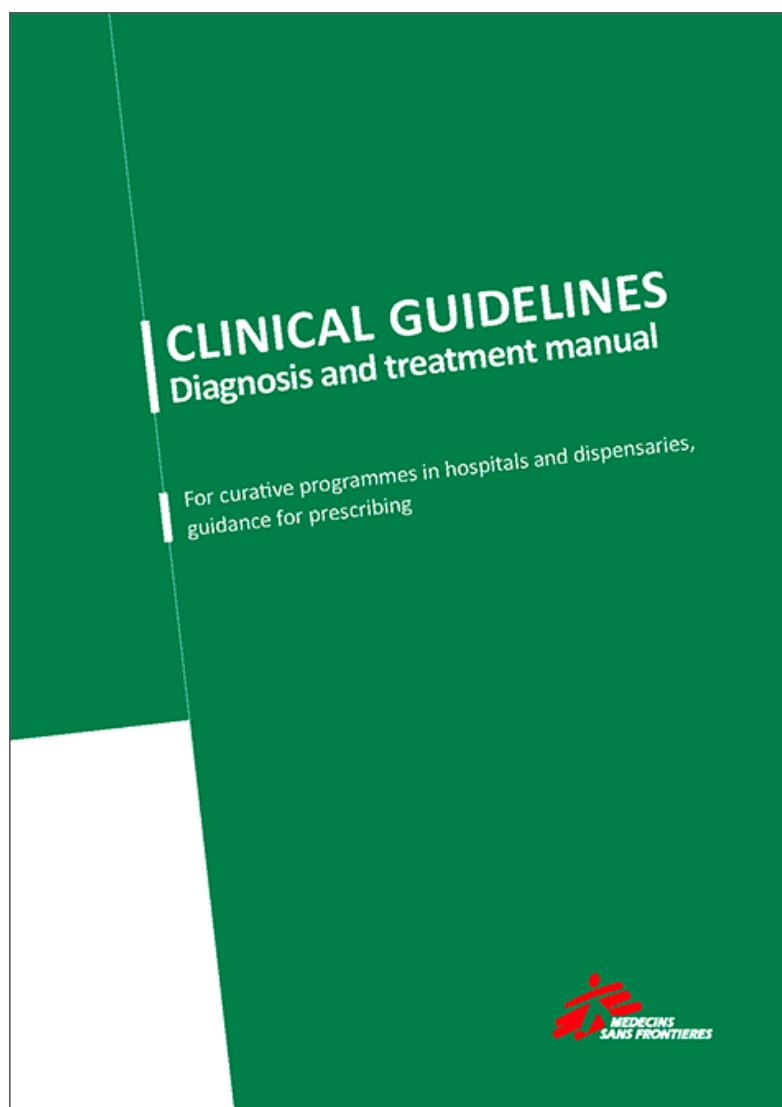




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# Clinical guidelines - Diagnosis and treatment manual

For curative programmes in hospitals and dispensaries  
Guidance for prescribing



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The *Clinical guidelines* has been developed by Médecins Sans Frontières.

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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, Spanish and Arabic 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**

**Last update: October 2023**

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 2 <sup>nd</sup> day, Day 3 or 3 <sup>rd</sup> day, etc.)
dl	decilitre
(e)FAST	(extended) focused assessment with sonography for trauma
FBC	full blood count
g	gram
HBP	high blood pressure (hypertension)
HF	heart failure
HIV	human immunodeficiency virus
HR	heart rate

Ig	immunoglobulin
IM	intramuscular
IO	intraosseous
IU	international unit
IV	intravenous
kcal	kilocalorie
kg	kilogram
LP	lumbar puncture
mg	milligram
MIU	million international units
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
PCR	polymerase chain reaction
PO	per os – oral administration
POCUS	point-of-care ultrasound
PRBC	packed-red blood cells
RR	respiratory rate
SAM	severe acute malnutrition
SC	subcutaneous
SMX	sulfamethoxazole

SMX + TMP	sulfamethoxazole + trimethoprim = co-trimoxazole
SpO <sub>2</sub>	arterial blood oxygen saturation measured by pulse oximetry
tab	tablet
TB	tuberculosis
TMP	trimethoprim
WHO	World Health Organization

# **Chapter 1: A few symptoms and syndromes**

Shock

Generalised tonic-clonic seizures and convulsive status epilepticus

Hypoglycaemia

Fever

Pain

Anaemia

Dehydration

Severe acute malnutrition

# Shock

Last updated: September 2023

Shock is a condition of widespread reduced tissue perfusion and inadequate oxygen delivery. Prolonged shock can result in cellular dysfunction and irreversible organ failure. Mortality is high without early diagnosis and treatment.

## Clinical features

Shock should be suspected in patients with:

- Sign(s) of hypotension: weak pulse, low or declining blood pressure (BP)<sup>a</sup>, narrow pulse pressure
- Acute onset of signs of tissue hypoperfusion:
  - Skin: pallor, mottled skin, sweating, cold extremities or lower limb temperature gradient<sup>b</sup>, capillary refill time (CRT)  $\geq 3$  seconds
  - Lungs: tachypnea, dyspnoea
  - Heart: tachycardia, which often occurs before BP decreases
  - Kidney: oliguria (urine output  $< 0.5$  to  $1$  ml/kg/hour) or anuria
  - Brain: thirst, anxiety, agitation, confusional state, apathy, altered mental status

In children, accurate BP measurement is difficult, and hypotension is a very late sign of shock. Therefore, critically ill children<sup>c</sup> should be treated for shock if they present at least one of the following signs: lower limb temperature gradient<sup>b</sup>, CRT  $\geq 3$  seconds, weak radial pulse or severe tachycardia<sup>d[1]</sup>.

