological signs) 24 hours after the injection, continue the treatment with ceftriaxone for 5 days.

Additional treatment

– Ensure that the patient is well fed and well hydrated (infusions or nasogastric tube if necessary).
– Seizures(see page 16) (Chapter 1).
– Coma: prevention of bed sores, care of the mouth and eyes, etc.
– Dexamethasone in not indicated.

[1](see page 0) The solvent of ceftriaxone for IM injection contains lidocaine. Ceftriaxone reconstituted using this solvent must never be administered by IV route. For IV administration, water for injection must always be used. [a(see page 0) b(see page 0)]

[2](see page 0) For IM administration, divide the dose into 2 injections if needed, half-dose in each buttock. [a(see page 0) b(see page 0) c(see page 0)]

References

1. D. van de Beek, C. Cabellos, O. Dzupova, S. Esposito, M. Klein, A. T. Kloek, S. L. Leib, B. Mourvillier, C. Ostergaard, P. Pagliano, H.W. Pfister, R. C. Read, O. Resat Sipahi, M.C. Brouwer. ESCMID guideline: diagnosis and treatment of acute bacterial meningitis, 2016. https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(16)00020-3/pdf

2. Sheldon L Kaplan, MD. Bacterial meningitis in children: Dexamethasone and other measures to prevent neurologic complications. UpToDate [Accessed 25 February 2019].

3. World Health Organization. Managing meningitis epidemics in Africa. A quick reference guide for health authorities and health-care workers. 2015. https://apps.who.int/iris/bitstream/handle/10665/154595/WHO_HSE_GAR_ERI_2010.4_Rev1_eng.pdf?sequence=1

Tetanus

- Clinical features(see page 163)
  - Children and adults(see page 163)
  - Neonates(see page 163)
- Treatment(see page 163)
  - General measures(see page 163)
  - Neutralisation of toxin(see page 163)
  - Inhibition of toxin production(see page 163)
  - Control of rigidity and spasms, and sedation of the patient(see page 164)
  - Treatment of pain(see page 166)
  - Treatment of the entry point and associated infections(see page 166)
  - Tetanus vaccination(see page 166)
- Prevention(see page 166)
  - 1) Post-exposure prophylaxis(see page 166)
  - 2) Routine vaccination (pre-exposure prophylaxis)(see page 167)

– Tetanus is a severe infection due to the bacillus *Clostridium tetani*, found in soil, and human and animal waste. The infection is noncontagious.
– *Clostridium tetani* is introduced into the body through a wound and produces a toxin whose action on the central nervous system is responsible for the symptoms of tetanus.
– Tetanus is entirely preventable by vaccination. It occurs in people who have not been fully vaccinated before exposure or have not received adequate post-exposure prophylaxis. In these individuals, most breaks in the skin or mucous membranes carry a risk of tetanus, but the wounds with the greatest risk are: the stump of the umbilical cord in neonates, puncture wounds, wounds with tissue loss or contamination with foreign material or soil, avulsion and crush injuries, sites of non-sterile injections, chronic wounds (e.g. lower extremity ulcers), burns and bites. Surgical or obstetrical procedures performed under non-sterile conditions also carry a risk of tetanus.

Clinical features

Generalised tetanus is the most frequent and severe form of the infection. It presents as muscular rigidity, which progresses rapidly to involve the entire body, and muscle spasms, which are very painful. Level of consciousness is not altered.

Children and adults

– Average time from exposure to onset of symptoms is 7 days (3 to 21 days).
– Muscular rigidity begins in the jaw muscles (difficulty with then inability to open mouth [trismus] preventing the patient from speaking, eating), spreading to the face (fixed smile), neck (difficulty with swallowing), to the trunk (restriction of respiratory muscles; hyperextension of spine [opisthotonus]), to the abdomen (guarding) and to the limbs (flexion of the upper limbs and extension of the lower limbs).
– Muscle spasms, which are very painful, appear at the onset or when muscular rigidity becomes generalised. They are triggered by stimuli (noise, light, touch) or arise spontaneously. Spasms of the thoracic and laryngeal muscles may cause respiratory distress or aspiration.

Neonates

– In 90% of cases, initial symptoms appear within 3 to 14 days of birth.
– The first signs are significant irritability and difficulty sucking (rigidity of the lips, trismus) then rigidity becomes generalised, as in adults. Any neonate, who initially sucked and cried normally, presenting with irritability and difficulty sucking 3 to 28 days after birth and demonstrating rigidity and muscle spasms should be assumed to have neonatal tetanus.

Treatment

Hospitalisation is needed and usually lasts 3 to 4 weeks. Correct management can reduce mortality even in hospitals with limited resources.

General measures

– Ensure intensive nursing care.
– The patient should be in a dark, quiet room. Blindfold neonates with a cloth bandage.
– Handle the patient carefully, while sedated and as little as possible; change position every 3 to 4 hours to avoid bedsores.
– Teach family the danger signs and instruct them to call the nurse for the slightest respiratory symptom (cough, difficulty breathing, apnoea, excessive secretions, cyanosis, etc.).
– Establish IV access for hydration, IV injections.
– Gentle suction of secretions (mouth, oropharynx).
– Insert a nasogastric tube for hydration, feeding and administration of oral medications.
– Provide hydration and nutrition in feeds divided over 24 hours. In neonates, give expressed breast milk every 3 hours (risk of hypoglycaemia).

Neutralisation of toxin

human tetanus immunoglobulin IM
Neonates, children and adults: 500 IU single dose, injected into 2 separate sites

Inhibition of toxin production

metronidazole (see page 0) IV infusion (30 minutes; 60 minutes in neonates) for 7 days
Neonates:
• 0 to 7 days: 15 mg/kg on D1 then, after 24 hours, 7.5 mg/kg every 12 hours

• 8 days to < 1 month (< 2 kg): same doses
• 8 days to < 1 month (≥ 2 kg): 15 mg/kg every 12 hours
Children 1 month and over: 10 mg/kg every 8 hours (max. 1500 mg daily)
Adults: 500 mg every 8 hours

Control of rigidity and spasms, and sedation of the patient

Diazepam should decrease the frequency and intensity of spams without causing respiratory depression. The dose and frequency of administration depend on the patient's clinical response and tolerance.

⚠ – There is a high risk of respiratory depression and hypotension when using diazepam, especially in children and elderly patients. Constant and close monitoring of the patient's respiratory rate (RR) and oxygen saturation (SpO_2) is essential, with immediate availability of equipment for manual ventilation (Ambu bag, face mask) and intubation, suction (electric if possible) and Ringer lactate.
– A continuous IV infusion of diazepam requires the use of a dedicated vein (no other infusion/injection in this vein); avoid the antecubital fossa if possible.
– Do not stop treatment abruptly; an abrupt stop can cause spasms.

Neonates	**diazepam emulsion** for injection (10 mg ampoule, 5 mg/ml, 2 ml) • 0.1 to 0.3 mg/kg by slow IV injection (3 to 5 minutes) every 1 to 4 hours depending on the severity and the persistence of the spasms as long as the RR is ≥ 30. • If despite hourly diazepam the spasms persist, start a continuous infusion of diazepam with an electric syringe: 0.1 to 0.5 mg/kg/hour (2.4 to 12 mg/kg every 24 hours). Start with 0.1 mg/kg/hour and if symptoms persist, increase by 0.1 mg/kg/hour as long as RR is ≥ 30. • If in spite of 0.5 mg/kg/hour symptoms persist, the dose can be increased up to 0.8 mg/kg/hour as long as the RR ≥ 30. • Diluted diazepam emulsion does not keep for more than 6 hours. *Example:* *Neonate weighing 3 kg (administration by electric syringe)* *0.1 mg/kg/hour x 3 kg = 0.3 mg/hour* *Dilute one 10 mg ampoule of **diazepam emulsion** for injection in 50 ml of 10% glucose to obtain a solution containing 0.2 mg of diazepam per ml.* *Administer 1.5 ml/hour [dose (in mg/hour) ÷ dilution (in mg/ml) = dose in ml/hour i.e. 0.3 (mg/hour) ÷ 0.2 (mg/ml) = 1.5 ml/hour].* If an electric syringe is not available, diluting the diazepam emulsion in an infusion bag for continuous infusion may be considered. Weigh the risks associated with this mode of administration (accidental bolus or insufficient dose). The infusion should be monitored closely to avoid any change, however small, of the prescribed rate.

Children > 1 month and adults	Same doses and protocol as in neonates but: • Use **diazepam solution** for injection 5 mg/ml: (10 mg ampoule, 5 mg/ml, 2 ml)[2](see page 0) . • These doses can be administered as long as the RR is: ≥ 30 in children under 1 year ≥ 25 in children 1 to 4 years ≥ 20 in children 5 to 12 years ≥ 14 in children over 12 years ≥ 12 in adults *Examples:* *• Child weighing 6 kg (continuous IV infusion using a pediatric infusion set; 1 ml = 60 drops)* *0.1 mg/kg/hour x 6 kg = 0.6 mg/hour* *Dilute one 10 mg ampoule of **diazepam solution** for injection in 50 ml of 5% glucose (10% glucose if child < 3 months) to obtain a solution containing 0.2 mg of diazepam per ml.* *Administer 3 ml/hour [dose (in mg/hour) ÷ dilution (in mg/ml) = dose in ml/hour i.e. 0.6 (mg/hour) ÷ 0.2 (mg/ml) = 3 ml/hour] or 3 drops/minute (in a paediatric infusion set ml/hour = drops/minute).* *• Adult weighing 60 kg (standard adult infusion set, 1 ml = 20 drops)* *0.1 mg/kg/hour x 60 kg = 6 mg/hour* *Dilute 5 ampoules of 10 mg of **diazepam solution** (50 mg) in 250 ml of 0.9% sodium chloride or 5% glucose to obtain a solution containing 0.2 mg of diazepam per ml.* *Administer 30 ml/hour [dose (in mg/hour) ÷ dilution (in mg/ml) = dose in ml/hour e.g. 6 (mg/hour) ÷ 0.5 (mg/ml) = 30 ml/hour] or 10 drops/minute.*

Count the volume of the infusion of diazepam as part of the patient's daily fluid intake.

When the frequency and severity of the spasms have decreased, start weaning the diazepam (gradually decrease the rate of infusion):
– Calculate the total daily dose of IV diazepam and administer it orally in 4 divided doses, 6 hours apart, via nasogastric (NG)[3](see page 0) tube.
– Give first NG dose and decrease rate of IV infusion by 50%.
– Give second NG dose and stop IV diazepam infusion.
– If withdrawal signs[4](see page 0) appear, wean more slowly.
– Once on diazepam PO, wean by 10 to 20% of the original dose daily, until at a dose of 0.05 mg/kg every 6 hours.
– Then increase the interval from every 6 hours to every 8 hours for 24 hours as tolerated (wean more slowly if withdrawal signs appear).
– Continue to increase the interval between the doses from every 8 hours to every 12 hours and then to every 24 hours before stopping the diazepam.
– Each step should be for 24 hours or more if withdrawal signs appear.

Notes:
– It is often at these smaller doses that it is difficult to wean diazepam. If this is the case, slow the wean further: dropping the % wean (e.g. 5% wean every 24 hours instead of 10% wean) or increasing the interval between weans (e.g. going from every 24 hours to every 48 hours).
– If the patient is also receiving morphine, wean diazepam first then, wean morphine.
– Non-pharmacological measures to reduce withdrawal: reduce environmental stimuli; swaddle infants, frequent feedings.
– Infants who have had tetanus remain hypertonic, even when they are no longer having spams.

Treatment of pain

morphine PO (via nasogastric tube) if necessary (see Pain(see page 23), Chapter 1).
When morphine is administered with diazepam the risk of respiratory depression is increased, thus closer monitoring is required. When morphine is no longer required, wean the same way as diazepam.

Treatment of the entry point and associated infections

– Search systematically the entry wound. Provide local treatment under sedation: cleansing and for deep wounds, irrigation and debridement.
– Cord infection: do not excise or debride; treat bacterial omphalitis and sepsis, add to metronidazole IV: cloxacillin IV + cefotaxime IV or cloxacillin IV + gentamicin IV (for doses, see Bacterial meningitis(see page 157)).

Tetanus vaccination

As tetanus does not confer immunity, vaccination against tetanus must be administered once the patient has recovered.
In case of neonatal tetanus, initiate the vaccination of the mother.

Prevention

Of critical importance, given the difficulty of treating tetanus once established.

1) Post-exposure prophylaxis

– In all cases:
• Cleansing and disinfection of the wound, and removal of any foreign body.
• Antibiotics are not prescribed routinely for prophylaxis. The decision to administer an antibiotic (metronidazole or penicillin) is made on a case-by-case basis, according to the patient's clinical status.

– Depending on pre-exposure vaccination status:
Tetanus vaccine (TV)5(see page 0) and immunoglobulin: see indications below.

Type of wound	**Complete vaccination** (3 or more doses) Time since administration of last dose:			**Incomplete vaccination** (less than 3 doses) or **no vaccination** or **unknown status**
	< 5 years	5-10 years	> 10 years	
Minor, clean	None	None	TV 1 booster dose	Initiate or complete TV
Other	None	TV 1 booster dose	TV 1 booster dose	Initiate or complete TV and administer tetanus immunoglobulin

tetanus vaccine IM
Children and adults: 0.5 ml per dose
If no vaccination or unknown vaccination status: administer at least 2 doses at an interval of 4 weeks.
If incomplete vaccination: administer one dose.
Then, to ensure long-lasting protection, administer additional doses to complete a total of 5 doses, as indicated in the table below.

human anti-tetanus immunoglobulin IM
Children and adults: 250 IU single dose; 500 IU for wounds more than 24 hours old.
Inject the vaccine and the immunoglobulin in 2 different sites, using a separate syringe for each.

2) Routine vaccination (pre-exposure prophylaxis)

– Children: 6 doses in total: a first series of 3 doses of DTP or DTP + HepB or DTP + HepB + Hib before the age of 1 year, administered at an interval of 1 month (e.g. at the age of 6, 10 and 14 weeks), then a dose of a vaccine containing tetanus toxoid between the age of 12 and 23 months, a dose between the age of 4 to 7 years, then a dose between the age of 12 and 15 years.

– Women of childbearing age: 5 doses during the reproductive years: a series of 3 doses of Td or TT[6](see page 0) with an interval of at least one month between the first and second dose and an interval of at least 6 months between the second and third dose, then two other doses, each at minimum interval of one year, e.g. during pregnancies (see table below).

– Pregnant women: if a woman has never been vaccinated or if her vaccination status is unknown: 2 doses of Td or TT[6](see page 0) during the pregnancy to reduce the risk of tetanus in mother and neonate: the first as soon as possible during the pregnancy and the second at least 4 weeks later and at least 2 weeks before delivery. This vaccination schedule protects more than 80% of neonates from tetanus. A single dose offers no protection

Dose	Vaccination schedule in adults	Degree and duration of protection
TV1	On first contact with the health care system or as soon as possible during pregnancy	No protection
TV2	At least 4 weeks after TV1	80% 1 to 3 years
TV3	6 months to 1 year after TV2 or during the following pregnancy	95% 5 years
TV4	1 to 5 years after TV3 or during the following pregnancy	99% 10 years
TV5	1 to 10 years after TV4 or during the following pregnancy	99% Throughout the reproductive years

[1](see page 0) Clindamycin IV for 7 days is an alternative (for doses, see Periorbital and orbital cellulitis(see page 119), Chapter 5).
[2](see page 0) Administer the first dose rectally if an IV cannot be placed immediately.
[3](see page 0) Administration of oral diazepam tablets to infants: calculate the exact dose of diazepam, e.g. to obtain 0.5 mg of diazepam, cut a scored diazepam 2 mg tablet in half along scoring then split in half again. Crush quarter tablet and dissolve in expressed breast milk or infant formula.
[4](see page 0) Withdrawal signs: excessive irritability, tremors, increased muscle tone, frequent yawning, poor feeding, watery stools and sweating.
[5](see page 0) Tetanus-containing vaccine, such as Td or TT or DTP or DTP + HepB or DTP + HepB + Hib according to availability and patient's age.

6(see page 0) Use preferably Td vaccine (tetanus toxoid-diphtheria) or, if not available, TT vaccine (tetanus toxoid). [a(see page 0) b(see page 0)]

Enteric (typhoid and paratyphoid) fevers

- Clinical features(see page 168)
- Laboratory(see page 168)
- Treatment(see page 169)
- Prevention(see page 170)
- References(see page 171)

– Enteric fevers are systemic infections caused by bacteria of the genus *Salmonella.* The organisms enter the body via the gastrointestinal tract and gain access to the bloodstream via the lymphatic system.
– Typhoid fever is due to *Salmonella enterica* serotype Typhi and paratyphoid fever is due to *Salmonella enterica* serotype Paratyphi A, B or C.
– Enteric fevers are acquired by the ingestion of water or food contaminated with excreta of symptomatic or asymptomatic carriers or by direct contact (dirty hands).
– Enteric fevers are endemic on the Indian subcontinent, Southeast Asia, sub-saharan Africa and, to a lesser extent, in Latin America[1](see page 171); they mainly affect children under 15 years.

Clinical features

Typhoid fever
Clinical manifestations vary from mild to severe forms.
– The characteristic sign is prolonged, mild (38-39 °C) or high (40-41 °C) fever. The fever gradually increases during the first week, plateaus the second week then decreases between the third and fourth week.
– Fever is accompanied by non-specific signs and symptoms: gastrointestinal disturbances (abdominal pain, constipation or diarrhoea, vomiting), headache, malaise, chills, asthenia, non productive cough and/or splenomegaly.
– Other more specific signs may be present: erythematous maculopapular rash on the trunk (5 to 30% of patients), stupor and extreme fatigue, relative bradycardia (heart rate-temperature dissociation).
– Serious complications, mainly gastrointestinal (gastrointestinal haemorrhage or perforation, peritonitis) occur in 10 to 15% of cases. In pregnant women, risk of foetal complications (miscarriage, preterm delivery, intrauterine death).

Clinical diagnosis is difficult as typhoid fever resembles other infections present in regions where enteric fevers are endemic. The main differential diagnoses are: malaria(see page 123), brucellosis(see page 171), leptospirosis(see page 175), typhus(see page 180) and dengue(see page 196).

Paratyphoid fever
The symptoms of paratyphoid fever are the same as those of typhoid fever, although the illness is usually shorter and less severe.

Laboratory

– In all cases, rule out malaria in endemic regions (rapid test).
– Diagnosis: culture of *S.* Typhi or Paratyphi and antibiotic susceptibility test (blood sample the first week or stool sample from second week). For blood cultures collect 10 ml of blood.
– Other tests:
• Blood cell count: a normal or low leucocyte count can be an indication.
• Widal-Felix agglutination reaction: this test is still used in certain endemic countries as it is cheap. Threshold titer vary according to the region. It should not be performed before the second week

of illness. Two samples must be collected 10-15 days apart to detect an increase in antibodies. Its specificity and sensitivity are low.

Treatment

– Hydrate and treat fever(see page 21) (Chapter 1), which will not decrease until 4 to 5 days after starting antibiotherapy.
– Uncomplicated cases (approximately 90% of patients): outpatient antibiotherapy by oral route for 7 days.
– Severe cases (e.g. alteration of the general state, neurological disorders, oral administration not possible due to persistant vomiting, etc.) and pregnant women: inpatient antibiotherapy by parenteral route, then switch to oral route as soon as possible to complete 14 days (or 21 days) of treatment. Closely monitor patients to rapidly detect any complications (worsening abdominal pain, meteorism and abdominal guarding, dehydration, etc.).
– Choice of antibiotherapy: the choice depends on the susceptibility of the strain to antibiotics, or if antibiotic susceptibility testing is not available, on recent regional data on susceptibility of isolated strains. The appearance of multiresistant strains (resistant to first-line antibiotics: chloramphenicol, ampicilin and cotrimoxazole) has led to the frequent use of fluoroquinolones. Fluoroquinolone resistance is currently endemic in Asia[2](see page 171).

Antibiotherapy (except in pregnant or breast-feeding women)

Uncomplicated cases	
No resistance to ciprofloxacin	**ciprofloxacin** PO Children: 15 mg/kg 2 times daily (max. 1 g daily) Adults: 500 mg 2 times daily
Resistance to ciprofloxacin	**azithromycin** PO Children: 10 to 20 mg/kg once daily (max. 1 g daily) Adults: 1 g once daily or **cefixime** PO Children: 10 mg/kg 2 times daily (max. 400 mg daily) Adults: 200 mg 2 times daily
Region with data on susceptibility to these antibiotics from recent drug susceptibility tests	**chloramphenicol** PO Children > 1 year and < 13 years: 25 mg/kg 3 times daily (max. 3 g daily) Children ≥ 13 years and adults: 1 g 3 times daily
	amoxicillin PO Children: 30 mg/kg 3 times daily (max. 3 g daily) Adults: 1 g 3 times daily
	co-trimoxazole PO Children: 20 mg SMX + 4 mg TMP/kg 2 times daily (max. 1600 mg SMX + 320 mg TMP daily) Adults: 800 mg SMX + 160 mg TMP 2 times daily
Severe cases	

No resistance to ciprofloxacin or **Resistance to ciprofloxacin**	**ceftriaxone** IV[1](see page 0) Children: 50 to 100 mg/kg once daily (max. 4 g daily) Adults: 2 g once daily or 2 times daily
Region with data on susceptibility to these antibiotics from recent drug susceptibility tests	**chloramphenicol** IV Children > 1 year and < 13 years: 25 mg/kg every 8 hours (max. 3 g daily) Children ≥ 13 years and adults: 1 g every 8 hours
	ampicillin IV Children: 50 mg/kg every 6 to 8 hours (max. 3 g daily) Adults: 1 g every 6 to 8 hours

Antibiotherapy in pregnant or breast-feeding women

Preferably use **cefixime** or **azithromycin** or **ceftriaxone**. If none of them are available, use ciprofloxacin, the life-threatening risk of typhoid outweighs the risk of adverse effects.

– In case of severe typhoid fever with neurological disorders (hallucinations, altered mental status): **dexamethasone** IV: initial dose of 3 mg/kg then 1 mg/kg every 6 hours for 2 days (8 doses)

– Treatment in intensive care unit in case of gastrointestinal haemorrhage; surgery in case of gastrointestinal perforation.

Prevention

– Hygiene measures common to all diarrhoeas: handwashing; consumption of treated water (chlorinated, boiled, bottled, etc.); washing/cooking of food, etc.
– In hospitals: disinfection of excreta with 2% chlorinated solution.
– Vaccination with the **typhoid conjugate vaccine** in endemic regions[3](see page 171):(see page 171)
• Routine vaccination: a single dose of 0.5 ml at the same time as other vaccines administered at the age of 9 months or during the second year of life.
• Catch-up vaccination (same dose) up to 15 years of age: according to national recommendations.
This vaccine can be used to control typhoid outbreaks.
It does not protect against paratyphoid fever.

[1](see page 0) The solvent of ceftriaxone for IM injection contains lidocaine. Ceftriaxone reconstituted using this solvent must NEVER be administered by IV route. For IV administration, water for injection must always be used.

References

1. Crump JA, Mintz ED. Global trends in typhoid and paratyphoid fever. *Clin Infect Dis*. 2010;50(2): 241-6. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2798017/pdf/nihms154999.pdf [Accessed 15 november 2018]

2. John Wain, Rene S Hendriksen, Matthew L Mikoleit, Karen H Keddy, R Leon Ochiai. Typhoid fever. Seminar. Lancet[4]. 2015 Mar 21;385(9973):1136-45.

3. World Health Organization. Weekly epidemiological record Relevé épidémiologique hebdomadaire 30 MARCH 2018, 93th YEAR / 30 MARS 2018, 93e ANNÉE No 13, 2018, 93, 153–172. http://apps.who.int/iris/bitstream/handle/10665/272272/WER9313.pdf?ua=1 [Accessed 12 november 2018]

Brucellosis

Last updated: October 2020

- Clinical features(see page 171)
- Paraclinical investigations(see page 172)
- Treatment(see page 172)
- Prevention(see page 173)

– Brucellosis is a zoonosis that mainly affects livestock animals.
– The main routes of transmission to humans are:
• digestive, by ingestion of unpasteurized milk (or unpasteurized milk products) from an infected animal;
• cutaneous, by direct contact with infected animals or carcasses of infected animals.
– Brucellosis is caused by bacteria of the genus *Brucella,* particularly *B. melitensis* (sheep and goats), *B. abortus* (cattle), *B. suis* (pigs).
– The disease is found worldwide and mainly in rural areas.
– After primary infection relapses may occur (5 to 15% of cases, even months after end of initial treatment) or the infection may become chronic.

Clinical features

Acute form (primary infection)
– Remittent or intermittent fever (39-40 °C), associated with several signs or symptoms: chills, night sweats, joint and muscle pain, weight loss, fatigue, malaise, headache; adenopathies (particularly in children).
– May be associated with: non-specific gastrointestinal disorders, cough, hepato and/or splenomegaly, arthritis (knee), orchitis.

Diagnosis is difficult because of the broad spectrum of fluctuating and non-specific clinical manifestations. In patients with unexplained fever, brucellosis should be considered when risk factors are present: consumption of unpasteurized milk products; exposure to livestock (e.g. livestock farmers, veterinarians, butchers, slaughterhouse workers).

4 https://www.ncbi.nlm.nih.gov/pubmed/25458731

Localised form
Primary infection may progress to localised infection (even several months or years later), mainly:
– osteoarticular: sacroiliac joint and often particularly lower limbs joints; spine (intervertebral disk infection, vertebral osteomyelitis)
– genito-urinary: orchitis, epididymitis
– pulmonary: bronchitis, pneumonia, pleurisy
– neurological : meningitis, encephalitis, polyneuritis

Paraclinical investigations

Laboratory
− Blood culture is the gold standard for diagnosis. It is positive only in the acute phase. The bacteria grow slowly (7 to 21 days).
– Serological tests (Rose Bengal, Wright agglutination test, indirect immunofluorescence, ELISA, etc.) provide presumptive diagnoses.
– In the event of neurological signs or meningitis, lumbar puncture shows clear cerebrospinal fluid (CSF) that may contain high white blood cell count; high protein concentration in CSF; low CSF glucose.
– Rule out malaria in endemic regions (rapid test).
– Exclude tuberculosis if cough > 2 weeks (sputum smear microscopy).

Radiography
− Joint pain (hips, knees, ankles, vertebrae, sacroiliac joint): small erosions or destruction or joint space narrowing. Often involves the spine, particularly the lumbar spine, causing spondylodiskitis.
− Pulmonary signs: chest x-ray often normal. There may be consolidation, nodules, lymphadenopathy, or pleural effusion.

Treatment

Check national recommendations on antibiotic therapy. For information:

Children under 8 years	co-trimoxazole + rifampicin or co-trimoxazole + gentamicin
Children 8 years and over	doxycycline + rifampicin or doxycycline + gentamicin
Adults	doxycycline + rifampicin or doxycycline + streptomycin or gentamicin
Pregnant/breast-feeding women	rifampicin

co-trimoxazole PO for 6 weeks
Children < 8 years: 20 mg SMX + 4 mg TMP/kg 2 times daily

doxycycline PO for 6 weeks
Children ≥ 8 years: 1 to 2 mg/kg 2 times daily
Adults: 100 mg 2 times daily

rifampicin PO for 6 weeks
Children: 15 to 20 mg/kg once daily (max. 600 mg daily)
Adults: 600 to 900 mg once daily

gentamicin IM for 2 weeks
Children and adults: 5 mg/kg once daily

streptomycin IM for 2 weeks
Adults: 1 g once daily

For localised forms of the infection, same treatment but for a period of 6 weeks to 4 months depending on the focus.

Prevention

– Washing of hands and clothing if in contact with animals.
– Boil milk, avoid ingestion of unpasteurized milk products, cook offal thoroughly.

Plague

- Clinical features and progress(see page 173)
- Laboratory(see page 174)
- Management and treatment(see page 174)
  - Treatment of suspected or confirmed cases(see page 174)
  - Chemoprophylaxis of contacts(see page 175)
- Prevention(see page 175)

– A zoonosis caused by the Gram-negative bacillus *Yersinia pestis* that mainly affects wild and domestic rodents.
– Plague is transmitted to man by the bite of an infected flea vector or through a break in the skin by contact with a rodent. Human-to-human transmission occurs through the bites of human fleas, or, in the case of pneumonic plague, by inhaling infected droplets expelled by coughing.
– Vast foci of infection remain in Asia, Africa, Madagascar, and in North and South America[1](see page 0).

Clinical features and progress

There are 3 main clinical forms:

– *Bubonic plague* is the most common form: high fever, chills, headache, associated with one (or more) very painful lymph node, usually inguinal (bubo). Frequent gastrointestinal signs: abdominal pain, vomiting, diarrhoea, etc. The mortality rate in untreated patients is approximately 50% as a result of septicaemia.

– *Septicaemic plague* is a complication of untreated bubonic plague and is a fulminant illness.

– *Pneumonic plague* is a very contagious form: high fever, chills, headache, myalgia associated with paroxysmal coughing, blood stained sputum and respiratory distress. This form progresses rapidly, and

is fatal unless treated. It occurs either as a complication of bubonic plague or as the result of a primary infection.

Occasionally, the disease can take the form of *meningitic plague*.

Laboratory

– Isolation of *Y. pestis* (direct examination and culture) from lymph node aspirate, blood, sputum, cerebrospinal fluid, depending on the form involved.
– Serodiagnosis: ELISA reads positive soon after the onset of the illness.
– Transportation of the samples requires a cold chain (failing that, the temperature must be kept below 30 °C).

Management and treatment

– When plague is suspected: take samples for cultures and antibiotic sensitivity testing and then treat immediately without waiting for the diagnosis to be confirmed. Inform the health authorities as soon as the diagnosis has been confirmed.

– Isolation:
• Patients suffering from bubonic plague do not have to be isolated. Treat the patient and his/her bedding and clothing with an insecticide (e.g. **permethrin 0.5%** powder; see Pediculosis(see page 95), Chapter 4). Observe standard precautions (handwashing, gowns, gloves, etc.).
• Patients with primary or secondary pneumonic plague must be strictly isolated. Their bedding, clothing, sputum and excreta must be disinfected with a chlorinated solution. Observe standard precautions (handwashing, gowns, gloves, etc.) and both the patient and carers should wear facemasks for 48 hours after beginning appropriate antibiotherapy .

Treatment of suspected or confirmed cases

If treatment is begun early, recovery is rapid and complete. Penicillins, cephalosporins and macrolides should not be used.
Aminoglycosides, tetracyclines, chloramphenicol and sulphonamides are effective. Follow national recommendations. For information:

streptomycin IM for 10 days
Children: 15 mg/kg every 12 hours (max. 2 g daily)
Adults: 1 g every 12 hours

gentamicin IM or IV for 10 days
Children: 2.5 mg/kg every 8 hours
Adults: 5 mg/kg once daily

doxycycline PO for 10 days
Children 8 years and over: 2 mg/kg 2 times daily (max. 200 mg daily)
Adults: 100 mg 2 times daily or 200 mg once daily

chloramphenicol PO or IV for 10 days
Children 1 year to 12 years: 25 mg/kg every 8 hours
Children 13 years and over and adults: 1 g every 8 hours

Indications	First choice	Alternative
Bubonic plague	doxycycline	chloramphenicol or streptomycin
Pneumonic plague	streptomycin	–

Indications	First choice	Alternative
Septicaemic plague	streptomycin	chloramphenicol
Meningitic plague	chloramphenicol	–
Pregnant or breast-feeding women	gentamicin	–

Chemoprophylaxis of contacts

In the event of contact with a pneumonic plague patient or direct contact with infected body fluids or tissues and within one week after the end of exposure:
doxycycline PO for 7 days
Children 8 years and over: 2 mg/kg 2 times daily (max. 200 mg daily)
Adults: 100 mg 2 times daily or 200 mg once daily
or
ciprofloxacin PO for 7 days
Children : 20 mg/kg 2 times daily (max. 1 g daily)
Adults: 500 mg 2 times daily

Prevention

– Flea vector control is essential to controlling an epidemic.
– Long-term prevention: environmental sanitation and control of rodent reservoir.
– Vaccination against plague is indicated for laboratory technicians handling rodents and is not as a method for controlling an epidemic.

1(see page 0) For more information on distribution of natural foci: http://www.who.int/csr/disease/plague/Plague-map-2016.pdf

Leptospirosis

- Clinical features(see page 176)
- Laboratory(see page 176)
- Treatment(see page 176)
- Prevention(see page 177)
- References(see page 177)

– Leptospirosis is a zoonosis that affects many domestic and wild animals, mainly rodents (particularly rats) but also dogs and cattle, etc.
– It is transmitted to humans by contact through skin lesions or mucous membranes (e.g. eyes, mouth) with:
• freshwater or moist soil contaminated with urine of an infected animal (indirect contact);
• urine, blood and other body fluids or tissues of an infected animal (direct contact).
– It is caused by bacteria of the genus *Leptospira*.
– Leptospirosis occurs worldwide, particularly in tropical and subtropical regions. There are often outbreaks after heavy rainfall or flooding.

Clinical features

Approximately 90% of cases are a moderate form of the disease with a favourable outcome. 5 to 15% of cases present a severe form with multiple organ dysfunction and a high mortality rate.

Moderate form
– Acute phase (septicaemic)
• Sudden onset of high fever with chills, headache, muscle pain (especially calf pain), photophobia, ocular pain, bilateral conjunctival haemorrhage very frequent.
• May be associated with: gastrointestinal symptoms (anorexia, abdominal pain, nausea, vomiting), non-productive cough, adenopathies, hepatomegaly.
– Immune phase: the signs of the acute phase regress after 5 to 7 days then reappear for a few days usually in a milder form (milder fever, less severe myalgia) then disappear.

Severe or ictero-haemorrhagic form
The onset is the same but a few days later the symptoms worsen: renal disorders (oliguria or polyuria), hepatic disorder (jaundice), widespread haemorrhages (purpura, ecchymoses, epistaxis, haemoptysis, etc.), pulmonary signs (chest pain) or cardiac signs (myocarditis, pericarditis).

Diagnosis is difficult because of the broad spectrum of clinical manifestations. Patients that present the following should be considered as suspected cases of leptospirosis:
• fever + 2 of the following signs: myalgia, calf pain, conjunctival haemorrhage, chills, abdominal pain, headache, jaundice or oliguria
and
• one or more risk factors for infection: contact with potentially contaminated surface freshwater (e.g. swimming, fishing, rice fields, flooding) or occupations at risk (e.g. crop and livestock farmers, veterinarians, butchers, slaughterhouse workers, miners).

Laboratory

In all cases, rule out malaria in endemic regions (rapid test).

Diagnosis
Laboratory diagnosis is difficult to obtain; it is only performed in the event of strongly suspected leptospirosis (on a blood sample):
– Serology:
• between 0 and 7 days: real-time PCR (early diagnosis);
• after 7 days: microscopic agglutination test (MAT); IgM ELISA test provides presumptive diagnosis
• after 10 days: MAT and IgM ELISA tests only.
– Culture: limited use (bacteria grow slowly, specific culture medium).

Other investigations (if available)
– Complete blood count: possible polymorphonuclear leukocytosis, thrombocytopenia or anaemia.
– Urine: proteinuria, leukocyturia, possible microscopic haematuria.

Treatment

According to the WHO recommendations, do not wait for diagnostic test results before starting antibiotherapy based on clinical and epidemiological suspicions[1](see page 177),[2](see page 177).

Moderate form (outpatient treatment)

– Rest and treatment of fever(see page 21): paracetamol PO (Chapter 1).
– Acetylsalicylic acid (aspirin) is contra-indicated (risk of haemorrhage).
– Antibiotherapy:
doxycycline PO (except in children under 8 years and pregnant or lactating women) for 7 days

Children 8 years and over: 1 to 2 mg/kg 2 times daily (max. 100 mg per dose)
Adults: 100 mg 2 times daily
or
azithromycin PO for 3 days
Children: 10 mg/kg on D1 (max. 500 mg) then 5 mg/kg once daily on D2 and D3 (max. 250 mg daily)
Adults: 1 g on D1 then 500 mg once daily on D2 and D3
or, if not available,
amoxicillin PO for 7 days
Children: 25 mg/kg 2 times daily
Adults: 1 g 2 times daily

Antibiotherapy can trigger a Jarisch-Herxheimer reaction (high fever, chills, fall in blood pressure and sometimes shock). It is recommended to monitor the patient for 2 hours after the first dose of antibiotic for occurrence and management of severe Jarisch-Herxheimer reaction (symptomatic treatment of shock).

Severe form (inpatient treatment)

– Specific management according to organs affected.
– Antibiotherapy:
ceftriaxone IV for 7 days
Children: 80 to 100 mg/kg once daily (max. 2 g daily)
Adults: 2 g once daily

Prevention

– Avoid bathing in endemic areas.
– Disinfect laundry and objects soiled by urine.
– Vaccination and protection clothing (only for professionals at risk of exposure).

For IV administration of ceftriaxone, dilute with water for injection only.

References

1. World Health Organization. Human leptospirosis : guidance for diagnosis, surveillance and control. Geneva, 2003. http://apps.who.int/iris/bitstream/handle/10665/42667/WHO_CDS_CSR_EPH_2002.23.pdf?sequence=1&isAllowed=y [Accessed 2 october 2018]

2. Cyrille Goarant. Leptospirosis: risk factors and management challenges in developing countries. Research and Reports in Tropical Medicine 2016:7 49–62. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6028063/pdf/rrtm-7-049.pdf [Accessed 2 october 2018]

Relapsing fever (borreliosis)

- Louse-borne relapsing fever (LBRF)(see page 178)
- Tick-borne relapsing fever (TBRF)(see page 179)

Relapsing fever (FR) is caused by spirochetes of the genus *Borrelia*, transmitted to humans by arthropod vectors.

Louse-borne relapsing fever (LBRF)

- Clinical features(see page 178)
- Laboratory(see page 178)
- Treatment(see page 179)

LBRF is caused by *Borrelia recurrentis*. It occurs in epidemic waves when conditions favourable to the transmission of body lice are met: cold climate/season, overcrowding and very poor sanitation (e.g. refugee camps, prisons). Endemic foci of LBRF are mainly the Sudan and the Horn of Africa (especially Ethiopia). LBRF can be associated with louse-borne typhus (see Eruptive rickettsioses(see page 180)). The mortality rate for untreated LBRF ranges from 15 to 40%.

Clinical features

– Relapsing fever is characterized by febrile episodes separated by afebrile periods of approximately 7 days (4 to 14 days).

– The initial febrile episode lasts up to 6 days:
• Sudden onset of high fever (axillary temperature > 39 °C), severe headache and asthenia, diffuse pain (muscle, joint, back pain), often associated with gastrointestinal disturbances (anorexia, abdominal pain, vomiting, diarrhoea).
• Splenomegaly is common; bleeding signs (e.g. petechiae, subconjunctival haemorrhage, epistaxis, bleeding gums), jaundice or neurological symptoms may be observed.
• The febrile episode terminates in a crisis with an elevation in temperature, heart rate and blood pressure, followed by a fall in temperature and blood pressure, which may last for several hours.

– Following the initial febrile episode, the cycle usually reccurs; each episode is less severe than the previous one and the patient develops temporary immunity.

– Complications:
• collapse during defervescence, myocarditis, cerebral haemorrhage;
• during pregnancy: abortion, preterm delivery, in utero foetal death, neonatal death.

In practice, in an applicable epidemiological setting (see above), a suspect case of LBRF is, according to the WHO, *a patient with high fever and two of the following symptoms: severe joint pain, chills, jaundice or signs of bleeding (nose or other bleeding) or a patient with high fever who is responding poorly to antimalarial drugs*. Clothing should be checked for the presence of body lice and nits.

Laboratory

The diagnosis is confirmed by detection of *Borrelia* in thick or thin blood films (Giemsa stain). Blood samples must be collected during febrile periods. Spirochetes are not found in the peripheral blood during afebrile periods. In addition, the number of circulating spirochetes tends to decrease with each febrile episode.

Treatment

– Antibiotherapy (suspect or confirmed cases and close contacts):
doxycycline PO[1](see page 0)
Children under 8 years: 4 mg/kg (max. 100 mg) single dose
Children 8 years and over: 100 mg single dose
Adults: 200 mg single dose
or
erythromycin PO
Children ≤ 5 years: 250 mg single dose
Children > 5 years and adults: 500 mg single dose

– Treatment of pain and fever(see page 21) (paracetamol PO) and prevention or treatment of dehydration in the event of associated diarrhoea.

– Elimination of body lice is essential in control of epidemics (see Pediculosis(see page 95), Chapter 4).

[1](see page 0) Doxycycline is usually contra-indicated in children under 8 years and pregnant or lactating women. However, if erythromycin is not available, it may be used for the treatment of LBRF, the administration of a single dose should not cause any adverse effects.

Tick-borne relapsing fever (TBRF)

- Clinical features(see page 179)
- Laboratory(see page 179)
- Treatment(see page 180)

TBRFs are caused by different *Borrelia* species. They are endemic in temperate and warm regions of the word, especially in Africa (Tanzania, DRC, Senegal, Mauritania, Mali, the Horn of Africa) and mainly in rural areas. TBRF is a major cause of morbidity and mortality in children and pregnant women. The mortality rate for untreated TBRF ranges from 2 to 15%.

Clinical features

The clinical manifestations and complications of TBRF are similar to those of LBRF but neurological symptoms (particularly, cranial nerve palsies and lymphocytic meningitis) are more frequent than in LBRF and the number of relapses is higher.

The clinical diagnosis is difficult, especially during the first episode: cases occur sporadically rather than in outbreaks; the tick bite is painless and usually unnoticed by the patient; symptoms are very similar to those of malaria, typhoid fever, leptospirosis, certain arbovirosis (yellow fever, dengue) or rickettsiosis, and meningitis.