Clinical features may vary according to the type of shock<sup>[2]</sup>:

Type	Specific clinical features	Risk factors
<b>Distributive</b> Severe vasodilation and increased capillary permeability resulting in maldistribution of blood flow	<b>Anaphylaxis:</b> likely when either of the following 2 criteria develop within minutes to hours <sup>[3]</sup> : <ul style="list-style-type: none"> <li>Involvement of skin and/or mucous membranes (e.g. generalised urticaria, itching, flushing, swollen lips/tongue/uvula) AND ≥ 1 of the following:               <ul style="list-style-type: none"> <li>respiratory symptoms (wheeze, dyspnoea);</li> <li>low BP or symptoms of end-organ dysfunction (hypotonia, incontinence);</li> <li>severe gastrointestinal symptoms (abdominal pain, repetitive vomiting).</li> </ul> </li> <li>Hypotension, bronchospasm or laryngeal involvement (stridor, vocal changes, odynophagia) after exposure to known or probable allergen for that patient.</li> </ul>	Recent exposure to an allergen (e.g. food, sting, medicine) or history of anaphylaxis
	<b>Septic shock:</b> signs of infection, fever or hypothermia, altered mental status, dyspnoea, persisting hypotension despite fluid resuscitation <sup>[4]</sup>	Infection, recent surgery, immunodeficiency
<b>Cardiogenic</b> Cardiac pump failure	Ischaemia: chest pain, dyspnoea Arrhythmia Murmur of valvular heart disease	History of cardiac disease, advanced age
	Acute heart failure: see <u>Heart failure in adults</u> , Chapter 12.	History of cardiac disease, viral illness, immunodeficiency
<b>Hypovolaemic</b> Direct blood/fluid loss or fluid sequestration into the extravascular space resulting in decreased intravascular volume	<b>Haemorrhagic:</b> external bleeding, signs and symptoms of internal bleeding, hypotension <sup>(a)</sup>	Trauma, recent surgery, obstetric haemorrhage
	<b>Non-haemorrhagic:</b> dry mouth, absence of tears, sunken eyes/fontanelle, low jugular venous pressure (JVP), altered mental status	Profuse diarrhoea and/or vomiting, intestinal obstruction
<b>Obstructive</b> Obstruction to blood flow to, or from, the heart or great vessels	Pulmonary embolism (PE): chest pain, tachycardia, tachypnoea, hypoxia Deep vein thrombosis (DVT): leg pain, swelling, warmth	Recent surgery or immobilisation, cancer, history of PE or DVT
	Tension pneumothorax: decreased breath sounds, raised JVP, weak radial pulse, tracheal deviation	Trauma, invasive medical procedure
	Cardiac tamponade: pulsus paradoxus <sup>(b)</sup> , raised JVP, narrow pulse pressure, muffled heart sounds	Trauma, immunodeficiency

(a) In children and young adults with hypovolaemic shock, BP may be maintained initially, but subsequently declines rapidly if fluid loss is not replaced.

- (b) Pulsus paradoxus is measured by taking the patient's BP during both expiration and inspiration. It is defined as a decrease of > 10 mmHg in the SBP during inspiration compared with expiration.

## Management

- Attend to the patient immediately even if the type of shock is not known. Call for help. Move to critical care unit if possible.
- Assess and manage A (airway), B (breathing), and C (circulation) according to [Basic Life Support](#) (see below). If anaphylaxis is suspected, immediately go to specific management.
- Take a rapid history to try to determine underlying cause.
- Monitor:
  - urine output hourly (insert a urinary catheter)
  - HR, RR, BP, temperature, CRT, SpO<sub>2</sub>, and level of consciousness
- Perform the following tests:
  - haemoglobin and blood glucose level
  - malaria rapid diagnostic test in endemic area: see [Malaria](#), Chapter 6
  - blood culture (if available) and blood group
- In children, administer **ceftriaxone IV<sup>e</sup>**: one dose of 80 mg/kg. Reassess need for further antibiotic treatment according to underlying cause.
- Treat pain: see [Pain](#), Chapter 1.

Primary objective of shock management is to restore adequate tissue perfusion, demonstrated by:

- Returning vital signs, CRT, SpO<sub>2</sub>, mental status, etc. to normal.
- Maintaining mean arterial pressure (MAP)<sup>f</sup> > 65 mmHg in adults (or higher if patient has pre-existing hypertension).
- Maintaining urine output > 0.5 to 1 ml/kg/hour.

After initial management:

- Take a more detailed history.
- Perform a comprehensive physical examination.
- In case of dehydration: see [Dehydration](#), Chapter 1.
- In case of blunt thoracic or abdominal trauma, perform POCUS<sup>g</sup> : (e)FAST exam to evaluate for pneumothorax or free fluid in pleural, pericardial and/or peritoneal spaces. Refer to surgeon as required.

On-going care:

- Re-evaluate patient's condition and response to treatment every 10 minutes until patient is stable.
- Perform a second comprehensive physical examination.
- Initiate nutritional support adapted to patient's needs as soon as possible and reassess regularly. Patients have high protein and energy requirements. Enteral route is preferred.

## Basic Life Support

### 1) Manage airways and breathing

- Lay the patient on their back. However:
  - if spinal trauma is suspected, do not move the patient;
  - in case of anaphylaxis, the patient may prefer a sitting position.
- In case of altered mental status:
  - be prepared with mask and bag if needed for ventilation;
  - remove any airway obstruction (e.g. secretions, foreign body);
  - open airway: stand at head of bed, place one hand on the forehead and gently tilt the head back. Simultaneously, place the fingertips of the other hand under the chin and lift the chin. If suspicion of spinal trauma, do not move the neck. Instead, place heels of both hands on patient's parietal areas, and use index and middle fingers of both hands to push the angle of mandible anteriorly (jaw thrust)

- if needed, insert an oropharyngeal airway.
- Auscultate lungs to assess ventilation.
- Administer 10 to 15 litres/minute of oxygen with mask to maintain  $\text{SpO}_2 > 94\%$ .
- If  $\text{SpO}_2$  remains  $\leq 94\%$  with oxygen, see [If resources allow](#).

## 2) Maintain circulation

- Control bleeding:
  - apply direct manual pressure and/or compression/haemostatic dressing to the wound;
  - in case of massive life-threatening bleeding from an extremity (e.g. leg) not controlled by direct pressure: apply a windlass tourniquet <sup>h[5]</sup>.
- Insert 2 peripheral IV lines (catheters 20-22G in children and 14-18G in adults) or an intraosseous (IO) needle.
- Administer **Ringer lactate (RL)<sup>i</sup>**, **glucose 5%-Ringer lactate (G5%-RL)<sup>j</sup>**, and/or blood, following specific management described below. Reassess before giving additional fluid therapy. Monitor for fluid overload<sup>k</sup>, especially in patients at risk, e.g. severely malnourished children; patients with severe malaria, heart disease, severe anaemia; older patients.
- Maintain normal body temperature.
- If unable to maintain BP, see [If resources allow](#).

## Anaphylaxis

- Remove exposure to causal agent.
- Administer **epinephrine (adrenaline)** IM into the mid-anterolateral thigh. Use undiluted solution and a 1 ml syringe graduated in 0.01 ml<sup>[6]</sup>:
  - Children under 6 months: 0.1 to 0.15 ml
  - Children 6 months to 5 years: 0.15 ml
  - Children 6 to 12 years: 0.3 ml
  - Children over 12 years<sup>l</sup> and adults: 0.5 ml

Repeat after 5 minutes if no or poor clinical improvement (up to a total of 3 IM injections).

- Monitor HR, BP, CRT and clinical response.
- In case of stridor, administer nebulized **epinephrine**: 0.5 mg/kg/dose (max. 5 mg) in 5 ml of 0.9% sodium chloride over 10 to 15 minutes
- If  $\text{SpO}_2$  is  $< 94\%$ , ventilate with bag mask.
- Administer a bolus of **RL**:
  - Children: 10 ml/kg as quickly as possible
  - Adults: 500 ml as quickly as possible

Repeat bolus once if signs of poor perfusion persist after 15 minutes.

- If shock persists after 3 IM injections of epinephrine, in particular if unable to maintain BP, see [If resources allow](#).
- After initial treatment with epinephrine and IV fluids, some patients (e.g. patients requiring continuing treatment after 2 doses of epinephrine IM or patients with ongoing asthma or shock) may benefit from a short course of corticosteroid therapy. When the patient is stable, **prednisolone** PO : 1 to 2 mg/kg (max. 50 mg) once daily in the morning for 3 to 5 days. Use an IV corticosteroid only if the patient cannot take oral treatment.

## Septic shock

Look for source of infection. If possible, take specimens for culture before starting antibiotic treatment.

- Fluid therapy:
  - Children and adolescents under 15 years: **G5%-RL** solution as maintenance fluids (see [Appendix 1](#))
  - Adolescents 15 years and over and adults: one bolus of 250 to 500 ml of **RL** as quickly as possible
- Antibiotic treatment:
  - Start antibiotics according to the suspected origin of infection within 1 hour of presentation<sup>[7]</sup> (see tables below).

- If source is unknown, administer a broad-spectrum antibiotic to cover gram-positive, gram-negative, and anaerobic bacteria. If possible, take into account local epidemiology (rates and types of resistance). Differentiate community acquired sepsis and nosocomial sepsis as pathogens and rates of resistance may be different. Simplify the antibiotic treatment (to narrower spectrum) whenever possible.
- Reassess treatment daily:
  - ▷ If culture results are available: adapt treatment accordingly.
  - ▷ If improvement after 24 to 48 hours: change to oral route, however some foci (e.g. meningitis) require prolonged IV treatment.
  - ▷ If no improvement after 48 to 96 hours: consider resistant pathogen<sup>m</sup> , in particular in patients with immunodeficiency or recent (in the last month) hospitalisation or antibiotic use and adapt treatment accordingly.
- Other measures to control infection:
  - If suspected catheter-related infection, insert a new catheter in another site and remove the suspected catheter.
  - Drain soft-tissue abscess (see [Cutaneous abscess](#), Chapter 10); irrigate and debride traumatic wounds. Refer to surgeon if needed for debridement, drainage, relieving obstruction, etc.
- Treatment of fever: see [Fever](#), Chapter 1.