Laboratory

– As for LBRF, the diagnosis is confirmed by detection of *Borrelia* in the patient's blood.
– Repeat the examination if the first smear is negative despite strong clinical suspicion.

Treatment

– Antibiotherapy:
doxycycline PO (except in children under 8 years and pregnant or lactating women)
Children 8 years and over: 50 mg 2 times daily or 100 mg once daily for 7 days
Adults: 100 mg 2 times daily or 200 mg once daily for 7 days
or
erythromycin PO
Children under 8 years: 25 mg/kg 2 times daily for 7 days
Pregnant or breastfeeding women: 1 g 2 times daily for 7 days

– Treatment of pain and fever(see page 21) (paracetamol PO) and prevention or treatment of dehydration in the event of associated diarrhoea.

⚠ Antibiotic therapy can trigger a Jarisch-Herxheimer reaction with high fever, chills, fall in blood pressure and sometimes shock. It is recommended to monitor the patient for 2 hours after the first dose of antibiotic, for occurrence and management of severe Jarisch-Herxheimer reaction (symptomatic treatment of shock). Jarisch-Herxheimer reaction appears to occur more frequently in LBRF than in TBRF.

Eruptive rickettsioses

- Clinical features(see page 180)
- Laboratory(see page 181)
- Treatment(see page 182)
- Prevention(see page 182)

Eruptive fevers caused by bacteria of the genus *Rickettsia* and transmitted to man by an arthropod vector. Three main groups are distinguished: typhus group, spotted fever group and scrub typhus group.

Clinical features

– Common to all forms:
• Sudden onset of fever (temperature of over 39 °C) with severe headache and myalgias.
• 3 to 5 days later; onset of generalised cutaneous eruption (see below).
• Hypotension; non-dissociated rapid heart rate (variable).
• Typhoid state: prostration, obnubilation, confusion and extreme asthenia, particularly marked in typhus forms.
• Inoculation eschar: painless, black crusted lesion surrounded by a erythematous halo at the site of the bite. Always check for this significant sign.
• Non-cutaneous signs vary from one form to another, and are atypical and variable (see below).

Group	**Typhus**		**Spotted fever**			**Scrub typhus**
Form	Epidemic typhus	Murine typhus	Mediterranean spotted fever	Rocky Mountain spotted fever	Other Old-World tick-borne fevers	Scrub typhus

Group	Typhus		Spotted fever			Scrub typhus
Pathogen	*R. prowasekii*	*R. typhi*	*R. conorii*	*R. rickettsii*	*R. sibirica, R. australis*	*O. tsutsugamushi*
Vector	body lice	rat fleas	ticks	ticks	ticks	mites
Reservoir	**man**	rats	dogs	rodents	rodents, dogs, etc.	rodents
Occurence	**epidemic**	endemic	endemic	endemic	endemic	sporadic
Geographical distribution	worldwide, conflicts; main sites: Burundi/ Rwanda, Ethiopia	worldwide	around the mediterranean, Sub-Saharan Africa	North America, Central America, Columbia, Brazil	Southern Africa, Australia, Siberia	Far East, India, South Pacific Area
Rash	maculopapular	maculopapular	maculopapular	purpural	maculopapular	macular
Eschar	0	0	**black necrotic area**	rare	**black necrotic area**	**black necrotic area**
Typhoid state	+++	+++	+/-	+/-	+/-	+++
Extra-cutaneous signs	cough, myalgia, meningeal signs	gastrointestinal signs	meningeal signs	gastrointestinal and neurological signs, hypotension	variables	meningeal signs
Case fatality (%)	30 (without treatment)	5	2	5	1	0-30

– Complications can be severe, and sometimes fatal: encephalitis, myocarditis, hepatitis, acute renal failure, haemorrhage etc.

Laboratory

Detection of specific IgM of each group by indirect immunofluorescence. The diagnosis is confirmed by 2 serological tests at an interval of 10 days. In practice, clinical signs and the epidemiological context are sufficient to suggest the diagnosis and start treatment.

Treatment

– Symptomatic treatment:
• Hydration (PO or IV if the patient is unable to drink).
• Fever(see page 21): paracetamol PO (Chapter 1). Acetylsalicylic acid (aspirin) is contra-indicated due to the risk of haemorrhage.

– Antibiotic therapy[1](see page 0) for 5 to 7 days or until 3 days after the fever has disappeared:
doxycycline PO (except in children under 8 years and pregnant or lactating women)
Children 8 years and over: 50 mg 2 times daily or 100 mg once daily
Adult: 100 mg 2 times daily or 200 mg once daily

– In a context of *epidemic typhus*, **doxycycline** PO is the choice treatment, but there is a risk of recurrence:
Children under 8 years: 4 mg/kg (max. 100 mg) single dose
Children 8 years and over: 100 mg single dose
Adults: 200 mg single dose

Note: doxycycline is usually contraindicated in children under 8 years and pregnant or lactating women. However, the administration of a single dose should not, in theory, provoke adverse effects. Check national recommendations.

Prevention

– Epidemic typhus: control of body lice (see Pediculosis(see page 95), Chapter 4).
– Murine typhus: control of fleas and then rats.
– Spotted fevers: avoid tick bites by wearing clothing and using repellents.
– Scrub typhus: use of repellents, chemoprophylaxis with **doxycycline** PO (200 mg once weekly in adults).

[1](see page 0) Unlike borrelioses, antibiotic treatment of rickettsioses does not provoke a Jarisch-Herxheimer reaction. However, the geographical distribution of borrelioses and rickettsioses may overlap, and thus a reaction may occur due to a possible co-infection (see Borreliosis(see page 178)).

Chapter 8: Viral diseases

- Measles(see page 183)
- Poliomyelitis(see page 186)
- Rabies(see page 187)
- Viral hepatitis(see page 192)
- Dengue(see page 196)
- Viral haemorrhagic fevers(see page 203)
- HIV infection and AIDS(see page 206)

Measles

- Clinical features(see page 183)
- Complications(see page 184)
- Case management(see page 184)
- Treatment(see page 184)
    - Supportive and preventive treatment(see page 184)
    - Treatment of complications(see page 185)
- Prevention(see page 185)

Measles is a highly contagious acute viral infection, transmitted by the airborne route (inhalation of respiratory droplets spread by infected individuals). The disease mainly affects children under 5 years of age and can be prevented by immunization.
For more information, refer to the guide Management of a measles epidemic, MSF.

Clinical features

The average incubation period is 10 days.

Prodromal or catarrhal phase (2 to 4 days)
– High fever (39-40 °C) with cough, coryza (nasal discharge) and/or conjunctivitis (red and watery eyes).
– Koplik's spots: tiny bluish-white spots on an erythematous base, found on the inside of the cheek. This sign is specific of measles infection, but may be absent at the time of examination. Observation of Koplik's spots is not required for diagnosing measles.

Eruptive phase (4 to 6 days)
– On average 3 days after the onset of symptoms: eruption of erythematous, non- pruritic maculopapules, which blanch with pressure. The rash begins on the forehead then spreads downward to the face, neck, trunk (second day), abdomen and lower limbs (third and fourth day).
– As the rash progresses, prodromal symptoms subside. In the absence of complications, the fever disappears once the rash reaches the feet.
– The rash fades around the fifth day in the same order that it appeared (from the head to the feet).

The eruptive phase is followed by skin desquamation during 1 to 2 weeks, very pronounced on pigmented skin (the skin develops a striped appearance).

In practice, a patient presenting with fever and erythematous maculopapular rash and at least one of the following signs: cough or runny nose or conjunctivitis, is a clinical case of measles.

Complications

Most measles cases experience at least one complication:
– Respiratory and ENT: pneumonia, otitis media, laryngotracheobronchitis
– Ocular: purulent conjunctivitis, keratitis, xerophthalmia (risk of blindness)
– Gastrointestinal: diarrhoea with or without dehydration, benign or severe stomatitis
– Neurological: febrile seizures; rarely, encephalitis
– Acute malnutrition, provoked or aggravated by measles (post-measles period)

Pneumonia and dehydration are the most common immediate causes of death.

Case management

– Admit as inpatient children with at least one major complication:
• Inability to eat/drink/suck, or vomiting
• Altered consciousness or seizures
• Dehydration
• Severe pneumonia (pneumonia with respiratory distress or cyanosis or $SpO_2 < 90\%$)
• Acute laryngotracheobronchitis (croup) 1(see page 0)
• Corneal lesions (pain, photophobia, erosion or opacity)
• Severe oral lesions that prevent eating
• Acute malnutrition

– Treat as outpatient children with no major complications, no complications or minor complications:
• Pneumonia without severe signs
• Acute otitis media
• Purulent conjunctivitis (no corneal lesions)
• Diarrhoea without dehydration
• Oral candidiasis that does not interfere with eating
If in doubt, keep the child under observation for a few hours.

– Isolation
• Isolation of hospitalized patients
• Measles cases treated as outpatients should be kept at home during this period.

Treatment

Supportive and preventive treatment

– Treat fever: paracetamol (Fever(see page 21), Chapter 1).
– Make the child drink (high risk of dehydration).
– Give smaller, more frequent meals or breastfeed more frequently (every 2 to 3 hours).
– Clear the nasopharynx (nose-blowing or nasal lavages) to prevent secondary respiratory infection and improve the child's comfort.
– Clean the eyes with clean water 2 times daily and administer retinol on D1 and D2 (see Xerophthalmia(see page 114), Chapter 5) to prevent ocular complications.
– In children under 5 years: amoxicillin PO for 5 days as a preventive measure (reduction of respiratory and ocular infections).
– In the event of watery diarrhoea without dehydration: oral rehydration according to WHO *Plan A* (see Dehydration(see page 34), Chapter 1).
– Insert a nasogastric tube for a few days if oral lesions prevent the child from drinking.

Treatment of complications

	Treatment of complications
Severe pneumonia	**ceftriaxone** IV or IM + **cloxacillin** IV then change to **amoxicillin/clavulanic acid** PO (see Chapter 2(see page 65)) + **oxygen** if cyanosis or SpO_2 < 90% + **salbutamol** if expiratory wheezing and sibilant rales on auscultation In all cases, close monitoring.
Pneumonia without severe signs	**amoxicillin** PO for 5 days
Croup	Inpatient monitoring (risk of worsening). Keep the child calm. Agitation and crying exacerbate the symptoms. For severe croup: **dexamethasone** IM: 0.6 mg/kg single dose + nebulized **epinephrine** (**adrenaline**, 1 mg/ml ampoule): 0.5 ml/kg (max. 5 ml) + **oxygen** if cyanosis or SpO_2 < 90% Intensive monitoring until symptoms resolve.
Acute otitis media	See Otitis(see page 57), Chapter 2.
Dehydration	Per oral route or IV depending on the degree of dehydration.
Oral candidiasis	See Stomatitis(see page 87), Chapter 3.
Purulent conjunctivitis	See Conjunctivitis(see page 116), Chapter 5.
Keratitis/keratoconjunctivitis	**tetracycline 1% eye ointment** 2 times daily for 7 days + **retinol** PO one dose on D1, D2 and D8 (see Xerophthalmia(see page 114), Chapter 5) + eye protection and pain management (see Pain(see page 23), Chapter 1). No topical corticosteroids.
Xerophthalmia	See Xerophthalmia(see page 114), Chapter 5.
Febrile seizures	See Seizures, Chapter 1.

Prevention

– No chemoprophylaxis for contacts.
– Vaccination:
• Between 9 and 12 months: one dose of 0.5 ml. The WHO recommends a second dose between 15 and 18 months. Respect an interval of at least 4 weeks between doses.
• Where there is high risk of infection (overcrowding, epidemics, malnutrition, infants born to a mother with HIV infection, etc.), administer a supplementary dose from 6 months of age then continue vaccination schedule.

• Children under 15 years who have missed either one or both doses of routine vaccination should be vaccinated when they come in contact with health services. Check national recommendations.

1 (see page 0) Symptoms (hoarse crying or voice, difficulty breathing, a high-pitched inspiratory wheeze [inspiratory stridor], characteristic "barking" cough) are caused by inflammation and narrowing of the larynx. Croup is considered benign or “moderate” if the stridor occurs when the child is agitated or crying, but disappears when the child is calm. The child should be monitored during this period, however, because his general and respiratory status can deteriorate rapidly. Croup is severe when the stridor persists at rest or is associated with signs of respiratory distress.

Poliomyelitis

- Clinical features (see page 186)
- Laboratory (see page 186)
- Treatment (see page 186)
- Patients with acute flaccid paralysis (AFP) (see page 187)
- Prevention (see page 187)

– Poliomyelitis is an acute viral infection due to a poliovirus (serotypes 1, 2 and 3). Human-to-human transmission is direct (faecal-oral) or indirect (ingestion of food and water contaminated by stool). Humans are the only reservoir of the virus. In principle the disease can be eradicated by mass vaccination.

– In endemic areas, epidemics usually affect children under 5 years of age.
In non- endemic areas, where vaccination coverage is low, young adults are most commonly affected.

Clinical features

– In more than 90% of cases, infection is asymptomatic.

– *Non-paralytic form*: a non-specific febrile illness with muscle pain, headache, vomiting, backache; no neurological involvement.
As spontaneous recovery usually occurs within 10 days, diagnosis is rarely made outside epidemic contexts.

– *Paralytic form*: in less than 1% of cases, after the non-specific signs, the patient develops rapid onset (from the morning to the evening) asymmetrical acute flaccid paralysis, predominantly of the lower limbs, with ascending progression. The muscles become soft with diminished reflexes. Sensation is maintained. The disease is life threatening if paralysis involves the respiratory muscles or muscles of swallowing. Initial urinary retention is common. Gastrointestinal disturbances (nausea, vomiting, diarrhoea), muscle pain and meningeal symptoms may also occur.

Laboratory

Look for the polio virus in stool samples. The virus is excreted for one month after infection, but only intermittently; therefore, 2 samples must be collected with an interval of 48 hours.

Treatment

– Hospitalise patients with the paralytic form: rest, prevent bed sores in bedridden patients, give analgesics (do not give IM injections to patients in the febrile phase), ventilate patients with respiratory

paralysis.
– Physiotherapy once the lesions are stable to prevent muscle atrophy and contractures.
– Care for sequelae: physiotherapy, surgery and prosthetics.

Patients with acute flaccid paralysis (AFP)

– Consider all patients with AFP as suspected cases of poliomyelitis.
– Confirm the diagnosis by isolating the virus: send the 2 stool samples to a reference laboratory, with a clinical description of the patient. The stool samples must be stored and transported between 0 °C and 8 °C.
– While waiting for laboratory confirmation, vaccinate all children under 5 years of age living in the area (from the same village or neighbouring villages), irrespective of their vaccination status.
– Once the case is confirmed, organize a mass vaccination campaign: the area and the age group are determined as a function of epidemiological data.
– Surveillance: for each case of AFP there are between 100 and 200 subclinical cases. Therefore, active surveillance to detect new cases is essential for epidemic control.

Prevention

– 2 types of vaccines exist:
• a trivalent injectable inactivated poliovirus vaccine (IPV),
• a bivalent oral live attenuated poliovirus vaccine (bOPV).

– Vaccination schedule: depends on the epidemiology of the virus.
Protocols vary according to the country, follow national recommendations. For information, the WHO recommends:

Schedule	Primary vaccination	
	Endemic or at risk zones*	**Other zones**
Birth	1 dose bOPV**	–
6 weeks	1 dose bOPV	1 dose bOPV
10 weeks	1 dose bOPV	1 dose bOPV
14 weeks	1 dose bOPV + 1 dose IPV	1 dose bOPV + 1 dose IPV

* Countries where poliomyelitis is endemic or zones at high risk of importation and subsequent spread of the virus.

** The 1st dose of bOPV is administered at birth, or as soon as possible, to optimise seroconversion rates after subsequent doses and induce mucosal protection.

In children who start routine vaccination late (after the age of 3 months), the dose of IPV is administered together with the 1st dose of bOPV, followed by 2 doses of bOPV alone administered 4 weeks apart.

There is also an 'IPV only' schedule: 3 doses administered 4 weeks apart (e.g. at 6, 10 and 14 weeks) and a booster dose at least 6 months later.
IPV should eventually completely replace bOPV.

Rabies

- Clinical features(see page 188)
- Post-exposure prophylaxis(see page 188)
  - Definitions of exposure categories (WHO)(see page 188)
  - Treatment of the wound(see page 189)
  - Passive and active immunisation(see page 189)
  - Other measures(see page 190)
- Prevention(see page 191)
- References(see page 192)

– Rabies is a viral infection of wild and domestic mammals, transmitted to humans by the saliva of infected animals through bites, scratches or licks on broken skin or mucous membranes.
– In endemic areas (Africa and Asia), 99% of cases are due to dog bites and 40% of cases are children under 15 years of age.[1](see page 192)
– Before symptoms develop, rabies can effectively be prevented by post-exposure prophylaxis.
– Once symptoms develop, rabies is fatal. There is no curative treatment; care is palliative.

Clinical features

– The incubation period averages 20 to 90 days from exposure (75% of patients), but can be shorter (in severe exposure, e.g. bites to face, head and hands; multiple bites), or longer (20% of patients develop symptoms between 90 days and 1 year, and 5% more than 1 year after exposure).

– Prodromal phase: itching or paraesthesiae or neuropathic pain around the site of exposure, and non-specific symptoms (fever, malaise, etc.).

– Neurologic phase:
• Encephalitic form (furious form): psychomotor agitation or hydrophobia (throat spasms and panic, triggered by attempting to drink or sight/sound/touch of water) and aerophobia (similar response to a draft of air); sometimes seizures. The patient is calm and lucid between episodes. Infection evolves to paralysis and coma.
• Paralytic form (less common, 20% of cases): progressive ascending paralysis resembling Guillain-Barré syndrome; evolves to coma.

Diagnosis is often difficult: there may be no history of scratch or bite (exposure through licking) or wounds may have healed; a reliable history may be difficult to obtain.

Post-exposure prophylaxis

Definitions of exposure categories (WHO)

Category I	Contact with animal, or licks on intact skin	**No exposure**
Category II	Nibbles on exposed skin Minor bite(s) or scratch(es) without bleeding	**Minor exposure**
Category III	Transdermal bite(s) or scratch(es) Licks on broken skin Contamination of mucous membranes by animal's saliva (licks) Direct contact with bats[1](see page 0)	**Severe exposure**

Post-exposure prophylaxis is carried out for Category II and III exposures.

Treatment of the wound

In all cases
Prolonged cleansing of the wound or contact site for 15 minutes to eliminate the virus, as soon as possible after exposure, is of critical importance. For skin: use soap, rinse copiously with running water, remove all foreign material; application of a disinfectant (povidone iodine 10% or other) is an additional precaution which does not take the place of thorough wound washing. For mucous membranes (eye, mouth, etc.): rinse thoroughly with water or 0.9% sodium chloride. Local cleansing is indicated even if the patient presents late.

According to condition/type of wound
In order to avoid inoculating virus deeper into the tissues, wounds are either not sutured at all (e.g. superficial, non-mutilating or puncture wounds), or are left open and re-evaluated in 48-72 hours, with a view to possible closure. Highly contaminated wounds, or wounds that may compromise function, require surgical management (exploration, removal of foreign material, excision of necrotic tissue, copious irrigation with sterile 0.9% sodium chloride or Ringer lactate, with local or general anaesthesia). When suturing is indicated (face), rabies immunoglobulin should be administered several hours before wound closure (see below). Infected wounds are not sutured and reassessed daily.

Passive and active immunisation

Given the duration of incubation, administration of vaccine/immunoglobulin is always a priority, even for patients exposed several months previously.

Anti-rabies serotherapy
Rabies immunoglobulin is indicated after:
– Category III exposures (except in patients who have received a full course of pre-exposure prophylaxis against rabies, see Prevention(see page 191));
– Category II and III exposures in immunocompromised patients[2](see page 0) (even in patients who have received a full course of pre-exposure prophylaxis against rabies).

It is intended to neutralize virus in the exposure site. It is given as a single dose on D0, with the first dose of rabies vaccine.
human rabies immunoglobulin:
Children and adults: 20 IU/kg
or
highly purified rabies immunoglobulin F(ab')2 fragments:
Children and adults: 40 IU/kg

Infiltrate rabies immunoglobulin into and around the previously washed wound(s). Ensure it is not injected into a blood vessel (risk of shock).
For finger wounds, infiltrate very cautiously to avoid increased pressure in the tissue compartment (compartment syndrome).
In the event of multiple wounds, dilute the dose 2- to 3-fold with sterile 0.9% sodium chloride to obtain a sufficient quantity to infiltrate all the sites exposed.
Infiltrate rabies immunoglobulin into the wound even if it has already healed.
For mucosal exposures with no wound, rinse with rabies immunoglobulin diluted in sterile 0.9% sodium chloride.

Monitor the patient during and after the injection (low risk of anaphylactic reaction).

If rabies immunoglobulin is not available on D0, the first dose of rabies vaccine is administered alone. Administer rabies immunoglobulin as soon as possible between D0 and D7; from D8, it is not necessary to administer rabies immunoglobulin as vaccine-induced antibodies begin to appear.[1](see page 192)

Post-exposure rabies prophylaxis

A complete prophylaxis series is indicated for Category II and III exposures. It should be started on D0 and continued to completion if the risk of rabies has not been excluded[3](see page 0). Several different types of rabies vaccines prepared from cell cultures (CCEEV) exist. These vaccines must replace nerve tissue vaccines (NTV).

Prophylaxis schedules may vary from country to country, check national recommendations. The patient must be administered the full course of doses indicated.

Main post-exposure prophylaxis regimens[1](see page 192)

Date	**No pre-exposure prophylaxis** or **unknown prophylaxis status** or **incomplete pre-exposure prophylaxis** or **complete pre-exposure prophylaxis with an NTV**		
	IM route[(a)] 1 dose = 0.5 or 1 ml depending on the manufacturer		**ID route**[(b)] 1 dose = 0.1 ml
D0	2 doses[(c)] (1 dose in each arm or thigh)	1 dose[(c)]	2 doses[(c)] (1 dose in each arm)
D3		1 dose	2 doses (1 dose in each arm)
D7	1 dose	1 dose	2 doses (1 dose in each arm)
D14		1 dose[(d)]	
D21	1 dose		

[(a)] IM route: there are two possible schedules, the Zagreb regimen (2-0-1-0-1) over 21 days or the 4-dose Essen regimen (1-1-1-1-0) over 14 to 28 days. The IM injection is administered into the anterolateral part of the thigh in children < 2 years; into the deltoid muscle (arm) in children ≥ 2 years and adults; do not administer into the gluteal muscle.

[(b)] ID route: inject into the deltoid muscle (or the suprascapular region or the anterolateral part of the thigh). Incorrect ID technique results in failure of post-exposure prophylaxis. If correct ID technique cannot be assured, use IM route.

[(c)] As well as a single dose of rabies immunoglobulin on D0 if indicated.

[(d)] The last injection can be administered between D14 and D28.

Notes:

• In immunocompromised patients: 1 dose on D0, 1 dose on D7 and 1 dose between D21 and D28.[1](see page 192)

• In patients that have received a full course of pre-exposure prophylaxis (see Prevention(see page 191)), the post-exposure regimen is: 1 dose on D0 and 1 dose D3 by IM or ID route or 4 doses by ID route on D0.

Other measures

Antibiotherapy/antibiotic prophylaxis[2](see page 192)

Infection present • local: redness, oedema, serosanguinous or purulent drainage • locoregional or general: lymphangitis, lymphadenopathy, localised cellulitis, bone or joint infection, fever	**No infection** and • wounds on the face or hands or genital region • wounds involving joint, tendon, ligament or fracture • deep puncture wounds • wounds with crush injury • wounds very contaminated or requiring debridement • wounds where correct debridement is not possible • immunocompromised patients	**No infection** and • no criteria requiring antibiotic prophylaxis • wounds more than 24-48 hours old
Antibiotherapy PO 7 days in the event of local non severe infection; 14 days in the event of severe local infection, or widespread generalised infection.	Antibiotic prophylaxis PO 5 to 7 days	No antibiotic prophylaxis

The same dosage is used for both treatment and prophylaxis:
The treatment of choice is **amoxicillin/clavulanic acid** (**co-amoxiclav**) PO [4](see page 0)
Use formulations in a ratio of 8:1 or 7:1. The dose is expressed in amoxicillin:
Children < 40 kg: 25 mg/kg 2 times daily
Children ≥ 40 kg and adults:
Ratio 8:1: 2000 mg daily (2 tablets of 500/62.5 mg 2 times daily)
Ratio 7:1: 1750 mg daily (1 tablet of 875/125 mg 2 times daily)

Tetanus vaccination and serotherapy
Check prophylaxis status. If unknown or not up-to-date, see Tetanus(see page 162), Chapter 7.

Prevention

Pre-exposure prophylaxis with a CCEEV for people at risk (prolonged stay in rabies endemic areas, professionals in contact with animals susceptible of carrying the virus, etc): 1 dose by IM route or 2 doses by ID route on D0 and D7.

[1](see page 0) In the event of direct contact with bats, check national recommendations.
[2](see page 0) For example, for HIV-infected patients: CD4 ≤ 25% in children < 5 years and < 200 cells/mm^3 in children ≥ 5 years and adults.[1](see page 192)
[3](see page 0) Either through observation of the captured animal (if domestic) or through laboratory diagnosis of the animal (killed). The WHO recommends a 10-day observation period of the animal, if captured. If no signs of rabies develop during the observation period, the risk of rabies is excluded, and post-exposure prophylaxis is discontinued. Laboratory diagnosis of the dead animal involves sending the head to a specialised laboratory, which confirms or excludes rabies in the animal. If laboratory diagnosis is negative, risk of rabies is excluded, and post-exposure prophylaxis is discontinued.

4(see page 0) In penicillin-allergic patients:
• Children: **co-trimoxazole** (30 mg SMX + 6 mg TMP/kg 2 times daily) + **clindamycin** (10 mg/kg 3 times daily)
• Adults: **co-trimoxazole** (800 mg SMX + 160 mg TMP 2 times daily) or **doxycycline** (100 mg 2 times daily or 200 mg once daily, except in pregnant and lactating women) + **metronidazole** (500 mg 3 times daily).

References

1. Weekly epidemiological record/Relevé épidémiologique hebdomadaire, 20 April 2018, 93th year/20 avril 2018, 93e année. N° 16, 2018, 93, 201–220. http://apps.who.int/iris/bitstream/handle/10665/272371/WER9316.pdf?ua=1 [Accessed 25 october 2018]

2. Spencer O, Banerjee S. Animal bites. BMJ Best practice 2018 [Accessed 25 october 2018]

Viral hepatitis

Last updated: November 2020

- Clinical features(see page 192)
- Laboratory(see page 194)
- Other investigations(see page 194)
- Treatment(see page 194)
- Vaccination(see page 195)
- References(see page 196)

– Several viral infections of the liver are grouped under the heading of viral hepatitis: hepatitis A, B, C, D (delta) and E.
– The different hepatitis viruses are present throughout the world, but their prevalence varies by country. Hepatitis A and B are common in developing countries where the vast majority of infections occur during childhood.
– The clinical characteristics of all five diseases are similar enough to make differential diagnosis difficult; however, there are epidemiological, immunological and pathological differences. Patients with hepatitis B, C and D may later develop chronic liver disease.
– The main characteristics of each type of viral hepatitis are summarized in the table below.

Clinical features

– *Asymptomatic forms*
Mild or anicteric forms are the most common, irrespective of the causal virus.

– *Icteric forms*
Insidious or sudden onset with symptoms of varying intensity: fever, fatigue, nausea, gastrointestinal disturbance, followed by jaundice, dark coloured urine and more or less claycoloured stool.

– *Fulminant forms*
Hepatocellular failure with severe cytolysis that can be fatal. This form is most frequent in hepatitis B

patients with secondary infection with the D virus, and in the event of pregnant women infected with hepatitis E during their third trimester.

– *Chronic hepatitis*
Hepatitis B, C and D may lead to cirrhosis and/or hepatocellular carcinoma (HCC).

The various forms of viral hepatitis

	Hepatitis A	Hepatitis B	Hepatitis C	Hepatitis D	Hepatitis E
Age group most at risk	Children	Children	Young adults	Young adults	Young adults
Transmission	Faecal-oral Contaminated food and water Transfusion (rare)	Vertical 1 (see page 0) Close contact with infected person (especially intra-familial). Exposure to blood (transfusion; material contaminated with blood) Sexual	Exposure to blood (transfusion; material contaminated with blood) Sexual (low) Intranasal (implements shared by intranasal drug users) Vertical 1 (see page 0)	Exposure to blood (transfusion; material contaminated with blood) Sexual Possibly vertical 1 (see page 0)	Faecal-oral Contaminated food and water
Incubation period	2 to 6 weeks	4 to 30 weeks (average 10 weeks)	2 to 25 weeks	Co-infection B/D: as for hepatitis B Secondary infection of hepatitis B: approximately 5 weeks	2 to 8 weeks
Fulminant forms	0.2 to 0.4%	1 to 3%	More rare than in hepatitis B	Much more common in patients with secondary infection of hepatitis B than in patients with B/D co-infection	20% mortality in pregnant women

Prognosis	No chronic forms	Chronicity: 0.2 to 10% (risk is inversely related to age, e.g. up to 90% if infected before the age of 1 year) of which 5 to 15% progress to cirrhosis. HCC possible	Chronicity: up to 50%, of which 10 to 25% progress to cirrhosis. HCC possible	Chronicity: < 5% for patients with B/D co- infection; > 90% if secondary infection of hepatitis B (rapid cirrhosis)	No chronic forms
Individual prevention	Polyvalent immunoglobulin	Specific anti-HBs immunoglobulin Safe sex (condoms)	Specific anti-HBs immunoglobulin may be effective	As for hepatitis B (the D virus can only develop with B)	Cook meat (pork)
Vaccination	Anti-hepatitis A	Anti-hepatitis B	Does not exist	Anti-hepatitis B	Does not exist
Collective prevention	Hygiene, sanitation	Limit transfusion, screen blood prior to transfusion Single use of disposable material			Hygiene, sanitation

Laboratory

Diagnosis

– HAV, HDV and HEV infection: detection of IgM anti-HAV, anti-HDV and anti-HEV antibodies, respectively.
– HBV infection: detection of HBsAg; chronic hepatitis B: presence of HBsAG for longer 6 months; chronic active hepatitis B: detection of HBeAg and/or HBV DNA.
– HCV infection: detection of anti-HCV antibodies and HCV RNA; chronic hepatitis C: viraemia persists for longer than 6 months.

Other tests

– ALT (or AST) level, platelet count, creatinine, HCV diagnosis and HBV viral load to decide treatment of chronic active hepatitis B.
– APRI score (evaluation of liver fibrosis in chronic hepatitis): [(patient's AST level/normal AST level) x 100]/platelet count (10^9 platelets/litre). An APRI score > 1 indicates probable severe fibrosis.
– HIV test.

Other investigations

– Elastrography (Fibroscan®): measures the elasticity of the liver to determine stage of liver fibrosis, scored from F0 (absence of fibrosis) to F4 (cirrhosis).

Treatment

– Rest, hydration, no special diet.
– Do not administer drug therapy for symptomatic treatment (analgesics, antipyretics, antidiarrhoeals, antiemetics etc.) during the acute phase as it may aggravate symptoms and the evolution of hepatitis. Corticosteroids are not indicated.
– Stop or reduce alcohol consumption.

Treatment of chronic active hepatitis B

The goal of treatment is to reduce the risk of cirrhosis and HCC.

– Patients with HIV co-infection
Lifelong antiretroviral therapy of HIV that includes tenofovir. Do not administer tenofovir monotherapy or tenofovir dual therapy with lamivudine or emtricitabine (risk of developing HIV drug resistance).

– Patients without HIV co-infection
Treatment is indicated in the event of cirrhosis or advanced hepatic fibrosis (APRI score > 1.5 or Fibroscan F3-F4 > 10 kPa); HBsAg positive with persistently elevated ALT or AST > 2 times the normal values in 2 samples taken 3 or 6 months apart; or persistently elevated ALT or AST with a high viral load (> 20 000 IU/ml).
tenofovir PO (300 mg tab, equivalent to 245 mg of tenofovir disoproxil), lifelong therapy:
Children ≥ 12 years and adults, including pregnant women: one tablet once daily taken with a meal

Treatment of chronic hepatitis C[1](see page 196)

Genotypes 1, 2, 3, 4, 5, 6 without cirrhosis or with compensated cirrhosis	**sofosbuvir/velpatasvir** PO (400 mg SOF/100 mg VEL tablet) 1 tablet once daily for 12 weeks
Genotypes 1, 2, 4, 5, 6 without cirrhosis or with compensated cirrhosis Genotype 3 without cirrhosis	**sofosbuvir** PO: 400 mg once daily for 12 weeks + **daclatasvir** PO: 60 mg once daily for 12 weeks
Genotype 3 with compensated cirrhosis	**sofosbuvir** PO: 400 mg once daily for 24 weeks + **daclatasvir** PO: 60 mg once daily for 24 weeks
Genotypes 1 and 4 without cirrhosis or with compensated cirrhosis	**sofosbuvir/ledipasvir** PO (400 mg SOF/90 mg LED tablet) 1 tablet once daily for 12 weeks

In case of decompensated cirrhosis (presence of ascites or jaundice or mental confusion or signs of gastrointestinal haemorrhage): same treatment but for 24 weeks.

Treatment is contra-indicated during pregnancy and breastfeeding.
For women of childbearing age: provide a contraceptive; do not start treatment in women who do not want contraception.

Vaccination

– Routine vaccination of neonates and infants[2](see page 196) (according to national vaccination schedule):
3 dose schedule: one dose as soon as possible after birth, preferably within the first 24 hours of life, then one dose at 6 weeks and one dose at 14 weeks[2](see page 0)
4 dose schedule: one dose as soon as possible after birth, preferably within the first 24 hours of life, then one dose at 6 weeks, one dose at 10 weeks and one dose at 14 weeks[2](see page 0)

– Catch-up vaccination (unvaccinated individuals):
3 dose schedule (0-1-6): 2 doses 4 weeks apart, then a third dose 6 months after the first dose

– Post-exposure prophylaxis:
One dose on D0, one dose on D7 and one dose between D21 and D30 then a booster dose 12 months after the first dose

1 (see page 0) Vertical transmission: transmission of the virus from the mother to the child during pregnancy, at the time of delivery, or during the first 28 days after birth. [a (see page 0) b (see page 0) c (see page 0)]

2 (see page 0) At birth, only the monovalent hepatitis B vaccine can be used.
For the following doses, a monovalent or tetravalent (diphtheria, tetanus, pertussis, hepatitis B) or pentavalent (diphtheria, tetanus, pertussis, hepatitis B and *Haemophilus influenzae*) vaccine can be used, depending on national recommendations.
If an infant was not administered the birth dose, this dose can be administered at anytime during the first contact with health-care providers, up to the time of the next dose of the primary schedule. [a (see page 0) b (see page 0)]

References

1. World Health Organization. Guidelines for the care and treatment of persons diagnosed with chronic hepatitis C virus infection. July 2018. http://apps.who.int/iris/bitstream/handle/10665/273174/9789241550345-eng.pdf?ua=1 [Accessed 21 December 2018]

2. Weekly epidemiological record/Relevé épidémiologique hebdomadaire 7 JULY 2017, 92th YEAR / 7 JUILLET 2017, 92e ANNÉE No 27, 2017, 92, 369–392 http://apps.who.int/iris/bitstream/handle/10665/255841/WER9227.pdf?sequence=1 [Accessed 22 November 2018]

Dengue

- Clinical features (see page 197)
- Major differential diagnoses (see page 197)
- Laboratory (see page 197)
- Treatment1 (see page 198)
  - Patients in Group A (see page 198)
  - Patients in Group B (see page 198)
  - Patients in Group C (see page 199)
- Prevention (see page 202)
- References (see page 203)

– Dengue fever is an arbovirus transmitted to humans by the bite of a mosquito (*Aedes*). Transmission by transfusion of contaminated blood and transplacental transmission to the foetus have also been reported.
– Four different serotypes of dengue have been described. Infection with one serotype provides a lifelong immunity to that specific serotype, but only partial, short-term immunity to other serotypes. There is no specific antiviral treatment.
– Dengue is a mainly urban disease, present in tropical and subtropical regions 1 (see page 0) , in particular in Asia, Central and South America and the Caribbean. Outbreaks have been described in Eastern Africa.
– Primary infection may be asymptomatic or present as mild dengue fever. Subsequent infections increase the risk of severe dengue.

Clinical features

After the incubation period (4 to 10 days), the illness occurs in 3 phases:
– *Febrile phase*: high fever (39 to 40 °C) lasting 2 to 7 days, often accompanied by generalized aches, a maculopapular rash and mild haemorrhagic manifestations.
– *Critical phase* (between the third and seventh day): decrease in temperature. The majority of patients will have dengue without warning signs and proceed to the recovery phase. Certain patients will develop dengue with warning sign(s) or severe dengue.
– *Recovery phase*: patient improves, vital signs normalise, gastrointestinal symptoms subside and appetite returns. At times, bradycardia and generalized pruritus.

Symptoms according to severity (adapted from the WHO)	
Dengue without warning signs	Fever + 2 of the following symptoms: • Nausea, vomiting • Rash resembling measles • Generalized aches (headache, retro-orbital pain, myalgias, arthralgias) • Benign mucocutaneous bleeding (petechiae, positive tourniquet test 2 (see page 0), epistaxis, gingival bleeding) • Leucopenia
Dengue with warning signs	Presence of at least one of these symptoms: • Abdominal pain • Persistent vomiting • Fluid accumulation (ascites, pleural effusion) • Mucosal bleeding • Hepatomegaly (> 2 cm) • Agitation or lethargy • Increasing haematocrit and rapidly dropping platelet count
Severe dengue	• Severe plasma leakage with: - Fluid accumulation (ascites, pleural effusion) + respiratory distress - Compensated shock: weak and rapid pulse, hypotension, cold extremities, capillary refill time > 3 seconds - Decompensated shock: heart rate and blood pressure unrecordable • Severe mucocutaneous bleeding • Multiorgan failure e.g.: hepatic or cardiac failure, obtundation, coma

Major differential diagnoses

Malaria, influenza, measles, Chikungunya, mononucleosis, primary HIV-infection, sepsis, meningococcemia, typhoid fever, viral haemorrhagic fever, leptospirosis.

Laboratory

Diagnosis

– Rapid diagnostic test (serum, plasma or whole blood) detects NS1 viral antigen during the febrile phase and IgM and IgG antibodies during the critical and recovery phases.
– This test indicates the likely presence of an infection with dengue virus but the results must be confirmed by molecular techniques (PCR) in a reference laboratory.

Monitoring the haematocrit (Hct) and complete blood count

– The haematocrit (and not the haemoglobin) is the only test that shows haemoconcentration or increased vascular permeability (plasma leakage). The Hct reflects disease evolution and suggests therapeutic response.
– In children and pregnant women and if possible, in all patients, measure a reference Hct (Hct 0) at the first visit (during the febrile phase or before the critical phase).
– Measure baseline Hct on admission before administering fluid boluses (Hct 1) for all patients in Groups B and C then monitor Hct to determine therapy.
– An increase in the Hct with a rapid drop in the platelet count (≤ 100 000/mm^3) is a warning sign.
– In case of hemodynamic instability or signs of shock:
• An increased or a persistently high Hct (> 50% in men or an increase relative to the previous Hct in women and children) indicates severe plasma leakage;
• A decrease in Hct (< 40-45% in men, < 35-40% in women and children 1 year and older, < 30-35% in children under 1 year) may indicate a haemorrhage.
– Leukopenia (< 5 000/mm^3) is frequent.

Treatment[1]

Patients in Group A

Patients with no warning signs, able to drink sufficiently and with a normal urine output.
– Treat as outpatients, bed rest and good hydration.
– Fever: **paracetamol** PO at the usual doses (see Fever(see page 21), Chapter 1), maintaining a strict 6 to 8 hour interval between doses. Do not prescribe acetylsalicylic acid, ibuprofen or other AINS drugs.
– Seek medical attention if: no clinical improvement, persistent vomiting, cold extremities, agitation or lethargy, breathing difficulties or absence of urine output.
– If follow-up is impossible or symptoms cannot be monitored at home (patients living far from the health care facility/living alone), hospitalise for observation.

Patients in Group B

Patients with warning sign(s) or co-morbidities (e.g. diabetes mellitus, hypertension, cardiac or renal failure, sickle cell anaemia) or at risk populations (pregnant women, infants, the elderly, patients with difficulty drinking).

In all cases:
– Hospitalise; place the patient under a mosquito net.
– Measure Hct 1 and baseline platelet count.
– Avoid invasive procedures (nasogastric tube, IM injections) to minimize the risk of bleeding.
– Fever: **paracetamol** PO as in Group A. In case of hepatitis, administer with caution and decrease the dose (children: 10 mg/kg 3 times daily; adults: 500 mg 3 times daily; maintaining a strict 8-hour interval between doses).

If warning signs or dehydration:
– Place an intravenous line and start hydration with Ringer lactate.
– Monitor the Hct every 4 to 6 hours until the patient is stabilized.
– The volume and rate of Ringer lactate administration is determined by the vital signs: heart rate (HR), blood pressure (BP) and by the evolution of the Hct. See Table 1 – Group B: dengue with warning signs or dehydration(see page 199).
– Monitor fluid balance: intake (IV and oral) and output (urine).
– Monitor urine output every 4 hours: administer the volume of IV fluids necessary to ensure that the

urine output is at least 1 ml/kg/hour in children and 0.5 ml/kg/hour in adults. If unavailable, ensure that the patient is urinating at least every 4 hours.