Origin	Antibiotics	Alternatives <sup>(c)</sup>
<b>Cutaneous</b> staphylococci, streptococci <sup>(d)</sup>	cloxacillin (+ vancomycin if risk factors for MRSA <sup>(e)</sup> )	cefazolin <sup>(f)</sup> (or vancomycin if risk factors for MRSA <sup>(e)</sup> )
<b>Pulmonary</b> pneumococci, <i>H. influenzae</i>	ceftriaxone + azithromycin (+ gentamicin if risk factors for MDR gram negative bacteria <sup>(g)</sup> )	clindamycin + ciprofloxacin + doxycycline
<b>Intestinal or biliary</b> enterobacteria, anaerobic bacteria, enterococci	ceftriaxone + metronidazole (+ gentamicin if risk factors for MDR gram negative bacteria <sup>(g)</sup> ) (+ ampicillin if biliary source)	clindamycin + ciprofloxacin
<b>Gynaecological</b> streptococci, gonococci, anaerobic bacteria, <i>E. coli</i>	ceftriaxone + metronidazole + azithromycin	clindamycin + gentamicin + azithromycin
<b>Urinary</b> enterobacteria, enterococci	ceftriaxone (+ amikacin if risk factors for pseudomonas <sup>(h)</sup> )	meropenem (+ amikacin if risk factors for pseudomonas <sup>(h)</sup> )
<b>Central nervous system</b>	See <u>Bacterial meningitis</u> , Chapter 7.	
	ampicillin + gentamicin in children	ceftriaxone or cloxacillin + amikacin in children
<b>Other or undetermined</b>	ceftriaxone (+ amikacin if risk factors for pseudomonas <sup>(h)</sup> ) in adults	clindamycin + ciprofloxacin in adults

(c) Only if first-line antibiotic is not available or in allergic patients.

(d) For necrotising infections, see Necrotising infection of skin and soft tissues, Chapter 10.

(e) Risk factors for MRSA: prior MRSA infection, recent hospitalisation or antibiotic use, recurrent skin infection, chronic wounds, invasive device, settings with high rates of MRSA.

(f) Do not administer if severe beta-lactam allergy

(g) Risk factors for multiresistant (MDR) gram negative bacteria: recent hospitalisation in intensive care unit or antibiotic use.

(h) Risk factors for pseudomonas: immunodeficiency, recent hospitalisation or antibiotic use, burns or presence of invasive device.

Antibiotics	Children over 1 month	Adults
<b>amikacin</b> IM or slow IV injection over 3 minutes	15 mg/kg (max. 1.5 g) once daily	15 mg/kg once daily
<b>ampicillin</b> IV infusion over 30 minutes	50 mg/kg (max. 2 g) every 8 hours	2 g every 6 to 8 hours (2 g every 4 hours for meningitis)
<b>azithromycin</b> PO (by NGT)	10 to 20 mg/kg (max. 500 mg) once daily	500 mg to 1 g once daily
<b>cefazolin</b> slow IV injection over 3 minutes or IV infusion over 30 minutes	25 mg/kg (max. 3 g) every 12 hours	2 g every 8 hours
<b>ceftriaxone</b> slow IV injection over 3 minutes or IV infusion over 30 minutes	80 mg/kg (max. 4 g) once daily (100 mg/kg, max. 4 g, once daily for meningitis)	2 g once daily (2 g every 12 hours for meningitis)
<b>ciprofloxacin</b> PO (by NGT)	15 to 20 mg/kg (max. 750 mg) every 12 hours	500 to 750 mg every 12 hours
<b>ciprofloxacin</b> IV infusion over 60 minutes	10 mg/kg (max. 400 mg) every 8 hours	400 mg every 8 to 12 hours
<b>clindamycin</b> IV infusion over 30 minutes	10 mg/kg (max. 600 mg) every 8 hours	600 to 900 mg every 8 hours
<b>cloxacillin</b> IV infusion over 60 minutes	25 to 50 mg/kg (max. 2 g) every 6 hours	2 g every 6 hours
<b>doxycycline</b> PO (by NGT)	4.4 mg/kg (max. 200 mg) on D1 then 2.2 mg/kg (max. 100 mg) every 12 hours	200 mg on D1 then 100 mg every 12 hours
<b>gentamicin</b> IM or slow IV injection over 3 minutes	7.5 mg/kg once daily	5 mg/kg once daily
<b>meropenem</b> IV infusion over 15 or 30 minutes	20 mg/kg (max. 2 g) every 8 hours	2 g every 8 hours
<b>metronidazole</b> PO (by NGT)	10 mg/kg (max. 500 mg) every 8 hours	500 mg every 8 hours
<b>metronidazole</b> IV infusion over 30 minutes	10 mg/kg (max. 500 mg) every 8 hours	500 mg every 8 hours
<b>vancomycin</b> IV infusion over	15 mg/kg (max. 500 mg) every 6	15 to 20 mg/kg (max. 2 g) every 12 hours

## Cardiogenic shock

- Administer **RL** with extreme caution and monitor closely for signs of fluid overload:
  - Adults: 100 to 250 ml over 30 minutes
  - Subsequent fluid administration should be based on thorough patient assessment, including urinary output, mental status and SpO<sub>2</sub>.
- Vasopressors are often required to maintain BP, see [If resources allow](#).
- In case of acute heart failure, see [Heart failure in adults](#), Chapter 12.
- Arrhythmias should be managed according to Advanced Life Support techniques as appropriate and where available.