<table>
<tr><th colspan="3">Table 1 – Group B: dengue with warning signs or dehydration</th></tr>
<tr><td colspan="3">Measure Hct 1 then
Children and adults:
Ringer lactate
5-7 ml/kg/h for 1-2 h
3-5 ml/kg/h for 2-4 h
2-3 ml/kg/h for 2-4 h or less depending on clinical response</td></tr>
<tr><td colspan="3">• Re-evaluate the clinical signs (vital signs, capillary refill time, urine output) hourly and measure Hct 2 then repeat the Hct every 4-6 hours or more if necessary.
• Adjust the rate of the IV infusion in order to maintain a urine output of 1-2 ml/kg/h in children and 0.5 ml/kg/h in adults.</td></tr>
<tr><td rowspan="3">Hct 2 identical to Hct 1
or minimally increased

Children and adults:
Ringer lactate
2-3 ml/kg/h for 2-4 h</td><td colspan="2">Hct 2 increased relative to Hct 1 and/or tachycardia and/or hypotension (if shock: see Group C)
Children and adults:
Ringer lactate
5-10 ml/kg/h for 1-2 h</td></tr>
<tr><td colspan="2">Re-evaluate the clinical signs and measure Hct 3.</td></tr>
<tr><td>Hct stable
Children and adults:
Ringer lactate
3-5 ml/kg/h for 2-4 h
2-3 ml/kg/h or less depending on clinical response</td><td>Hct increased or vital signs unstable
Children and adults:
Ringer lactate
5-10 ml/kg/h for 1-2 h and re-evaluate as above</td></tr>
<tr><td colspan="3">• If no improvement treat as a Group C patient.
• If improvement (disappearance of the danger signs, improvement of the urine output or PO fluid intake or normalisation of the Hct) gradually reduce the rate of IV fluid administration. Duration of IV fluid administration: 24-48 h.</td></tr>
</table>

Patients in Group C

Patients with severe dengue requiring emergency treatment.

In all cases:

– Hospitalise in intensive care; place the patient under a mosquito net.
– Administer oxygen (O_2) continuously:

• to maintain the SpO_2 between 94 and 98% if it is ≤ 90% 3 (see page 0) or if the patient has cyanosis or respiratory distress;
• if pulse oxymeter is not available: at least 5 litres/minute or to relieve the hypoxia and improve respiration.
– Before first bolus, measure Hct 1, baseline platelets count and blood group, then monitor the Hct every 1 to 4 hours until the patient is stabilized.
– Check for the presence of the shock: rapid and weak pulse, low BP or narrow pulse pressure, cold extremities, capillary refill time > 3 seconds.
– Mark the size of the liver with a pen on admission.

– The volume and rate of Ringer lactate or plasma substitute administration is determined by the vital signs (HR, BP) and by the evolution of the Hct. See Table 2 – Group C: dengue with compensated shock(see page 200) or Table 3 – Group C: dengue with decompensated shock(see page 201).
– Monitor urine output: same monitoring as in Group B.
– Monitor signs of fluid overload (especially in children):
• Increase in RR ≥ 10/minute or tachypnoea;
• Increase in HR ≥ 20/minute or tachycardia and SpO_2 < 90%;
• Rales and/or pulmonary oedema (fine crackles);
• Gallop rhythm on cardiac auscultation;
• Increase in liver size;
• Peripheral oedema (e.g. eyelid oedema).
– In the event of fluid overload, stop the IV infusion if vital signs are stable.
– In the event of respiratory distress with rales, administer furosemide IV (see Heart failure(see page 300), Chapter 12) if the patient is not in shock.
– Avoid invasive procedures (nasogastric tube, IM injections) to minimize the risk of bleeding.
– Transfuse patients with fresh whole blood 4(see page 0) in case of significant bleeding or if a low Hct does not improve with resuscitation. The post-transfusion Hct should be interpreted with caution.
– When the patient improves, stop the IV infusion to avoid fluid overload.

Table 2 – Group C: dengue with compensated shock
(BP maintained but signs of shock present)

Measure Hct 1 then give **Ringer lactate** (first bolus) Children: 10-20 ml/kg in 1 h Adults: 5-10 ml/kg in 1 h		
If improvement (no signs of shock present) ***Reduction of rate:*** Children: **Ringer lactate** 10 ml/kg/h for 1-2 h 7 ml/kg/h for 2 h 5 ml/kg/h for 4 h 3 ml/kg/h Adults: **Ringer lactate** 5-7 ml/kg/h for 1-2 h 3-5 ml/kg/h for 2-4 h 2-3 ml/kg/h for 2-4 h	If no improvement (signs of shock present): measure Hct 2.	
	Hct 2 increases or stays elevated[a] Children: **plasma substitute** 10-20 ml/kg in 1 h (second bolus) 10 ml/kg in 1 h 7 ml/kg in 1 h Adults: **Ringer lactate** or **plasma substitute** 10-20 ml/kg in 1 h (second bolus)	Hct 2 decreases[b] Look for severe haemorrhage.

	If improvement (no signs of shock present) Children: **Ringer lactate** according to "*Reduction of rate in children*" Adults: **Ringer lactate** 7-10 ml/kg/h for 1-2 h Then according to "*Reduction of rate in adults*"	If no improvement (signs of shock present) Measure Hct 3 and proceed as above from "Measure Hct 2".	No severe haemorrhage Children and adults: **plasma substitute** 10-20 ml/kg in 1 h Evaluate need for transfusion if no improvement.	Severe haemorrhage Transfuse Children and adults: **fresh whole blood** 10-20 ml/kg
		Verify presence of signs of shock, of fluid overload and measure Hct, then reduce the rate as in "*Reduction of rate*" if signs of shock are absent.		
• Reduce the rate when the HR and BP normalise. Always check for signs of fluid overload. • Continue for 24-36 h (less if PO hydration is tolerated). Supplemental boluses of crystalloids or colloids may be necessary in the next 24 h. Do not administer IV fluids for more than 48 h.				

[a] > 50% in men or increased relative to Hct 1 in women and children.

[b] < 40-45% in men, < 35-40% in women and children 1 year and older, < 30-35% in children less than 1 year.

Table 3 – Group C: dengue with decompensated shock (pulse and blood pressure unrecordable)
Measure Hct 1 then **Ringer lactate** or **plasma substitute** (if pulse pressure < 10 mmHg or severe hypotension) IV or IO : Children and adults: 20 ml/kg in 15-30 min (first bolus)

<table>
<tr><td rowspan="6">If improvement (no signs of shock present)

Children:
plasma substitute
10 ml/kg in 1 h
Adults:
Ringer lactate or plasma substitute
10 ml/kg in 1 h

Reduction of rate:
Ringer lactate
Children:
10 ml/kg in 1 h
7 ml/kg/h for 2 h
5 ml/kg/h for 4 h
3 ml/kg/h
Adults:
5-7 ml/kg/h for 1-2 h
3-5 ml/kg/h for 2-4 h
2-3 ml/kg/h for 2-4 h</td><td colspan="5">If no improvement (signs of shock present)

Compare Hct 1 (obtained before the first bolus) to Hct 0[a] (obtained during the febrile phase or before the critical phase).</td></tr>
<tr><td colspan="3">Hct 1 increases or stays elevated relative to Hct 0

Children and adults:
plasma substitute 10-20 ml/kg in 30-60 min (second bolus)
Verify the presence of signs of shock or of fluid overload.</td><td colspan="2">Hct 1 decreases[b] relative to Hct 0

Verify the vital signs and look for signs of severe haemorrhage.</td></tr>
<tr><td rowspan="4">If improvement

Children and adults:
plasma substitute
7-10 ml/kg/h for 1-2 h

Then
Children and adults:
Ringer lactate as in “Reduction of rate”</td><td colspan="2">If no improvement: measure Hct 2</td><td rowspan="2">No severe haemorrhage

Children and adults:
plasma substitute
10-20 ml/kg in 30-60 min (second bolus)
Transfuse if no improvement.</td><td rowspan="2">Severe haemorrhage

Transfuse
Children and adults:
fresh whole blood
10-15 ml/kg</td></tr>
<tr><td>If Hct 2 < Hct 1:
Severe haemorrhage

Transfuse
Children and adults:
fresh whole blood
10-15 ml/kg</td><td>If Hct 2 ≥ Hct 1:
No severe haemorrhage

Children and adults:
plasma substitute (third bolus)
10-20 ml/kg in 30-60 min
7-10 ml/kg/h for 1-2 h</td></tr>
<tr><td>If improvement

Children and adults:
Ringer lactate as in “Reduction of rate”</td><td>If no improvement

Measure Hct 3 and proceed as above from “Measure Hct 2”.</td><td colspan="2" rowspan="2">Verify the presence of signs of shock or of fluid overload and measure Hct.</td></tr>
<tr><td colspan="4">Reduce the IV fluid rate when HR and BP normalise; continue for 24-48 h (or less if PO hydration tolerated). Supplemental boluses of crystalloids or colloids may be necessary in the next 24 h. Do not administer IV fluids for more than 48 h.</td></tr>
</table>

[a] If not available, compare to population norms of haematocrit according to age. If these are not know use the following norms as a reference: < 45% in men, < 40% in women and children 1 year or older, < 35% in children less than 1 year.

[b] < 40-45% in men, < 35-40% in women and in children 1 year and older, < 30-35% in children less than 1 year.

Prevention

Individual protection: long sleeves and trousers, repellents, mosquito net (*Aedes* bites during the day).

1 (see page 0) For more information: http://gamapserver.who.int/mapLibrary/Files/Maps/Global_DengueTransmission_ITHRiskMap.png?ua=1

2 (see page 0) Tourniquet test: inflate a blood pressure cuff on the upper arm to a point midway between the systolic and diastolic pressure for 5 min. The test is positive when 20 or more petechiae per 2.5 cm square are observed.

3 (see page 0) If possible it is better to treat all patients with a SpO_2 < 95% with oxygen.

4 (see page 0) Fresh whole blood: that has never been refrigerated, that has never kept at a temperature below 16 °C and collected from the donor for less than 6 hours.

References

1. World Health Organization. Handbook for clinical management of dengue. Geneva, 2012. http://www.wpro.who.int/mvp/documents/handbook_for_clinical_management_of_dengue.pdf

Viral haemorrhagic fevers

- Clinical features (see page 203)
- Laboratory (see page 204)
- Management (see page 205)
- Treatment (see page 206)
- Prevention (see page 206)
- References (see page 206)

– Several diseases with different aetiologies and different modes of transmission are grouped under this term as they present with common clinical signs.
– Dengue haemorrhagic fever is a viral haemorrhagic fever that is described in a specific chapter (see Dengue (see page 196), Chapter 8).

Clinical features

– Common syndrome (CS):
• Fever higher than 38.5 °C;
• Haemorrhagic symptoms (purpura, epistaxis, haematemesis, melaena, etc.).

– The clinical signs are often nonspecific; the severity varies depending on the aetiology.

	Reservoir/ Vector ***Geographical distribution***	**Isolation of patients**	**Clinical features**	**Estimated case fatality rate**
Ebola* Marburg	Bats (?) *Africa*	Strict isolation	CS + sudden onset general malaise, vomiting and diarrhoea	60-80%

	Reservoir/ Vector ***Geographical distribution***	**Isolation of patients**	**Clinical features**	**Estimated case fatality rate**
Lassa*	Rodents *West Africa* 1 (see page 0)	Strict isolation	CS + general malaise, headache, muscle pain, facial oedema, pharyngitis, proteinuria on reagent strip	15-20%
Junin and Machupo*	Rodents *South America*	Isolation	CS + vomiting, erythema of the face and, depending on the aetiology: • periorbital oedema, cervical adenopathy, pharyngitis	15-30%
Omsk	Ticks *Europe, Asia*	None		2-5%
Crimean Congo*	Livestock/Ticks *Africa, Asia*	Strict isolation	• pharyngitis, reddened conjunctivae	5-20%
FHSR (hantavirus)*	Rodents *Asia and Europe*	None	• oedema of the soft palate, generalised petechial rash • proteinuria on reagent strip	< 1%
Kyasanur	Small mammals/ Ticks *India*	None	CS + headache, muscle pain, prostration	2-10%
Rift Valley*	Livestock/ Mosquitoes *Africa*	Mosquito nets	Clinical signs: • isolated fever • SC • encephalitis • retinitis and blindness	30-50%
Yellow fever*	Primates/ Mosquitoes *Africa, South America*	Mosquito nets	CS + jaundice, proteinuria on reagent strip, oliguria, headache	10-30%

* Viral haemorrhagic fever with epidemic potential.

Laboratory

– A sample of whole blood must be send to a reference laboratory for serological diagnosis, with a clinical description of the patient. The sample may also be sent on filter paper. It is easier to transport, but the small volume of blood only allows a limited number of aetiologies to be tested.
– Protective clothing must be worn while taking or handling the sample (gown, gloves, glasses, mask, etc.).
– The sample must be sent in a triple packaging system for Category A infectious substances.

Management

Suspicion of haemorrhagic fever

(isolated case of fever with haemorrhagic symptoms in an endemic area)

– Isolation: isolation room (or if not available, use screens/partitions); restrict visitors (if a carer is strictly necessary, s/he must be protected with gown, gloves, mask).
– Standard precautions:
The majority of hospital-acquired infections have occurred due to a lack of respect for these precautions:
• Hand washing;
• Gloves for patient examination and when touching blood, body fluids, secretions, excretions, mucous membranes, non-intact skin;
• Gowns to protect skin and prevent soiling of clothing during consultations and activities that are likely to generate splashes or sprays of blood, body fluids, secretions, or excretions;
• Surgical mask and goggles, or face shield, to protect mucous membranes of the eyes, nose, and mouth during activities that may generate splashes of blood, body fluids, secretions, and excretions;
• Adequate procedures for the routine cleaning and disinfection of objects and surfaces;
• Rubber gloves to handle soiled laundry;
• Safe waste management;
• Safe injection practices.

Confirmed cases of Ebola, Marburg, Lassa, Crimean-Congo fevers or epidemics of unknown origin

– Strict isolation in a reserved area separate from other patient areas, with a defined circuit for entrance/exit and changing room at the entrance/exit; dedicated staff and equipment/supplies; use of disposable material if possible.
– Standard precautions (as above)
PLUS
– Droplet precautions AND contact precautions including personal protective equipment (PPE):
• two pairs of gloves,
• double gown or coverall suit,
• surgical cap or hood, mask, protective glasses,
• impermeable apron,
• rubber boots.
The PPE is to be worn systematically prior to entry into isolation area, regardless the tasks to be performed (care, cleaning, distribution of meals, etc.) and to be removed before leaving the isolation area.
– Disinfection of surfaces, objects, clothing and bedding with chlorine solution; safe handling and on site disposal of waste and excreta, etc.
– In the event of a death, do not wash the body. Prompt and safe burial of the dead as quickly as possible, using a body bag.

Confirmed cases of Yellow fever or Rift Valley fever

– Standard precautions.
– Patient under a mosquito net to prevent transmission.

For all patients: report to the Ministry of Health of the country.

Treatment

– Aetiological treatment: ribavirine for Lassa fever and Crimean-Congo fever.
– Symptomatic treatment:
• Fever(see page 21): paracetamol (Chapter 1). Acetylsalicylic acid (aspirin) is contra-indicated.
• Pain: mild (paracetamol), moderate (tramadol), severe (sublingual morphine): see Pain(see page 23), Chapter 1.
• Dehydration: oral rehydration salts and/or IV rehydration with Ringer lactate, see Dehydration(see page 34), Chapter 1.
• Seizures(see page 16) (Chapter 1).
• Vomiting: **ondansetron** PO
Children 6 months to < 2 years: 2 mg once daily
Children 2 to < 4 years: 2 mg 2 times daily
Children 4 to < 12 years: 4 mg 2 times daily
Children ≥ 12 years and adults: 4 to 8 mg 2 times daily
– For Ebola and Marburg haemorrhagic fevers: invasive procedures must be strictly limited. Health care staff is at risk of contamination when inserting and maintaining IV lines. An IV line must be well secured so that the patient, often confused, cannot pull it out.

Prevention

– Vaccination against yellow fever[1](see page 206) :
Children and adults: 0.5 ml single dose
• Routine vaccination : children from 9 months of age, along with the measles vaccine.
• Mass vaccination campaign during an epidemic: children from 6 months and adults ; for pregnant women, only administer during an epidemic.
– Vaccination against Rift Valley fever: only during an epidemic.
– Vector control programmes for known vectors.
– Infection control measures are essential in all cases.

1(see page 0) For more information on geographic distribution of Lassa fever: https://www.who.int/emergencies/diseases/lassa-fever/geographic-distribution.png?ua=1

References

1. Weekly epidemiological record-Relevé épidémiologique hebdomadaire 5 july 2013, 88$_{th}$ year / 5 juillet 2013, 88^{e} année No. 27, 2013, 88, 269–284. https://www.who.int/wer/2013/wer8827.pdf?ua=1 [Accessed 10 december 2018]

HIV infection and AIDS

- Evolution of the disease(see page 207)
- Laboratory(see page 207)
- Treatment of HIV infection(see page 208)
- Prevention of HIV infection(see page 209)

- Prevention of opportunistic infections(see page 209)
  - Primary prophylaxis(see page 209)
  - Secondary prophylaxis(see page 210)
- References(see page 220)

– Acquired immune deficiency syndrome (AIDS) is the most advanced stage of infection with human immunodeficiency virus (HIV).
– Two subtypes of HIV have been identified. HIV-1 is more widespread than HIV-2, the latter mainly being found in West Africa. HIV-2 is less virulent and less transmissible than HIV-1.
– HIV weakens the immune system by causing a deficit in CD4 T lymphocytes.

Evolution of the disease

– *Primary infection or acute retroviral syndrome*: 50 to 70% of newly infected individuals develop during seroconversion (from 15 days to 3 months post exposure), a viral syndrome with fever, malaise, and lymphadenopathy.

– *Asymptomatic HIV infection* (after seroconversion): a period of clinical latency, but not viral latency. The time period for progression from HIV infection to the development of severe immune deficiency in western countries is approximately 10 years. This period appears to be shorter in developing countries.

– *Symptomatic HIV infection*: with progressive destruction of the immune system, common and more severe diseases occur more frequently, and with higher mortality, in seropositive individuals.

– *AIDS*: this stage corresponds to the development of severe opportunistic infections and neoplasms. From a biological point of view, AIDS is defined as a CD4 count < 200 cells/mm^3. Without treatment the disease progresses rapidly towards death.

The World Health Organization (WHO) has proposed a clinical classification of HIV infection in 4 stages of severity for adults and adolescents and for children[1](see page 220).

Laboratory

Diagnosis of HIV infection
– The diagnosis is made with serological (detection of antibodies against the virus) or virological (especially in infants) testing.
– Testing should always be done *voluntarily with informed consent*.
– All HIV test results must be strictly *confidential* in order to avoid discrimination.
– The individual should have access to services offering pre-test and post-test counselling, treatment and support.
– A diagnosis of HIV infection can be made only after at least 2 different test results (2 different brands) are clearly positive: the positive result of an initial (highly sensitive) test must be confirmed through use of a second (highly specific) test. In areas where HIV prevalence is low, diagnosis is confirmed after 3 positive test results.

CD4 lymphocyte counts
– CD4 cell depletion is a marker of the progression of immune depression. The level of the CD4 cell count is a predictor of the development of opportunistic infections or neoplasms and can be used to orient their diagnosis, e.g. cerebral toxoplasmosis or cryptococcal meningitis appear when the CD4 count is below 100 cells/mm^3 in adults. If clinical symptoms/signs are present suggesting one of these infections, but the CD4 count is greater than or equal to 200 cells/mm^3, it is unlikely that that particular infection is present.

Opportunistic infections
It is important to screen for serious opportunistic infections in those at risk (e.g. testing for cryptococcal antigen for all adults with a CD4 count < 100 cells/mm^3 regardless of symptoms).

Treatment of HIV infection

Antiretroviral (ARV) treatment
A multi-drug (at least 3) antiretroviral therapy (ART) is the reference treatment. It does not eradicate the virus, but slows the progression of the disease and improves the patient's clinical state by reducing viral replication and consequently increasing the CD4 cell count to levels beyond the threshold of opportunistic infections.

For more information: The use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach. World Health Organization, second edition, 2016. http://apps.who.int/iris/bitstream/10665/208825/1/9789241549684_eng.pdf?ua=[5]1

Therapeutic classes
Four major classes ARV are used:
– NRTI (nucleoside/nucleotide reverse transcriptase inhibitors): zidovudine (AZT), lamivudine (3TC), abacavir (ABC), tenofovir (TDF), emtricitabine (FTC).
– NNRTI (non-nucleoside reverse transcriptase inhibitors): efavirenz (EFV), nevirapine (NVP), etravirine (ETR). HIV-2 is naturally resistant to NNRTIs.
– PI (protease inhibitors): atazanavir (ATV), lopinavir (LPV), ritonavir (RTV), darunavir (DRV).
– INI (integrase inhibitors): dolutegravir, raltegravir.

Principles of ARV treatment
– Daily triple therapy must be taken for life to prevent the rapid development of resistance. It is important that the patient understands this and that adherence to treatment is optimal.
– Follow the ART protocols recommended by national HIV program.
– The most widely used and easiest regimens to administer are 2 NRTI + 1 NNRTI: e.g. TDF/3TC/EFV.
– In the event of treatment failure, all 3 drugs should be replaced with a second-line regimen: 2 other NRTIs + 1 PI.
Other possible combinations exist which are less commonly used or more difficult to manage.

Criteria for ARV treatment
As a priority ART should be initiated in all patients with WHO clinical stage 3 or 4 and patients with CD4 < 350 /mm^3. However, those with higher CD4 counts can initiate ART.

Monitoring of ARV treatment
HIV viral load is an essential tool for monitoring the effectiveness of ARV. CD4 count is useful for identifying severely immunosuppressed. Other tests such as blood count, tests for liver (ALAT) and renal function (creatinine clearance) are not essential, but can be useful in detecting adverse effects.

Treatment of opportunistic and other infections
With progressive immunosuppression, HIV-infected patients who are not receiving triple therapy (or patients on ART but with poor adherence) become increasingly susceptible to infections. For conditions of clinical stages 2 and 3, standard treatments are usually effective. Patients may benefit from primary prophylaxis against opportunistic infections (see Primary prophylaxis(see page 209)). Tuberculosis (TB) is the most common serious opportunistic infection. It can be difficult to diagnose in HIV-infected patients however.

Treatment of pain
Treat all patients for associated pain (see Pain(see page 23), Chapter 1).

5 http://apps.who.int/iris/bitstream/10665/208825/1/9789241549684_eng.pdf?ua=1

Prevention of HIV infection

Sexual transmission
The most reliable method of prevention is the use of male or female condoms.
Male circumcision decreases significantly the risk of HIV transmission.
Early diagnosis and treatment of sexually transmitted infections is essential as they increase the transmission of HIV (see Chapter 9(see page 221)).
ART to HIV positive and adherent partner does protect the negative partner from HIV infection.

Occupational transmission (accidental needle stick injuries or injuries with contaminated objects, contact between a patient's blood and unprotected broken skin or mucous membranes)
Prevention is based on use of standard precautions to avoid contamination with soiled material or potentially infected body fluids.
Post-exposure prophylaxis (PEP): e.g. in the event of rape or occupational accidental exposure to blood, ARV treatment initiated as soon as possible within 72 hours of exposure for a duration of 1 month may reduce the risk of infection.

Nosocomial transmission
Prevention of nosocomial HIV infection is based on the rational use of injections and strict respect for hygiene and sterilization and disinfection procedures for medical material.
For transfusion: strict respect of indications for transfusion and systematic serological screening of the donor's blood are the two indispensable precautions in the prevention of HIV transmission through transfusions.

Transmission in injection drug users
Needle and syringe exchange programs with disposable needles and syringes for users can reduce the risk.

Mother-to-child transmission (MTCT)
The global rate of vertical transmission varies from 20 to 40%. The risk of transmission through breast-feeding is evaluated at approximately 12% and persists for the duration of breast-feeding.
• *In pregnant women*: HIV transmission from mother-to-child may be reduced by ART. The protocol called Option B+ is the internationally preferred protocol. All HIV-infected pregnant women receive lifelong triple-drug therapy, regardless of the CD4 count or clinical stage, both for their own health and to prevent transmission to the child. The most commonly recommended ART is TDF/3TC/EFV or TDF/FTC/EFV. Check national recommendations. In addition, ARVs are administered to the newborn.
Programs targeting pregnant women also include other preventive measures such as avoiding artificial rupture of the membranes and systematic episiotomy.
• *In breast-feeding women*: exclusive breast-feeding for the first 6 months of life, introduction of complementary (solid) foods at 6 months, gradual cessation of breast-feeding to the age of 12 months.

Prevention of opportunistic infections

In the absence of ARV treatment, all HIV-infected individuals become symptomatic and evolve towards AIDS. However, some opportunistic infections can be prevented.

Primary prophylaxis

For HIV infected patients who have not previously contracted an opportunistic infection, in order to prevent the development of some opportunistic infections.

Infections	Primary prophylaxis
Pneumocystosis Cerebral toxoplasmosis Isosporiasis Various bacterial infections Malaria	**co-trimoxazole** PO Children: 50 mg SMX + 10 mg TMP/kg once daily Adults: 800 mg SMX + 160 mg TMP once daily

Secondary prophylaxis

For patients who develop a specific opportunistic infection, in order to prevent recurrence once treatment for the infection is completed.

Infections	Secondary prophylaxis	Comments
Pneumocystosis	**co-trimoxazole** PO Children: 50 mg SMX + 10 mg TMP/kg once daily Adults: 800 mg SMX + 160 mg TMP once daily	Alternative **dapsone** PO Children: 2 mg/kg once daily (max. 100 mg daily) Adults: 100 mg once daily
Toxoplasmosis		Alternative Adults: **dapsone** PO: 200 mg once weekly or 50 mg once daily + **pyrimethamine** PO: 75 mg once weekly + **folinic acid** PO: 25 to 30 mg once weekly
Isosporiasis		–
Penicilliosis Histoplasmosis	**itraconazole** PO Adults: 200 mg once daily	–
Cryptococcal meningitis	**fluconazole** PO Children: 6 mg/kg once daily Adults: 200 mg once daily	–
Oral or oesophageal candidiasis	**fluconazole** PO Children: 3 to 6 mg/kg once daily Adults: 100 to 200 mg once daily	Only for frequent and severe recurrences
Herpes simplex	**aciclovir** PO Children under 2 years: 200 mg 2 times daily Children 2 years and over and adults: 400 mg 2 times daily	Only for frequent and severe recurrences

Symptoms	Definitions and aetiologies	Diagnosis	Treatment
Diarrhoea with or without blood (also see Chapter 3(see page 79))	Diarrhoea is defined as at least 3 liquid stools per day. Aetiologies: **Parasitic infections** • *Isospora belli* • *Cryptosporidium* • *Microsporidium* • *Giardia lamblia* • *Entamoeba histolytica* **Bacterial infections** • *Shigella* • *Salmonella enteritis* • *Campylobacter enteritis* **Mycobacterial infections** • *Mycobacterium tuberculosis* (gastrointestinal TB) • *Mycobacterium avium* complex **Helminthiasis** • *Strongyloides stercoralis* **Viral infections** • Cytomegalovirus (CMV) **Other causes** • Kaposi sarcoma • Lymphoma • Idiopathic (HIV infection) • Antiretrovirals (especially lopinavir and ritonavir)	1. History and clinical examination 2. Microscopic examination of stool for ova and parasites (2 to 3 samples) *Note:* *I. belli, Cryptosporidium, Microsporidium*, MAC and CMV are unlikely if CD4 count > 200 cells.	• Persistent (> 2 weeks) or chronic (> 4 weeks) diarrhoea is often associated with weight loss and dehydration. • Prevention or treatment of dehydration is critical (Dehydration(see page 34), Chapter 1). • Depending on the results of the stool examinations: give appropriate treatment. • If there is no laboratory support: ***Acute bloody diarrhoea*** • First-line treatment: Children: **azithromycin** PO: 20 mg/kg once daily for 5 days or **ciprofloxacin** PO: 15 mg/kg 2 times daily for 7 days Adults: **ciprofloxacin** PO: 500 mg 2 times daily for 7 days • If amoebiasis suspected: **tinidazole** or **metronidazole** PO (Amoebiasis(see page 83), Chapter 3). ***Non-bloody persistent or chronic diarrhea*** Persistent or chronic diarrhoea suggests advanced immunocompromised state. For patients who qualify for ARVs by CD4 count (or unknown CD4 count), ARV initiation is urgent and will usually resolve symptoms in 14 to 28 days. • *Isospora belli*: **co-trimoxazole** PO Children: 40 mg SMX + 8 mg TMP/kg 2 times daily for 10 days then 25 mg SMX + 5 mg TMP/kg 2 times daily for 3 weeks Adults: 800 mg SMX + 160 mg TMP 2 times daily for 7 to 10 days then 400 mg SMX + 80 mg TMP 2 times daily for 3 weeks • *Cryptosporidium*: no specific treatment in HIV-infected patients • *Microsporidium*: **albendazole** PO (limited efficacy) Children: 10 mg/kg 2 times daily (max. 800 mg daily) for 7 days Adults: 400 mg 2 times daily for 2 to 4 weeks • Helminthiasis: **albendazole** PO for 3 days Children > 6 months but ≤ 10 kg: 200 mg once daily Children > 6 months and adults: 400 mg once daily • Giardiasis: **tinidazole** or **metronidazole** (Intestinal protozoan infections(see page 139), Chapter 6).

Symptoms	Definitions and aetiologies	Diagnosis	Treatment
			• If no improvement (and no contra-indications such as bloody diarrhoea), symptomatic treatment with **loperamide** PO: Children < 2 years: contra-indicated Children 2 to 5 years: 1 mg 3 times daily Children 6 to 8 years: 2 mg 2 times daily Children > 8 years: 2 mg 3 times daily Adults: initial dose 4 mg then 2 mg after each liquid stool (max. 16 mg daily) **Nutrition** ++++ Children: continue to breastfeed; increase daily calorie intake: 6-11 months: add 150 kcal daily 12-23 months: add 200 kcal daily 2-5 years: add 250 kcal daily 6-9 years: add 350 kcal daily 10-14 years: add 400 kcal daily Eliminate fresh milk, give porridge prepared with rice water or soup or yoghurts. Give 2.5 ml of oil per meal. Any child 0-5 years should receive zinc sulfate (Acute diarrhoea(see page 79), Chapter 3). Adults: increase the calorie and protein intake (at least 2 g protein/kg daily). No food is excluded but avoid raw food, fresh milk and foods high in fibre. Encourage small, frequent meals.

Symptoms	Definitions and aetiologies	Diagnosis	Treatment
Oral and oesophageal lesions	**Fungal infections** • Oral candidiasis: see Stomatitis(see page 87), Chapter 3. • Oesophageal candidiasis: pain on swallowing, dysphagia. May result in weight loss. **Viral infections** • Oral hairy leukoplakia (keratosis on the lateral sides of the tongue due to the Epstein-Barr virus) • Oral and oesophageal herpes **Aphthous ulcers**	Clinical examination is enough to make a diagnosis. Consider all severe oral candidiasis (if the pharynx is involved) as oesophageal candidiasis even in the absence of dysphagia.	• Mild oral candidiasis **nystatin** PO Children and adults: 100 000 IU (= 1 ml) 4 times daily or **miconazole** oral gel Children 6 months-2 years: 1.25 ml 4 times daily Children over 2 years and adults: 2.5 ml 4 times daily The treatment lasts 7 to 14 days. • Moderate to severe oral candidiasis and oesophageal candidiasis **fluconazole** PO Children: 3 to 6 mg/kg once daily Adults: 50 to 200 mg once daily up to 400 mg daily if necessary The treatment lasts 7 to 14 days for oral candidiasis and 14 to 21 days for oesophageal candidiasis. *Candidiasis is an indication for prophylaxis with co-trimoxazole.* • Oral hairy leukoplakia: no treatment • Oral herpes: Analgesics (paracetamol, ibuprofen). For recurrent or extensive forms affecting the oesophagus, add: **aciclovir** PO for 7 days Children under 2 years: 200 mg 5 times daily Children 2 years and over and adults: 400 mg 5 times daily *Secondary prophylaxis only for patients with frequent recurrences.*

Symptoms	Definitions and aetiologies	Diagnosis	Treatment
Respiratory problems (also see Chapter 2(see page 43))	Cough and/or thoracic pain and/or dyspnoea in a symptomatic HIV infected patient. Aetiologies: **Bacterial infections** • *Streptococcus pneumoniae* • *Haemophilus influenzae* • *Staphylococcus aureus* **Mycobacterial infections** • *M. tuberculosis,* MAC **Protozoal infections** • *Pneumocystis jiroveci* (PCP) **Fungal infections** • *Cryptococcus neoformans* • *Histoplasma capsulatum* • *Coccidioides immitis* • *Aspergillus* spp • *Penicillium marneffei* **Viral infections** • CMV **Neoplasms** • Kaposi sarcoma • Non-Hodgkin's lymphoma	1. History and clinical examination: Blood in the sputum? If fever < 7 days, dyspnoea: unlikely TB. If cough > 21 days, weight loss, thoracic pain > 15 days, no dyspnoea: likely TB. Pulmonary auscultation: bilateral lobar pneumonia? 2. If possible: a) Look for AFB in sputum b) Chest x-ray • PCP: bilateral interstitial infiltrates • TB: miliary shadowing, large heart, pleural effusion, enlarged lymph nodes inside the chest. *Notes* • MAC, PCP, CMV and fungal infections are unlikely in patients with a CD4 count > 200 cells/mm^3. • Staphylococcal pneumonia is often associated with a pyomyositis or an abscess.	• For the diagnosis and treatment of upper respiratory tract infections, particularly pneumonia: see Chapter 2(see page 43). • If the chest x-ray is consistent with staphylococcal pneumonia: Children: see Staphylococcal pneumonia(see page 70), Chapter 2. Adults: **ceftriaxone** IM or slow IV 1 g once daily + **cloxacillin** IV 2 g every 6 hours • If the sputum examination is AFB+, treat for TB. • If the sputum examination is negative and the chest x-ray is consistent with PCP: **co-trimoxazole** PO for 21 days Children: 50 mg SMX + 10 mg TMP/kg 2 times daily Adults: 1600 SMX + 320 TMP 3 times daily *Note*: the symptoms may become worse during the first phase of treatment, effectiveness can only be evaluated after one week of treatment. Add **prednisolone** PO for patients with severe PCP with hypoxia: Children: start with 2 mg/kg daily then decrease the dose following the adult example Adults: 40 mg 2 times daily for 5 days, then 40 mg once daily for 5 days then 20 mg once daily for 10 days *Secondary prophylaxis is recommended.* • Fungal infections (cryptococcosis, penicilliosis, histoplasmosis): Adults: **amphotericin B** IV: 0.7 to 1 mg/kg once daily for 2 weeks (cryptococcosis, penicilliosis) or 1 to 2 weeks (histoplasmosis), then: **fluconazole** PO: 400 mg daily for 8 weeks (cryptococcosis) **itraconazole** PO: 200 mg 2 times daily for 10 weeks (penicilliosis) **itraconazole** PO: 200 mg 3 times daily for 3 days then 200 to 400 mg daily for 12 weeks (histoplasmosis) *Secondary prophylaxis is recommended.*

Symptoms	Definitions and aetiologies	Diagnosis	Treatment
	Others • Lymphoid interstitial pneumonia • Pleural effusion (often TB) • Pericardial effusion (often TB) • Pneumothorax (may be due to PCP)		
Lymphadenopathy	Enlarged lymph nodes in a symptomatic HIV-infected patient Persistent generalised lymphadenopathy (PGL): • 2 or more extra-inguinal sites • lymph nodes > 1.5 cm • enlarged for 3 or more months PGL is usually due to HIV infection. Aetiologies: **HIV infection** **Infections** • TB • Syphilis • Histoplasmosis • Toxoplasmosis • CMV **Neoplasms** • Kaposi sarcoma • Lymphoma	1. Clinical examination: look for a local cause (skin or dental infection etc.); TB or syphilis. 2. Suspected TB: lymph node aspiration, look for AFB, chest x-ray *Note*: in HIV infected patients, TB is often extrapulmonary. 3. Suspected syphilis: serology 4. If all examinations are negative: biopsy is useful to exclude lymphoma, Kaposi's sarcoma and fungal or mycobacterial infections (see notes for patients in stage 1).	• Treat according to the aetiology or empirical treatment with, for example **doxycycline** PO. • TB: see the guide Tuberculosis, MSF. • Early syphilis: **benzathine benzylpenicillin** IM Adults: 2.4 MIU single dose (1.2 MIU in each buttock) or, if not available: **azithromycin** PO Adults: 2 g single dose *Note*: in patients in stage 1, no further investigation (other than 1, 2 and 3 in this table) or treatment are required.

Symptoms	Definitions and aetiologies	Diagnosis	Treatment
Skin lesions (also see Chapter 4(see page 91))	**Bacterial infections** • Furunculosis • Impetigo and pyoderma • Axillary hidradenitis • Pyomyositis • Syphilis **Viral infections** • Herpes zoster • Herpes simplex • Genital warts • *Molluscum contagiosum* **Fungal infections** • Candidiasis, dermatophytoses and deep mycoses (penicilliosis, cryptococcosis, histoplasmosis, etc.) **Neoplasms** • Kaposi sarcoma **Other skin infections** • Chronic prurigo or urticaria • Severe seborrhoeic dermatitis • Psoriasis • Scabies • Diffuse cutaneous xerosis **Rash caused by medication** **Bed sores**		**Bacterial infections** • Furunculosis, impetigo, chronic folliculitis: see Bacterial skin infections(see page 98), Chapter 4. • Suppurative axillary hidradenitis: local treatment + **doxycycline** PO: 200 mg once daily for 6 weeks (in adults) • Pyomyositis: antibiotics and surgical drainage, see Pyomyositis(see page 268), Chapter 10. • Primary and secondary syphilis: see Genital ulcers(see page 235), Chapter 9. **Viral infections** • Herpes zoster: see Herpes simplex and herpes zoster(see page 110), Chapter 4. For necrotic, extensive forms, eruption on the face, ophthalmic zoster, add **aciclovir** within 48 hours of the onset of lesions: Children (IV route): 5 to 10 mg/kg every 8 hours for 7 days Adults (oral route): 800 mg 5 times daily for 7 days • Herpes simplex: see Herpes simplex and herpes zoster(see page 110), Chapter 4. • Genital warts: see Venereal warts(see page 241), Chapter 9. **Fungal infections** • Candidiasis: **2% miconazole** cream, one application 2 times daily • Dermatophytoses: see Superficial fungal infections(see page 96), Chapter 4. **Treatment of Kaposi sarcoma (KS)** • Start promptly ART. • KS tumours with oedema or ulceration or presence of extensive oral or gastrointestinal or pulmonary KS +/- systemic illness: chemotherapy **Other skin infections** • Prurigo, urticaria: see Other skin disorders(see page 111), Chapter 4. • Seborrhoeic dermatitis: **Whitfield's** ointment or **2% miconazole**, one application 2 times daily. For severe inflammation, use a topical corticosteroid in combination with miconazole. • Xerosis: **zinc oxide** ointment or **calamine** lotion • Psoriasis: **corticosteroids** and **zinc oxide** ointment • Scabies: local treatment. For crusted or profuse scabies, add **ivermectin** PO (see Scabies(see page 92), Chapter 4).

Symptoms	Definitions and aetiologies	Diagnosis	Treatment
Neurological disorders in adults	Aetiologies: **Infections** • TB meningitis • Cryptococcal meningitis • Cerebral toxoplasmosis • Neurosyphilis • CMV encephalitis • HIV encephalopathy • Progressive multifocal leuko-encephalopathy • Cerebral malaria **Neoplasms** • Primary CNS lymphoma **Common causes of headache unrelated to HIV infection**: sometimes more frequent in HIV infected patients (sinusitis, problems with accommodation etc.) **Adverse effects of ARVs**	History and clinical examination: • Change in mental state • Focal deficits • Seizures • Signs of meningeal irritation • Raised intercranial pressure • Motor problems, ataxia In settings where cryptococcal infection is common, screen all adults with CD4 < 100 prior to initiation of ART, using a rapid CrAg test on serum or plasma. In endemic areas: check for malaria (if febrile). Lumbar puncture (LP) if not contra-indicated. Elements in favour of neurosyphilis: • VDRL positive in blood and/or CSF • cells in the CSF • high protein in the CSF	Positive malaria test: see Malaria(see page 123), Chapter 6. If focal signs, treat for toxoplasmosis: **co-trimoxazole** PO: 25 mg SMX + 5 mg TMP/kg 2 times daily for 4 to 6 weeks or **pyrimethamine** PO: 100 mg morning and evening on D1, then 75 to 100 mg daily + **sulfadiazine** PO: 2 g 2 to 3 times daily + **folinic acid** PO: 15 mg once daily, for 6 weeks *A secondary prophylaxis is recommended.* If the LP is positive: • Bacterial meningitis(see page 157): see Chapter 7. • TB meningitis: see the guide Tuberculosis, MSF. • Cryptococcal meningitis[2](see page 220): **amphotericin B** IV: 1 mg/kg once daily + **flucytosine** PO: 25 mg/kg 4 times daily for 1 week then **fluconazole** PO: 1200 mg once daily for 1 week then 800 mg once daily for 8 weeks or, if not available **amphotericin B** IV: 1 mg/kg once daily + **fluconazole** PO: 1200 mg once daily for 2 weeks then **fluconazole** PO alone: 800 mg once daily for 8 weeks or **fluconazole** PO: 1200 mg once daily + **flucytosine** PO: 25 mg/kg 4 times daily for 2 weeks then **fluconazole** PO alone: 800 mg once daily for 8 weeks During the induction phase: give fluconazole IV (same doses) if the patient cannot take oral treatment; liposomal amphotericin B (3 mg/kg daily 2 weeks) may be used instead of conventional amphotericin B in case of renal impairment. *A secondary prophylaxis is recommended.* *Note*: intracranial pressure (ICP) is often raised in cryptococcal meningitis. To lower ICP, repeated 'therapeutic' punctures to drain CSF may be necessary at the beginning of treatment. Neurosyphilis: **benzylpenicillin** IV: 2 to 4 MIU (1.2 to 2.4 g) every 4 hours for 14 days or **ceftriaxone** IV or IM: 2 g once daily for 10 to 14 days Headache of unknown origin: symptomatic treatment starting with a step 1 analgesic (see Pain(see page 23), Chapter 1).