## Hypovolemic non-haemorrhagic shock

- Administer **RL**:
  - Children under 1 year: 30 ml/kg over 1 hour then 70 ml/kg over 5 hours
  - Children/adolescents 1 to 14 years: 30 ml/kg over 30 minutes then 70 ml/kg over 2.5 hours
  - Adolescents 15 years and over and adults: 250 to 500 ml as quickly as possible (to be repeated once if required) then adjusted to patient's condition, providing up to 70 ml/kg over 2.5 hours

## Hypovolaemic haemorrhagic shock

In order to prevent the “lethal trauma triad” of hypothermia, acidosis and coagulopathy:

- Determine blood group and if needed transfuse, as quickly as possible:
  - Children under 20 kg: 20 ml/kg of whole blood
  - Children 20 kg and over and adults: an adult unit of whole blood

Repeat if needed.
- If blood is not immediately available, administer a bolus of **RL** with caution (i.e. minimize the use of RL) while waiting for blood:
  - Children: 20 ml/kg as quickly as possible
  - Adults: 250 to 500 ml as quickly as possible

When blood is available, stop RL and administer blood only.
- Warm the patient (blankets, warm room, warm IV fluids).
- In case of trauma presenting within 3 hours, administer **tranexamic acid** slow IV (over 10 minutes):
  - Children: 15 mg/kg (max. 1 g)
  - Adults: 1 g

Then immediately start a second dose, administered by IV infusion over 8 hours.
- In case of postpartum haemorrhage, refer to the guide [Essential obstetric and newborn care](#), MSF.
- Refer to surgery if needed.

## Obstructive shock

The management described up to this point will provide only temporary stabilization. Treat the cause or refer for aetiological treatment:

- Pulmonary embolism: anticoagulation +/- thrombolysis.
- Tension pneumothorax: needle decompression/finger thoracostomy, followed by insertion of chest tube.
- Cardiac tamponade: pericardial tap.

## If resources allow:

- Manage airways and breathing:
  - complete airway obstruction: endotracheal intubation or cricothyroidotomy
  - respiratory failure: non-invasive or invasive mechanical ventilation
- Maintain circulation:
  - If unable to achieve management objectives (in particular BP) using fluid therapy (and no signs of fluid overload are present) or, in the case of anaphylaxis, if shock persists after 3 IM epinephrine injections, vasopressors-inotropes (see below) can be used in the following conditions:
    - ▷ close monitoring in a critical care unit;
    - ▷ a large peripheral IV catheter<sup>n</sup> (proximal forearm or above), a central venous catheter or an IO line dedicated to the infusion;
    - ▷ use of an electric syringe or pump to control flow rate<sup>o</sup>;
    - ▷ intensive monitoring of drug administration, particularly during syringe changes.
  - All infused volumes must be accounted for when recording fluid balance.

These protocols are for peripheral IV administration. Titrate according to patient's clinical situation. Refer to management objectives (including BP) under [Management](#).

	Norepinephrine (NEP) tartrate <sup>(l)</sup>	Epinephrine (EPN) (adrenaline)
Indication	Children: 2 <sup>nd</sup> choice Adults: 1 <sup>st</sup> choice	Children: 1 <sup>st</sup> choice Adults: 2 <sup>nd</sup> choice
Preparation of diluted solution <sup>(l)</sup>	Children: Add 1 ml (2 mg) of NEP tartrate to 39 ml of 0.9% NaCl to obtain a 0.05 mg/ml (50 micrograms/ml) solution.  Adults: Add 2 ml (4 mg) of NEP tartrate to 38 ml of 0.9% NaCl to obtain a 0.1 mg/ml (100 micrograms/ml) solution.	Children: Add 2 ml (2 mg) of EPN to 38 ml of 0.9% NaCl to obtain a 0.05 mg/ml (50 micrograms/ml) solution.  Adults: Add 4 ml (4 mg) of EPN to 36 ml of 0.9% NaCl to obtain a 0.1 mg/ml (100 micrograms/ml) solution.
Starting rate <sup>(k)</sup>	0.1 microgram/kg/minute	
Rate for increasing <sup>(k)</sup>	Increase by 0.05 micrograms/kg/minute every 10 minutes for the first hour, then every hour. Max. 1 microgram/kg/minute.	
Rate for decreasing <sup>(k)</sup>	Taper down doses when management objectives are attained. Do not stop abruptly. Decrease by 0.05 micrograms/kg/minute every hour.	

(i) 2 mg of NEP tartrate = 1 mg of NEP base.

(j) 0.9% sodium chloride or 5% glucose or RL can be used for dilution.