Symptoms	Definitions and aetiologies	Diagnosis	Treatment
Neurological disorders in children	Aetiologies: • Bacterial meningitis • TB meningitis • Cryptococcal meningitis • Cerebral toxoplasmosis • CMV meningo-encephalitis • Cerebral malaria	Good history taking as only patients with acute episodes benefit from specific aetiological treatment (seizures, meningeal syndrome, focal signs). In endemic areas, check for malaria (if febrile). Lumbar puncture (LP) if not contra-indicated.	Positive malaria test: see Malaria(see page 123), Chapter 6. If LP is not possible: • Treat for bacterial meningitis(see page 157) if patient febrile and/or meningeal syndrome (see Chapter 7). • If focal signs, treat for toxoplasmosis: **co-trimoxazole** PO: 25 mg SMX + 5 mg TMP/kg 2 times daily for 4 to 6 weeks or **pyrimethamine** PO: 1 mg/kg 2 times daily for 2 days then 1 mg/kg once daily + **sulfadiazine** PO: 40 mg/kg 2 times daily + **folinic acid** PO: 10 mg once daily, for 8 weeks *A secondary prophylaxis is recommended.* If the LP is positive: • Bacterial meningitis(see page 157): see Chapter 7. • TB meningitis: see the guide Tuberculosis, MSF. • Cryptococcal meningitis (in order of preference)[2](see page 220): **amphotericin B** IV: 1 mg/kg once daily + **flucytosine** PO: 25 mg/kg 4 times daily for 1 week then **fluconazole** PO: 12 mg/kg once daily (max. 800 mg daily) for 1 week then 6-12 mg/kg once daily (max. 800 mg daily) for 8 weeks or, if not available **amphotericin B** IV: 1 mg/kg once daily + **fluconazole** PO: 12 mg/kg once daily (max. 800 mg daily) for 2 weeks then **fluconazole** PO alone: 6-12 mg/kg once daily for 8 weeks (max. 800 mg daily) or **fluconazole** PO: 12 mg/kg once daily (max. 800 mg daily) + **flucytosine** PO: 25 mg/kg 4 times daily for 2 weeks then **fluconazole** PO alone: 6-12 mg/kg once daily (max. 800 mg daily) for 8 weeks During the induction phase: give fluconazole IV (same doses) if the child cannot take oral treatment; liposomal amphotericin B (3 mg/kg daily, 2 weeks) may be used instead of conventional amphotericin B in case of renal impairment. *A secondary prophylaxis is recommended.*

Symptoms	Definitions and aetiologies	Diagnosis	Treatment
Persistent or recurrent fever	Temperature > 38 °C, chronic (lasting more than 5 days) or recurrent (multiple episodes in a period of more than 5 days) Aetiologies: **Infections** • Common childhood diseases • Severe bacterial infections (TB, pneumonia, typhoid fever, septicaemia, meningitis, endocarditis, etc.) • Occult bacterial infections (sinusitis, otitis, urinary tract infections) • Opportunistic infections (TB, mycosis, toxoplasmosis) • Malaria **Neoplasms** • Non-Hodgkin's lymphoma **HIV infection** **Fever caused by medication**	1. History and clinical examination: look for a ENT or urinary infection, TB, skin infection, enlarged lymph nodes etc. 2. In endemic areas, check for malaria. 3. Suspected TB: look for AFB. 4. Chest x-ray, CBC, blood cultures, urinalysis, stool culture, serology, lumbar puncture (LP). If the child is under treatment, consider adverse effects of medication.	Positive malaria test: see Malaria(see page 123), Chapter 6. If testing is not available: in endemic areas, treat malaria. Suspected meningitis: treat according to the results of the LP. If LP is not available, treat for bacterial meningitis(see page 157), see Chapter 7. Identified or suspected focus of infection: • ENT: see Chapter 2(see page 43); urinary: see Chapter 9(see page 221), etc. • TB: see the guide Tuberculosis, MSF.

References

1. World Health Organization. WHO case definitions of HIV for surveillance and revised clinical staging and immunological classification de HIV-related disease in adults and children, 2007. http://www.who.int/hiv/pub/guidelines/HIVstaging150307.pdf [Accessed 17 May 2018]

2. Word Health Organization. Guidelines for the diagnosis, prevention, and management of cryptococcal disease in HIV-infected adults, adolescents and children, Geneva, 2018. http://apps.who.int/iris/bitstream/handle/10665/260399/9789241550277-eng.pdf?sequence=1 [Accessed 17 May 2018]

Chapter 9: Genito-urinary diseases

- Nephrotic syndrome in children(see page 221)
- Urolithiasis(see page 224)
- Acute cystitis(see page 225)
- Acute pyelonephritis(see page 226)
- Acute prostatitis(see page 228)
- Genital infections(see page 229)
- Urethral discharge(see page 231)
- Abnormal vaginal discharge(see page 233)
- Genital ulcers(see page 235)
- Lower abdominal pain in women(see page 238)
- Upper genital tract infections (UGTI)(see page 239)
- Venereal warts(see page 241)
- Major genital infections (summary)(see page 243)
- Metrorrhagia (unrelated to pregnancy)(see page 246)

Nephrotic syndrome in children

- Clinical features(see page 221)
- Laboratory(see page 222)
- Treatment(see page 222)
- Management of complications(see page 223)

– Nephrotic syndrome (NS) is characterized by the presence of oedema, heavy proteinuria, hypoalbuminemia, and hyperlipidaemia.

– Primary or idiopathic NS is the most common cause of NS in children between 1 and 10 years. It usually responds to corticosteroids.

– Secondary NS is associated with infectious diseases (e.g. post-infectious glomerulonephritis, endocarditis, hepatitis B and C, HIV infection, malaria, and schistosomiasis) and may respond to treatment of the underlying cause.

– Children with NS are at increased risk of thromboembolism, severe bacterial infections (in particular, due to *S. pneumoniae*) and malnutrition. Untreated NS may progress to renal failure.

Clinical features

– Typically, the child presents with soft, pitting and painless oedema, which varies in location based on position and activity. Upon awaking, the child has periorbital or facial oedema, which over the day decreases as oedema of the legs increases. As oedema worsens, it may localize to the back or genitals, or become generalized with ascites and pleural effusions.

– This oedema should be differentiated from the oedema of severe acute malnutrition (SAM): in SAM, the child presents with bilateral pitting oedema of the feet and lower legs that does not vary with position. Oedema extends upwards to hands and face in severe cases. It is usually associated with typical skin and hair changes (see Kwashiorkor: Severe acute malnutrition(see page 38), Chapter 1).

– Once SAM is excluded, the following two criteria must be met to make a clinical diagnosis of primary NS:
• Presence of heavy proteinuria,

and
• Absence of associated infections: see Hepatitis B and C(see page 192) and HIV infection(see page 206) (Chapter 8), Malaria(see page 123) and Schistosomiases(see page 142) (Chapter 6).

Laboratory

– Urine
• Measure protein with urinary dipstick on three separate voided urine samples (first voided urine if possible). In NS, proteinuria is equal or greater than +++ or equal or greater than 300 mg/dl or 30 g/litre 1(see page 0) . NS is excluded if heavy proteinuria is not consistently present.
• In case of macroscopic haematuria, or microscopic haematuria ≥ +, consider glomerulonephritis.

– Blood tests (if available)
• Serum albumin concentration less than 30 g/litre and hyperlipidaemia.
• Blood urea nitrogen (BUN) and creatinine most often in the normal range.

– Perform all necessary laboratory tests to exclude secondary NS.

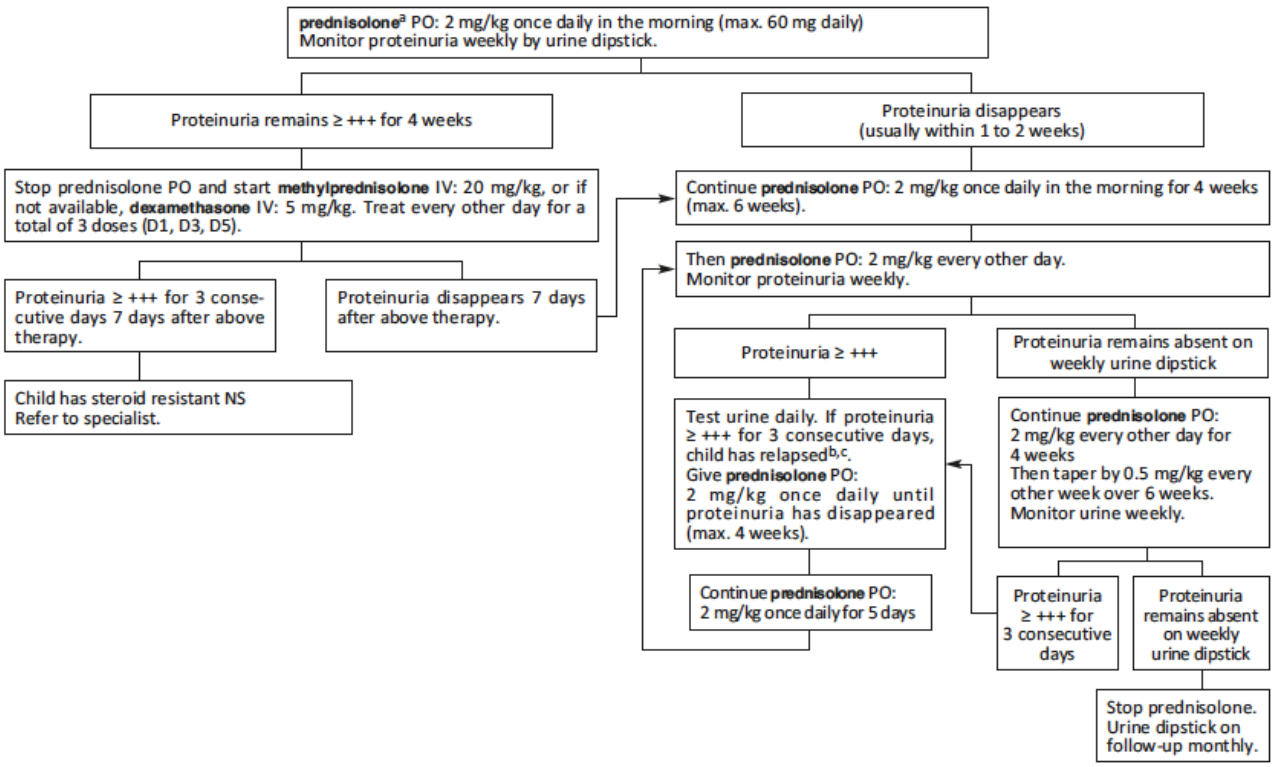
Treatment

– Hospitalize the child for initial therapy.

– Corticosteroids (prednisolone or prednisone) are indicated in primary NS.

– Before starting corticosteroid treatment:
• Treat any concomitant acute infections such as pneumonia, peritonitis, sepsis, pharyngitis, or cellulitis.
• Exclude active tuberculosis and/or start antituberculous treatment.

– Corticosteroid treatment
See algorithm below. Total length of initial treatment is 2 to 4 months.



[a] Prednisone may be used interchangeably with prednisolone in this algorithm.

[b] If child has relapsed more than once, treat until proteinuria disappears but then taper prednisolone down to 0.5 mg/kg every other day rather than discontinuing entirely and treat for 12 months. Continue

as long as proteinuria remains negative. If proteinuria recurs, treat as relapse. Child has steroid dependent NS.

[c] Frequent relapses: 2 or more in the first 6 months or 4 or more in a 12 month period.

– Nutrition, fluid intake, nursing and follow-up
• No salt-added diet.
• Do not restrict fluids (risk of thrombosis due to hypercoagulability). If oedema is very severe, fluids may initially be restricted (e.g. 75% of usual intake) while monitoring urine output.
• Encourage child to walk and play to prevent thromboembolism.
• Discharge child when stable, follow-up at least monthly, more frequently if indicated, weight and urine dipstick at each visit.
• Instruct the parent to continue no salt-added diet and to seek medical advice in case of fever, abdominal pain, respiratory distress or signs of thromboembolism.

– Management of infections
Treat infections as soon as they appear but do not routinely give prophylactic antibiotics.

– Immunization
• Children under 5 years: check that the child has received all EPI vaccines including *Haemophilus influenzae* type B, conjugated pneumococcal vaccine and (if in an endemic area) meningococcal A conjugate vaccine. If not, administer catch-up vaccines.
• Children over 5 years: check that the child has received tetanus, measles, pneumococcal conjugate and (if in an endemic area) meningococcal A conjugate vaccine. If not, administer catch-up vaccines.

Management of complications

– Intravascular volume depletion potentially leading to shock, present despite oedematous appearance
Signs include decreased urine output with any one of the following: capillary refill ≥ 3 seconds, poor skin perfusion/mottling, cold extremities, low blood pressure.
If signs are present, administer **human albumin 5%** IV: 1 g/kg. If albumin is not available, administer **Ringer lactate** or **0.9% sodium chloride**: 10 ml/kg over 30 minutes.
If signs of shock are present, see Shock(see page 10), Chapter 1.

– Respiratory distress due to severe oedema (rare)
This is the only situation in which diuretics should be used and only if there are no signs of intravascular volume depletion or after hypovolaemia has been corrected:
furosemide PO: 0.5 mg/kg 2 times daily
If not effective, discontinue furosemide. If creatinine is normal, administer **spironolactone** PO: 1 mg/kg 2 times daily. The dose can be increased to 9 mg/kg daily in resistant cases of ascites.
While on diuretics, monitor for dehydration, thromboembolism and hypokalaemia.

Specialized advice and management (including further investigations such as renal biopsy) are required:
– In children less than 1 year or more than 10 years,
– In case of steroid resistant NS,
– In case of mixed nephrotic and nephritic clinical picture.

In case of steroid-resistant NS, when referral is impossible and as a last resort, the following palliative measure may reduce proteinuria and delay renal failure:
enalapril PO: 0.1 to 0.3 mg/kg 2 times daily (start with the lowest dose and increase gradually if necessary until reduction of proteinuria). If available, monitor for hyperkalaemia.
This is a palliative measure and the prognosis for steroid-resistant NS is poor in the absence of specialized treatment.

[1](see page 0) Nephrotic range proteinuria in children is defined as urinary protein excretion greater than 50 mg/kg daily. Quantitative measurement of protein excretion is normally based on a timed 24-hour urine collection. However, if this test cannot be performed, urine dipstick measurements can be substituted.

Urolithiasis

- Clinical features(see page 224)
- Treatment(see page 224)

Urolithiasis is the formation and passage of calculi (stones) in the urinary tract.

Clinical features

– Many calculi do not cause symptoms; they may be found incidentally through radiology exams.
– Symptoms arise when calculi cause partial or complete obstruction and/or infection:
• Intermittent, acute flank to pelvic pain (renal colic). Pain can be severe and typically causes nausea and vomiting. Abdomen/flank may be tender to palpation. Patients are typically restless, finding no comfortable position.
• Haematuria and/or gravel (calculi) passed in urine.
• Fever and signs of pyelonephritis if secondary infection develops (see Acute pyelonephritis(see page 226), Chapter 9).

Note: if available, ultrasound may demonstrate calculi and hydronephrosis.

Treatment

– Encourage the patient to drink fluids.

– Administer analgesics according to the intensity of pain:
Adults:
ibuprofen PO + **paracetamol** PO (see Pain(see page 23), Chapter 1) +/- **hyoscine butylbromide** PO[1](see page 0) (10 to 20 mg every 8 hours if necessary) for 1 to 3 days
or
diclofenac IM: 75 mg to be repeated after 6 hours if necessary (max. 150 mg daily) +/- **hyoscine butylbromide** IM[1](see page 0) : 20 mg every 8 hours if necessary
Change to oral treatment, if necessary, after 1 to 2 days (**ibuprofen** PO and/or **paracetamol** PO).

In the event of failure to respond or contra-indications: **morphine** IV (see Pain(see page 23), Chapter 1).

– In case of secondary infection: antibiotic treatment as for pyelonephritis(see page 226). The effectiveness will depend on the passage of calculi.

Note: the majority of calculi pass spontaneously. If there are signs of significant renal dysfunction or secondary infection that does not improve with antibiotic treatment, consider surgical referral.

[1](see page 0) Hyoscine butylbromide may cause urinary retention, dryness of the mouth, constipation, blurred vision and tachycardia. If patients are able to tolerate the adverse effects, it may be helpful in controlling the pain of renal colic. [a(see page 0) b(see page 0)]

Acute cystitis

- Clinical features(see page 225)
- Laboratory(see page 225)
- Treatment(see page 225)
  - Cystitis in girls ≥ 2 years(see page 225)
  - Cystitis in non pregnant women(see page 226)
  - Cystitis in pregnant or lactating women(see page 226)

Cystitis is an infection of the bladder and urethra that affects mainly women and girls from 2 years of age. *Escherichia coli* is the causative pathogen in at least 70% of cases. Other pathogens include *Proteus mirabilis*, *Enterococcus* sp, *Klebsiella* sp and in young women, *Staphylococcus saprophyticus*.

Clinical features

– Burning pain on urination and urinary urgency and frequency; in children: crying when passing urine; involuntary loss of urine.
AND
– No fever (or mild fever), no flank pain; no systemic signs and symptoms in children.

It is essential to rule out pyelonephritis(see page 226).
The symptom 'burning pain on urination' alone is insufficient to make the diagnosis. See Abnormal vaginal discharge(see page 233).

Laboratory

– Urine dipstick test:
Perform dipstick analysis for nitrites (which indicate the presence of enterobacteria) and leukocytes (which indicate an inflammation) in the urine.
• If dipstick analysis is negative for both nitrites and leukocytes, a urinary infection is excluded.
• If dipstick analysis is positive for nitrites and/or leukocytes, a urinary infection is likely.
– Microscopy/culture: when a dipstick analysis is positive, it is recommended to carry out urine microscopy/culture in order to confirm the infection and identify the causative pathogen, particularly in children and pregnant women.

When urine microscopy is not feasible, an empirical antibiotherapy should be administered to patients with typical signs of cystitis and positive dipstick urinalysis (leucocytes and/or nitrites).

Note: aside of these results, in areas where urinary schistosomiasis is endemic, consider schistosomiasis in patients with macroscopic haematuria or microscopic haematuria detected by dipstick test, especially in children from 5 to 15 years, even if the patient may suffer from concomitant bacterial cystitis.

Treatment

Cystitis in girls ≥ 2 years

cefixime PO: 8 mg/kg once daily for 3 days
or
amoxicillin/clavulanic acid PO (dose expressed in amoxicillin): 12.5 mg/kg 2 times daily for 3 days

Cystitis in non pregnant women

– If dipstick analysis is positive for both nitrites and leukocytes:
fosfomycin-trometamol PO: 3 g single dose
or
nitrofurantoin PO: 100 mg 3 times daily for 5 to 7 days
– If dipstick analysis is negative for nitrites but positive for leukocytes, the infection may be due to *S. saprophyticus*. Fosfomycin is not active against this pathogen. Use nitrofurantoin as above.
– Whatever the antibiotic used, symptoms may persist for 2 to 3 days despite adequate treatment.
– In the event of treatment failure (or recurrent cystitis i.e. > 3-4 episodes per year), **ciprofloxacin** PO: 500 mg 2 times daily for 5 days
– For patients with recurrent cystitis, consider bladder stones, urinary schistosomiasis, urinary tuberculosis or gonorrhoea (examine the partner).

Cystitis in pregnant or lactating women

fosfomycin-trometamol PO: 3 g single dose
or
cefixime PO: 200 mg 2 times daily for 5 days

Acute pyelonephritis

- Clinical features(see page 226)
- Laboratory(see page 227)
- Treatment(see page 227)
- References(see page 228)

– Pyelonephritis is an infection of the renal parenchyma, more common in women than in men.
– The pathogens causing pyelonephritis are the same as those causing cystitis (see Acute cystitis(see page 225), Chapter 9).
– Pyelonephritis is potentially severe, especially in pregnant women, neonates and infants.
– Management depends on the presence of signs of severity or complications or risk of complications.

Clinical features

Neonates and infant

– Symptoms are not specific: fever, irritability, vomiting, poor oral intake. Palpation of the lower abdomen may show abdominal tenderness. The absence of fever does not rule out the diagnosis. On the other hand, fever –with no obvious cause– may be the only manifestation.
– Neonates may present with fever or hypothermia, altered general condition, altered conscious state, pale/grey colour, shock.

In practice, a urinary tract infection should be suspected in children with unexplained fever or septic syndrome with no obvious focus of infection.

Older children and adults

– Signs of cystitis (burning pain on urination and urinary urgency and frequency, etc.)
AND

– Fever > 38 °C and unilateral flank pain or abdominal tenderness
– Nausea and/or vomiting are common.

Laboratory

See Acute cystitis(see page 225), Chapter 9.

Treatment

– Criteria for hospital admission:

• Patients at risk of complications: children, pregnant women, men[1](see page 0) , functional or structural abnormality of the urinary tract (lithiasis, malformation, etc.), severe immunodeficiency;
• Patients with complicated pyelonephritis: urinary tract obstruction, renal abscess, emphysematous pyelonephritis in diabetic patients;
• Patients with signs of severe infection: sepsis (infection with signs of organ dysfunction) and septic shock, dehydration or nausea/vomiting preventing hydration and oral treatment;
• No clinical improvement 24 hours after the start of oral antibiotherapy in women treated as outpatients.

– Antibiotherapy in children

• *Children under one month*
ampicillin slow IV (3 minutes) for 7 to 10 days
Children 0 to 7 days (< 2 kg): 50 mg/kg every 12 hours
Children 0 to 7 days (≥ 2 kg): 50 mg/kg every 8 hours
Children 8 days to < 1 month: 50 mg/kg every 8 hours
+ **gentamicin** slow IV (3 minutes) for 5 days
Children 0 to 7 days (< 2 kg): 3 mg/kg once daily
Children 0 to 7 days (≥ 2 kg): 5 mg/kg once daily
Children 8 days to < 1 month: 5 mg/kg once daily
or
cefotaxime slow IV (3 minutes) for 7 to 10 days
Children 0 to 7 days (< 2 kg): 50 mg/kg every 12 hours
Children 0 to 7 days (≥ 2 kg): 50 mg/kg every 8 hours
Children 8 days to < 1 month: 50 mg/kg every 8 hours

• *Children one month and over*
ceftriaxone IM or slow IV[2](see page 0) (3 minutes): 50 mg/kg once daily until the child's condition improves (at least 3 days)
then change to oral route to complete 10 days of treatment with:
amoxicillin/clavulanic acid PO (dose expressed in amoxicillin)
Children < 40 kg: 25 mg/kg 2 times daily
Children ≥ 40 kg:
Ratio 8:1: 2000 mg daily (2 tablets of 500/62.5 mg 2 times daily)
Ratio 7:1: 1750 mg daily (1 tablet of 875/125 mg 2 times daily)

– Antibiotherapy in adults[1](see page 228)

• *Uncomplicated pyelonephritis*
ceftriaxone IM: 1 g single dose or **gentamicin** IM: 5 mg/kg single dose
+
ciprofloxacin PO: 500 mg 2 times daily for 7 days
or
amoxicillin/**clavulanic acid** PO (dose expressed in amoxicillin) for 10 to 14 days
Ratio 8:1: 2000 mg daily (2 tablets of 500/62.5 mg 2 times daily)
Ratio 7:1: 1750 mg daily (1 tablet of 875/125 mg 2 times daily)

or
cefixime PO: 200 mg 2 times daily or 400 mg once daily for 10 to 14 days

• *Pyelonephritis with criteria for hospital admission*
ampicillin slow IV (3 minutes): 2 g every 6 hours for at least 3 days + **gentamicin** IM: 5 mg/kg once daily for 3 days then change to amoxicillin/clavulanic acid PO (or another antibiotic depending on the antibiotic susceptibility test) to complete 10 to 14 days of treatment
or
ceftriaxone IV[2](see page 0) : 1 g once daily for at least 3 days + **gentamicin** IM: 5 mg/kg once daily for 3 days in the event of sepsis then change to amoxicillin/clavulanic acid PO (or another antibiotic depending on the antibiotic susceptibility test) to complete 10 to 14 days of treatment

Preferably use the combination ampicillin + gentamicin to cover enterococci.
Pyelonephritis with abscess formation or emphysematous pyelonephritis may require longer antibiotherapy.

– Treatment of fever and pain: do not administer NSAID (Fever(see page 21), Chapter 1).
– Maintain proper hydration (1.5 litres daily in adults), especially in children (risk of dehydration); treat dehydration if present (see Dehydration(see page 34), Chapter 1).
– Management of septic shock if needed.

[1](see page 0) Pyelonephritis is rare in men; bacterial prostatitis should be suspected in the event of febrile urinary tract infection.
[2](see page 0) The solvent of ceftriaxone for IM injection contains lidocaine. Ceftriaxone reconstituted using this solvent must never be administered by IV route. For IV administration, water for injection must always be used. [a(see page 0) b(see page 0)]

References

1. Gupta K, Hooton TM, Naber KG, Wullt B, Colgan R, Miller LG, Moran GJ, Nicolle LE, Raz R, Schaeffer AJ, Soper DE, Infectious Diseases Society of America, European Society for Microbiology and Infectious Diseases. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. Clin Infect Dis. 2011;52(5):e103.
https://academic.oup.com/cid/article/52/5/e103/388285 [Accessed 17 December 2018]

Acute prostatitis

- Clinical features(see page 229)
- Treatment(see page 229)
- References(see page 229)

– Prostatitis is an acute bacterial infection of the prostate.
– The most common causative pathogen is *Escherichia coli*. Other pathogens include *Proteus mirabilis, Klebsiella* sp, *Pseudomonas aeruginosa* and *Enterococcus* sp.
– Progression to chronic prostatitis is possible.

Clinical features

– Fever (often high) and chills.
– Signs of cystitis (burning on urination and urinary frequency).
– Perineal, urethral, penile or rectal pain.
– Urinary retention.

On examination:
– Very painful digital rectal examination. Fluctuant mass in case of prostatic abscess.
– Leukocyturia, pyuria, possible macroscopic haematuria.

Treatment

– Antibiotic therapy:
ciprofloxacin PO: 500 mg 2 times daily for 14 days then review the patient. Stop treatment if signs and symptoms have completely resolved. If signs and symptoms are ongoing continue the same treatment for a further 14 days.[1](see page 229)

– Symptomatic treatment:
• Ensure adequate hydration (1.5 litres daily).
• Treat fever(see page 21) (Chapter 1) and pain(see page 23) (Chapter 1).

– Refer to a surgeon in case of suspected prostatic abscess.

References

1. National Institute for Health and Care Excellence. NICE guideline [NG110] Prostatitis (acute): antimicrobial prescribing, 2018. https://www.nice.org.uk/guidance/ng110/resources/visual-summary-pdf-6544018477 [Accessed 4 March 2020]

Genital infections

- Basic principles of GI management(see page 230)
- Special situation: sexual violence(see page 230)

The diagnosis and treatment of genital infections (GI) present several difficulties: clinical features are not specific; many infections are asymptomatic; laboratory tests available in the field are not always reliable; mixed infections are common; partners need to be treated simultaneously in case of sexually transmitted infections[1](see page 0) and the risk of recurrence or treatment failure is increased in HIV-infected patients.

Thus, the WHO has introduced the syndromic management of GI and developed standardised case management flowcharts: based on the identification of consistent groups of signs and symptoms (syndromes), patients are treated for the pathogens/ infections[2](see page 0) that may cause each syndrome.

Look for a GI if a patient complains of:	See
Urethral discharge Painful or difficult urination (dysuria)	Urethral discharge(see page 231)
Abnormal vaginal discharge Vulvar itching/burning Pain with intercourse (dyspareunia) Painful or difficult urination (dysuria)	Abnormal vaginal discharge(see page 233)
Genital blisters or sores Burning sensation in the vulva or perineum	Genital ulcers(see page 235)
Skin growths in the genital (or anal) area	Venereal warts(see page 241)
Lower abdominal pain (in women)	Lower abdominal pain(see page 238) Upper genital tract infections(see page 239)

Basic principles of GI management

– The patient can be effectively treated without laboratory testing. Some tests may help in diagnosing vaginal and urethral discharge, but they should never delay treatment (results should be available within one hour).

– The patient should be treated at his/her first encounter with the health care provider (no patient should be sent home without treatment, e.g. while waiting for laboratory results).

– Single dose regimens are preferred when indicated.

– In the case of urethral discharge, abnormal vaginal discharge (except candidiasis), genital ulcers (except herpes) and sexually transmitted upper genital tract infection, the sexual partner should receive a treatment. In the case of candidiasis, genital herpes and venereal warts, the partner is treated only if symptomatic.

– Patients with sexually transmitted infections should receive information on their disease(s) and treatment and be counselled on risk reduction and HIV testing. Condoms should be provided for the duration of treatment.

Special situation: sexual violence

Taking into consideration the physical, psychological, legal and social consequences of sexual violence, *medical care* is not limited to the diagnosis and treatment of genital lesions or infections.

Care includes listening to the victim's story, a complete physical examination, laboratory tests if available, and completion of a medical certificate.

During the consultation, prophylactic or curative treatments must be proposed to the patient.

– **Prophylactic treatment:**

• priority is given to:
a) the risk of HIV transmission. Start antiretroviral therapy as early as possible if the patient is seen within 48-72 hours after exposure (see HIV infection and AIDS(see page 206), Chapter 8);
b) the risk of pregnancy resulting from rape. Administer emergency contraception as soon as possible, ideally within 72 hours after the rape: **levonorgestrel** PO, one 1.5 mg tablet single dose (including in women receiving HIV post-exposure prophylaxis)[3](see page 0); double the dose (3 mg)

only if the patient was already taking enzyme-inducing drug(s) (e.g. rifampicin, carbamazepine, certain antiretrovirals) before the rape;

• prevention of sexually transmitted infections includes a single dose treatment with **azithromycin** PO 2 g + **ceftriaxone** IM 250 mg (or, if ceftriaxone is not available, **cefixime** PO 400 mg). If necessary, treatment of trichomoniasis may be started later than the other treatments (**tinidazole** or **metronidazole** PO, 2 g single dose);

• tetanus prophylaxis and/or vaccination (see Tetanus(see page 162), Chapter 7) if there are any wounds;

• vaccination against hepatitis B (accelerated vaccination schedule, see Viral hepatitis(see page 192), Chapter 8).

– **Curative treatment:**

• of wounds,
• of any related pathologies/infections if the assault is not recent.

Mental health care is necessary irrespective of any delay between the event and the patient arriving for a consultation. Care is based on immediate attention (one-on-one reception and listening) and if necessary, follow-up care with a view to detecting and treating any psychological and/or psychiatric sequelae (anxiety, depression, post-traumatic stress disorder, etc.). See Chapter 11(see page 278).

1(see page 0) GI may be sexually transmitted (e.g. gonorrhoea, chlamydia) or not (e.g. most cases of candidiasis).
2(see page 0) Keep in mind that in *Schistosoma haematobium* endemic areas, genital symptoms may also be due to, or associated with, genitourinary schistosomiasis (see Schistosomiasis(see page 142), Chapter 6).
3(see page 0) Nevertheless, between 72 and 120 hours (5 days) after the rape, emergency contraception is still sufficiently effective to be administered.

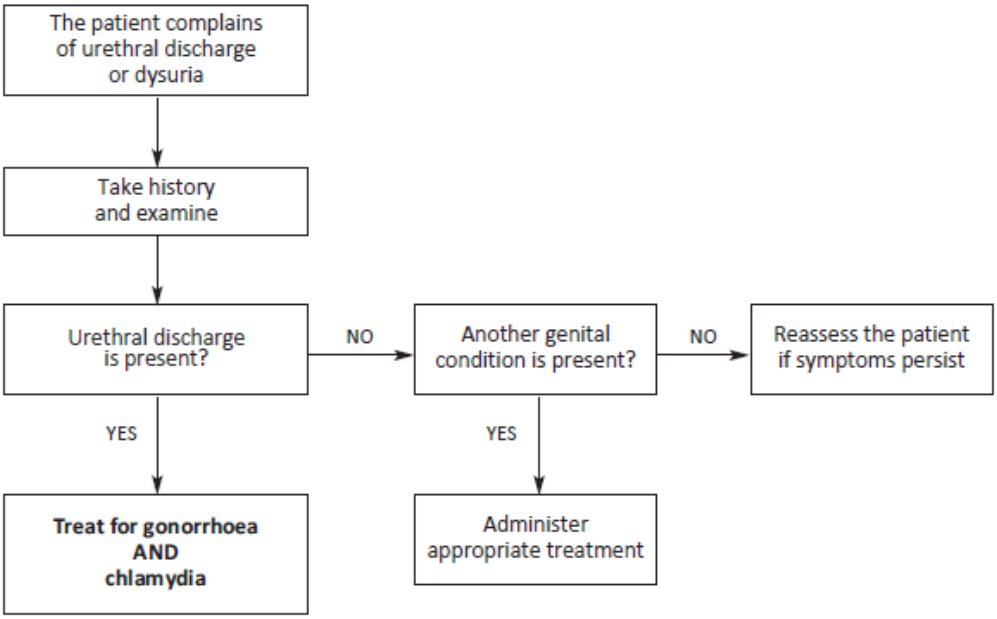
Urethral discharge

- Case management(see page 232)
- Laboratory(see page 232)
- Treatment of the patient(see page 232)
- Treatment of the partner(see page 233)

Urethral discharge is seen almost exclusively in men. The principal causative organisms are *Neisseria gonorrhoeae* (gonorrhoea) and *Chlamydia trachomatis* (chlamydia).

Abnormal discharge should be confirmed by performing a clinical examination 1(see page 0) . In males, the urethra should be milked gently if no discharge is visible. Furthermore, specifically check for urethral discharge in patients complaining of painful or difficult urination (dysuria).

Case management



Laboratory

– *C. trachomatis* cannot easily be identified in a field laboratory. In the absence of validated rapid diagnostic tests, the treatment is empiric.
– In men, a methylene blue or Gram stained smear from a urethral swab may be used to detect gonococci (Gram negative intracellular diplococci).

Treatment of the patient

– In women: same treatment as cervicitis(see page 235).

– In men:
• If microscopy of a urethral smear has been performed: in the absence of gonococci, treat for chlamydia alone; in the presence of gonococci, treat for chlamydia AND gonorrhoea.
• When no laboratory is available, treat for chlamydia AND gonorrhoea as below:

Treatment for chlamydia	**PLUS**	**Treatment for gonorrhoea**
azithromycin PO: 1 g single dose or **doxycycline** PO: 100 mg 2 times daily for 7 days		**ceftriaxone** IM: 250 mg single dose or, if ceftriaxone is not available, **cefixime** PO: 400 mg single dose or **spectinomycin** IM: 2 g single dose

If urethral discharge persists or reappears after 7 days:
– Verify that the patient has received an effective treatment (i.e. one of the combinations above).
– Gonococcal resistance is a possibility if another treatment (e.g. co-trimoxazole or kanamycin) has been administered: re-treat for gonorrhoea as above (chlamydia is rarely resistant).
– If an effective antibiotic therapy has been given, consider trichomoniasis (**tinidazole** or **metronidazole** PO, 2 g single dose); also consider re-infection.

Treatment of the partner

The sexual partner receives the same treatment as the patient, whether or not symptoms are present.

1 (see page 0) In areas where lymphatic filariasis is endemic, be careful not to confuse purulent urethral discharge with milky or rice-water urine (chyluria) suggestive of lymphatic filariasis.

Abnormal vaginal discharge

- Case management (see page 234)
- Laboratory (see page 234)
- Treatment of the patient (see page 235)
- Treatment of the partner (see page 235)

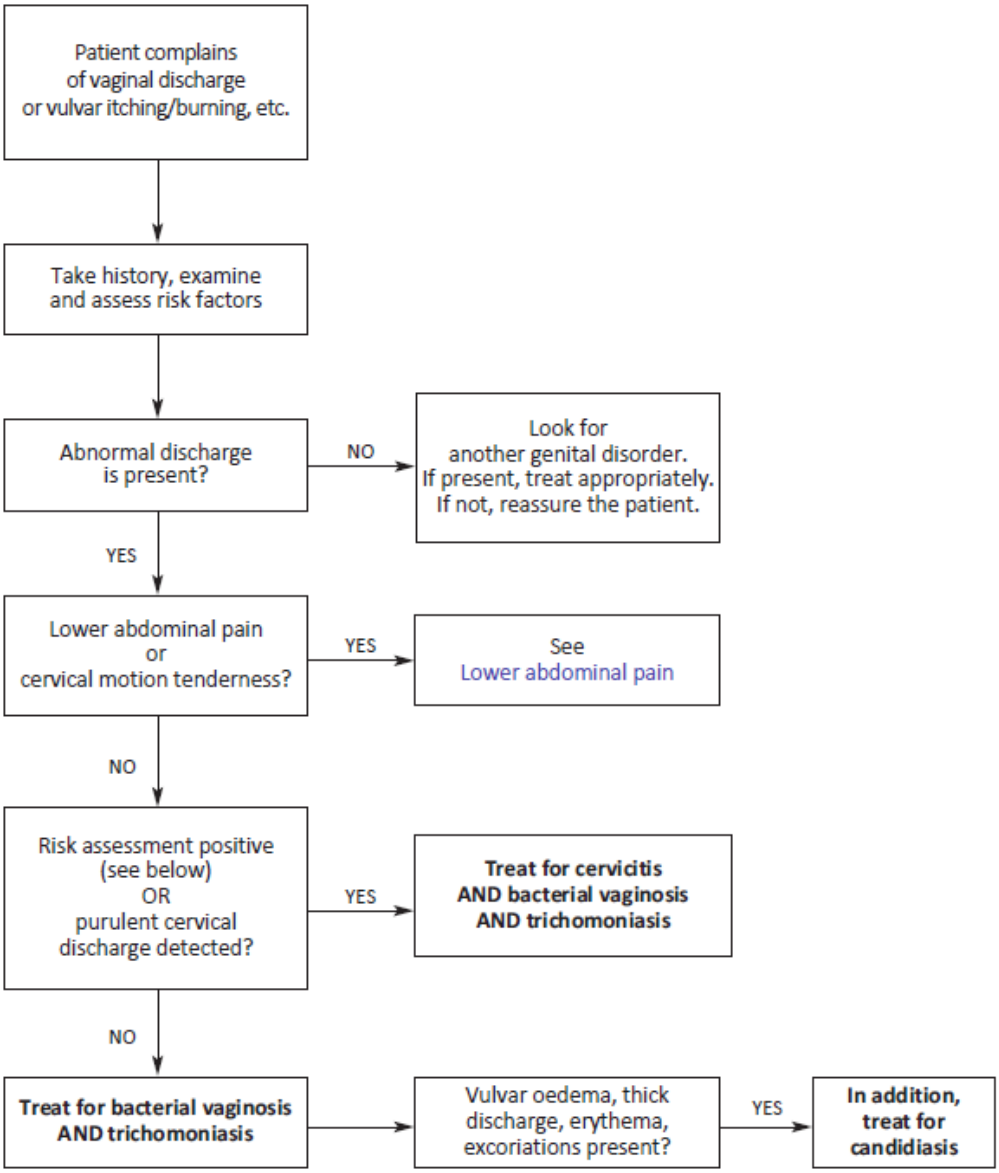
Abnormal vaginal discharge is defined as discharge that differs from usual with respect to colour/odour/consistency (e.g. discoloured or purulent or malodorous).

Abnormal discharge is often associated with vulvar pruritus or pain with intercourse (dyspareunia), or painful or difficult urination (dysuria) or lower abdominal pain. Routinely check for abnormal vaginal discharge in women presenting with these symptoms.

Abnormal vaginal discharge may be a sign of infection of the vagina (vaginitis) and/or the cervix (cervicitis) or upper genital tract infection.
Abnormal discharge must be clinically confirmed: inspection of the vulva, speculum exam checking for cervical/vaginal inflammation or discharge.
Abdominal and bimanual pelvic examinations should be performed routinely in all women presenting with vaginal discharge to rule out upper genital tract infection (lower abdominal pain and cervical motion tenderness).

The principal causative organisms are:
– In vaginitis: *Gardnerella vaginalis* and other bacteria (bacterial vaginosis), *Trichomonas vaginalis* (trichomoniasis) and *Candida albicans* (candidiasis).
– In cervicitis: *Neisseria gonorrhoeae* (gonorrhoea) and *Chlamydia trachomatis* (chlamydia).
– In upper genital tract infections: see UGTI (see page 239).

Case management



Cervicitis may be difficult to diagnose. When in doubt, administer treatment for cervicitis to women with abnormal vaginal discharge and any of the following risk factors:
– Urethral discharge in the partner
– Context of sexual violence or prostitution
– New partner or more than one partner in the preceding 3 months

Laboratory

– Tests usually available in the field can only identify causes of vaginitis, and thus are of limited usefulness.
Microscopic examination of a fresh wet smear may show mobile *T. vaginalis*, yeast cells and hyphae in candidiasis, and “clue cells” in bacterial vaginosis.
– Identification of *N. gonorrhoeae* by Gram stained smear is not sensitive in women and is not recommended.

Treatment of the patient

Cervicitis

Treat for both chlamydia AND gonorrhoea.

Non-pregnant women		
Treatment for chlamydia **azithromycin** PO: 1 g single dose or **doxycycline** PO: 100 mg 2 times daily for 7 days	**PLUS**	**Treatment for gonorrhoea** **ceftriaxone** IM: 250 mg single dose or, if not available, **cefixime** PO: 400 mg single dose or **spectinomycin** IM: 2 g single dose
Pregnant women		
azithromycin PO: 1 g single dose or **erythromycin** PO: 1 g 2 times daily or 500 mg 4 times daily for 7 days	**PLUS**	**ceftriaxone** IM: 250 mg single dose or, if not available, **cefixime** PO: 400 mg single dose

Bacterial vaginosis and trichomoniasis

tinidazole PO: 2 g single dose
or **metronidazole** PO: 2 g single dose

In the case of treatment failure:
tinidazole PO: 500 mg 2 times daily for 5 days
or **metronidazole** PO: 400 to 500 mg 2 times daily for 7 days

Vulvovaginal candidiasis

clotrimazole (500 mg vaginal tab): 1 tablet inserted deep into the vagina at bedtime, single dose

If the patient has extensive vulvar involvement, **miconazole 2%** cream (one application to the vulva 2 times daily for 7 days) may be used in combination with the intravaginal treatment above. Miconazole cream may complement, but does not replace, treatment with clotrimazole.

Treatment of the partner

When the patient is treated for vaginitis or cervicitis, the partner receives the same treatment as the patient, whether or not symptoms are present.

In the case of vulvovaginal candidiasis, the partner is treated only if symptomatic (itching and redness of the glans/prepuce): **miconazole 2%** cream, one application 2 times daily for 7 days.

Genital ulcers

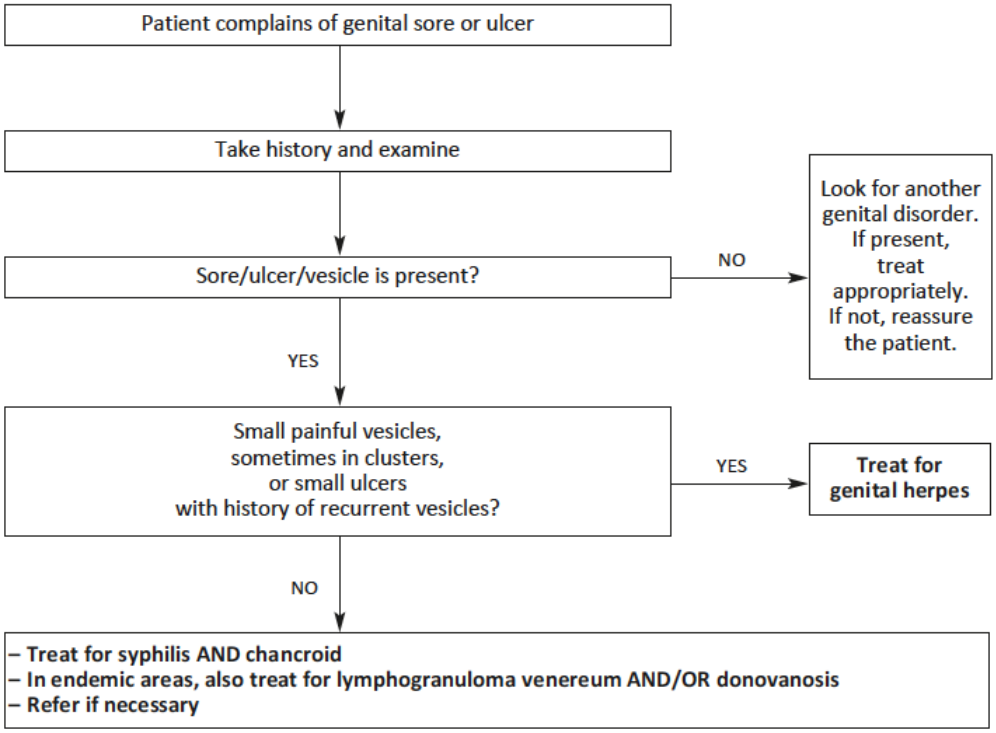
- Case management(see page 236)
- Laboratory(see page 236)
- Treatment of the patient(see page 236)
  - Genital herpes(see page 236)
  - Syphilis(see page 237)

- Chancroid(see page 237)
- Lymphogranuloma venereum(see page 237)
- Donovanosis(see page 237)
- Treatment of the partner(see page 238)
- References(see page 238)

Genital ulcers, defined as single or multiple vesicular, ulcerative or erosive lesions of the genital tract, with or without inguinal lymphadenopathy, should lead to consideration of sexually transmitted infection.

The principal causative organisms are *Treponema pallidum* (syphilis), *Haemophilus ducreyi* (chancroid) and *Herpes simplex* (genital herpes). *Chlamydia trachomatis* (lymphogranuloma venereum) and *Calymmatobacterium granulomatis* (donovanosis)[1](see page 0) are less frequent.

Case management



Laboratory

Laboratory testing available in the field is of little value: e.g., in syphilis, a negative RPR or VDRL result does not exclude primary syphilis in early stage, and a positive test may reflect previous infection in a successfully treated patient.

Treatment of the patient

Genital herpes

– Local treatment: clean the area with soap and water.

– Antiviral treatment: **aciclovir** PO
In patients with a first episode, treatment may reduce the duration of symptom when given within 5 days after the onset of symptoms: 400 mg 3 times daily for 7 days.

In patients with recurrence, give the same dose for 5 days, but treatment is only effective if initiated during the prodromal phase or within 24 hours after the onset of symptoms.
In patients with frequent recurrences (more than 6 episodes par year), see HIV infection and AIDS(see page 206), Chapter 8.

– Treatment of pain(see page 23): paracetamol PO (Chapter 1).

Syphilis

benzathine benzylpenicillin IM: 2.4 MUI per injection (half the dose in each buttock)[1](see page 238).
Early syphilis (primary, secondary, or early latent infection of less than 12 months duration): single dose
Late latent syphilis (infection of more than 12 months duration or of unknown duration): one injection weekly for 3 weeks
or, for penicillin-allergic patients or if penicillin is not available:
erythromycin PO: 1 g 2 times daily or 500 mg 4 times daily for 14 days (early syphilis) or 30 days (late latent syphilis)
or
doxycycline PO: 100 mg 2 times daily for 14 days (early syphilis) or 30 days (late latent syphilis)[2](see page 0)
or
azithromycin PO: 2 g single dose (only in cases of early syphilis and only if the strain is sensitive).[2](see page 238)

Chancroid

azithromycin PO: 1 g single dose
or
ceftriaxone IM: 250 mg single dose
or
erythromycin PO: 1 g 2 times daily or 500 mg 4 times daily for 7 days

Fluctuant lymph nodes may be aspirated through healthy skin as required. Do not incise and drain lymph nodes.

Note: treat simultaneously for syphilis AND chancroid as both are frequent, and cannot be correctly distinguished on clinical grounds.

Lymphogranuloma venereum

erythromycin PO: 1 g 2 times daily or 500 mg 4 times daily for 14 days
or
doxycycline PO: 100 mg 2 times daily for 14 days[2](see page 0)

Fluctuant lymph nodes may be aspirated through healthy skin as required. Do not incise and drain lymph nodes.

Donovanosis

Treatment is given until the complete disappearance of the lesions (usually, several weeks; otherwise risk of recurrence):
azithromycin PO: 1 g on D1 then 500 mg once daily
or
erythromycin PO: 1 g 2 times daily or 500 mg 4 times daily
or
doxycycline PO: 100 mg 2 times daily[2](see page 0)

In HIV infected patients, add **gentamicin** IM: 6 mg/kg once daily.

Treatment of the partner

The sexual partner receives the same treatment as the patient, whether or not symptoms are present, except in the case of genital herpes (the partner is treated only if symptomatic).

1 (see page 0) Lymphogranuloma venereum is endemic in East and West Africa, India, Southeast Asia, South America and the Caribbean. Donovanosis is endemic in South Africa, Papua New Guinea, India, Brazil and the Caribbean.

2 (see page 0) Doxycycline is contra-indicated in pregnant and breast-feeding women. [a (see page 0) b (see page 0) c (see page 0)]

References

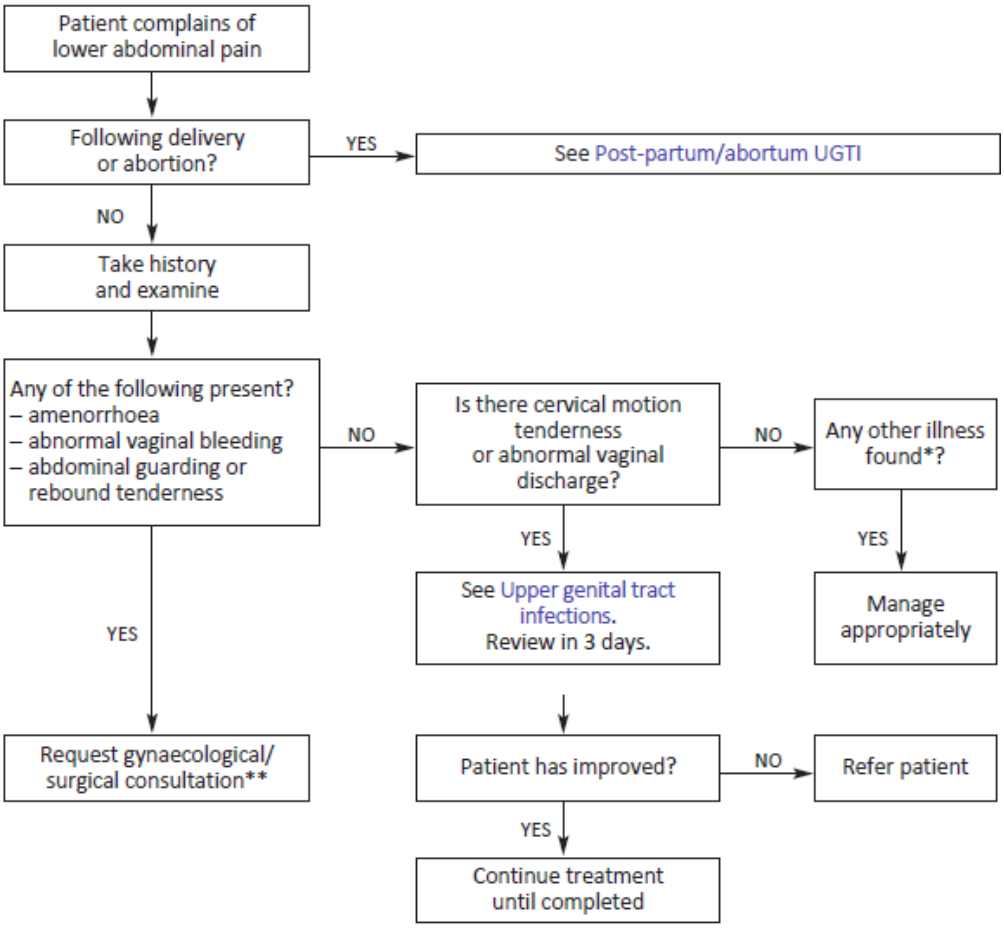
1. Centers for Disease Control and Prevention. Syphilis Pocket Guide for Providers. 2017. https://www.cdc.gov/std/syphilis/Syphilis-Pocket-Guide-FINAL-508.pdf

2. World Health Organization. WHO guidelines for the treatment of *Treponema pallidum* (syphilis), Geneva, 2016. http://apps.who.int/iris/bitstream/handle/10665/249572/9789241549806-eng.pdf?sequence=1

Lower abdominal pain in women

Upper genital tract infection should be suspected in women with lower abdominal pain (see Upper genital tract infections (see page 239)).
Gynaecological examination should be routinely performed:
– Inspection of the vulva, speculum examination: check for purulent discharge or inflammation, and
– Abdominal exam and bimanual pelvic exam: check for pain on mobilising the cervix.

Case management



* Look for another cause (in particular, gastrointestinal or urinary pathology).
** Look for a pregnancy related pathology (threatened abortion, extra-uterine pregnancy) or a complication (peritonitis, pelvic abscess).

Upper genital tract infections (UGTI)

- Clinical features(see page 240)
  - Sexually transmitted infections(see page 240)
  - Infections after childbirth or abortion(see page 240)
- Treatment(see page 240)
  - Sexually transmitted infections(see page 240)
  - Infections after childbirth or abortion(see page 241)

Upper genital tract infections are bacterial infections of the uterus (endometritis) and/or the fallopian tubes (salpingitis), which may be complicated by peritonitis, pelvic abscess or septicaemia.
UGTI may be sexually transmitted or arise after childbirth or abortion. Antibiotic choices are directed by the most common pathogens in each scenario.
If peritonitis or pelvic abscess is suspected, request a surgical opinion while initiating antibiotic therapy.

Clinical features

Sexually transmitted infections

Diagnosis may be difficult, as clinical presentation is variable.
– Suggestive symptoms are: abdominal pain, abnormal vaginal discharge, fever, dyspareunia, menometrorrhagia, dysuria.
– Infection is probable when one or more of the above symptoms are associated with one or more of the following signs: cervical motion tenderness, adnexal tenderness, tender abdominal mass.

Infections after childbirth or abortion

– Most cases present with a typical clinical picture, developing within 2 to 10 days after delivery (caesarean section or vaginal delivery) or abortion (spontaneous or induced):
• Fever, generally high
• Abdominal or pelvic pain
• Malodorous or purulent lochia
• Enlarged, soft and/or tender uterus

– Check for retained placenta.

– In the early stages, fever may be absent or moderate and abdominal pain may be mild.

Treatment

– Criteria for hospitalisation include:
• Clinical suspicion of severe or complicated infection (e.g. peritonitis, abscess, septicaemia)
• Diagnostic uncertainty (e.g. suspicion of extra-uterine pregnancy, appendicitis)
• Significant obstacles to ambulatory oral treatment
• No improvement after 48 hours, or deterioration within 48 hours, of outpatient treatment

– All other patients may be treated on an ambulatory basis. They should be reassessed routinely on the third day of treatment to evaluate clinical improvement (decrease in pain, absence of fever). If it is difficult to organise routine follow-up, advise patients to return to clinic if there is no improvement after 48 hours of treatment, or sooner if their condition is worsening.

Sexually transmitted infections

– Antibiotic therapy combines 3 antibiotics to cover the most frequent causative organisms: gonococci, chlamydiae, and anaerobes.

• *Ambulatory treatment:*
cefixime PO: 400 mg single dose or **ceftriaxone** IM: 250 mg single dose
+ **doxycycline** PO: 100 mg 2 times daily for 14 days 1 (see page 0)
+ **metronidazole** PO: 500 mg 2 times daily for 14 days

• *Treatment in hospital:*
ceftriaxone IM: 250 mg once daily
+ **doxycycline** PO: 100 mg 2 times daily for 14 days 1 (see page 0)
+ **metronidazole** PO or IV infusion: 500 mg 2 times daily for 14 days
Continue triple therapy for 24 to 48 hours after signs and symptoms have improved (resolution of fever, decrease in pain), then continue doxycycline (or erythromycin) + metronidazole to complete 14 days of treatment.

– If an IUD is in place, it should be removed (offer another method of contraception).

– Analgesic treatment according to pain intensity.

– Treatment of the partner: single dose treatment for both gonorrhoea AND chlamydia (as for Urethral discharge(see page 231)), whether or not symptoms are present.

Infections after childbirth or abortion

– Antibiotic therapy: treatment must cover the most frequent causative organisms: anaerobes, Gram negatives and streptococci.

• *Ambulatory treatment* (early stages only):
amoxicillin/clavulanic acid (**co-amoxiclav**) PO for 7 days
Use formulations in a ratio of 8:1 or 7:1 exclusively. The dose is expressed in amoxicillin:
Ratio 8:1: 3000 mg daily (2 tablets of 500/62.5 mg 3 times daily)
Ratio 7:1: 2625 mg daily (1 tablet of 875/125 mg 3 times daily)
or
amoxicillin PO: 1 g 3 times daily + **metronidazole** PO: 500 mg 3 times daily doses for 7 days

• *Treatment in hospital:*
amoxicillin/clavulanic acid (**co-amoxiclav**) IV (dose expressed in amoxicillin): 1 g every 8 hours
+ **gentamicin** IM: 5 mg/kg once daily
or
ampicillin IV: 2 g every 8 hours
+ **metronidazole** IV infusion: 500 mg every 8 hours
+ **gentamicin** IM: as above
Stop antibiotic therapy 48 hours after resolution of fever and clinical signs and symptoms.
In penicillin-allergic patients, use **clindamycin** IV (900 mg every 8 hours) + **gentamicin** (as above).

– In case of placental retention: perform digital curettage or manual vacuum extraction (refer to the guide Essential obstetric and newborn care, MSF) 24 hours after initiation of antibiotic therapy.

– Analgesic treatment according to pain intensity.

– If the patient's condition deteriorates or if fever persists after 48-72 hours of treatment, consider the possibility of complication requiring additional treatment (e.g. pelvic abscess drainage), otherwise change the antibiotic to ceftriaxone + doxycycline + metronidazole as in hospital-based treatment of sexually transmitted UGTI.

1(see page 0) In pregnant/breastfeeding women: **erythromycin** PO: 1 g 2 times daily or 500 mg 4 times daily for 14 days
Single dose azithromycin is not effective against chlamydia in the treatment of sexually transmitted UGTI. [a(see page 0) b(see page 0)]

Venereal warts

- Clinical features(see page 242)
- Treatment(see page 242)
  - External warts < 3 cm and vaginal warts(see page 242)
  - External warts > 3 cm; cervical, intra-urethral, rectal and oral warts; warts in pregnant or breastfeeding women(see page 242)

Venereal warts are benign tumours of the skin or mucous membranes due to certain papilloma viruses (HPV).

Clinical features

– Venereal warts are soft, raised, painless growths, sometimes clustered (cauliflower- like appearance) or macules (flat warts), which are more difficult to discern. Warts can be external (vulva, penis, scrotum, perineum, anus) and/or internal (vagina, cervix, urethra, rectum; oral cavity in HIV infected patients).
– In women, the presence of external warts is an indication for a speculum examination to exclude vaginal or cervical warts. Speculum exam may reveal a friable, fungating tumour on the cervix, suggestive of cancer associated with papilloma virus[1] .

Treatment

Choice of treatment depends on the size and location of the warts. Treatment may be less effective, and relapses more frequent, in HIV infected patients.

External warts < 3 cm and vaginal warts

podophyllotoxin 0.5%[2] solution may be self-applied by the patient, but in the event of vaginal warts, the treatment must be applied by medical staff.
Explain the procedure to the patient: apply the solution to the warts using an applicator or cotton bud, sparing the surrounding healthy skin, allow to air dry. On vaginal warts, the solution should be allowed to dry before the speculum is withdrawn.
Apply the solution 2 times daily, 3 consecutive days per week, for up to 4 weeks.
Podophyllum preparations are contra-indicated in pregnant[3] or breastfeeding women. They should not be applied on cervical, intra-urethral, rectal, oral or extensive warts. Improper use may result in painful ulceration.

External warts > 3 cm; cervical, intra-urethral, rectal and oral warts; warts in pregnant or breastfeeding women

Surgical excision or cryotherapy or electrocoagulation.

[1] Certain types of HPV may cause cancer. Presence of genital warts in women is an indication to screen for precancerous lesions of the cervix, if feasible in the context (visual inspection with acetic acid, or cervical smear, or other available techniques), and to treat any lesions identified (cryotherapy, conisation, etc., according to diagnosis).

[2] **Podophyllum 10%**, **15%** or **25% resin** is another preparation which is much more caustic, and should be applied only by medical staff. Protect the surrounding skin (vaseline or zinc oxide ointment) before applying the resin. Wash off with soap and water after 1 to 4 hours. Apply once weekly for 4 weeks.

[3] Treatment of warts is not an emergency and may be deferred if alternatives to podophyllum preparations are not available. Genital warts are not an indication for caesarean section: it is uncommon for warts to interfere with delivery, and the risk of mother-to-child transmission is very low.

Major genital infections (summary)

Pathogens/ Infections	Clinical features	Laboratory	Treatment

Neisseria gonorrhoeae (gonorrhoea)	• In women:
	  • vaginal discharge, cervicitis (mucopurulent cervical discharge), dysuria (50% of infections are asymptomatic);
	  • UGTI (salpingitis, endometritis).
	• In men: purulent urethral discharge and sometimes dysuria (5 to 50% of infections are asymptomatic).
		• In women: not valid (not sensitive).
		• In men: Gram or methylene blue stain: intracellular diplococci and polymorphonuclear leucocytes (more than 4 per field).
			ceftriaxone IM: 250 mg single dose
			or, if not available,
			cefixime PO: 400 mg single dose
			Treat also for chlamydia.
			In case of upper genital tract infection, see UGTI(see page 239).

Chlamydia trachomatis (chlamydia)	• In women:
	  • vaginal discharge, cervicitis, and rarely dysuria (> 50% of infections are asymptomatic);
	  • UGTI (salpingitis, endometritis).
	• In men: mild urethral discharge and/or dysuria but up to 90% of infections are asymptomatic.
		The best method is PCR (not feasible under field conditions).	**azithromycin** PO: 1 g single dose
			or **doxycycline** PO[1](see page 0): 200 mg daily for 7 days
			Treat also for gonococcal infection (except when a Gram stain in males shows no *N. gonorrhoeae*).
			In case of upper genital tract infection, see UGTI(see page 239).

Pathogens/ Infections	Clinical features	Laboratory	Treatment
Trichomonas vaginalis (trichomoniasis)	• In women: yellow-green vaginal discharge, sometimes foul smelling, vulvar irritation (10 to 50% of infections are asymptomatic). • In men: most infections are asymptomatic. Can produce balanitis, urethritis with mild discharge and sometimes dysuria.	• Wet mount of fresh vaginal fluid shows motile trichomonas (low sensitivity). • pH of urethral/vaginal fluid > 4.5.	**tinidazole** or **metronidazole** PO: 2 g single dose
Bacterial vaginosis (*Gardnerella vaginalis* and other associated bacteria)	Diagnosis is made in the presence of 3 of the following 4 signs: • Homogenous grey-white adherent vaginal discharge • pH of vaginal fluid > 4.5 • Vaginal fluid has an amine (fishy) odour, especially when mixed with 10% KOH • Presence of clue cells in wet mount or Gram stain of vaginal fluid		**tinidazole** or **metronidazole** PO: 2 g single dose
Candida albicans (candidiasis)	• Mainly seen in women: pruritus and vulvovaginitis, frequently creamy-white vaginal discharge, sometimes dysuria. • In men: balanitis/ balanoposthitis (inflammation of the glans/ prepuce, erythema, pruritus, white pustules) and rarely urethritis	• Saline of KOH wet mount of fresh vaginal fluid shows budding yeast cells and pseudohyphae. • pH of vaginal fluid: normal	• In women: **clotrimazole** 500 mg: one vaginal tablet single dose • In men: **miconazole 2%** cream: 1 application 2 times daily for 7 days
Herpes simplex virus type 2 (genital herpes)	Many asymptomatic carriers. Multiple vesicles on genitals leading to painful ulcerations. In women, affects vulva, vagina and cervix; in males, penis and sometimes urethra. In primary episodes, fever (30%) and lymphadenopathy (50%). Recurrences in 1/3 of infections with shorter and milder symptoms.	Diagnosis by culture, serology and PCR done exclusively at a reference laboratory.	Analgesics, local disinfection. If available, **aciclovir** PO: • Primary episode: 1200 mg daily for 7 days, given within 5 days after onset of lesions. • Recurrent infections: same dose for 5 days, given within 24 hours after onset of lesions.

Pathogens/ Infections	Clinical features	Laboratory	Treatment
Treponema pallidum (syphilis)	Single firm painless genital ulcer, often unnoticed.	RPR/VDRL lack sensitivity and specificity, but may be useful for following treatment effectiveness (decrease in titer) or confirming re-infection (rise in titer). Treponemal tests (TPHA, FTA-ABS, rapid tests such as SD Bioline®) are more sensitive and specific.	**benzathine benzylpenicillin** IM: 2.4 MIU per injection, single dose (syphylis < 12 months) or once weekly for 3 weeks (syphilis > 12 months or unknown duration) or **azithromycin** PO: 2 g single dose or **erythromycin** PO: 2 g daily for 14 days or **doxycycline** PO[1](see page 0) : 200 mg daily for 14 days Treat also for chancroid.
Haemophilus ducreyi (chancroid)	Painful single (or multiple) genital ulcer (soft chancre, bleeds easily when touched). Painful and voluminous inguinal lymphadenitis in 50%. Fistulae develop in 25% of cases.	*H. ducreyi* bacillus is difficult to identify on microscopy or by culture.	**azithromycin** PO: 1 g single dose or **ceftriaxone** IM: 250 mg single dose or **ciprofloxacin** PO[2](see page 0) : 1 g daily for 3 days or **erythromycin** PO: 2 g daily for 7 days Treat also for syphillis.
Human papillomavirus (venereal warts)	Soft, raised, painless growths, sometimes clustered (acuminate condyloma) or macules (flat warts). Warts can be external (vulva, penis, scrotum, perineum, anus) and/or internal (vagina, cervix, urethra, rectum; oral cavity in HIV infected patients).	The diagnosis is based on clinical features. It feasible in the context, the presence of genital warts in women in an indication to screen for pre-cancerous lesions of the cervix (visual inspection with acetic acid, or cervical smear, or other available techniques).	• External warts < 3 cm and vaginal warts: **podophyllotoxin 0.5%** • External warts > 3 cm; cervical, intra-urethral, rectal and oral warts; warts in pregnant or breastfeeding women: surgical excision or cryotherapy or electrocoagulation.

[1](see page 0) Doxycycline is contra-indicated in pregnant women. It should not be administered to breast-feeding women if the treatment exceeds 7 days (use erythromycin).

[a(see page 0) b(see page 0)]
[2](see page 0) Ciprofloxacin should be avoided in pregnant women.

Metrorrhagia (unrelated to pregnancy)

- In all events(see page 246)
- According to clinical examination(see page 246)

Genital bleeding unrelated to the menstrual period.

In women of childbearing age, always assess if the bleeding is related to a pregnancy.

For the management of pregnancy-related bleeding, refer to the guide Essential obstetric and newborn care, MSF.

In all events

– Rapidly assess the severity of bleeding.
– In the event of heavy haemorrhage or shock :
• Start an IV infusion of Ringer lactate; monitor vital signs (heart rate, blood pressure);
• Prepare for a possible blood transfusion (determine patient's group, identify potential donors);
• If a transfusion is performed, only use blood that has been screened (HIV, hepatitis B and C, syphilis; malaria in endemic areas).
– In the event of referral to a surgical facility, difficult transport conditions might aggravate the haemorrhage: the patient should have an IV line and be accompanied by family members who are potential blood donors.
– Prevent or treat anaemia (measure haemoglobin if possible).

According to clinical examination

Speculum examination: determine the origin of the bleeding [vagina, cervix, uterinen cavity]; appearance of the cervix; estimation of blood loss;
Bimanual pelvic examination: look for uterine motion tenderness, increased volume or abnormalities of the uterus.

– Friable, hard, ulcerated, hypertrophic mass on the cervix: possible cervical cancer; surgical treatment is required. While waiting for surgery, **tranexamic acid** PO (1 g 3 times daily for 3 to 5 days) may be used to reduce bleeding.

– Inflammation of the cervix, light or moderate bleeding, purulent cervical discharge, pelvic pain: consider cervicitis (see Abnormal vaginal discharge(see page 233)) or salpingitis (see Upper genital tract infections(see page 239)).

– Enlarged, misshapen uterus: uterine fibroids; surgical treatment if large fibroids cause significant bleeding. While waiting for surgery or if surgery is not indicated, treat as a functional uterine bleeding.

– Normal uterus and cervix: possible functional uterine bleeding: **tranexamic acid** PO as above. In situations of repeated bleeding, it can be combined with an NSAID (**ibuprofen** PO for 3 to 5 days, see Pain(see page 23), Chapter 1) and/or a long-term treatment with oral estroprogestogens or injectable progestogens.
Note: rule out other causes of vaginal bleeding before diagnosing functional uterine bleeding. Consider for example poorly tolerated contraceptive, endometrial cancer in postmenopausal women, genitourinary schistosomiasis in endemic areas (see Schistosomiasis(see page 142), Chapter 6).

Chapter 10: Medical and minor surgical procedures

- Dressings(see page 247)
- Treatment of a simple wound(see page 249)
- Burns(see page 258)
- Cutaneous abscess(see page 265)
- Pyomyositis(see page 268)
- Leg ulcers(see page 269)
- Necrotising infections of the skin and soft tissues(see page 271)
- Venomous bites and stings(see page 273)
- Dental infections(see page 276)

Dressings

- Equipment(see page 247)
- Organisation of care(see page 248)
- Technique(see page 248)
    - Removal of an old dressing(see page 248)
    - Observe the wound(see page 248)
    - Technique for cleaning and dressing of the wound(see page 249)
    - Subsequent dressings(see page 249)

– The objective of dressing wounds is to promote healing. The procedure includes cleaning, disinfection and protection of the wound while respecting the rules of hygiene.
– Not all wounds need to be covered by a dressing (e.g. a clean wound that has been sutured for several days; a small dry wound not requiring sutures).

Equipment

Sterile instruments

– One Kocher or Pean forceps
– One dissecting forceps
– One pair of surgical scissors or one scalpel to excise necrotic tissue and to cut gauze or sutures
Instruments for one dressing for one patient must be wrapped together in paper or fabric (or can be placed in a metallic box) and sterilised together to limit handling and breaks in asepsis. 5 to 10 compresses may be included in this set.
If there are no sterile instruments, a dressing can be done using sterile gloves.

Renewable supplies

– Sterile compresses
– Non-sterile disposable gloves
– Adhesive tape and/or crepe or gauze bandage
– Sterile 0.9% sodium chloride or sterile water

– Depending on the wound: antiseptic (7.5% povidone iodine scrub solution, 10% povidone iodine dermal solution), paraffin compresses, analgesics

Organisation of care

Proper organization of care helps maintain the rules of asepsis and decreases the risk of contamination of the wound or transmission of organisms from one patient to another:
– Assign one room for dressings. It must be cleaned and the waste removed every day. The dressing table must be disinfected after each patient.
– Dressings may be applied at the bedside if the patient's condition requires. Use a clean, disinfected dressing trolley with: on the upper tray, sterile and/or clean material (dressing set, extra compresses, etc.) and on the lower tray, septic material (container for contaminated instruments, sharps disposal container and a container or garbage bag for waste).
– Prepare all the necessary material in a well lit area. If necessary, arrange for an assistant to be present.
– Wear protective glasses if there is a risk of projection from an oozing wound.
– Always proceed from clean to dirty: start with patients with uninfected wounds. If there are multiple dressings for one patient, start with the cleanest wound.

Technique

– If the procedure may be painful, give an analgesic and wait the necessary time for the drug to take effect before starting the procedure.
– Settle the patient comfortably in an area where his privacy is respected throughout the procedure.
– Explain the procedure to the patient and obtain his co-operation.
– Instruments (or sterile gloves) must be changed between patients.
– To prevent drug interactions, use the same antiseptic for all care of one patient.

Removal of an old dressing

– Wash hands (ordinary soap) or disinfect them with an alcohol-based hand rub.
– Put on non-sterile gloves and remove the adhesive tape, bandage and superficial compresses.
– Proceed gently with the last compresses. If they stick to the wound, loosen them with 0.9% sodium chloride or sterile water before removal.
– Observe the soiled compresses. If there is significant discharge, a greenish colour or a foul odour, a wound infection is likely.
– Discard the dressing and the non-sterile gloves in the waste container.

Observe the wound

– In the case of an open wound, loss of cutaneous tissue or ulcer, the colour is an indicator of the stage in the healing process:
• *black* area = necrosis, wet or dry infected eschar
• *yellow* or *greenish* area = infected tissue and presence of pus
• *red* area = granulation, usually a sign of healing (unless there is hypertrophy), however, red edges indicate inflammation or infection
• *pink* area = process of epithelisation, the final stage of healing that begins at the edges of the wound

– In the case of a sutured wound, the existence of local signs of suppuration and pain requires the removal of one or more sutures to avoid the infection spreading. Local signs include:
• red, indurated and painful edges
• drainage of pus between the sutures, either spontaneously or when pressure is applied on either side of the wound
• lymphangitis
• sub-cutaneous crepitations around the wound

In any case, if local signs of infection are observed, look for general signs of infection (fever, chills, changes in the overall condition).

Technique for cleaning and dressing of the wound

– Wash hands again or disinfect them with an alcohol-based hand rub.
– Open the dressing set or box after checking the date of sterilisation and that the wrapping is intact.
– Pick up one of the sterile forceps being careful not to touch anything else.
– Pick up the second forceps with the help of the first one.
– Make a swab by folding a compress in 4 using the forceps.

– *Clean sutured wound or clean open wound with red granulation*:
• clean with 0.9% sodium chloride or sterile water to remove any organic residue; work from the cleanest to the dirtiest area (use a clean swab for each stroke);
• dab dry with a sterile compress;
• re-cover a sutured wound with sterile compresses or an open wound with paraffin compresses; the dressing should extend a few cm beyond the edges of the wound;
• keep the dressing in place with adhesive tape or a bandage.

– *Necrotic or infected open wounds*:
• clean with povidone iodine (7.5% scrub solution, 1 part of solution + 4 parts of sterile 0.9% sodium chloride or sterile water). Rinse thoroughly then dab dry with a sterile compress; or if not available, sterile 0.9% sodium chloride or sterile water and apply an antiseptic (10% povidone iodine dermal solution).
• apply sterile vaseline and remove all necrotic tissue at each dressing change until the wound is clean.

– Discard any sharp materials used in an appropriate sharps container and the rest of the waste in a waste container.
– As quickly as possible, soak the instruments in disinfectant.
– Wash hands again or disinfect them with an alcohol-based hand rub.

The principles remain the same if the dressing is done using instruments or sterile gloves.

Subsequent dressings

– Clean, sutured wound: remove the initial dressing after 5 days if the wound remains painless and odourless, and if the dressing remains clean. The decision to re-cover or to leave the wound uncovered (if it is dry) often depends on the context and local practices.
– Infected, sutured wound: remove one or more sutures and evacuate the pus. Change the dressing at least once daily.
– Open, dirty wound: daily cleaning and dressing change.
– Open granulating wound: change the dressing every 2 to 3 days, except if the granulation is hypertrophic (in this case, apply local corticosteroids).

Treatment of a simple wound

- Equipment(see page 250)
- Technique(see page 250)
  - Initial cleaning(see page 250)
  - Exploration(see page 251)
  - Wound excision(see page 251)
  - Immediate suturing of a simple wound(see page 251)
  - Delayed suturing of a simple wound(see page 251)
  - Healing by second intention of infected wounds(see page 251)

– A simple wound is a break in the continuity of the skin limited in depth at the sub-cutaneous fatty tissue, that does not affect the underlying structures (muscle, bone, joints, major arteries, nerves, tendons) and without significant loss of tissue.
– The goal of treatment is to assure rapid healing of the wound without complications or sequelae.
Several basic rules apply:
• rapidly treat wounds, while maintaining the rules of asepsis and the order of the initial procedures: cleaning-exploration-excision;
• identify wounds that need to be sutured and those for which suturing would be harmful or dangerous;
• immediately suture recent, clean, simple wounds (less than 6 hours old) and delay suturing contaminated wounds and/or those more than 6 hours old;
• prevent local (abscess) or general (gas gangrene; tetanus) infections.

Equipment

Instruments

(Figures 1a to 1d)

– One dissecting forceps, one needle-holder, one pair of surgical scissors and one Pean or Kocher forceps are usually enough.
– One or two other artery forceps, a pair of Farabeuf retractors and a scalpel may be useful for a contused or deep wound.

Instruments to suture one wound for one patient must be packaged and sterilised together (suture box or set) to limit handling and breaks in asepsis.

Renewable supplies

– For local anaesthesia: sterile syringe and needle; 1% lidocaine (without epinephrine)
– Sterile gloves, fenestrated sterile towel
– Sterile absorbable and non-absorbable sutures
– Antiseptic and supplies for dressings
– For drainage: corrugated rubber drain or equivalent, nylon suture

Technique

– Settle the patient comfortably in an area with good lighting and ensure all the necessary material is prepared.
– Explain the procedure to the patient and ensure his co-operation.
– If the patient is a young child, arrange to have an assistant hold the child if necessary.

Initial cleaning

– Wear suitable clothing: sterile gloves for all wounds and a gown and protective glasses if there is a risk of projection from a bleeding wound.
– Start by washing the wound, prolong the cleaning if the wound is particularly soiled. Use ordinary soap or 7.5% povidone iodine scrub solution and water and rinse.
– If necessary use a sterile brush. Cleaning with running water is preferable to cleaning by immersion.
– If the wound is infected and the patient has general signs of infection (fever, chills, changes in the overall condition) systemic antibiotic therapy may be required. Administer antibiotics at least one hour prior to starting care.

Exploration

– Wash hands and put on sterile gloves.
– Disinfect the wound and surrounding area with 10% povidone iodine.
– Cover the wound with a fenestrated sterile towel.
– Local anaesthetic: infiltrate **1% lidocaine** into the edges of the wound and wait at least 2 minutes for the anaesthetic to take effect.
– Proceed carefully from the superficial to the deepest parts of the wound to explore the extent of the wound, if necessary, aided by an assistant.
– Consider the anatomical location of the wound and look for injury to any underlying structures (the clinical examination of a limb must include evaluation of sensitivity and motor functioning, as well as that of tendons in order to orient surgical exploration):
• a wound that communicates with a fracture is an open fracture,
• a wound close to a joint may be a joint wound,
• a wound on the hands or feet may affect the nerves and/or tendons.
– Look for and remove any foreign bodies.
– In the event of significant pain or bleeding, the exploration must be completed in an operating room.

Wound excision

– The goal of the excision is to remove non-viable tissue, which favours the proliferation of bacteria and infection.
– The wound may require little or no excision if it is clean. The excision is more extensive if the wound is bruised, irregular or extensive.
– Limit excision of the skin around the wound, particularly in facial wounds.
– Sub-cutaneous fat and tissue of doubtful viability should be generously excised in order to leave only well vascularised tissue.

Immediate suturing of a simple wound

– Immediate suturing may have serious consequences for the patient if precautions to prevent infection and promote healing are not taken.
– The decision to suture immediately can only be taken after the cleaning, exploration and satisfactory excision, and if the following conditions are met: simple wound, no more than 6 hours old with no devitalised or contused tissue (the wound may be as long as 24 hours old if on the face, scalp, upper limbs or hands).
– Bites (for local treatment see Rabies(see page 187), Chapter 8) and bullet, shell or mine shrapnel wounds should not be immediately sutured.

Delayed suturing of a simple wound

– Wounds that do not fill the above conditions should not be immediately sutured.
– After cleaning, exploration and excision a simple dressing is applied to the open wound.
– Further cleaning and removal of any remaining necrotic tissue is completed with daily dressing changes.
– If after 72 hours there are no signs of local infection, the wound may be sutured.

Healing by second intention of infected wounds

If the wound does not meet the conditions of cleanliness described above, the wound cannot be sutured. It will heal either spontaneously (healing by secondary intention), or will require a skin graft (once the wound is clean) if there is significant loss of tissue.

Figures 1: *Basic instruments*

Figure 1a
Kocher forceps,
straight, toothed

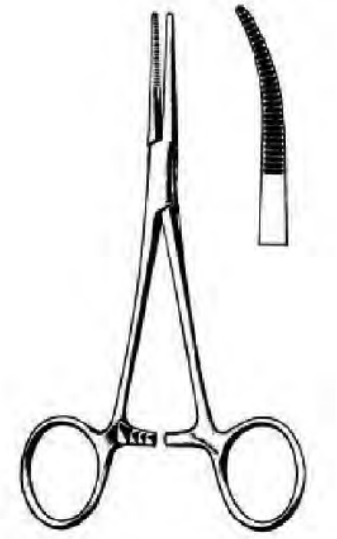


Figure 1b
Kelly forceps,
curved, non-toothed

Figure 1c
Small artery forceps,
curved, non-toothed

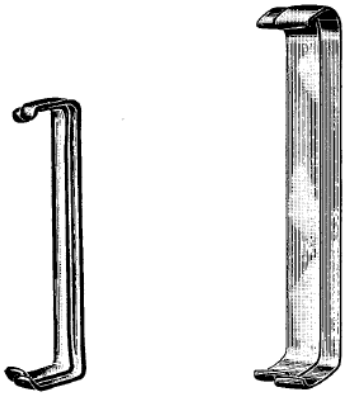


Figure 1d
Farabeuf retractors

Figures 2: *How to hold instruments*

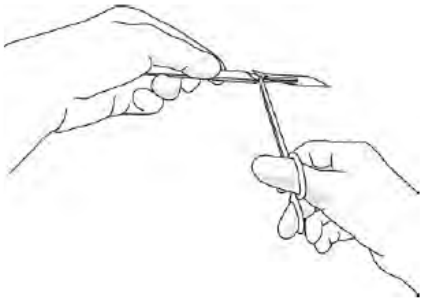


Figure 2a
Always mount a surgical blade using a needle holder.
Change the blade for each new procedure.