(k) The infusion rate is calculated as follows: [desired dose (microgram/kg/min) x weight (kg) x 60 min] ÷ concentration (microgram/ml).

- Ongoing care: measure serum potassium, magnesium, calcium and phosphate levels and correct any abnormalities. Additional investigations (e.g. X-rays, other laboratory tests) may be indicated, depending on aetiology suspected.

## Footnotes

- (a) Hypotension is based on systolic blood pressure (SBP) in adults: SBP < 90 mmHg or decrease in SBP  $\geq$  40 mmHg from baseline or mean arterial pressure MAP < 65 mmHg. Shock is often accompanied by hypotension but may also occur with normal or elevated BP.
- (b) Run the back of the hand from the toe to the knee. A notable temperature change from the cold foot to the warm knee is a positive temperature gradient, indicating distal hypoperfusion.
- (c) 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.
- (d) Children under 1 year: > 180 bpm; Children 1 to 5 years: > 160 bpm; Children 5 years and over: > 140 bpm.
- (e) For IV administration of ceftriaxone, dissolve only in water for injection.
- (f) MAP = diastolic BP (DBP) + 1/3 (SBP-DBP). A patient with BP 90/60 has a MAP = 60 + 1/3 (90-60) = 70.
- (g) POCUS should only be performed and interpreted by trained clinicians.
- (h) The patient should receive surgery within 1 hour of the application of a windlass tourniquet. After 1 hour, there is a risk of ischaemic injury of the limb. If surgery is not possible and the tourniquet is required to save the patient's life, it should be left in place. Any tourniquet that has been applied for more than 6 hours should be left in place until arrival at a facility capable of providing definitive surgical care.
- (i) Crystalloids should be used. Colloids (e.g. modified fluid gelatin, albumin) are not recommended.
- (j) Remove 50 ml of RL from a 500 ml RL bottle or bag, then add 50 ml of 50% glucose to the remaining 450 ml of RL to obtain 500 ml of 5% glucose-RL solution.
- (k) In case of fluid overload: sit the patient up, reduce the infusion rate to a minimum and administer **furosemide** IV (0.5 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 necessity of continuing IV fluids. If IV fluids are still required, re-start at half the previous infusion rate and monitor closely.
- (l) If small or prepubertal children, administer 0.3 ml of **epinephrine**.
- (m) For example: methicillin-resistant *Staphylococcus aureus* (MRSA), pseudomonas species, and gram-negative bacteria with extended-spectrum beta-lactamase (ESBL) activity.
- (n) When using a peripheral vein, monitor infusion site closely for signs of extravasation, in particular in young children.
- (o) If no system to control volume delivery and flow rate (e.g. syringe pump), an infusion using an infusion bag and standard paediatric giving set can be considered in extreme situations as a temporary measure. 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.

## References

1. Houston KA, George EC, Maitland K. Implications for paediatric shock management in resource-limited settings: a perspective from the FEAST trial. *Crit Care*. 2018;22(1):119.  
<https://doi.org/10.1186/s13054-018-1966-4>
2. Cecconi M, De Backer D, Antonelli M, et al. Consensus on circulatory shock and hemodynamic monitoring. Task force of the European Society of Intensive Care Medicine. *Intensive Care Med*. 2014;40(12):1795-1815.  
<https://doi.org/10.1007/s00134-014-3525-z>
3. Cardona V, Ansotegui IJ, Ebisawa M, et al. World allergy organization anaphylaxis guidance 2020. *World Allergy Organ J*.

2020;13(10):100472. Published 2020 Oct 30.  
<https://doi.org/10.1016/j.waojou.2020.100472>

4. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*. 2016;315(8):801-810.  
<https://doi.org/10.1001/jama.2016.0288>
5. Richey SL. Tourniquets for the control of traumatic hemorrhage: a review of the literature. *World J Emerg Surg*. 2007;2:28. Published 2007 Oct 24.  
<https://doi.org/10.1186/1749-7922-2-28>
6. Emergency treatment of anaphylaxis. Guidelines for healthcare providers. Resuscitation Council UK. Updated 2021 [Accessed May 31 2023].  
[https://www.resus.org.uk/sites/default/files/2021-05/Emergency%20Treatment%20of%20Anaphylaxis%20May%202021\\_0.pdf](https://www.resus.org.uk/sites/default/files/2021-05/Emergency%20Treatment%20of%20Anaphylaxis%20May%202021_0.pdf)
7. Evans L, Rhodes A, Alhazzani W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. *Intensive Care Med*. 2021;47(11):1181-1247.  
<https://doi.org/10.1007/s00134-021-06506-y>

# Generalised tonic-clonic seizures and convulsive status epilepticus

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Generalised tonic-clonic seizures are involuntary movements of both sides of the body associated with impaired or loss of consciousness. They result from abnormal brain activity.

Most seizures are brief (less than 5 minutes) and resolve spontaneously. They may occur once or may recur.

In young children, seizures frequently occur in the context of fever, with no underlying causes. These are defined as "febrile seizures".

A seizure lasting longer than 5 minutes or 2 or more seizures in 5 minutes without complete restoration of baseline consciousness between seizures is defined as "status epilepticus" [1][2]. Status epilepticus is a medical emergency requiring immediate management. The longer a seizure lasts, the more difficult it is to stop, and the greater the risk for permanent brain damage and death.

In pregnancy and the postpartum period, seizures may be a manifestation of eclampsia. Refer to [Essential obstetric and newborn care](#), MSF.

## Clinical features

### During a seizure

- contraction of muscles, including respiratory muscles (tonic phase), followed by rhythmic jerking of the arms and legs (clonic phase)
- and
- loss of consciousness

These signs may be associated with loss of urine, breathing difficulty, and cyanosis.

### Immediately after a seizure (postictal phase)

The patient experiences fatigue and temporary symptoms such as confusional state, headache, memory loss, focal deficits. Recovery usually occurs within 30 to 60 minutes [3] but may be delayed.

## First aid during a seizure

- Note the time. Call for help.
- Protect from falls and trauma, loosen clothing.
- Maintain airway, place patient in recovery position to avoid aspiration, do not put anything in the mouth.
- Treat hypoglycaemia if present or administer glucose if unable to measure capillary blood glucose immediately (see [Hypoglycaemia](#), Chapter 1).
- Depending on the context:
  - Administer oxygen if available.
  - If febrile seizures are likely, see [Febrile seizures](#).
  - In adults, **thiamine** (100 mg by IV infusion in 100 ml 0.9% NaCl over 30 minutes) may be administered at the same time as glucose if vitamin B<sub>1</sub> deficiency is suspected (e.g. in case of alcohol-related seizures)<sup>a</sup>.
- If seizures stop spontaneously in 5 minutes or less, see [Postictal management](#).

## Febrile seizures

Febrile seizures frequently occur in children aged 6 months to 5 years with fever (usually due to viral infection) and no signs of central nervous system (CNS) infection, metabolic disturbances, or history of afebrile seizures<sup>[4]</sup>. They may be either "simple" or "complex".

- A simple febrile seizure is defined as a single generalised seizure, without focal signs, that lasts less than 15 minutes, and does not recur within a 24-hour period<sup>[4]</sup>. Most of these seizures last less than 5 minutes and if so, no antiseizure treatment is required. The risk of subsequent epilepsy is low after this type of seizure. Observe the child at least until full recovery, and discharge when child returns to neurological baseline. Give instructions for home-based management: symptomatic treatment of fever to make the child more comfortable (see [Fever](#), Chapter 1) and of underlying viral infection if relevant.
- A complex febrile seizure is a seizure meeting at least one the following criteria: presence of focal signs, a duration more than 15 minutes, or multiple seizures within a 24-hour period<sup>[4]</sup>.
- In all cases:
  - Provide [first aid during a seizure](#).
  - After a seizure, see [Postictal management](#).
  - If a seizure lasts more than 5 minutes or recurs within 5 minutes, start treatment for status epilepticus.

## Status epilepticus

In case of status epilepticus, start antiseizure medication (ASM).



- ASMs may cause respiratory depression, bradycardia, and hypotension, especially in children and older patients.
- During and after ASM administration:
  - have ventilation equipment (Ambu and mask) and solutions for fluid replacement ready for use,
  - monitor RR, SpO<sub>2</sub>, HR, and BP at least every 15 minutes until stable.
- Never administer ASMs by rapid IV injection. Reduce the administration rate in the event of drop in RR, HR, or BP.

### Step 1 - First-line ASM treatment

- Administer one of the following benzodiazepines (BZD). The choice depends on the situation, i.e. if seizures occur in pre-hospital or hospital setting.
- In any case, do not administer more than 2 doses of BZD.

#### Status epilepticus in pre-hospital setting

- Administer **midazolam** (5 mg/ml solution) by buccal or intranasal route or **diazepam** (5 mg/ml solution) by rectal route. For doses to be administered, see [Table 1](#).
- If seizures do not stop 5 minutes after the first dose of BZD, readminister the same dose.
- If seizures do not stop after the second dose of BZD, refer urgently to hospital for treatment with second-line ASM(s).
- If seizures stop after 1 or 2 doses of BZD, refer to hospital for further management (aetiological treatment and potential maintenance treatment).
- While awaiting transfer, monitor vital signs, administer oxygen if available to maintain SpO<sub>2</sub> > 94%. If seizures stop, see [Postictal management](#).

#### Status epilepticus in hospital setting

Check whether a BZD has been administered before arrival at the hospital and the number of doses. If one dose was administered, give a second dose. If 2 doses were administered, start [Step 2 - Second-line ASM treatment](#).

If no pre-hospital dose of BZD was administered:

- If IV or IO access: **diazepam** (5 mg/ml solution) by slow IV injection (over 3 to 5 minutes). For doses to be administered, see [Table 1](#).
- If no IV or IO access: **midazolam** (5 mg/ml solution) by buccal or intranasal route or **midazolam** (1 mg/ml solution) by IM route or **diazepam** (5 mg/ml solution) by rectal route. For doses to be administered, see [Table 1](#).
- If seizures do not stop 5 minutes after the first dose of BZD, readminister the same dose.
- If seizures do not stop after the second dose of BZD, start [Step 2 - Second-line ASM treatment](#).
- If seizures recur:
  - 6 hours or more after seizures stop, restart treatment from [Step 1 - First-line ASM treatment](#) as for a new seizure,
  - Less than 6 hours after seizures stop, continue treatment at the last point, e.g.:
    - if seizures recur < 6 hours after a first dose of BZD, readminister the same dose,
    - if seizures recur < 6 hours after 2 doses of BZD, start [Step 2 - Second-line ASM treatment](#).
- If seizures stop after 1 or 2 doses of BZD and do not recur, see [Postictal management](#) and evaluate the need for [maintenance ASM treatment](#).