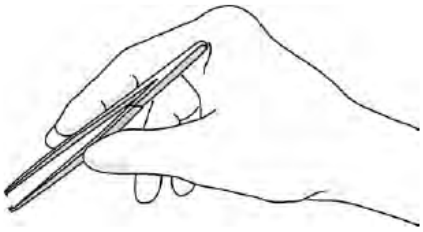


Figure 2b
Dissecting forceps should not be held in the palm of the hand, but rather between the thumb and index finger. Toothed dissecting forceps should only be used on skin.

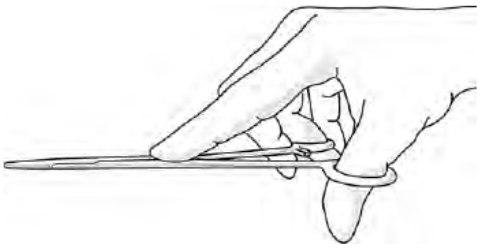


Figure 2c
Insert the thumb and the ring finger into the handle of a needle holder (or scissors), and stabilize the instrument using the index finger.

Figures 3: *Wound debridement*
This should be done sparingly, limited to excision of severely contused or lacerated tissue that is clearly becoming necrotic.

Figure 3a
Debridement of a contused, ragged wound: straightening of the wound edges with a scalpel. Be conservative in facial wounds.

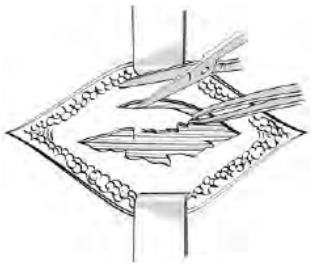


Figure 3b
Excision of edges of the aponeurosis to prevent necrosis.

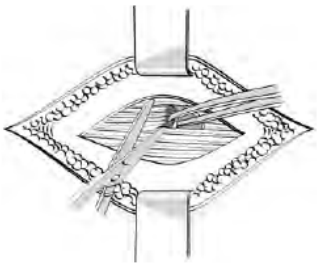


Figure 3c
Excision of contused muscle.

Figures 4: *Practising making knots using forceps*

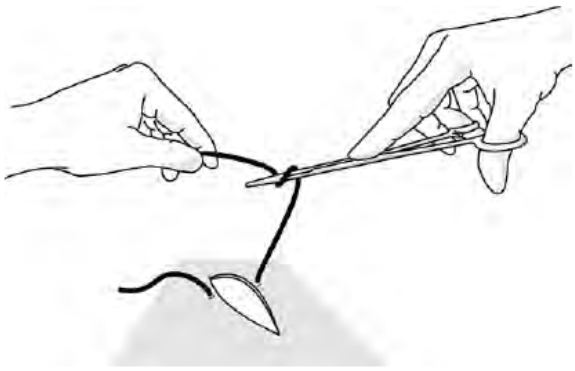


Figure 4a
Loop the suture around the needle holder in one direction and remember the direction of the loop. Grasp the loose end with the needle holder and pull it through the loop to make the first knot. Lower the knot so that it closes the wound.

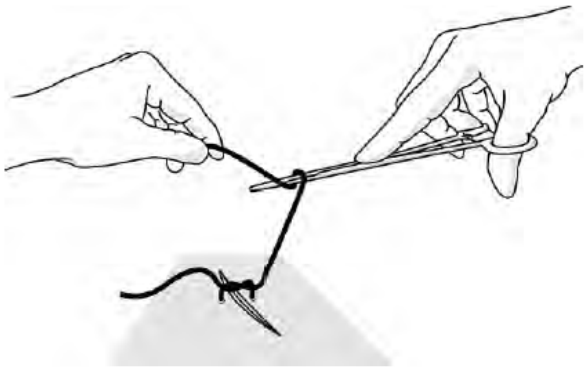


Figure 4b
The second loop should be in the opposite direction.
At least 3 knots are needed to make a suture, alternating from one direction to the other.

Figure 4c
In principle the first knot lies flat.

Figure 4d
Second knot in the opposite direction.

Figure 4e

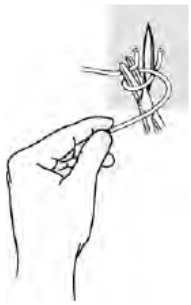


Figure 4f

Grasp the loose end with the needle holder.

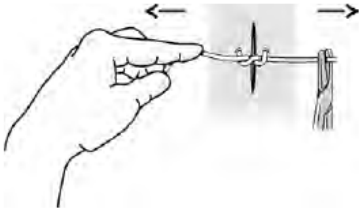


Figure 4g

First flat knot.

Slide the knot towards the wound using the hand holding the loose end while holding the other end with the needle holder. Tighten the knot without causing tissue ischaemia.

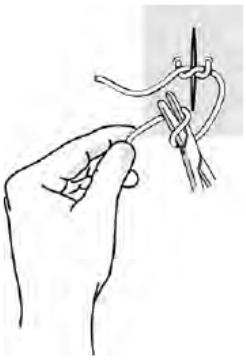


Figure 4h

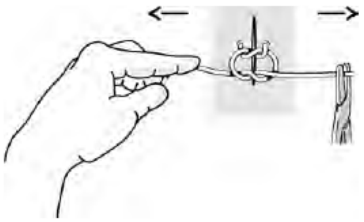


Figure 4i

Second knot in the opposite direction.

Figures 5: *Particular problems*

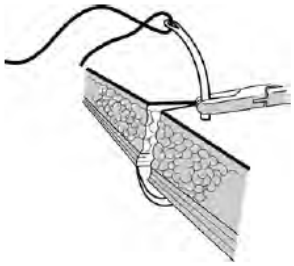


Figure 5a

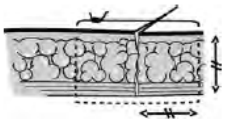


Figure 5b

The suture should be as deep as it is wide.

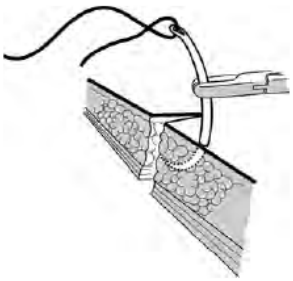


Figure 5c

Figure 5d

The suture is too shallow, the edges are invaginated.

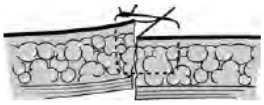


Figure 5e
Poor lining of the edges.

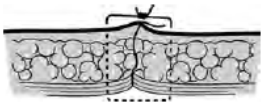


Figure 5f
Do not make the knot directly over the wound.

Figure 6: *Closing a corner*

Figure 7: *Closure of the skin, simple interrupted sutures with non-absorbable sutures*

Burns

- Classification of burns(see page 258)
- Evaluation of burns(see page 258)
- Treatment of severe burns(see page 260)
    - I. Initial management(see page 260)
    - II. General measures during the first 48 hours(see page 261)
    - III. Local treatment(see page 263)
    - IV. Surgical care(see page 264)
    - V. Pain management(see page 264)
- Minor burns(see page 265)

Burns are cutaneous lesions caused by exposure to heat, electricity, chemicals or radiation. They cause significant pain and may threaten survival and/or compromise function.

Classification of burns

Severe burns: one or more of the following parameters:
– Involving more than 10% of the body surface area (BSA) in children and 15% in adults
– Inhalation injury (smoke, hot air, particles, toxic gas, etc.)
– Major concomitant trauma (fracture, head injury, etc.)
– Location: face, hands, neck, genitalia/perineum, joints (risk of functional deficit)
– Electrical and chemical burns or burns due to explosions
– Age < 3 years or > 60 years or significant co-morbidities (e.g. epilepsy, malnutrition)

Minor burns: involving less than 10% of the BSA in children and 15% in adults, in the absence of other risk factors

Evaluation of burns

Extent of burns

Lund-Browder table – Percentage of body surface area according to age

Location	< 1 year	1-4 years	5-9 years	10-15 years	Adults
Head	19	17	13	10	7
Neck	2	2	2	2	2
Anterior trunk	13	13	13	13	13
Posterior trunk	13	13	13	13	13
Right buttock	2.5	2.5	2.5	2.5	2.5

Location	< 1 year	1-4 years	5-9 years	10-15 years	Adults
Left buttock	2.5	2.5	2.5	2.5	2.5
Perineum/genitalia	1	1	1	1	1
Right upper arm	4	4	4	4	4
Left upper arm	4	4	4	4	4
Right lower arm	3	3	3	3	3
Left lower arm	3	3	3	3	3
Right hand	2.5	2.5	2.5	2.5	2.5
Left hand	2.5	2.5	2.5	2.5	2.5
Right thigh	5.5	6.5	8.5	8.5	9.5
Left thigh	5.5	6.5	8.5	8.5	9.5
Right leg	5	5	5.5	6	7
Left leg	5	5	5.5	6	7
Right foot	3.5	3.5	3.5	3.5	3.5
Left foot	3.5	3.5	3.5	3.5	3.5

This table helps to accurately calculate the % of BSA involved according to patient's age: e.g. burn of the face, anterior trunk, inner surface of the lower arm and circumferential burn of left upper arm in a child 2 years of age: 8.5 + 13 + 1.5 + 4 = 27% BSA.

Depth of burns

Apart from first-degree burns (painful erythema of the skin and absence of blisters) and very deep burns (third-degree burns, carbonization), it is not possible, upon initial examination, to determine the depth of burns. Differentiation is possible after D8-D10.

	Superficial burn on D8-D10	Deep burn on D8-D10
Sensation	Normal or pain	Insensitive or diminished sensation
Colour	Pink, blanches with pressure	White, red, brown or black Does not blanch with pressure
Texture	Smooth and supple	Firm and leathery
Appearance	Minimal fibrinous exudate Granulation tissue evident Bleeds when incised	Covered with fibrinous exudate Little or no bleeding when incised

	Superficial burn on D8-D10	Deep burn on D8-D10
Healing	Heals spontaneously within 5-15 days	• Very deep burn: always requires surgery (no spontaneous healing) • Intermediate burn: may heal spontaneously in 3 to 5 weeks; high risk of infection and permanent sequelae

Evaluation for the presence of inhalation injury

Dyspnoea with chest wall indrawing, bronchospasm, soot in the nares or mouth, productive cough, carbonaceous sputum, hoarseness, etc.

Treatment of severe burns

I. Initial management

On admission

– Ensure airway is patent; high-flow oxygen, even when SpO_2 is normal.
– Establish IV access, through unburned skin if possible (intraosseous access if IV access is not possible).
– **Ringer lactate** (RL): 20 ml/kg during the first hour, even if the patient is stable.
– **Morphine** SC: 0.2 mg/kg (Step 1 and Step 2 analgesics are not effective).
– In the event of chemical burns: flush with copious amounts of water for 15 to 30 minutes, avoiding contamination of healthy skin; do not attempt to neutralize the chemical agent.

Once the patient is stabilized

– Remove clothes if they are not adherent to the burn.
– Take history of the burn injury: mechanism, causative agent, time, etc.
– Assess the burn injury: extent, depth, carbonization; ocular burns, burns at risk of secondary functional deficits; circumferential burns of the extremities, chest or neck. Wear face mask and sterile gloves during the examination.
– Assess for associated injuries (fractures, etc.).
– Protect the patient and keep him warm: clean/sterile sheet, survival blanket.
– Insert a urinary catheter if burns involve > 15% of BSA, and in the case of electrical burns or burns of the perineum/genitalia.
– Insert a nasogastric tube if burns involve > 20% of BSA (in the operating room while carrying out dressing procedure).
– Calculate and initiate fluid and electrolyte requirements for the first 24 hours.
– Intensive monitoring: level of consciousness, heart rate, blood pressure, SpO_2, respiratory rate (RR) hourly; temperature and urine output every 4 hours.
– Additional testing: haemoglobin, blood group, urine dipstick test.
– Prepare the patient for the first dressing procedure in the operating room.

Notes:
– Burns do not bleed in the initial stage: check for haemorrhage if haemoglobin level is normal or low.
– Burns alone do not alter the level of consciousness. In the case if altered consciousness, consider head injury, intoxication, postictal state in epileptic patients.
– Clinical manifestations of electrical burns vary significantly according to the type of current. Look for complications (arrhythmia, rhabdomyolysis, neurological disorders).

II. General measures during the first 48 hours

Resuscitative measures

Intravenous replacement fluid to correct hypovolaemia:

Fluid and electrolyte requirements during the first 48 hours according to age

	Children < 12 years	Children ≥ 12 years and adults
0 - 8 h	2 ml/kg x % BSA of RL + maintenance fluid* per hour x 8 h	2 ml/kg x % BSA of RL
8 - 24 h	2 ml/kg x % BSA of RL + maintenance fluid* per hour x 16 h	2 ml/kg x % BSA of RL
24 - 48 h	Daily maintenance IV fluid requirements* minus oral fluids such as milk, broth, gavage feeds (do not include drinking water in the calculation).	40 ml/kg RL minus oral fluids (do not include drinking water in the calculation).

* maintenance fluid: alternate RL and 5% glucose: 4 ml/kg/h for first 10 kg of body weight + 2 ml/kg/h for next 10 kg + 1 ml/kg/h for each additional kg (over 20 kg, up to 30 kg)

Note: increase replacement volumes by 50% (3 ml/kg x % BSA for the first 8 hours) in the event of inhalation injury or electrical burn. For burns > 50% BSA, limit the calculation to 50% BSA.

This formula provides a guide only and should be adjusted according to systolic arterial pressure (SAP) and urine output. Avoid fluid overload. Reduce replacement fluid volumes if urine output exceeds the upper limit.

Target endpoints for IV replacement fluids

	Non-electrical burns			Electrical burns
	Children < 1 year	Children 1-12 years	Children > 12 years/adults	All ages
AP (mmHg)	SAP ≥ 60	SAP 70 to 90 + (2 x age)	SAP ≥ 100	Age appropriate SAP
Urine output	1 to 2 ml/kg/h	1 to 1.5 ml/kg/h	0.5 to 1 ml/kg/h	1 to 2 ml/kg/h

In patients with oliguria despite adequate fluid replacement:
dopamine IV: 5 to 15 micrograms/kg/minute by IV pump
or
epinephrine IV: 0.1 to 0.5 micrograms/kg/minute by IV pump
Stop the infusion after 48 hours, if fluid requirements can be met by the oral route or gavage.

Respiratory care

– In all cases: continuous inhalation of humidified oxygen, chest physiotherapy.
– Emergency surgical intervention if necessary: tracheotomy, chest escharotomy.
– Do not administer corticosteroids (no effect on oedema; predisposition to infection). No specific treatment for direct bronchopulmonary lesions.

Analgesia

See Pain management(see page 264)

Nutrition

Start feeding early, beginning at H8:
– Daily needs in adults
• calories: 25 kcal/kg + 40 kcal/% BSA
• proteins: 1.5 to 2 g/kg
– High energy foods (NRG5, Plumpy'nut, F100 milk) are necessary if the BSA is > 20% (normal food is inadequate).
– Nutritional requirements are administered according to the following distribution: carbohydrates 50%, lipids 30%, proteins 20%.
– Provide 5-10 times the recommended daily intake of vitamins and trace elements.
– Enteral feeds are preferred: oral route or nasogastric tube (necessary if BSA > 20%).
– Start with small quantities on D1, then increase progressively to reach recommended energy requirements within 3 days.
– Assess nutritional status regularly (weigh 2 times weekly).
– Reduce energy loss: occlusive dressings, warm environment (28-33 °C), early grafting; management of pain, insomnia and depression.

Patients at risk of rhabdomyolysis

In the event of deep and extensive burns, electrical burns, crush injuries to the extremities:
– Monitor for myoglobinuria: dark urine and urine dipstick tests.
– If present: induce alkaline diuresis for 48 hours (20 ml of **8.4% sodium bicarbonate** per litre of RL) to obtain an output of 1 to 2 ml/kg/hour. Do not administer dopamine or furosemide.

Infection control

Precautions against infection are of paramount importance until healing is complete. Infection is one of the most frequent and serious complications of burns:
– Hygiene precautions (e.g. sterile gloves when handling patients).
– Rigorous wound management (dressing changes, early excision).
– Separate “new” patients (< 7 days from burn) from convalescent patients (≥ 7 days from burn).
– Do not administer antibiotherapy in the absence of systemic infection.
Infection is defined by the presence of at least 2 of 4 following signs: temperature > 38.5 °C or < 36 °C, tachycardia, tachypnoea, elevation of white blood cell count by more than 100% (or substantial decrease in the number of white blood cells).
– In the event of systemic infection, start empiric antibiotherapy:
cefazolin IV
Children > 1 month: 25 mg/kg every 8 hours
Adults : 2 g every 8 hours
+ **ciprofloxacin** PO
Children > 1 month: 15 mg/kg 2 times daily
Adults: 500 mg 3 times daily
– Local infection, in the absence of signs of systemic infection, requires topical treatment with silver sulfadiazine. Not to be applied to children under 2 months.

Other treatments

– **Omeprazole** IV from D1
Children: 1 mg/kg once daily
Adults: 40 mg once daily

– Tetanus vaccination (see Tetanus(see page 162), Chapter 7).
– Thromboprophylaxis: **nadroparin** SC beginning 48 to 72 hours post-injury. High risk dosing protocol if the BSA is > 50% and/or in the event of high-voltage electrical injury; moderate risk dosing protocol if the BSA is 20 to 50% and/or in the event of burns of the lower limbs.
– Physiotherapy from D1 (prevention of contractures), analgesia is necessary.
– Intentional burns (suicide attempt, aggression): appropriate psychological follow-up.

III. Local treatment

Regular dressing changes[1](see page 0) prevent infection, decrease heat and fluid losses, reduce energy loss, and promote patient comfort. Dressings should be occlusive, assist in relieving pain, permit mobilisation, and prevent contractures.

Basic principles

– Rigorous adherence to the principles of asepsis.
– Dressing changes require morphine administration in the non-anaesthetised patient.
– The first dressing procedure is performed in the operating room under general anaesthesia, the following in an operating room under general anaesthesia or at the bedside with morphine.

Technique

– At the time of the first dressing procedure, shave any hairy areas (armpit, groin, pubis) if burns involve the adjacent tissues; scalp (anteriorly in the case of facial burns, entirely in the case of cranial burns). Cut nails.
– Clean the burn with povidone iodine scrub solution (1 volume of 7.5% povidone iodine + 4 volumes of 0.9% sodium chloride or sterile water). Scrub gently with compresses, taking care to avoid bleeding.
– Remove blisters with forceps and scissors.
– Rinse with 0.9% sodium chloride or sterile water.
– Dry the skin by blotting with sterile compresses.
– Apply **silver sulfadiazine** directly by hand (wear sterile gloves) in a uniform layer of 3-5 mm to all burned areas (except eyelids and lips) to children 2 months and over and adults.
– Apply a greasy dressing (Jelonet® or petrolatum gauze) using a back and forth motion (do not use a circular movement).
– Cover with a sterile compresses, unfolded into a single layer. Never encircle a limb with a single compress.
– Wrap with a crepe bandage, loosely applied.
– Elevate extremities to prevent oedema; immobilise in extension.

Frequency

– Routinely: every 48 hours.
– Daily in the event of superinfection or in certain areas (e.g. perineum).

Monitoring

– Distal ischaemia of the burned limb is the main complication during the first 48 hours. Assess for signs of ischaemia: cyanosis or pallor of the extremity, dysaesthesia, hyperalgia, impaired capillary refill.
– Monitor daily: pain, bleeding, progression of healing and infection.

IV. Surgical care

Emergency surgical interventions

– Escharotomy: in the case of circumferential burns of arms, legs or fingers, in order to avoid ischaemia, and circumferential burns of chest or neck that compromise respiratory movements.
– Tracheotomy: in the event of airway obstruction due to oedema (e.g. deep cervicofacial burns). Tracheotomy can be performed through a burned area.
– Tarsorrhaphy: in the event of ocular or deep eyelid burns.
– Surgery for associated injuries (fractures, visceral lesions, etc.).

Burn surgery

– Excision-grafting of deep burns, in the operating room, under general anaesthesia, between D5 and D6: excision of necrotic tissue (eschar) with simultaneous grafting with autografts of thin skin. This intervention entails significant bleeding risk, do not involve more than 15% of BSA in the same surgery.
– If early excision-grafting is not feasible, default to the process of sloughing-granulation-reepithelisation. Sloughing occurs spontaneously due to the action of sulfadiazine/ petrolatum gauze dressings and, if necessary, by mechanical surgical debridement of necrotic tissue. This is followed by granulation, which may require surgical reduction in the case of hypertrophy. The risk of infection is high and the process is prolonged (> 1 month).

V. Pain management

All burns require analgesic treatment. Pain intensity is not always predictable and regular assessment is paramount: use a simple verbal scale (SVS) in children > 5 years and adults and NFCS or FLACC scales in children < 5 years (see Pain(see page 23), Chapter 1).

Morphine is the treatment of choice for moderate to severe pain. Development of tolerance is common in burn patients and requires dose augmentation. Adjuvant treatment may complement analgesic medication (e.g. massage therapy, psychotherapy).

Continuous pain (experienced at rest)

– Moderate pain:
paracetamol PO + **tramadol** PO (see Pain(see page 23), Chapter 1)

– Moderate to severe pain:
paracetamol PO + **sustained release morphine** PO (see Pain(see page 23), Chapter 1)
In patients with severe burns, oral drugs are poorly absorbed in the digestive tract during the first 48 hours, morphine is administered by SC route.

Acute pain experienced during care

Analgesics are given in addition to those given for continuous pain.

– Significant medical interventions and extensive burns: general anaesthesia in an operating room.
– Limited non-surgical interventions (dressings, painful physiotherapy):
• Mild to moderate pain, 60 to 90 minutes before giving care:
tramadol PO (see Pain(see page 23), Chapter 1) rarely allows treatment to be completed comfortably. In the event of treatment failure, use morphine.
• Moderate or severe pain, 60 to 90 minutes before giving care:
immediate release morphine PO: initial dose of 0.5 to 1 mg/kg; the effective dose is usually around 1 mg/kg, but there is no maximum dose.
or **morphine** SC: initial dose of 0.2 to 0.5 mg/kg; the effective dose is usually around 0.5 mg/kg, but there is no maximum dose.

Note: these doses of morphine are for adults, dosing is the same in children > 1 year, should be halved in children less than 1 year, and quartered in infants less than 3 months.

– Pain management using morphine during dressing changes at the bedside requires:
• A trained nursing team.
• Availability of immediate release oral morphine and naloxone.
• Close monitoring: level of consciousness, RR, heart rate, SpO_2, every 15 min for the first hour following dressing change, then routine monitoring.
• Assessment of pain intensity and sedation during the intervention and for 1 hour thereafter.
• Necessary equipment for ventilation by mask and manual suction.
• Gentle handling of the patient at all times.

– Adjustment of morphine doses for subsequent dressings:
• If pain intensity (SVS) is 0 or 1: continue with the same dose.
• If SVS score ≥ 2: increase the dose by 25 to 50%. If pain control remains inadequate, the dressing change should be carried out in the operating room under anaesthesia.

– Take advantage of the residual analgesia following dressing changes to carry out physiotherapy.

– As a last resort (morphine unavailable and no facilities to give general anaesthesia), in a safe setting (trained staff, resuscitation equipment, recovery room), adding **ketamine** IM at analgesic doses (0.5 to 1 mg/kg) reinforces the analgesic effect of the paracetamol + tramadol combination given before a dressing change.

Chronic pain (during the rehabilitation period)

– The treatment is guided by self-evaluation of pain intensity, and utilises paracetamol and/or tramadol. Patients may develop neuropathic pain (see Pain(see page 23), Chapter 1).
– All other associated pain (physiotherapy, mobilization) should be treated as acute pain.

Minor burns

– Treat as outpatients.
– Wound care: dressings with silver sulfadiazine (to children 2 months and over and adults) or petrolatum gauze (except for first degree superficial burns).
– Pain: paracetamol ± tramadol usually effective.

1(see page 0) Open technique « naked burn patient under a mosquito net » and water immersion therapy are obsolete and should no longer be used.

Cutaneous abscess

- Clinical features(see page 266)
- Paraclinical investigations(see page 266)
- Treatment(see page 266)
- Equipment(see page 266)
- Anaesthesia(see page 266)
- Technique(see page 266)

– A cutaneous abscess is a collection of pus within the dermis or subcutaneous tissue.
– It is most commonly due to *Staphylococcus aureus*.

Clinical features

– Painful, red, shiny nodule with or without fluctuance; suppuration or surrounding cellulitis (see Erysipelas and cellulitis(see page 100), Chapter 4).
– Regional adenopathy and fever may be present.
– Complications: osteomyelitis, septic arthritis, septic shock (see Shock(see page 10), Chapter 1).

Paraclinical investigations

– Radiography in case of suspected osteomyelitis or septic arthritis.

Treatment

– Treatment is surgical incision and drainage, under aseptic conditions (i.e. sterile consumables and instruments, antiseptic skin preparation).
– Refer to a surgeon any cutaneous abscess:
• located in anterior and lateral neck, central triangle of the face, hand, perirectal region, breast, or
• adjacent to major blood vessels (e.g. femoral artery), or
• involving joint and bone.
– Antibiotic therapy only if signs of systemic infection, extensive surrounding cellulitis or for individuals with risk factors e.g. immunosuppression or diabetes (for antibiotic therapy, see Erysipelas and cellulitis(see page 100), Chapter 4).

Equipment

– Sterile scalpel
– Sterile curved, non-toothed artery forceps (Kelly type)
– Sterile disposable gloves and compresses
– Antiseptic solution and 0.9% sodium chloride
– 5 or 10 ml syringe

Anaesthesia

– For small (approximately < 5 cm), well delineated abscess in adults: use local anaesthesia with **1% lidocaine without epinephrine** (10 mg/ml): 15 to 20 ml.
– For larger (approximately > 5 cm), deep or poorly delineated abscess in adults or for abscess in children: consider procedural sedation or general anaesthesia (**ketamine** IM: 10 mg/kg).

For analgesia, see Pain(see page 23), Chapter 1.

Technique

Incision (Figure 8a)
– Hold the scalpel between the thumb and middle finger of the dominant hand, the index finger presses on the handle. Hold the abscess between the thumb and index finger of the other hand. The scalpel blade should be perpendicular to the skin.
– The incision is made in a single stroke along the long axis of the abscess. The incision must be long enough for a finger to be inserted.

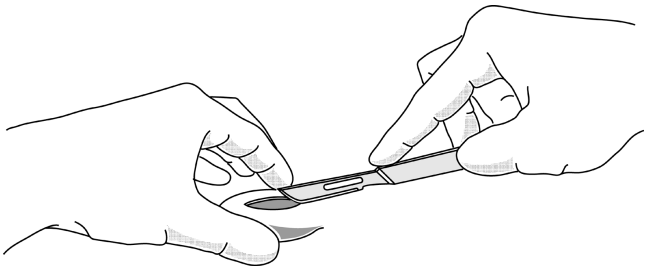


Figure 8a
Incision with a scalpel

Digital exploration (Figure 8b)
– Explore the cavity with the index finger, breaking down all loculi (a single cavity should remain), evacuate the pus (and foreign body, if present) and explore to the edges of the cavity.
– The exploration also allows an assessment of the extent of the abscess, the depth, and location with respect to underlying structures (arterial pulsation) or any possible contact with underlying bone. In this last case, seek surgical advice.

Figure 8b
Exploration of the cavity, breaking down any loculi

Washing
Abundant washing of the cavity using a syringe filled with 0.9% sodium chloride.

Drainage (Figure 8c)
Only necessary for deep abscesses.
Insert a drain (or, failing that a gauze wick) into the base of the cavity. If possible, fix it to the edge of the incision with a single suture. The drain is withdrawn progressively and then, after 3 to 5 days removed completely.

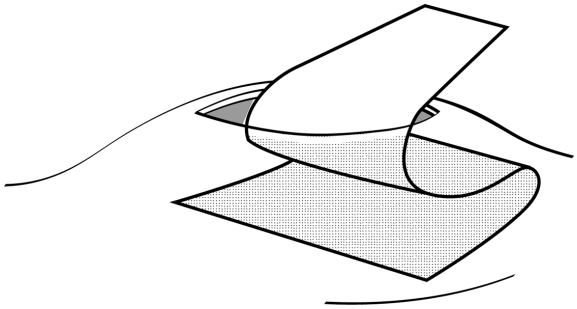


Figure 8c
Drain fixed to the skin

Dressing
Cover with sterile compresses.

Pyomyositis

- Clinical features(see page 268)
- Paraclinical investigations(see page 268)
- Treatment(see page 268)
- Equipment and anaesthesia(see page 269)
- Technique(see page 269)

– Pyomyositis is an infection of the muscle, almost always due to *Staphylococcus aureus*. It most commonly affects the muscles of the limbs and torso. Infections may occur simultaneously in multiple sites.
– Risk factors include immunosuppression, concurrent *S. aureus* infection, malnutrition, trauma and injection drug use. Risk of mortality is significant if treatment is delayed.

Clinical features

– Signs and symptoms:
• local: exquisite muscle tenderness, oedema giving muscles "woody" texture on palpation.
• systemic: regional adenopathy and fever.
• pyomyositis of the psoas muscle: patient keeps hip flexed and experiences pain on hip extension. If the abscess is on the right side, the clinical signs are the same as for appendicitis with pain in the right iliac fossa.
– Complications: septic emboli, endocarditis and septic arthritis, septic shock (see Shock(see page 10), Chapter 1).

Paraclinical investigations

– Point of care ultrasound (POCUS): assists in characterisation of abscess; can rule out deep venous thrombosis.
– Radiography: may demonstrate a foreign body, signs of osteomyelitis or osteosarcoma.

Treatment

– Immobilise the limb.
– Systematic antibiotic therapy (see Erysipelas and cellulitis(see page 100), Chapter 4).
– Adapt analgesics to the pain level (see Pain(see page 23), Chapter 1).
– Apply compresses soaked in 70% alcohol 2 times daily (max. 3 times daily to prevent burns to the skin) until incision and drainage.
– Treatment is surgical incision and drainage, under aseptic conditions (sterile consumables and instruments, antiseptic skin preparation) following the rules for incision and drainage of abscesses (see Cutaneous abscess(see page 265), Chapter 10). Muscle abscesses are often deeper than other abscesses. As a result, aspiration with a large bore needle may be necessary to locate the abscess. Needle aspiration is insufficient treatment even if pus is evacuated and should be followed by surgical incision and drainage.
– In case of pyomyositis of the psoas muscle, start antibiotics and refer to a surgeon.

Equipment and anaesthesia

As for Cutaneous abscess(see page 265), Chapter 10.

Technique

– Generous incision along the axis of the limb, over the site of the abscess and avoiding underlying neurovascular stuctures; incise the skin, subcutaneous tissues and muscular fascia with a scalpel (Figure 9a).
– Dissect the muscle fibres with non-toothed forceps (Kelly type) or round tipped scissors. Insert the instrument or a finger into the muscle until the purulent cavity is reached. If an instrument is used, during insertion, keep the instrument closed and perpendicular to the muscle fibres. Withdraw gently with the scissors or forceps slightly open, keeping instrument perpendicular to the fibres (Figure 9b). If abscess is found to be very deep, it may be necessary to refer to a surgeon.
– Use a forefinger to explore the cavity, break down any loculi and evacuate the pus (Figure 9c).
– Wash abundantly with 0.9% sodium chloride.
– Insert a large drain.
– Fix the drain to the edge of the wound using a single suture. Remove the drain on about the 5th day (Figure 9d).

Figures 9: *Surgical incision-drainage of a pyomyositis*

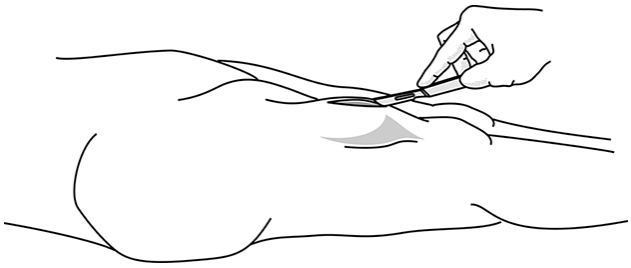


Figure 9a
Long incision

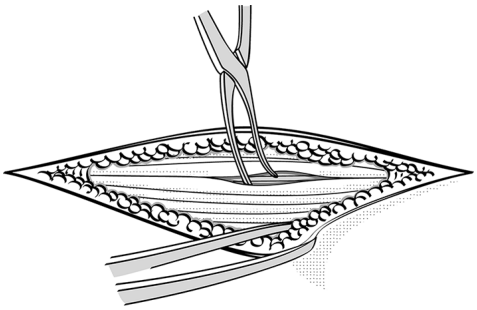


Figure 9b
Dissection of the muscle using Kelly forceps, insert closed then withdraw with the instrument slightly open

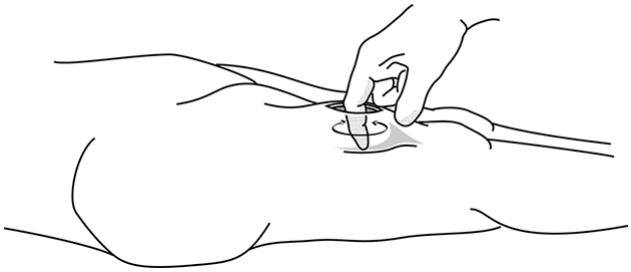


Figure 9c
Exploration and evacuation of pus with the finger

Figure 9d
Drain fixed to the skin

Leg ulcers

- Daily local treatment(see page 270)
- Systemic treatment(see page 270)

– Leg ulcers are chronic losses of cutaneous tissue. They are common in tropical regions, resulting from varied aetiologies:
• vascular: venous and/or arterial insufficiency,
• bacterial: leprosy, Buruli ulcer (*Mycobacterium ulcerans*), phagedenic ulcer, yaws, syphilis,
• parasitic: dracunculiasis (Guinea-worm disease), leishmaniasis,
• metabolic: diabetes,
• traumatic: trauma is often a precipitating factor combined with another underlying cause.

– The history of the disease and a complete clinical examination (paying particular attention to the neurological examination to determine if there is a peripheral neuropathy caused by leprosy or diabetes) usually leads to an aetiological diagnosis.

– All ulcers may become complicated with either local or regional secondary infections (abscess, lymphadenopathy, adenitis, osteomyelitis, erysipela, pyodermitis), generalised infection (septicaemia), tetanus and after many years of evolution, skin cancer.

Daily local treatment

– Bathe the leg for 10 to 15 minutes in **NaDCC** and rinse in boiled water.

– Remove any necrotic (black) and fibrinous (yellowish) tissue using compresses or excise the tissue with a scalpel.

– Apply:
• to a clean ulcer, with little discharge: **10% povidone iodine** and vaseline;
• to a dirty ulcer, with little discharge: **silver sulfadiazine** to a limited area (monitor for systemic adverse effects);
• to an oozing ulcer: **10% povidone iodine** alone;
• to an extensive, oozing ulcer or multiple ulcers: diluted **povidone iodine** (1/4 of 10% povidone iodine + 3/4 of 0.9% sodium chloride or clean water) for one minute then rinse with 0.9% sodium chloride or clean water to reduce the risk of transcutaneous iodine absorption.

– Cover with a dry sterile dressing.

Systemic treatment

– Treatment with analgesics in the event of pain: adapt the level and dosage to the individual (see Pain(see page 23), Chapter 1).

– Give systemic antibiotics in case of:

• Secondary infection (see Bacterial skin infections(see page 98), Chapter 4).

• Phagedenic ulcer (in the early stages, antibiotics may be useful. They are often ineffective in the chronic stages):
doxycycline PO (except in children under 8 years and pregnant or lactating women)
Children 8 years and over: 4 mg/kg once daily
Adults: 200 mg once daily
or
metronidazole PO
Children: 10 mg/kg 3 times daily
Adults: 500 mg 3 times daily
If after 7 days, antibiotherapy is effective, continue with doxycycline or metronidazole as above.
Treatment duration varies according to the clinical evolution.

– Treat the cause.

– Complementary therapy:
• Elevate the legs in cases of venous and/or lymphatic insufficiency.
• Tetanus prophylaxis if appropriate (see Tetanus(see page 162), Chapter 7).
• Skin graft if the ulcer is extensive, clean, red and flat. Skin grafts are often necessary after surgical excision to heal phagedenic and Buruli ulcers.

Necrotising infections of the skin and soft tissues

- Clinical features(see page 271)
- Laboratory(see page 271)
- Paraclinical investigations(see page 271)
- Treatment(see page 272)

– Invasive infections of the soft tissues: skin, subcutaneous tissue, superficial or deep fascia, muscles. They include necrotising cellulitis, necrotising fasciitis, myonecrosis, gas gangrene, etc.
– Clinical presentation depends on the causative organism and the stage of progression. Group A streptococcus is frequently isolated, as are *Staphylococcus aureus*, enterobacteriaceae and anaerobic bacteria including *Clostridium* sp.
– Delay in treatment of a minor wound or certain types of wounds (gunshot wounds or stabbings, open fractures or non-sterile intramuscular injections/circumcisions) or certain infections (varicella or omphalitis), favours the development of a necrotising infection. Patient risk factors include immunosuppression, diabetes, malnutrition and advanced age.
– A necrotising infection is a surgical emergency and has a high mortality rate.

Clinical features

– Initial signs and symptoms include erythema, oedema and pain disproportionate to appearance of infection. Location depends on the portal of entry. It may be difficult to differentiate necrotising infections from nonnecrotising infections (see Erysipelas and cellulitis(see page 100), Chapter 4). Systemic signs of infection (fever, tachycardia etc.) may be present.
– Lesions progress rapidly despite antibiotic therapy, with the development of the typical signs of a necrotizing infection: haemorrhagic blisters and necrosis (cold bluish or blackish hypoaesthetic macules).
– Signs of late infection: crepitus on palpation and fetid odour (gas gangrene) with signs of severe systemic infection (see Shock(see page 10), Chapter 1).

Laboratory

– If available, the following tests can help identify an early necrotising infection: white blood cell count > 15 000/mm^3 or < 4000/mm^3; serum creatinine > 141 micromol/litre; serum glucose > 10 mmol/litre (180 mg/dl) or < 3.3 mmol/litre (60 mg/dl). However, normal results do not exclude a necrotising infection.
– Obtain specimens for bacterial culture in the operating room and blood cultures if possible.

Paraclinical investigations

– Radiography: may demonstrate gas in muscles or along the fascia planes. Can rule out foreign body, osteomyelitis or osteosarcoma.

Treatment

Prompt surgical management accompanied by IV antibiotic therapy is essential to reduce the high mortality. Refer immediately to a surgeon. Start resuscitation if necessary (see Shock(see page 10), Chapter 1).

– Emergency surgical treatment:
• Debridement, drainage, wide excision of necrotic tissue and rapid amputation if necessary.
• Surgical re-evaluation within 24 to 36 hours to check for eventual progression of the necrosis and need for further debridement.

– IV antibiotic therapy for at least 14 days or more depending on clinical response:
cloxacillin + ceftriaxone + clindamycin or amoxicillin/clavulanic acid + clindamycin. For doses, see below.

cloxacillin IV infusion (60 minutes)[1](see page 0)
Children < 40 kg: 50 mg/kg every 6 hours
Children ≥ 40 kg and adults: 3 g every 6 hours

ceftriaxone slow IV (3 minutes) or IV infusion (30 minutes)[2](see page 0)
Children 1 month and over: 100 mg/kg once daily
Adults: 2 g once daily

clindamycin IV infusion (30 minutes)[3](see page 0)
Neonates 0 to 7 days (< 2 kg): 5 mg/kg every 12 hours
Neonates 0 to 7 days (≥ 2 kg): 5 mg/kg every 8 hours
Neonates 8 days to < 1 month (< 2 kg): 5 mg/kg every 8 hours
Neonates 8 days to < 1 month (≥ 2 kg): 10 mg/kg every 8 hours
Children 1 month and over: 10 to 13 mg/kg every 8 hours (max. 2700 mg daily)
Adults: 900 mg every 8 hours

amoxicillin/clavulanic acid (**co-amoxiclav**) slow IV injection (3 minutes) or IV infusion (30 minutes)[4](see page 0)

Children less than 3 months: 50 mg/kg every 12 hours
Children ≥ 3 months and < 40 kg: 50 mg/kg every 8 hours (max. 6 g daily)
Children ≥ 40 kg and adults: 2 g every 8 hours

– Other treatments:
• Deep vein thrombosis prophylaxis;
• Appropriate management of pain (see Pain(see page 23), Chapter 1);
• Early nutritional support.

[1](see page 0) Cloxacillin powder for injection should be reconstituted in 4 ml of water for injection. Then dilute each dose of cloxacillin in 5 ml/kg of 0.9% sodium chloride or 5% glucose in children less than 20 kg and in a bag of 100 ml of 0.9% sodium chloride or 5% glucose in children 20 kg and over and in adults.

[2](see page 0) For administration by IV route, ceftriaxone powder should to be reconstituted in water for injection only. For administration by IV infusion, dilute each dose of ceftriaxone in 5 ml/kg of 0.9% sodium chloride or 5% glucose in children less than 20 kg and in a bag of 100 ml of 0.9% sodium chloride or 5% glucose in children 20 kg and over and in adults.

[3](see page 0) Dilute each dose of clindamycin in 5 ml/kg of 0.9% sodium chloride or 5% glucose in children less than 20 kg and in a bag of 100 ml of 0.9% sodium chloride or 5% glucose in children 20 kg and over and in adults.

4(see page 0) Dilute each dose of amoxicillin/clavulanic acid in 5 ml/kg of 0.9% sodium chloride in children less than 20 kg and in a bag of 100 ml of 0.9% sodium chloride in children 20 kg and over and in adults. Do not dilute in glucose.

Venomous bites and stings

- Snake bites and envenomation(see page 273)
- Scorpion stings and envenomation(see page 275)
- Spider bites and envenomation(see page 275)
- Hymenoptera stings (honeybees, wasps and hornets)(see page 276)

Snake bites and envenomation

– More than 50% of the bites are dry bites, i.e. no envenomation occurred. In the event that venom is injected, the severity of envenomation depends on the species, the amount of venom injected, the location of the bite (bites on the head and neck are the most dangerous) and the weight, general condition and age of the individual (more serious in children).

– It is rare that the snake involved is identified. However, observation of the clinical signs may orient diagnosis and management. Two major syndromes are identified:
• neurological disorders that evolve towards respiratory muscle paralysis and coma are common manifestations of elapid envenomation (cobra, mamba, etc.);
• extensive local lesions (intense pain, inflammation with oedema and necrosis) and coagulation abnormalities are common manifestations of viperid or crotalid (rattle snake) envenomation.
Clinical manifestations and management of bites and envenomations are described in the table(see page 273) below.

– Early diagnosis and monitoring of coagulation abnormalities is based on whole blood clotting tests performed in a dry tube (at the patient's arrival and then every 4 to 6 hours for the first day).
Take 2 to 5 ml of whole blood, wait 30 minutes and examine the tube:
• Complete clotting: no coagulation abnormality
• Incomplete clotting or no clotting: coagulation abnormality, susceptibility to bleeding1(see page 0)
In the event of coagulation abnormalities, continue to monitor once daily until coagulation returns to normal.

– Aetiological treatment is based on the administration of snake antivenom serum, only if there are clear clinical manifestations of envenomation or coagulation abnormalities are observed.
Antivenom sera are effective, but rarely available (verify local availability) and difficult to store.
Antivenom serum should be administered as early as possible: by IV infusion (in 0.9% sodium chloride) if using a poorly purified serum; by slow IV in the event of severe envenomation if the serum is known to be well purified. Repeat antivenom serum administration after 4 or 6 hours if the symptoms of envenomation persist.

⚠ For all patients, be prepared for an anaphylactic reaction, which, despite its potential severity (shock), is usually more easily controlled than coagulation disorders or serious neurological disorders.

– In asymptomatic patients (bites without signs of envenomation and with normal coagulation), monitoring must continue for at least 12 hours (24 hours preferred).

Clinical signs and treatment

Time since bite	Clinical manifestations	Possible aggressor	Treatment
Bite			
0	Fang marks Pain at the site of bite	?	Strict rest, immobilisation of the limb with a splint to slow the diffusion of venom[a]. Wound cleansing. Tetanus prophylaxis (Tetanus(see page 162), Chapter 7). Observe for manifestations of envenomation. A the dispensary level, prepare patient evacuation to a referral centre.
Envenomation			
10-30 minutes	Hypotension, myosis, excessive salivation and sweating, dysphagia, dyspnoea Local paraesthesia, paresis	Elapids	Insert a peripheral IV line. IV antivenom serum as soon as possible.
	Inflammatory syndrome: intense pain, extensive regional oedema	Viperids Crotalids	Insert a peripheral IV line. IV antivenom serum as soon as possible. Analgesics[b]. IV or PO[b] anti-inflammatories.
30 minutes-5 hours	Cobra syndrome: bilateral eyelid drooping, trismus, respiratory muscle paralysis Shock	Elapids	Intubation and assisted ventilation. See Shock(see page 10), Chapter 1.
30 minutes-48 hours	Haemorrhagic syndome: epistaxis, purpura, haemolysis or disseminated intra-vascular coagulation Shock	Viperids Crotalids	Monitor coagulation (blood clotting test in a dry tube). Transfusion of fresh blood in the event of severe anaemia. See Shock(see page 10), Chapter 1.
6 hours or more	No signs or changes in coagulation (non-venomous snakes or snake bite without envenomation)	?	Reassure the patient. Send him home after 12 hours.
	Tissue necrosis		Remove blisters, clean; daily (non occlusive) dressings. Surgical intervention for necrosis, depending on the extent, after the lesions stabilise (minimum 15 days).

[a] Tourniquets, incision-suction and cauterisation are ineffective and may be dangerous.

[b] Do not use acetylsalicylic acid (aspirin).

– In case of clinical evidence of infection only: drainage of any abscess; amoxicillin/clavulanic acid (co-amoxiclav) for 7 to 10 days in case of cellulitis.
Infections are relatively rare, and most often associated with traditional treatment or with nosocomial transmission after unnecessary or premature surgery.

Scorpion stings and envenomation

– In most cases, the sting causes local effects including: pain, oedema, erythema. Management includes strict rest, wound cleansing, analgesics PO, and tetanus prophylaxis (see Tetanus(see page 162), Chapter 7). In patients with significant pain, infiltrate the area around the sting with local anaesthetic (**1% lidocaine**). Observe for 12 hours.

– General signs appear in the event of severe envenomation: hypertension, excessive salivation and sweating, hyperthermia, vomiting, diarrhoea, muscle pain, respiratory difficulties, seizures; rarely, shock.

– Aetiological treatment:
The use of scorpion antivenom sera is controversial (most of them are not very effective; they may be poorly tolerated due to insufficient purification).
In practice, in countries where scorpion envenomations are severe (North Africa, the Middle East, Central America and Amazonia), check local availability of antivenom sera and follow national recommendations.
The criteria for administration are the severity of the envenomation, the age of the patient (more severe in children) and the time elapsed since the sting. This should not exceed 2 to 3 hours. If the time elapsed is more than 2 or 3 hours, the benefit of antivenom serum is poor in comparison with the risk of anaphylaxis (in contrast to envenomation by snakes).

– Symptomatic treatment:
• In the event of vomiting, diarrhoea or excessive sweating: prevention of dehydration (oral rehydration salts), especially in children.
• In the event of muscle pain: **10% calcium gluconate** slow IV (children: 5 ml per injection, adults: 10 ml per injection, administered over 10 to 20 minutes).
• In the event of seizures: diazepam may be used with caution; the risk of respiratory depression is increased in envenomated patients (see Seizures(see page 16), Chapter 1).

Spider bites and envenomation

– Treatment is usually limited to wound cleansing, strict rest, analgesics PO and tetanus prophylaxis (see Tetanus(see page 162), Chapter 7).

– Severe envenomations are rare. There are two main clinical syndromes:

- Neurotoxic syndrome (black widow spider): severe muscle pain, tachycardia, hypertension, nausea, vomiting, headache, excessive sweating. The signs develop for 24 hours and then resolve spontaneously over a few days.
- Necrotic syndrome (recluse spider): local tissue lesions, possible necrosis and ulceration; mild general signs (fever, chills, malaise and vomiting) which usually resolve over a few days. If present, haemolysis may sometimes be life threatening.

As well as the general measures listed above, treatment includes administration of **10% calcium gluconate** by slow IV in the event of muscle spasms (children: 5 ml per injection, adults: 10 ml per injection, administered over 10 to 20 minutes).
Incision and debridement of necrotic tissue are not recommended (not useful; may impair healing).

Hymenoptera stings (honeybees, wasps and hornets)

– Local care: remove the embedded sting (bee); clean with soap and water; **calamine** lotion if pruriginous (children and adults: one application 3 to 4 times daily in a thin layer).

– Analgesics if necessary (paracetamol PO).

– In the event of an anaphylactic reaction:
epinephrine (**adrenaline**) IM
Use *undiluted* epinephrine solution (1:1000 = 1 mg/ml) and a 1 ml syringe graduated in 0.01 ml in children:
Children under 6 years: 0.15 ml
Children from 6 to 12 years: 0.3 ml
Children over 12 years and adults: 0.5 ml

For children, if 1 ml syringe is not available, use a diluted solution, i.e. add 1 mg epinephine to 9 ml of 0.9% sodium chloride to obtain a 0.1 mg/ml solution (1:10 000):
Children under 6 years: 1.5 ml
Children from 6 to 12 years: 3 ml

Repeat after 5 minutes if no clinical improvement.

In patients with circulatory collapse or those who deteriorate despite receiving IM epinephrine, use IV epinephrine (for doses, see Anaphylactic shock(see page 13), Chapter 1).

1(see page 0) There can be a considerable delay between the decrease in coagulation factors (less than 30 minutes after the bite) and the first signs of bleeding (other than bleeding at the site of the bite and/or the development of sero-sanguinous blisters), which may appear only 3 days after the bite. Conversely, bleeding may resolve prior to normalization of coagulation parameters.

Dental infections

- Clinical features and treatment(see page 276)
  - Infection localised to a tooth and its surroundings (acute dental abscess)(see page 276)
  - Infections extending to adjacent anatomical structures (acute dento-alveolar abscess)(see page 277)
  - Infections extending into the cervico-facial tissues(see page 277)

Infection arising as a secondary complication of an inflammation of the dental pulp. The severity and the treatment of dental infections depend on their evolution: localised to the infected tooth, extended to adjacent anatomical structures or diffuse infections.

Clinical features and treatment

Infection localised to a tooth and its surroundings (acute dental abscess)

– Intense and continuous pain.

– On examination: swelling limited to the gum surrounding the infected tooth. Purulent exudate may be present draining either through the root canal, or through the periodontal ligament (loosening the tooth) or through a gingival fistula. There are no signs of the infection extending to adjacent anatomical structures nor general signs of infection.

– Treatment:
• Treatment is only surgical (the source of infection is inaccessible to antibiotics): root canal therapy (disinfection of the root canal) if possible or extraction of the tooth.
• Pain: paracetamol or ibuprofen PO (see Pain(see page 23), Chapter 1).

Infections extending to adjacent anatomical structures (acute dento-alveolar abscess)

Local spreading of an acute dental abscess into the surrounding bone and tissue.

– Painful gingival and buccal swelling with warm and tender skin, developing into a ripe abscess: intense pain, with trismus, particularly if the infection is in a posterior tooth, presence of general signs (fever, fatigue, cervical lymphadenopathy).

– In patients with acute gangrenous cellulitis (crepitations on palpation), treat as an infection extending into the cervico-facial tissues (see below).

– Treatment:
• First surgical: incision and drainage of the pus or extraction of the tooth.
• Then antibiotic treatment for 5 days following the procedure: **amoxicillin** PO
Children: 25 mg/kg 2 times daily
Adults: 1 g 2 times daily
Notes:
If the dental procedure has to be delayed (local anaesthesia not possible due to inflammation, significant trismus), start an antibiotherapy, but the dental procedure must be completed in the following days.
If there is no improvement within 48 to 72 hours after the dental procedure, do not change antibiotic, but start a new procedure on the tooth.
• Pain: paracetamol or ibuprofen PO (see Pain(see page 23), Chapter 1).

Infections extending into the cervico-facial tissues

– Extremely serious cellulitis, with rapidly spreading cervical or facial tissue necrosis and signs of septicaemia.

– Treatment:
• treatment in an intensive care unit.
• high dose antibiotic treatment (see Necrotising infections of the skin and soft tissues(see page 271)).
• extraction of the tooth.

Chapter 11: Mental disorders in adults

- Anxiety(see page 278)
- Insomnia(see page 279)
- Agitation(see page 279)
- Mental confusion(see page 280)
- Post-traumatic stress disorder(see page 281)
- Depression(see page 282)
- Psychotic disorders(see page 283)
    - Acute psychotic episode(see page 284)
    - Chronic psychoses(see page 284)
    - Bipolar disorder(see page 286)

Anxiety

A patient suffering from anxiety has:
– psychological symptoms: pervasive worries, e.g. fear of having a serious illness, fear with no clearly-defined object or phobias;
– behavioural changes: nervousness, avoidance behaviour, self-isolating tendency, irritability;
– physical symptoms: e.g. dry mouth, “lump in the throat,”; sometimes medically unexplained symptoms (e.g. feeling of malaise, hot flashes or chills, diffuse pain);
– concentration difficulties, sleep problems (difficulty getting to sleep, recurrent nightmares).

Anxiety is a common feature in depression(see page 282), post-traumatic stress disorder(see page 281) and psychosis(see page 283). It can also occur in isolation, not associated with any other mental disorders. Anxiety disorders often occur immediately after a difficult life event. Medically unexplained symptoms are frequent in refugees and people exposed to adversity; in certain cultures they may be the only expression of psychological distress.

Management

Try to determine the source of the anxiety and reassure the patient (without minimising the distress or symptoms). If necessary, use simple relaxation techniques to alleviate the symptoms[1](see page 0) .

If symptoms are exacerbated (e.g., tachycardia, feeling of suffocation, fear of dying or “going crazy,” agitation, or conversely, prostration), it may be necessary to administer **diazepam**: 5 to 10 mg PO or 10 mg IM, to be repeated after one hour if required.

Acute severe anxiety may justify a short course (max. 1 or 2 weeks) of:
diazepam PO: 2.5 to 5 mg 2 times daily; reducing the dose by half in the last few days of treatment
or
hydroxyzine PO: 25 to 50 mg 2 times daily (max. 100 mg daily)
If symptoms recur after treatment discontinuation, do not resume diazepam or hydroxyzine. Re-evaluate for possible depression or post-traumatic stress disorder.

For generalised anxiety, an antidepressant with anxiolytic properties is preferred (**paroxetine** PO: 10 to 20 mg max. once daily at bedtime), to be continued for 2 to 3 months after symptoms resolve then, stop gradually over 2 weeks.

For example, in case of hyperventilation, use a technique that controls the respiratory rate: get the patient in a comfortable position with his eyes closed. Help him focus on his breathing so that it becomes calmer and more regular, with three-phase breathing cycles: inhalation (count to three), exhalation (count to three), pause (count to three), etc.

Insomnia

Complaints may be: difficulty falling or remaining asleep, waking up too early in the morning, nightmares, or fatigue.

Management

If the insomnia is related to an organic cause, treat the cause (e.g., administer analgesics for pain).

If the insomnia is related to the use of alcohol, drugs or a medication, management depends on the substance responsible.

If the insomnia is related to a particular life event (e.g. bereavement), a short term treatment with a sedating antihistamine may be useful:
promethazine PO: 25 mg once daily at bedtime for 7 to 10 days
or **diazepam** PO: 2 to 5 mg once daily at bedtime for 7 days max.

If the insomnia persists, re-evaluate the patient. Insomnia is a common feature in depression, post-traumatic stress disorder and anxiety disorders. In such cases, the underlying disorder should be addressed.

The main drugs known to cause sleep problems are corticosteroids, beta blockers, levodopa/carbidopa, fluoxetine, levothyroxin, etc.

Agitation

People who have recently suffered violent events, or with anxiety, psychotic disorders or mental confusion, may have periods of psychomotor agitation.
Agitation is common in acute intoxication (alcohol/psychostimulant drugs) and withdrawal syndrome.
Certain drugs may cause agitation (selective serotonin reuptake inhibitors (SSRIs), levodopa, mefloquine, efavirenz, etc.).
Agitation may be accompanied by oppositional behaviour, violence or fleeing.

Management

Clinical evaluation is best performed in pairs, in a calm setting, with or without the person's family/friends, depending on the situation.

It is essential to check for signs of mental confusion. If present, the priority is to detect the cause and treat it (see Mental confusion).

It may be necessary to administer **diazepam** 10 mg PO to reduce the agitation and conduct the clinical exam, without over-sedating the patient. If agitation is related to acute alcohol intoxication:
use **haloperidol** PO, 2 to 10 mg (risk of respiratory depression with diazepam).

If the patient is violent or dangerous, urgent sedation is required: **diazepam** IM 10 mg, to be repeated after 30 to 60 minutes if necessary.

Physical restraint may be required in certain circumstances. However, its use should be viewed as a temporary measure, always in combination with sedation and close medical supervision.

Alcoholic patients can experience withdrawal symptoms within 6 to 24 hours after they stop drinking. Withdrawal syndrome should be taken into consideration in patients who are hospitalised and therefore forced to stop drinking abruptly. In the early phase (pre-delirium tremens), the manifestations include irritability, a general feeling of malaise, profuse sweating and shaking. Treatment consists in:
diazepam PO (10 mg every 6 hours for 1 to 3 days, then reduce and stop over 7 days)
+ oral hydration (3 litres of water daily)
+ **thiamine** IM (100 mg once daily for at least 3 days)

If the agitation is associated with anxiety, see Anxiety(see page 278); if associated with psychotic disorders, see Psychotic disorders(see page 283).

Mental confusion

Clinical features

The clinical picture includes:
– disorientation in time and space;
– impaired consciousness;
– concentration problems;
– memory impairment.
These symptoms develop rapidly (hours or days), and often fluctuate during the course of the day. Agitation, delusions, behavioural disorders and hallucinations (often visual) may complicate the picture.

Management

Mental confusion almost always has an organic cause:
– Infectious: meningitis, cerebral malaria, encephalitis, septicaemia, syphilis, AIDS, etc.
– Metabolic: hyper/hypoglycaemia, electrolyte imbalance, niacin or B_1 deficiencies, etc.
– Endocrine: thyroid disorders
– Neurological: epilepsy, raised intracranial pressure, head trauma, meningeal haemorrhage, brain tumour, etc.
Also consider the use of drugs which may cause mental confusion (opioid analgesics, psychotropic drugs, fluoroquinolones, etc.), use of toxic substances (alcohol/drugs), or withdrawal from these substances.

Mental confusion requires hospitalisation. Treat the underlying cause.

In case of agitation, the administration of diazepam may increase mental confusion.
If it is absolutely necessary to sedate the patient, use a low dose of **risperidone** PO (one dose of 2 mg) or **haloperidol** IM (one dose of 2.5 mg).

In case of mental confusion related to stopping alcohol (delirium tremens):
– Admit the patient to an intensive care unit.
– Administer **diazepam** IV: 10 to 20 mg 4 to 6 times daily, under close supervision with ventilation equipment near at hand. The goal is to achieve mild sedation without provoking respiratory depression. The doses and duration of the treatment are adapted according to the clinical progress.
– Add **chlorpromazine** IM if necessary: 25 to 50 mg 1 to 3 times daily.
– IV hydration: 2 to 4 litres **0.9% sodium chloride** per 24 hours.
– Administer **thiamine** IM: 100 mg daily for at least 3 days.
– Monitor vital signs and blood glucose levels.

Post-traumatic stress disorder

An event is “traumatic” when someone has been directly confronted with death, either by seeing another person being killed or seriously injured as the result of violence, or by experiencing serious harm, such as a threat to his/her life or physical integrity (e.g. rape, torture). These events cause feelings of helplessness and horror.

Immediate, transitory disorders (prostration, disorientation, fleeing, automatic behaviours, etc.) are to be distinguished from secondary, long-lasting problems that appear several weeks or months after the event: post-traumatic stress, often associated with depression (Depression(see page 282)), or sometimes acute psychosis (Psychotic disorders(see page 283)), even in people with no history of psychotic symptoms.

Post-traumatic stress disorder (PTSD) is characterised by three types of psychological response, generally seen in combination:

– *Persistent re-experiencing*
The patient describes:
• images, thoughts or perceptions related to the traumatic experience, which intrude despite efforts to block them out, including at night in the form of distressing dreams;
• flashbacks during which the patient “relives” parts of the traumatic scene.

– *Avoidance*
The patient tries to avoid:
• places, situations and people that might be associated with the trauma;
• having thoughts or feelings related to the trauma; patients may use alcohol, drugs or any psychotropic agents for this purpose.

– *Increased arousal*
Constant state of alert, exaggerated startle response, anxiety, insomnia, poor concentration. The patient may develop somatic symptoms such as hypertension, sweating, shaking, tachycardia, headache, etc.).

Re-experiencing is highly distressing and causes disorders that may worsen over time; people isolate themselves, behave differently, stop fulfilling their family/social obligations, and experience diffuse pain and mental exhaustion.

Management

Psychological intervention is essential to reduce the suffering, disabling symptoms and social handicaps resulting from PTSD.

It is important to reassure the patient that his symptoms are a comprehensible response to a very abnormal event. Sessions should be conducted with tact. The patient should be encouraged to talk about his experience. Avoid over active explorations of the patient’s emotions: leave it to the patient to decide how far he wants to go.

Associated symptoms (anxiety or insomnia), if persistent, can be relieved by symptomatic treatment (diazepam) for no more than two weeks[1](see page 0).

If the patient has severe symptoms (obsessive thoughts, pronounced arousal, etc.), the pharmacological treatment is **paroxetine** PO (10 to 20 mg once daily at bedtime) or **sertraline** PO (50 mg once daily with a meal), to be continued for 2 to 3 months after symptoms resolve then, stop gradually.

[1](see page 0) Benzodiazepines can lead to dependence and tolerance. They should be used only for severe conditions and for a limited amount of time.

Depression

Depression is characterised by a set of symptoms lasting at least two weeks and causing a change from the patient's previous functioning.

The classic diagnostic criteria for a major depressive episode are:
– Pervasive sadness and/or a lack of interest or pleasure in activities normally found pleasurable
And
– At least four of the following signs:
• Significant loss of appetite or weight
• Insomnia, especially early waking (or, more rarely, hypersomnia)
• Psychomotor agitation or retardation
• Significant fatigue, making it difficult to carry out daily tasks
• Diminished ability to make decisions or concentrate
• Feeling of guilt or worthlessness, loss of self-confidence or self-esteem
• Feeling of despair
• Thoughts of death, suicidal ideation or attempt

The features of depression can vary, however, from one culture to another 1(see page 0) . For example, the depressed patient may express multiple somatic complaints rather than psychological distress. Depression may also manifest itself as an acute psychotic disorder in a given cultural context.

Management

When faced with symptoms of depression, consider an underlying organic cause (e.g. hypothyroidism or Parkinson's disease) or adverse effects from medical treatment (corticosteroids, cycloserine, efavirenz, mefloquine, etc.). Look for a triggering event (e.g. rape, recent childbirth and post-partum depression).

Depressive symptoms are the most common mental disorders in patients with severe chronic infectious diseases such as HIV infection or tuberculosis. These symptoms should not be neglected, especially as they have a negative impact on adherence to treatment.

Symptoms of depression are common directly after a major loss (bereavement, exile, etc.). They gradually subside, in most cases, with support from relatives. Psychological support may be useful.

Pharmacological treatment is justified if there is a risk of suicide or in the event of severe or long-lasting problems with significant impact on daily life, or if psychological follow-up alone is not enough.

Before prescribing, make sure that a 9-month treatment and follow-up (psychological support, adherence and response) is possible.

Preferably use a serotonin reuptake inhibitor (SRI), particularly in elderly patients:
fluoxetine PO: 20 mg once daily in the morning (max. 40 mg daily); use with caution in patients with severe anxiety disorders or who are immobilised (e.g. wounded)
or
paroxetine PO: 20 mg once daily at bedtime (max. 40 mg daily), especially if the depression is accompanied by severe anxiety
or
sertraline PO: 50 mg once daily during a meal (max. 100 mg daily)

If the response is insufficient after 4 weeks and the SRI is well tolerated, increase the dose. If the SRI is poorly tolerated, replace with another SRI without waiting any interval between the two.
If antidepressants are not available, **amitriptyline** PO may be used as an alternative: start with 25 mg once daily at bedtime and gradually increase over 8 to 10 days to 75 mg once daily (max. 150 mg daily). The therapeutic dose is close to the lethal dose; in elderly patients, reduce the dose by half.

There is a delay of 2 to 3 weeks before the antidepressant effect of SRIs occurs, at least 4 weeks for amitriptyline. During this period, anxiety may be exacerbated and the risk of suicide increased, especially with fluoxetine. **Diazepam** PO (2.5 to 5 mg 2 times daily) may be given for the first 2 weeks of treatment.

During the first month, the patient should be followed weekly. During this period, do not give the patient more tablets than the quantity required for each week or entrust the treatment to someone in the patient's close entourage that can initially ensure administration of the drug.

All serious depression carries the risk of suicide. Talking to patients about this will not increase the risk of suicide attempt. On the contrary – depressed people are often anxious and ambivalent about suicide and feel relieved when able to talk about it.

If major symptoms have not resolved at all after a month at a normally-effective dose, refer the patient to a psychiatrist, if possible; if not, try a different antidepressant.

The treatment should always be stopped gradually over a 4-week period. Inform the patient about problems associated with abrupt treatment discontinuation (very common with paroxetine).

Special situations: pregnant or breast-feeding women

– *Pregnancy in a woman under antidepressants:*
It is always preferable to stop treatment. If it is necessary to pursue treatment, continue normal treatment. Nevertheless, if the woman is taking paroxetine, change to sertraline.

– *Depression during pregnancy or during post-partum period:*
Depression is more frequent in the post-partum (breast-feeding) period than in pregnancy. In case of severe post-partum depression in a breast-feeding woman: use paroxetine, do not administer fluoxetine. In case of severe depression during pregnancy: use sertraline, avoid paroxetine.

1 (see page 0) Hence the importance of working with an “informant” (in the anthropological sense of the word) when dealing with unfamiliar cultural contexts.

Psychotic disorders

- Acute psychotic episode (see page 284)
- Chronic psychoses (see page 284)
- Bipolar disorder (see page 286)

Psychoses are characterised by delusions. The patient is convinced of things that are not real, based on intuition, interpretation or hallucinations – especially auditory ones.
Delusions are often accompanied by behaviour disorders, for example agitation, prostration, mutism, opposition, and fleeing.

Management includes psychosocial support and antipsychotic medication.
Treatment efficacy and the prognosis depend in large part on the quality of the relationship established with the patient and his family.
Keeping the patient at home with outpatient follow-up is preferred if the patient is not a danger to himself or others, and if the family is capable of managing the disorder.

The meaning of psychoses varies with the cultural context 1 (see page 0). For example, psychotic disorders may be attributed to charms or to ancestor intervention. Therapeutic approach should take those beliefs into account. Patient are usually already under “traditional” treatments, this should not be seen as an obstacle to conventional medical treatment.

1(see page 0) Hence the importance of working with an “informant” (in the anthropological sense of the word) when dealing with unfamiliar cultural contexts.

Acute psychotic episode

An acute psychotic episode can be a one-time occurrence, usually of sudden onset, or can occur repeatedly or may be the early phase of chronic psychosis. It can occur following a life event (e.g. loss, acute stress or trauma). In postpartum psychosis, the delusions centre on the mother-child relationship.

Before prescribing antipsychotic medication, consider the possibility of an underlying organic cause (see Mental confusion(see page 280)) or use of toxic substances.

Antipsychotic therapy is the same as that for chronic psychoses(see page 284) (risperidone or haloperidol) and should last at least 3 months. After 3 months, if the patient is stable, stop the treatment gradually over 4 weeks, monitoring for potential relapse.

For severe anxiety or agitation, a short-course anxiolytic(see page 285) or sedative treatment may be added to the antipsychotic treatment, at the beginning of treatment.

Chronic psychoses

Chronic psychoses (schizophrenia, paranoid psychosis, etc.) are defined by specific clinical characteristics and their long-term nature.
In schizophrenia, delusions are accompanied by dissociation; patients seem odd, their speech and thoughts are incoherent, their behaviour unpredictable and their emotional expression discordant. Such patients are often very anxious. Delusions of persecution are common.

The goal of treatment is to reduce psychological suffering and disabling symptoms, particularly on the relational level. It offers real benefits, even if chronic symptoms persist (tendency toward social isolation, possible relapses and periods of increased behavioural problems, etc.).

Treatment should last at least one year, possibly for life, particularly in schizophrenic patients. Uncertainty about the possibility of follow-up at one year or beyond is no reason not to treat. However, it is better not to start pharmacological treatment for patients who have no family/social support (e.g. homeless), provided they do not have severe behavioural disorders.

Only prescribe one antipsychotic at a time. To limit the risk of adverse effects, start treatment at a low dose and gradually increase until the minimum effective dose is reached. In elderly patients, reduce the dose by half, whichever medication is used.

Haloperidol is the most commonly used antipsychotic in many countries. Preferably use oral haloperidol with a view to switching to long-acting haloperidol (haloperidol decanoate) if the patient is likely to need long-term treatment (e.g. schizophrenic patients).
haloperidol PO: start with 0.5 mg 2 times daily for 3 days then 1 mg 2 times daily until the end of the first week; increase to 2.5 mg 2 times daily the second week; if necessary increase to 5 mg 2 times daily as of the third week (max. 20 mg daily)

If haloperidol is not available, contratindicated or poorly tolerated, possible alternative are1(see page 0) :
risperidone PO: 1 mg 2 times daily for one week, then 2 mg 2 times daily for one week; if insufficient, increase to 3 mg 2 times daily as of the third week (max. 10 mg daily)
or
chlorpromazine PO (especially if a sedative effect is required):

25 to 75 mg once daily in the evening for one week; increase if necessary to 50 mg in the morning and 100 mg in the evening for one week; if insufficient, 100 mg 3 times daily as of the third week.

In case of extrapyramidal effects, which are more common with haloperidol than with risperidone, try reducing the dose of antipsychotic or, if the extrapyramidal symptoms are severe, add **biperiden** PO: 2 mg once daily, increase if necessary up to 2 mg 2 to 3 times daily (if biperiden is not available, use **trihexphenidyl** PO at the same dosage).

For severe anxiety, it is possible to add to the antipsychotic treatment an anxiolytic for a few days: **diazepam** PO: 2.5 to 5 mg 2 times daily

For major agitation:
− If the patient is not under antipsychotic treatment:
haloperidol PO 5 mg + **promethazine** PO 25 mg (if violent or oppositional behaviour, use IM route), to be repeated after 60 minutes if necessary (max. 15 mg of haloperidol and 100 mg of promethazine in 24 hours). High doses of haloperidol can induce extrapyramidal effects, add biperiden if necessary.
− If the patient is already under antipsychotic treatment:
diazepam PO or IM: 10 mg to be repeated after 60 minutes if necessary
Do not combine two antipsychotics.

For long-term treatment (e.g. schizophrenic patients) a long-acting antipsychotic drug can be used once the patient has been stabilised on oral therapy. The dosage depends of the oral dose the patient is taking:
– For a patient on **haloperidol** PO, change to haloperidol decanoate, one injection every 3 to 4 weeks:

Daily dose of haloperidol PO	**Monthly dose of haloperidol decanoate IM** [2](see page 0)
2.5 mg	25 mg
5 mg	50 mg
10 mg	100 mg
15 mg	150 mg

– For a patient on **risperidone** PO: gradually decrease the dose of risperidone by slowly introducing haloperidol PO then, once the patient is stabilised, change to haloperidol decanoate every 3 to 4 weeks as above.

Special situations: pregnant or breast-feeding women

– In the event of pregnancy in a woman taking antipsychotics: re-evaluate the need to continue the treatment. If treatment is still necessary, administer the minimal effective dose and avoid combination with an anticholinergic (biperiden or trihexphenidyl). Monitor the neonate for extrapyramidal symptoms during the first few days of life.
– Post-partum psychosis: if the woman is breast-feeding, haloperidol should be preferred.
– Long-acting antipsychotics should not be administered.

[1](see page 0) In the event of intolerance or treatment failure with other antipsychotics, use **olanzapine** PO: 5 mg once daily, increase gradually to 10 mg daily (max. 20 mg daily).
[2](see page 0) If haloperidol decanoate is not available, **fluphenazine** IM: 12.5 to 50 mg/injection every 3 to 4 weeks.

Bipolar disorder

Bipolar disorder is characterised by alternating manic and depressive episodes[1](see page 0), generally separated by “normal” periods lasting several months or years.

Episodes of mania are characterised by elation, euphoria and hyperactivity accompanied by insomnia, grandiose ideas, and loss of social inhibitions (sexual, in particular).
Depressive episodes are often severe, with significant risk of suicide.
Search family history of similar symptoms (particularly suicide), very frequent in bipolar patients.

Pharmacologically:
– Episodes of mania are treated with **risperidone** PO starting at a low dose (2 mg once daily), increase if necessary in steps of 1 mg daily (max. 6 mg daily) or **haloperidol** PO (5 to 15 mg daily) for 3 to 6 weeks.
– **Diazepam** PO (5 mg daily) can be added during the first weeks.
– At the end of antipsychotic treatment, medication should be stopped gradually, monitoring for possible relapse. Continue treatment if necessary.
– Depressive episodes are treated as depression (see Depression(see page 282)).
– If the patient has an episode of mania while on antidepressants, immediately stop antidepressants and treat the episode of mania as above. An episode of mania while on antidepressants is indicative of bipolar disorder.

The primary treatment for bipolar disorder is a mood stabilizer taken for life. Treatment can be initiated by a physician trained in mental health, but a consultation should be set up as soon as possible with a specialist.
valproic acid PO: 200 mg 2 times daily (Week 1) then 400 mg 2 times daily (Week 2) then 500 mg 2 times daily (Week 3). This is usually sufficient to stabilise the patient; if necessary the dose may be increased by 500 mg weekly (max. 1000 mg 2 times daily).
or
carbamazepine PO: 100 mg 2 times daily (Week 1) then 200 mg 2 times daily (Week 2) then 200 mg 3 times daily (Week 3). This is usually sufficient to stabilise the patient; if necessary the dose may be increased by 200 mg weekly (max. 1200 mg daily).

Valproic acid is not recommended in women of childbearing age. If it is necessary to start treatment, use carbamazepine.
If a woman of childbearing age is already taking valproic acid, switch to carbamazepine by gradually decreasing the dose of valproic acid over a period of 2 weeks (do not stop treatment abruptly) while gradually starting carbamazepine.
If a woman becomes pregnant or is planning pregnancy it is essential to contact a specialist to re-evaluate whether the treatment is still necessary and adjust the dose if needed.

1(see page 0) “Unipolar forms” are characterized by recurring episodes of depression.

Chapter 12: Other conditions

- Sickle cell disease(see page 287)
- Diabetes type 2 in adults(see page 293)
- Essential hypertension in adults(see page 297)
- Heart failure in adults(see page 300)
    - Chronic heart failure(see page 301)
    - Acute heart failure (acute pulmonary oedema)(see page 303)
- Endemic goitre and iodine deficiency(see page 305)

Sickle cell disease

- Clinical features(see page 287)
- Major acute manifestations(see page 288)
    - Painful vaso-occlusive crises (VOC)(see page 288)
    - Fever(see page 288)
    - Acute severe anaemia(see page 288)
    - Stroke(see page 288)
    - Acute chest syndrome (ACS)(see page 288)
    - Priapism(see page 288)
- Laboratory and other investigations(see page 289)
    - Diagnosis(see page 289)
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- Management of major acute manifestations(see page 289)
    - Painful vaso-occlusive crisis (VOC)(see page 289)
    - Fever and infection(see page 290)
    - Acute severe haemolysis(see page 290)
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    - Splenic sequestration(see page 291)
    - Stroke(see page 291)
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    - Priapism(see page 292)
- Prevention of complications(see page 292)
    - Education of patients (including children) and families(see page 292)
    - Routine preventive care(see page 292)
    - Routine follow-up of patients(see page 293)

– Homozygous sickle cell disease (SCD) is a life-threatening genetic disorder of haemoglobin (Hb). The abnormal Hb (HbS) results in the distortion of red blood cells into a sickle shape leading to increased destruction (haemolysis), an increase in blood viscosity and obstruction of capillaries (vaso-occlusion).
– SCD is common in sub-Saharan Africa (1 to 3% of births), on the American continent, in India and in the Mediterranean basin.

Clinical features

– Symptoms generally begin after 6 months of age.
– Major signs: recurrent painful crises, chronic anaemia, splenomegaly and frequently, growth retardation and malnutrition in children.
– Serious acute life threatening complications such as stroke, overwhelming infections and acute chest

syndrome.
– In populations in whom the disease is frequent, diagnosis is suggested by a family history of similar clinical signs.

Major acute manifestations

Painful vaso-occlusive crises (VOC)

– Children under 2 years present with the hand-foot syndrome or dactylitis (acute pain and swelling in the hands or feet).
– Children older than 2 years and adults present with acute pain affecting the back, chest, abdomen (can resemble an acute abdomen) and extremities.
– Young children may have non-specific signs of a VOC: refusal to walk, irritability, lack of appetite, crying, whimpering or moaning when touched, etc.
– Look for an associated infection that might have precipitated the VOC.
– In case of bony pain in a single location, unresponsive to analgesics (or a persistent limp in a child) associated with fever and erythema or swelling, consider an osteomyelitis.

Fever

Look for infection: in particular pneumonia, cellulitis, meningitis, osteomyelitis and sepsis (patients are particularly susceptible to infections especially due to pneumococcus, meningococcus and *Haemophilus influenzae*); malaria.

Acute severe anaemia

– The chronic anaemia is often complicated by acute severe anaemia with gradually appearing fatigue, pallor of the conjunctivae and palms, shortness of breath, tachycardia, syncope or heart failure.
– The acute anaemia can be due to:
• Acute severe haemolysis often secondary to malaria: fever, haemoglobinuria (dark urine) and yellow conjunctivae.
• Splenic sequestration (trapping of blood cells in the spleen), mostly in children 1 to 4 years: sudden enlargement of the spleen, severe left upper quadrant pain, thrombocytopenia. Can lead to shock.
• Aplastic crisis (transient suspension of red blood cell production by the bone marrow): impalpable spleen and absence of reticulocytes.

Stroke

– Most often ischaemic (due to vaso-occlusion in cerebral vessels) but a stroke can also be haemorrhagic.
– Sudden loss of motor function or aphasia, in children and in adults.
– Signs can resemble meningitis and cerebral malaria: headache, photophobia, vomiting, stiff neck, alteration of consciousness and neurologic signs or rarely seizures.

Acute chest syndrome (ACS)

– Chest pain, tachypnoea, respiratory distress, hypoxia; fever (more frequent in children); pulmonary infiltrate on chest x-ray. Often proceeded by a VOC.
– Complications: multiorgan failure (lung, liver, kidney).

Priapism

Painful prolonged erection in the absence of sexual stimulation, also occurring in young boys. Risk of necrosis and irreversible erectile dysfunction.

Laboratory and other investigations

Diagnosis

– Hb electrophoresis confirms the diagnosis but is often unavailable.
– If not available, a positive Emmel test (or sickling test) in the presence of clinical signs of sickle cell disease supports the diagnosis.

Other examinations

Tests	Indications
Haemoglobin	• At the time of diagnosis and annually (frequently 7 to 9 g/dl). • In case of VOC, fever, acute anaemia (≤ 5 g/dl or drop in Hb ≥ 2 g/dl below the patient's baseline), stroke, ACS. • For monitoring of transfused patients.
Platelets	• At the time of diagnosis and annually. • In case of acute anaemia (thrombocytopenia - platelet count ≤ 100 000/mm^3 if splenic sequestration).
Urine dipstick	• In case of fever: look for a urinary tract infection. • In case of acute severe anaemia: look for haemoglobinuria.
Malaria test	In case of VOC, fever, acute anaemia or stroke.
Lumbar puncture	In case of fever with meningeal signs or unexplained coma.
Other (if available)	• Complete blood count and reticulocyte count. • Blood culture in case of fever. • X-Ray if suspicion of pneumonia, osteomyelitis, ACS.

Management of major acute manifestations

Painful vaso-occlusive crisis (VOC)

– Moderate pain (at home):
• Generous oral hydration (water, soup, juice, coconut water): minimum 100 ml/kg daily in children and 50 ml/kg daily in adults (2.5 to 3 litres daily);
• Warm compresses (application of cold is contra-indicated);
• Level 1 (paracetamol and ibuprofen) and level 2 (tramadol) analgesics;
• If pain is not controlled at home within 24 hours, seek medical attention.

– Severe pain or pain not controlled at home (in hospital):
• IV hydration (Appendix 1b(see page 308)) and PO; monitor for fluid overload, discontinue IV fluids progressively after 24 to 48 hours;
• Level 3 analgesics (morphine);
• Do not give routine antibiotics in the absence of fever; do not transfuse for VOC.

For the treatment of pain according to intensity, see Pain(see page 23) (Chapter 1).

Fever and infection

– Admit to hospital:
• All children less than 2 years;
• Children with fever ≥ 38.5 °C and adults with fever ≥ 39.5 °C; patients who are critically ill appearing 1(see page 0) or have acute anaemia.

– PO or IV hydration (Appendix 1a(see page 307)).
– Treat malaria if present.
– Treat bacterial infections according to cause.
– Treat all patients with respiratory symptoms for pneumonia and ACS.
– In case of osteomyelitis:
ceftriaxone slow IV 2(see page 0) injection (3 minutes) or IV infusion (30 minutes)
Children < 40 kg: 50 mg/kg every 12 hours
Children ≥ 40 kg and adults: 2 g every 12 hours
+ **cloxacillin** IV infusion (60 minutes) 3(see page 0)
Children < 40 kg: 50 mg/kg every 6 hours
Children ≥ 40 kg and adults: 3 g every 6 hours
Administer IV therapy for at least 14 days. Then if the patient has improved, change to the oral route for an additional 14 days of treatment with a combination of:
ciprofloxacin PO
Children < 35 kg: 15 mg/kg 2 times daily
Children ≥ 35 kg and adults: 500 mg 2 times daily
+ **amoxicillin/clavulanic acid** PO (see below)

– If the source of infection is unknown:
ceftriaxone IM or slow IV 2(see page 0) injection (3 minutes) or IV infusion (30 minutes)
Children < 20 kg: 50 mg/kg once daily (max. 2 g/day)
Children ≥ 20 kg and adults: 1 to 2 g once daily

After 48 hours re-evaluate the patient:
• If the patient is improving (afebrile, can drink), change to:
amoxicillin/clavulanic acid (**co-amoxiclav**) PO for 7 to 10 days. Use formulations in a ratio of 8:1 or 7:1 exclusively. The dose is expressed in amoxicillin:
Children < 40 kg: 50 mg/kg 2 times daily
Children ≥ 40 kg and adults:
Ratio 8:1: 3000 mg daily (2 tab of 500/62.5 mg 3 times daily)
Ratio 7:1: 2625 mg daily (1 tab of 875/125 mg 3 times daily)
Patients over 2 years without acute anaemia can continue treatment as outpatients.
Patients under 2 years or with acute anaemia or who cannot be monitored and treated at home by their family should complete PO antibiotherapy in hospital.
• If the patient is not improving, continue ceftriaxone until the patient is afebrile, then, change to PO treatment. Monitor for acute anaemia.

Acute severe haemolysis

– Admit to hospital.
– Treat malaria if present.
– Transfuse packed red blood cells 4(see page 0) 5(see page 0) if Hb < 5 g/dl or drop of 2 g/dl below the patient's baseline. Target a Hb level of 9 g/dl.
• Start with 10 to 15 ml/kg in 3 to 4 hours. For information, 10 ml/kg of packed red blood cells usually raise the Hb by 2.5 g/dl.
• Repeat the Hb. If a second transfusion is needed, check for signs of fluid overload before starting the

transfusion.
• Measure Hb and perform urine dipstick in the following days. Further transfusions may be necessary if haemolysis is ongoing.

Aplastic crisis

– Admit to hospital.
– Treat an associated bacterial infection if present.
– Transfuse as for haemolysis. Repeat the Hb every other day. An increasing reticulocyte count and a gradual increase of the Hb indicate improvement. Follow patient until they have reached their baseline Hb.

Splenic sequestration

– Admit to hospital.
– Treat hypovolaemic shock if present.
– Monitor the size of the spleen.
– Transfuse if Hb < 5 g/dl, target a Hb level of 7 to 8 g/dl maximum.
– Administer ceftriaxone as above.
– After clinical improvement, monitor for relapse (follow the size of the spleen).
Note: splenectomy is contra-indicated (high operative mortality).

Stroke

– Admit to hospital.
– The treatment of choice for ischaemic stroke is an exchange transfusion to lower the concentration of HbS. Transfer the patient to a specialized facility for further management (including prophylactic therapy to prevent recurrences with transfusion program, hydroxyurea).
– If the patient is awaiting transfer or if transfer is not possible:
• Oxygen continuously, at least 5 litres/minute or to maintain the SpO_2 between 94 and 98%.
• Treat seizures if present.
• Transfuse if the Hb ≤ 9 g/dl. Target Hb of 10 g/dl.
• After the transfusion provide IV hydration (Appendix 1a(see page 307)).

Acute chest syndrome

– Admit to hospital.
– Measure SpO_2 and administer oxygen as in stroke.
– IV hydration (Appendix 1a(see page 307)) while monitoring for fluid overload.
– Antibiotics:
ceftriaxone slow IV 2(see page 0) injection (3 minutes) or IV infusion (30 minutes) for 7 to 10 days
Children < 20 kg: 50 mg/kg once daily (max. 2 g daily)
Children ≥ 20 kg and adults: 1 to 2 g once daily
+ **azithromycin** PO for 5 days
Children: 10 mg/kg once daily (max. 500 mg daily)
Adults: 500 mg on D1 then 250 mg once daily from D2 to D5

– Transfuse if symptoms are unresponsive to antibiotics and Hb < 9 g/dl.
– If wheezing is present treat with:
salbutamol aerosol (100 micrograms/puff)
Children and adults: 2 to 4 puffs with a spacer every 10 to 30 minutes as needed
– Encourage deep breathing (incentive spirometry hourly).
– Treat pain (see Pain(see page 23), Chapter 1).

Priapism

– PO and IV hydration (Appendix 1b(see page 308)), encourage urination, apply warm compresses, treat pain.
– Erection > 4 hours: consider transfusion and refer to surgery.

Prevention of complications

Certain complications can be avoided with appropriate health education of patients/families, routine preventive care and regular follow-up.

Education of patients (including children) and families

Basic knowledge	
• Disease • Treatment • Monitoring	Chronic, necessarily transmitted by both parents, non-contagious. Routine (see below) and symptomatic (pain). Size of the spleen, temperature, baseline Hb.
Major precipitating factors of a painful crisis and how to prevent them	
• Cold • Excessive heat • Tight clothing • Dehydration • Excessive effort • Infections	Wear warm clothing, avoid bathing in cold water. For example, avoid going out at mid-day. Wear wide comfortable clothing without elastics. Drink plenty of fluids. Moderate physical activity is beneficial. Follow routine treatments (including vaccination).
Principal complications requiring the patient to seek urgent medical advice	
• Pain unresponsive to analgesia after 24 hours or severe from the start. • Any fever (do not treat at home). • Respiratory problems (cough, difficulty breathing, chest pain). • Diarrhoea/vomiting and inability to drink. • Dehydration (dark, infrequent urine). • Anaemia (pale or yellow conjunctivae, pale palms, enlarged spleen).	

Routine preventive care

– Prevention of pneumococcal infections
phenoxymethylpenicillin (**penicillin V**) PO until age 15 years (at least until 5 years):
Children < 1 year: 62.5 mg 2 times daily
Children 1 to < 5 years: 125 mg 2 times daily
Children 5 to 15 years: 250 mg 2 times daily

– Immunization
Ensure that the child's immunisations are up to date; if not, administer catch up vaccines:

Children < 5 years	• DTP, hepatitis B, polio, measles, *H. influenzae* type B vaccines • Pneumococcal conjugate vaccine (PCV13 or, if not available, PCV10) • Meningococcal conjugate vaccine in endemic areas • At 2 years: pneumococcal 23-valent polysaccharide vaccine, at least 8 weeks after the last PCV13 or 10
Children > 5 years	• DTP or Td, hepatitis B, polio, measles, *H. influenzae* type B vaccines • Pneumococcal conjugate vaccine PCV13 (or PCV10) • Meningococcal conjugate vaccine in endemic areas

– To support red blood cell production
folic acid PO [6](see page 0) (life-long treatment)
Children < 1 year: 2.5 mg once daily
Children ≥ 1 year and adults: 5 mg once daily

– Malaria chemoprophylaxis (if malaria prevalence ≥ 5%)
mefloquine PO
Children 6 months to 5 years and > 5 kg: 5 mg base/kg once weekly
Do not use to treat malaria.

– Provide nutritional support at hospital discharge.

Routine follow-up of patients

– Between crises, for information:
Children < 5 years: every 1 to 3 months;
Children ≥ 5 years and adults: every 3 to 6 months.
– After a crisis: as often as necessary, according to the clinical course.

[1](see page 0) Critically ill appearing child: weak grunting or crying, drowsy and difficult to arouse, does not smile, disconjugate or anxious gaze, pallor or cyanosis, general hypotonia.

[2](see page 0) For administration by IV route, ceftriaxone powder should to be reconstituted in water for injection only. For administration by IV infusion, dilute each dose of ceftriaxone in 5 ml/kg of 0.9% sodium chloride or 5% glucose in children less than 20 kg and in a bag of 100 ml of 0.9% sodium chloride or 5% glucose in children 20 kg and over and in adults. [a(see page 0) b(see page 0) c(see page 0)]

[3](see page 0) Cloxacillin powder for injection should be reconstituted in 4 ml of water for injection. Then dilute each dose of cloxacillin in 5 ml/kg of 0.9% sodium chloride or 5% glucose in children less than 20 kg and in a bag of 100 ml of 0.9% sodium chloride or 5% glucose in children 20 kg and over and in adults.

[4](see page 0) Always inquire how many transfusions a patient has previously received (risk of iron overload).

[5](see page 0) Do not transfuse whole blood if possible (risk of fluid overload).

[6](see page 0) Iron is contraindicated in patients who have received multiple transfusions. Avoid combined preparations of iron and folic acid.

Diabetes type 2 in adults

- Clinical features(see page 294)

- Diagnosis(see page 294)
- Treatment(see page 294)
- Surveillance and monitoring(see page 296)
- References(see page 297)

− Diabetes is a metabolic disorder that leads to hyperglycaemia.
− Type 2 diabetes usually occurs in adults and accounts for 90% of diabetes cases worldwide.
− Type 2 diabetes can lead to acute complications, as well as chronic complications that result in serious organ damage (cardiovascular events; diabetic retinopathy, neuropathy, nephropathy).

Clinical features

− Few or no symptoms; symptoms of hyperglycaemia may be present: polyuria (frequent urination) and polydypsia (excessive thirst and drinking).
− In rare cases, patients may present with severe hyperglycaemia (impaired consciousness, coma or acute dehydration).

Diagnosis

− Look for diabetes in the event of:
• symptoms of hyperglycaemia;
• cardiovascular disorders: stroke, myocardial infarction, hypertension;
• peripheral neuropathies**,** foot ulcers, absence of tendon reflexes or peripheral pulse.

− Diagnosis is made on one of the following results[1](see page 297):

	Fasting blood glucose[(a)]	**Random blood glucose**[(b)]	**Glycated Hb**[(d)]
Sympto matic patient	1 fasting blood glucose ≥ 7 mmol/litre (or ≥ 126 mg/dl)	1 random blood glucose ≥ 11 mmol/litre (or ≥ 200 mg/dl)	1 HbA1c ≥ 6.5%
Asympto matic patient	2 fasting blood glucose ≥ 7 mmol/litre on 2 samples collected at 2 different times[(c)]	1 random glucose ≥ 11 mmol/litre followed by 1 fasting blood glucose ≥ 7 mmol/litre	2 HbA1c ≥ 6.5% on 2 samples collected at 2 different times[(c)]

[(a)] Fasting blood glucose test: performed on patient that has fasted at least 8 hours.
[(b)] Random blood glucose test: performed at any moment of the day.
[(c)] For example, interval of at least one or more days.
[(d)] Glycated Hb (HbA1c) reflects average glycaemia over around 3 months.

Note: even in a symptomatic patient, it is preferable to perform a second blood glucose test to confirm the result.

Treatment

Glycaemic targets[2](see page 297)

Fasting blood glucose < 8.3 mmol/litre (or < 150 mg/dl) or HbA1c between 7 and 7.5.
The closer blood glucose levels remain to these values, the more cardiovascular complications are prevented or delayed.
Depending on the context (healthcare provision) or patient profile (elderly patient, history of severe

hypoglycaemia or long-standing poorly controlled diabetes), fasting blood glucose < 10 mmol/litre (or < 180 mg/dl) or HbA1c of around 8 are acceptable.
Blood glucose should not fall < 4.5 mmol/litre (or < 80 mg/dl) or HbA1c < 6.5.

Lifestyle and dietary advice [1](see page 0)

− Avoid sugared foods and drinks (but no excessive restriction of carbohydrates).
− High fibre intake; limit animal fats and alcohol.
− Physical activity.
− Weight control. If BMI ≥ 25, try to reduce weight by 5 to 10%.
− Stop smoking.

Pharmacological treatment

First-line treatment **metformin** PO [2](see page 0) .
The usual dose is 1 to 2 g daily. For information:
Week 1: 500 mg once daily in the morning at breakfast
Week 2: 500 mg 2 times daily (morning and evening) during meals
Increase in increments of 500 mg per week as long as the drug is well tolerated (max. 2 g daily, i.e. 1 g morning and evening) [3](see page 297).

If glycaemic control is not acheived, administer metformin in combination with a sulfonylurea. Sulfonylurea doses are adjusted in increments to avoid the risk of hypoglycaemia, based on blood glucose results.
• In patients under 60, **glibenclamide** PO:
The usual dose is 5 mg 2 times daily. For information:
Week 1: 2.5 mg once daily in the morning at breakfast
Week 2: 5 mg once daily in the morning at breakfast
Increase in increments of 2.5 mg weekly until fasting blood glucose reaches target levels (max.15 mg daily).
• In patients over 60, **gliclazide** PO (immediate release tablet):
The usual dose is 40 to 80 mg 2 times daily. For information:
Weeks 1 and 2: 40 mg once daily in the morning at breakfast
Increase in increments of 40 mg every 2 weeks (weeks 3 and 4: 80 mg once daily in the morning at breakfast) until fasting blood glucose reaches target levels (max. 240 mg daily, i.e. 120 mg morning and evening).

If glycaemic control is not acheived with the combination of metformin + a sulfonylurea, continue metformin but replace the sulfonylurea with **intermediate-acting insulin** SC: start with 0.2 IU/kg at bedtime. The dose is adjusted after measuring fasting blood glucose in the morning. Once blood glucose levels have stabilized, test levels once weekly then after each consultation. Doses of 1 IU/kg/day or more may be necessary to reach glycaemic targets. If the necessary dose is over 0.5 IU/kg/day, administer in 2 injections daily.

Adjustment of intermediate-acting insulin dosage based on blood glucose levels

Morning blood glucose	Action

< 4 mmol/litre < 70 mg/dl	Treat hypoglycaemia (see Hypoglycémie(see page 20), Chapter 1). Reduce daily dose of insulin by 2 to 4 units. Maintain new dose for 4 days. Check blood glucose after 4 days, readjust dose if glycaemic target has not been not reached. Check blood glucose again after 4 days and repeat the process until glycaemic target is reached.
≥ 4 and < 8.3 mmol/litre ≥ 70 and < 150 mg/dl	Do not change dose.
≥ 8.3 and < 11 mmol/litre ≥ 150 and < 200 mg/dl	Increase daily dose of insulin by 2 units. Check blood glucose after 4 days, readjust dose if glycaemic target has not been not reached. Check blood glucose again after 4 days and repeat the process until glycaemic target is reached.
≥ 11 and < 16,5 mmol/litre ≥ 200 and < 300 mg/dl	Increase daily dose of insulin by 4 units. Check blood glucose after 4 days, readjust dose if glycaemic target has not been not reached. Check blood glucose again after 4 days and repeat the process until glycaemic target is reached.
≥ 16.5 mmol/litre ≥ 300 mg/dl	Perform dipstick analysis for ketones. Treat hyperosmolar hyperglycaemia or ketoacidosis if present.

Example for a man weighing 79 kg:
Start with 16 IU per day (79 kg x 0.2 IU).
On D4, blood glucose is 14.6 mmol/litre. Add 4 IU (daily dose of insulin is 20 IU).
On D8, blood glucose is 10.4 mmol/litre. Add 2 IU (daily dose of insulin is 22 IU).
On D12, blood glucose is 6.1 mmol/litre. Glycaemic target is reached.

Surveillance and monitoring

Laboratory surveillance
− Patients on oral hypoglycemic agents: blood glucose test once a month to begin with, then during monitoring visits.
− Patients on insulin: fasting blood glucose test during the dose adjustment phase then, if possible, once weekly, once the insulin dose stabilised.
− HbA1c if available: every 3 months, then every 6 months if well stabilised.
− Other necessary tests according to comorbidities and chronic complications.

Clinical monitoring
− Routine consultations: check blood pressure (should remain < 140/80 mmHg) and weight, examine feet. Consultations once a month for the first 6 months, then individualised frequency of consultations depending on the patient's characteristics (e.g. once every 6 months if the diabetes is well controlled).
− Annual check-up: check for cardiovascular and neurological complications, evaluate renal function (serum creatinine and proteinuria dipstick test), examination of teeth and gums.
− Management of diabetes complications.

Patient education
− Lifestyle and dietary measures (diet, physical activity, etc.).
− Patients on sulfonylurea or insulin therapy: signs of hypoglycaemia/hyperglycaemia and management.

– Patients on insulin therapy: auto-administration (schedule, injection sites and techniques); storage of insulin; self-monitoring of blood glucose and adjustment of doses in patients using glucometers.
– Patients with sensory neuropathy or peripheral arterial disease: autoexamination of feet; prevention of foot lesions.

1 (see page 0) These measures concern all patients regardless of medication prescribed. They can be sufficient alone to normalize blood glucose levels in certain patients.
2 (see page 0) If metformin is contraindicated or not tolerated, replace with a sulfonylurea.

References

1. Partners in Health. Chronic care integration for endemic non-communicable diseases, Chapter 7, Table 7.1. PIH, Boston, 2013. https://www.pih.org/sites/default/files/2017-07/PIH_NCD_Handbook.pdf.pdf [Accessed 13 June 2018]

2. American Diabetes Association**.** Glycemic targets**.** Diabetes Care 2017 Jan; 40 (Supplement 1): S48-S56. https://doi.org/10.2337/dc17-S009 [Accessed 13 June 2018]

3. Joint Formulary Committee. *British National Formulary* (online) London: BMJ Group and Pharmaceutical Press http://www.medicinescomplete.com[6] [Accessed 18 June 2018]

Essential hypertension in adults

- Clinical features (see page 298)
- Paraclinical investigations (see page 298)
- Long-term treatment (see page 298)
- Surveillance and monitoring (see page 299)
- Treatment of hypertensive crisis (see page 300)
- References (see page 300)

Hypertension (or high blood pressure - HBP) is defined as elevated blood pressure (BP) at rest that persists over time i.e. measured 3 times during 3 separate consultations over a period of three months. Essential hypertension is defined as HBP of undetermined cause (the large majority of cases).

The global overall prevalence of HBP in adults aged 25 and over is around 40%.[1] (see page 300)

Serious complications of HBP can be acute (hypertensive encephalopathy, left-sided heart failure, acute renal failure) or delayed i.e. occur after a long period during which HBP has not been controlled (stroke, ischaemic heart disease, peripheral arterial disease, chronic renal impairment).

For pregnancy-induced hypertension, see Essential obstetric and newborn care, MSF.

6 http://www.medicinescomplete.com/

Clinical features

– HBP thresholds:

HBP classification	**Blood pressure** (BP) in mmHg	
	Systolic (SBP)	**Diastolic** (DBP)
Mild	140 or over	90 or over
Moderate	160 or over	100 or over
Severe	180 or over	110 or over

– Severe HBP is defined more by the presence of serious end-organ damage than the blood pressure reading:
• Uncomplicated hypertensive crisis:
SBP ≥ 180 and/or DBP ≥ 110 and some symptoms (moderate headaches, epistaxis, dizziness, tinnitus, eye floaters) but no signs of end-organ damage;
• Hypertensive emergency:
SBP ≥ 180 and/or DBP ≥ 110 and signs of end-organ damage:
- intense headaches, nausea/vomitting, confusion, seizures, coma in the event of hypertensive encephalopathy;
- dyspnoea, chest pain in the event of heart failure or cardiac ischaemia;
- rapid and/or irregular heart rate in the event of heart failure;
- anuria, oliguria in the event of renal impairment.

– History and clinical examination should look for:
• medications being taken that can cause or aggravate HBP;1(see page 0)
• focal neurological sign(s) suggestive of stroke;
• comorbidities and risk factors: heart failure, diabetes, renal impairment; excessive smoking or consumption of alcohol, excess weight (BMI ≥ 25), etc.

Paraclinical investigations

– Blood test: ionogram (particularly serum potassium levels), serum creatinine.
– Other necessary laboratory tests according to comorbidities (e.g. diabetes).
– ECG and echocardiogram to look for signs of heart failure, coronary disease, or arrhythmia.

Long-term treatment

– The goal of treatment is to lower BP. Target BP are:
• SBP < 140 and/or DBP < 90
• SBP < 140 and/or DBP < 80 in diabetic patients
• SBP < 150 and/or DBP < 90 in patients aged > 80 years

– In patients with mild HBP (SBP ≥ 140 and/or DBP ≥ 90) without associated cardiovascular disorders or stroke or diabetes, start with lifestyle and dietary advice.

– Pharmacological treatment is indicated in the following cases:
• SBP ≥ 160 and/or DBP ≥ 100;
• HBP associated with cardiovascular disorder, stroke or diabetes;
• HBP not controlled by lifestyle and dietary changes alone.

Lifestyle and dietary advice
Recommended for all hypertensive patients:
− Reduce calorie and salt intake.
− Regular physical activity.
− Weight loss if BMI ≥ 25.
− Stop smoking and alcohol consumption.

Pharmacological treatment
Start with a monotherapy. One of four classes of antihypertensive drugs can be chosen as first line treatment, according to the patient's characteristics (e.g. age, contra-indications, etc.). For information:

Patient with no comorbidities	**Patient with comorbidities**
Thiazide diuretic	After a stroke: thiazide diuretic
Patient > 65 years: thiazide diuretic or calcium channel blocker	Diabetic patient: angiotensin converting enzyme (ACE) inhibitor or beta blocker if concomitant cardiovascular disorder
Patient with black skin: thiazide diuretic or calcium channel blocker (avoid ACE inhibitors)	Renal impairment: ACE inhibitor
Thiazide diuretic **hydrochlorothiazide** PO: 12.5 to 25 mg once daily in the morning (max. 25 mg daily) *Angiotensin converting enzyme inhibitor* **enalapril** PO: start with 5 mg once daily. Gradually increase, every 1 to 2 weeks, according to BP, up to 10 to 20 mg once daily (max. 40 mg daily). In elderly patients or patients taking a diuretic or patients with renal impairment: start with 2.5 mg once daily. *Calcium channel blocker* **amlodipine** PO: 5 mg once daily. Increase to 10 mg once daily if necessary (max. 10 mg daily). In elderly patients or patients with hepatic impairment: start with 2.5 mg once daily. *Beta-blocker* (contra-indicated in patients with asthma) **bisoprolol** PO: 5 to 10 mg once daily in the morning Do not stop treatment abruptly (risk of malaise, angina).	

In patients with no comorbidity start with a thiazide diuretic and check BP after 4 weeks of treatment. If the treatment has been correctly taken but there is no improvement after 4 weeks, add a second antihypertensive drug.
After 4 weeks of bitherapy, reevaluate. If the patient's BP remains too high, consider triple-therapy.

In diabetic patients, if there is no improvement after 4 weeks of AEC inhibitor treatment taken correctly, add a calcium channel blocker.

In patients with a cardiac disorder (heart failure or coronary heart disease), bitherapy is usually necessary from the start (AEC inhibitor + beta-blocker).

Surveillance and monitoring

Laboratory surveillance
According to treatment (diuretic, AEC inhibitor, etc.): ionogram and serum creatinine every 6 to 12 months.

Clinical monitoring
– Consultations every 3 months (BP, weight), then every 6 months, then individualised frequency of consultations depending on the patient's characteristics.
– Management of comorbidities (e.g. diabetes).

Patient education
– Lifestyle and dietary advice.
– Treatment observance: do not stop treatment abruptly, particularly if taking beta blockers (risk of malaise, angina).
– Consultation in the event of epistaxis, tinnitus, eye floaters; adverse effects of treatment (e.g. cough with AEC inhibitors, erectile dysfunction with beta blockers, oedema with calcium channel blockers).

Treatment of hypertensive crisis

Uncomplicated hypertensive crisis
Most frequent. Reassure the patient and prescribe rest. Check BP a few days later to start or adapt treatment.

Hypertensive emergency
Treat in an intensive care unit.
– Hypertensive encephalopathy:
The aim is to reduce BP by 10 to 15% within the first hour and to not reduce it more than 25% during the first 24 hours.
labetalol IV (contra-indicated in patients with asthma[2](see page 0)):
20 mg over at least 1 minute. Administer another dose after 10 minutes if BP has not decreased. If necessary, 40 mg doses are administered every 10 minutes until hypertension is controlled (max. 300 mg total dose).
– Stroke: do not try to decrease BP during the first 3 days unless SBP is ≥ 220 and/or DBP ≥ 120 (in this event administer labetalol).
– Acute pulmonary oedema: see Acute heart failure(see page 303).

[1](see page 0) Consider secondary hypertension caused by medications being taken, mainly NSAID, corticosteroids, opioids, oral estroprogestogens, etc. Treatment, in this event, consists in stopping or replacing the causative drug.
[2](see page 0) In patient with asthma, **hydralazine** IV: 5 to 10 mg diluted in 10 ml of 0,9% sodium chloride administered by slow IV, to be repeated after 20 to 30 minutes if necessary.

References

1. World Health Organization. Media center. High blood pressure: a public health problem, 2018 http://www.emro.who.int/media/world-health-day/public-health-problem-factsheet-2013.html [Accessed 12 September 2018]

Heart failure in adults

Heart failure (HF) is defined as the inability of the heart to maintain adequate cardiac output.
It is a serious condition, particularly frequent in people over 70 years.
There are two types:
– chronic HF: gradual onset of signs of HF;

– acute HF: sudden onset of life-threatening HF (cardiogenic acute pulmonary oedema or shock), in most cases in patients with known cardiopathy.

- Chronic heart failure(see page 301)
- Acute heart failure (acute pulmonary oedema)(see page 303)

Chronic heart failure

- Clinical features(see page 301)
- Paraclinical investigations(see page 302)
- Treatment(see page 302)
  - Lifestyle and dietary advice(see page 302)
  - Treatment of fluid retention(see page 302)
  - Long-term (lifelong) treatment(see page 302)
  - Other treatments(see page 303)
  - Treatment of causative or aggravating factors(see page 303)
- Surveillance and monitoring(see page 303)
- References(see page 303)

Clinical features

– Left-sided HF (left ventricle failure; most frequent form)
Fatigue and/or progressive onset of dyspnoea, occurs on exertion and then at rest, accentuated by the decubitus position, preventing the patient from lying down; peripheral oedema.
– Right-sided HF (right ventricle failure)
Oedema of the lower limbs, hepatomegaly, jugular vein distention, hepatojugular reflux; ascites in advanced stages.
– Global HF (failure of both ventricles)
Left and right-sided signs; right-sided signs are often the most prominent.

Evaluate severity of HF[1](see page 303):

Class I	No limitation of physical activity. No symptoms during ordinary physical activity.
Class II	Slight limitation of physical activity. Comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnoea.
Class III	Marked limitation of physical activity. Comfortable at rest. Less than ordinary activity causes fatigue, palpitation, or dyspnoea.
Class IV	Unable to carry on any physical activity without discomfort. Symptoms of heart failure at rest.

Identify causative or aggravating factors:
– Coronary or valvular heart disease, hypertension, viral or toxic cardiopathy, pericarditis.
– Anaemia, American trypanosomiasis, rheumatic fever, diabetes, thyroid disorder, drug/alcohol addiction.

Paraclinical investigations

− Cardiac ultrasound: if available, method of choice to confirm cardiopathy.
− Electrocardiogram (ECG): can diagnose left ventricular cardiomyopathy (left ventricular hypertrophy and/or left bundle branch block) or arrhythmia and particularly atrial fibrillation (AF or Afib) or signs of myocardial ischemia or infarction.
− Chest x-ray: can exclude lung disease in patients with dyspnoea or can show cardiomegaly or pleural effusion (often bilateral) and alveolar-interstitial syndrome.
− Blood test: full blood count, ionogram, serum creatinine.
− Other necessary laboratory tests according to comorbidities (e.g. diabetes, thyroid disorder).

Treatment

Lifestyle and dietary advice

− Reduce salt intake to limit fluid retention.
− Normal fluid intake except in cases of very severe oedema.
− Stop smoking.
− Physical activity adapted to the patient's capacity.
− Weight loss if BMI ≥ 25.

Treatment of fluid retention

furosemide PO: start with 20 mg once daily; increase if necessary, according to clinical response (certain patients need doses of 80 mg 1 to 2 times daily) then reduce once oedema decrease (20 to 40 mg once daily).
The reabsorption of oedema can sometimes be slow, taking up to 2 to 3 weeks.
The gradual worsening of HF may require an increase in dosage. Lifelong treatment with diuretics is not always necessary.
In the event of resistant oedema, add **hydrochlorothiazide** PO (25 mg 1 to 2 times daily for a few days) but only in hospital settings and monitoring renal function.

Long-term (lifelong) treatment

− ACE inhibitors are the first line treatment. Start with low doses, especially in patients with hypotension, renal impairment, hyponatraemia.
While increasing the dose monitor: drug tolerance (dry cough), blood pressure (the systolic BP should remain above > 90 mmHg), serum potassium and creatinine levels.
In patients taking diuretics, reduce the dose of the diuretic if possible while introducing ACE inhibitors (risk of hypotension if the patient is on high doses of diuretics).
enalapril PO:
Week 1: 2.5 mg once daily for 3 days then 5 mg once daily
Week 2: 10 mg once daily for 3 days then 20 mg once daily
The effective dose is usually 20 mg once daily (or 10 mg 2 times daily). Doses of 10 mg daily are sometimes enough; conversely, doses of 40 mg daily (maximum) are sometimes necessary.

− Once the patient has been stable for at least 2 weeks taking ACE inhibitors and in the absence of any contra-indications (asthma, hypotension, bradycardia, conduction disorders, particularly atrio-ventricular heart blocks), add a beta blocker.
bisoprolol PO: start with a low dose and gradually increase as long as the drug is well tolerated (monitor for signs of worsening HF, blood pressure, heart rate).
Week 1: 1.25 mg once daily
Week 2: 2.5 mg once daily
Week 3: 3.75 mg once daily
Weeks 4 to 8: 5 mg once daily

If insufficient:
Weeks 9 to 12: 7.5 mg once daily
As from week 13: 10 mg once daily (max. 10 mg daily)
In the event of temporarily worsening HF, hypotension or bradycardia, readjust doses of associated treatments and reduce the dose of bisoprolol or gradually stop treatment (stopping abruptly can lead to acute deterioration of the patient's condition). Once the patient is stabilized, re-increase/recommence bisoprolol.

Other treatments

− Antagonist of aldosterone: only if serum potassium levels and ECG can be monitored (risk of severe hyperkalaemia), add **spironolactone** PO (25 mg once daily) to long-term treatment, particularly in cases of severe HF (Classes III and IV).
− Nitrates: can be used in left-sided or global HF in patients with intolerance to ACE inhibitors (cough is not tolerated, renal impairment, severe hypotension).
isosorbide dinitrate PO: start with 5 to 40 mg 2 to 3 times daily and increase up to the effective dose, usually 15 to 120 mg daily.
− Digitalis glycosides: administer with caution, in intensive care unit (the therapeutic dose is close to the toxic dose), only in patients with AF with rapid ventricular response confirmed by ECG: no visible P waves, irregularly irregular QRS complex (120-160).

Treatment of causative or aggravating factors

According to the cause.

Surveillance and monitoring

Laboratory surveillance
According to treatment (ACE, diuretic, etc.).

Clinical monitoring
− Once stabilised, consultations once a month for the first 6 months, then individualised frequency of consultations depending on the patient's characteristics.
− Routine consultations: weight curve, BP, progress of signs (dyspnoea, oedema, etc.).
− Monitoring of comorbidities and causative or aggravating.

Patient education
− Lifestyle and dietary measures (diet, weight control, physical activity adapted to the patient's capacity, etc.).
− Warning signs (shortness of breath or oedema of the lower limbs, serious adverse effects of treatment) and management (timely/urgent medical consultation).

References

1. Chop WM, Jr. Extending the New York Heart Association classification system. JAMA. 1985;254:505.

Acute heart failure (acute pulmonary oedema)

- Clinical features(see page 304)
- Paraclinical investigations(see page 304)

- Treatment(see page 304)

Clinical features

– Onset or sudden exacerbation of dyspnoea
– Anxiety, agitation
– Peripheral oedema
– On auscultation: wet rales in both lung fields, sometimes muffled heart sounds and/or cardiac gallop.

Signs of severity:
– Severe respiratory distress (intercostal retractions, nasal flaring, see-saw breathing, SpO_2 < 90% while breathing ambient air), cyanosis, profuse sweating, confusion
– Systolic blood pressure < 90 mmHg
– Heart rate (HR) > 150/minute or < 40/minute
– Respiratory rate (RR) > 30/minute or < 12/minute
– Chest pain if underlying cardiac ischemia

Paraclinical investigations

Diagnosis is mainly clinical.
− ECG: look for signs of myocardial ischemia or arrhythmia.
If available:
− Chest x-ray: signs vary depending on the severity of pulmonary oedema. In early stage, dilation of vessels in upper lobes then perihilar haze and thickening of septa. In advanced stage, prominent opacities in hilar and perihilar regions. Can exclude other lung disease, such as pulmonary infection.
– Lung and pleural ultrasound: presence of B-lines, presence of bilateral pleural effusion.
– Cardiac ultrasound: look for signs of circulatory overload.
– Monitoring: full blood count, ionogram, serum creatinine.

Treatment

Systolic blood pressure is < 90 mmHg

See Shock(see page 10), Chapter 1.

Systolic blood pressure is ≥ 90 mmHg

Treatment common to all patients:
– Place patient is semi-seated position, legs down
– Oxygen mask, 6-10 litres/minute
– Insert an IV line
– Diuretic: **furosemide** IV, 40 mg to be repeated once if the patient has not urinated within 30 to 60 minutes. If the patient was already taking furosemide at doses of > 40 mg, administrer his usual dose by IV route.
– Monitor: HR, RR, BP, SpO_2, mental status

Other treatments :
– Add an rapid-acting nitrate (vasodilator) if systolic blood pressure is ≥ 180 mmHg and/or diastolic ≥ 110 mmHg.
The objective is to lower the systolic blood pressure to 120-150 mmHg and the diastolic pressure to under 110 mmHg.
isosorbide dinitrate IV (10 ml ampoule, 1 mg/ml)
2 mg (= 2 ml) by slow IV injection (over 2 minutes) then if necessary 2 to 10 mg/hour by continuous infusion with an electric syringe
Use sublingual route if IV route is not feasible:

isosorbide dinitrate sublingual (5 mg tablet)
5 mg per dose; if necessary up to 2 doses taken 10 minutes apart, on condition that systolic blood pressure is > 120 mmHg
or **glyceryl trinitrate**, sublingual (0.5 mg tablet)
0.5 mg per dose; if necessary up to 3 doses taken 5 minutes apart, on condition that systolic blood pressure is > 120 mmHg
– In patients with severe dyspnea, a nitrate can be considered if breathing does not improve 10 minutes after the adminstration of oxygen and furosemide. Treatment is only administered if the systolic blood pressure is > 120 mmHg.

Subsequent treatment depends on the underlying pathology (chronic heart failure(see page 301), hypertension(see page 297), acute coronary syndrome, etc.).

Endemic goitre and iodine deficiency

- Clinical features(see page 305)
- Prevention and treatment(see page 305)

– Goitre is an enlargement of the thyroid gland. Endemic goitre occurs in iodine-deficient areas. Goitre can also be caused or aggravated by the regular consumption of goitrogens such as manioc, cabbage, turnips, millet etc.

– Goitre is an adaptive process: iodine is essential for the production of thyroid hormones; iodine deficiency impairs thyroid hormone synthesis; to compensate, the thyroid gland increases in volume. Thyroid function usually remains normal.

– As well as the development of goitre, iodine deficiency in pregnant women has serious consequences for the child (foetal and perinatal mortality, physical and mental retardation, cretinism). These risks must be prevented by providing iodine supplementation in iodinedeficient areas.

Clinical features

– The WHO proposes a simplified classification based on the significance of goitre:

Group 0: normal thyroid, no palpable or visible goitre
Group 1: enlarged thyroid, palpable but not visible when the neck is in the normal position
Group 2: thyroid clearly visible when the neck is in the normal position

– Possible mechanical complications (rare): compression, deviation of the trachea or of the oesophagus.

Prevention and treatment

The objective of prevention is to reduce the consequences of iodine deficiency in neonates and children. Supplying iodised salt through national programmes is the recommended method of prevention.

For prevention in populations living in iodine deficient areas where iodised salt is not available and for curative treatment of patients with goitre: use **iodised oil**, according to national protocols. For information (according to the WHO):

Population	**Iodised oil** PO once yearly (190 mg capsule)
Children under 1 year	1 capsule

Children from 1 to < 6 years	2 capsules
Children from 6 to 15 years	3 capsules
Pregnant or lactating women or women of childbearing age	2 capsules

Curative and preventive single-doses are the same. Oral treatment is preferred. The target populations are pregnant and breastfeeding women, women of childbearing age and children.

In children, goitre disappears after several months. It disappears more slowly (or never) in adults despite restoration of normal thyroid function in 2 weeks. Surgery is only indicated for patients with local mechanical dysfunction.

Appendices

- Appendix 1a. Normal daily maintenance IV fluids in children 1 month(see page 307)
- Appendix 1b. 1.5 x daily maintenance IV fluids in children 1 month(see page 308)

Appendix 1a. Normal daily maintenance IV fluids in children 1 month

- Indications(see page 307)
- Fluid to be administered(see page 307)

Indications

Basic hydration needs 1(see page 0) for patients unable to drink sufficiently. After 48 hours, it is essential to provide nutrition to the patient orally or by nasogastric tube and to gradually reduce IV fluids.

⚠ This protocol should not be used for surgical or burns patients, those with renal, cardiac disease or diabetic ketoacidosis.

Fluid to be administered

The fluid of choice in children is *Ringer lactate-Glucose 5% (RL-G5%)*. Use a premixed solution if available. If not, add 50 ml of G50% to 500 ml of RL or 100 ml of G50% to 1000 ml of RL. If RL is not available, use 0.9% sodium chloride instead.

For ease of prescription and administration, the daily volumes and rates in drops per minute have been rounded off.

Weight	**Volume /24 hours**	**Rate*** (paediatric infusion set 1 ml = 60 drops)
3 to < 4 kg	350 ml/24 h	16 drops/min
4 to < 5 kg	450 ml/24 h	18 drops/min
5 to < 6 kg	550 ml/24 h	22 drops/min
6 to < 7 kg	650 ml/24 h	26 drops/min
7 to < 8 kg	750 ml/24 h	30 drops/min
8 to < 9 kg	850 ml/24 h	36 drops/min
9 to < 11 kg	950 ml/24 h	40 drops/min
11 to < 14 kg	1100 ml/24 h	46 drops/min
14 to < 16 kg	1200 ml/24 h	50 drops/min

16 to < 18 kg	1300 ml/24 h	54 drops/min
18 to < 20 kg	1400 ml/24 h	58 drops/min

Weight	**Volume /24 hours**	**Rate*** (paediatric infusion set 1 ml = 60 drops)	**Rate** (standard infusion set 1 ml = 20 drops)
20 to < 22 kg	1500 ml/24 h	62 drops/min	20 drops/min
22 to < 26 kg	1600 ml/24 h	66 drops/min	22 drops/min
26 to < 30 kg	1700 ml/24 h	70 drops/min	24 drops/min
30 to < 35 kg	1800 ml/24 h	74 drops/min	26 drops/min
≥ 35 kg	2000 ml/24 h	82 drops/min	28 drops/min

* In a paediatric infusion set, the number of drops per minute is equal to the number of ml per hour. For example: 15 drops/min = 15 ml/hour

1 (see page 0) Daily needs are calculated according the following formula:
Children 0-10 kg: 100 ml/kg per day
Children 11-20 kg: 1000 ml + (50 ml/kg for every kg over 10 kg) per day
Children > 20 kg: 1500 ml + (20-25 ml/kg for every kg over 20 kg) per day
Adults: 2 litres per day

Appendix 1b. 1.5 x daily maintenance IV fluids in children 1 month

- Indications (see page 308)
- Fluid to be administered (see page 308)

Indications

Increased hydration (more than maintenance fluids) is indicated in certain exceptional situations such as in sickle cell patients with painful vaso-occlusive crises (unless acute chest syndrome is suspected) and priapism.
Do not administer these volumes for more than 24 hours; encourage early oral hydration and simultaneously, gradually reduce IV fluids. Monitor for signs of fluid overload.

Fluid to be administered

The fluid of choice in children is *Ringer lactate-Glucose 5%*. For preparation, see Appendix 1a (see page 307).

For ease of prescription and administration, the daily volumes and rates in drops per minute have been rounded off.

1.5 X maintenance fluids

Weight	Volume /24 hours	Rate (paediatric infusion set 1 ml = 60 drops)
3 to < 4 kg	550 ml/24 h	22 drops/min
4 to < 5 kg	650 ml/24 h	26 drops/min
5 to < 6 kg	850 ml/24 h	34 drops/min
6 to < 7 kg	950 ml/24 h	40 drops/min
7 to < 8 kg	1100 ml/24 h	46 drops/min
8 to < 9 kg	1250 ml/24 h	52 drops/min
9 to < 11 kg	1450 ml/24 h	60 drops/min
11 to < 14 kg	1650 ml/24 h	68 drops/min
14 to < 16 kg	1800 ml/24 h	76 drops/min
16 to < 18 kg	1950 ml/24 h	82 drops/min
18 to < 20 kg	2100 ml/24 h	86 drops/min

Weight	Volume /24 hours	Rate (paediatric infusion set 1 ml = 60 drops)	Rate (standard infusion set 1 ml = 20 drops)
20 to < 22 kg	2200 ml/24 h	92 drops/min	30 drops/min
22 to < 26 kg	2400 ml/24 h	100 drops/min	34 drops/min
26 to < 30 kg	2600 ml/24 h	108 drops/min	36 drops/min
30 to < 35 kg	2800 ml/24 h	–	38 drops/min
≥ 35 kg	3000 ml/24 h	–	42 drops/min

Main references

Websites consulted between June 2016 and January 2019

British National Formulary (BNF) and *British National Formulary for Children* (BNFc)
MedicinesComplete

Martindale. The Complete Drug Reference
MedicinesComplete

UpToDate. Evidence-based clinical decision support resource

BMJ Group. BMJ Best Practice.

La revue *Prescrire*

Centre belge d'information pharmacothérapeutique (CBIP)
http://www.cbip.be/fr/start

Centers for Disease Control and Prevention
http://www.cdc.gov/DiseasesConditions/

Cochrane Library

World Health Organization
http://www.who.int/publications/en/

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7 https://confluence-uat.medicalguidelines.msf.org/viewport/essdrarabic/%D8%A7%D9%84%D8%B5%D9%81%D8%AD%D8%A9-%D8%A7%D9%84%D8%B1%D8%A6%D9%8A%D8%B3%D9%8A%D8%A9-%D8%A7%D9%84%D8%B9%D9%82%D8%A7%D9%82%D9%8A%D8%B1-%D8%A7%D9%84%D8%A3%D8%B3%D8%A7%D8%B3%D9%8A%D8%A9-26378528.html

8 https://confluence-uat.medicalguidelines.msf.org/viewport/eoncarabic/home-26379388.html