**Table 1 - Dosage of benzodiazepines**

Age	1 to < 4 months	4 to < 12 months	1 to < 3 years	3 to < 5 years	5 to < 9 years	9 to < 12 years	≥ 12 years adults
Weight	3 to < 6 kg	6 to < 10 kg	10 to < 15 kg	15 to < 20 kg	20 to < 30 kg	30 to < 40 kg	≥ 40 kg
<b>midazolam</b> buccal <sup>(a)</sup> or intranasal route <sup>(b)</sup> , dose in ml (5 mg/ml solution)							
	0.25 ml	0.4 ml	0.6 ml	1 ml	1.2 ml	2 ml	2 ml
<b>midazolam</b> IM route, dose in ml (1 mg/ml solution)							
	0.6 ml	1.2 ml	2 ml	3 ml	4 ml	6 ml	10 ml
<b>diazepam</b> rectal route <sup>(c)</sup> , dose in ml (5 mg/ml solution)							
	0.4 ml	0.7 ml	1.2 ml	1.5 ml	2 ml	2 ml	2 to 4 ml <sup>(d)</sup>
<b>diazepam</b> slow IV route, dose in ml (5 mg/ml solution)							
	0.25 ml	0.4 ml	0.6 ml	1 ml	1.2 ml	2 ml	2 ml <sup>(d)</sup>

(a) Midazolam buccal route: lay the patient on their side. Withdraw the required dose using a 1 ml or 2 ml syringe. Remove the needle. Insert the tip of the syringe into the space between the gum and cheek. Administer the dose by slowly pushing the syringe plunger.

(b) Midazolam intranasal route: lay the patient on their back or side. Withdraw the required dose using a 1 ml or 2 ml syringe (add an additional 0.1 ml to the calculated dose to account for the remaining liquid in the atomising device). Remove the needle. Attach the intranasal atomisation device to the syringe. Briskly push the syringe plunger to spray the dose into the nostril. The dose can be split in both nostrils to reduce irritation.

(c) Diazepam rectal route: lay the patient on their side. For volumes up to 1 ml, use a 1 ml syringe. Withdraw the required dose. Remove the needle. Insert the syringe into the rectum for a length of 1 to 3 cm (depending on age) to administer the dose. For volumes greater than 1 ml, use a 2 ml syringe and attach to the tip of the syringe a nasogastric tube n°8 cut to a length of 2 to 3 cm to administer the dose. After administration, hold the buttocks together for at least one minute.

- (d) In patients ≥ 65 years: for diazepam rectal, do not exceed 2 ml (= 10 mg) per dose; for diazepam IV, reduce the dose by half (1 ml = 5 mg per dose).

## Step 2 - Second-line ASM treatment

### Patients with no known epilepsy

Second-line ASMs are indicated for:

- Children, if seizures do not stop within 5 minutes of second dose of BZD.
- All adults, even if seizures stop after 1 or 2 doses of BZD, unless a reversible cause of seizure can be quickly treated (e.g. hypoglycaemia, electrolyte disturbances).

The choice of the ASM depends on the patient's characteristics: age, sex, pregnancy or breastfeeding status, and comorbidities. See [Table 2](#).

For doses to be administered, see [Table 3](#)

**Table 2** - Choice of a second-line antiseizure medication

	<b>Children 1 month to &lt; 2 years Girls ≥ 10 years and women</b>	<b>Girls 2 to &lt; 10 years Boys ≥ 2 years and men</b>
First choice	levetiracetam (LEV) <sup>(e)</sup>	levetiracetam (LEV) <sup>(e)</sup> or valproic acid (VPA) <sup>(f)</sup>
Second choice	phenobarbital (PB) <sup>(g)</sup>	phenobarbital (PB) <sup>(g)</sup>
Third choice	phenytoin (PHT) <sup>(h)</sup>	phenytoin (PHT) <sup>(h)</sup>

- (e) LEV can be used in all patients but with caution in patients with renal impairment or heart disorders.
- (f) VPA is contraindicated:
  - in children under 2 years and patients with hepatic disease;
  - in women and girls who are or may become pregnant. Every effort should be made to find a safer alternative to VPA in pregnant women and girls. However, prolonged status epilepticus is a life-threatening condition both for the mother and the unborn child. If VPA is the only ASM available, use the lowest possible dose.
- (g) PB is contraindicated in patients with severe impairment of respiratory, renal or hepatic function. It should be administered with caution in children, older patients and patients with mild to moderate impairment of respiratory, renal or hepatic function.
- (h) PHT is contraindicated in patients with bradycardia, atrioventricular block. It should be administered with caution in patients with hepatic impairment, heart failure, cardiac rhythm disorders, hypotension.
  - If seizures do not stop after second-line ASM, change to another second-line ASM.
  - If seizures do not stop or recur in < 6 hours despite 2 second-line ASMs, transfer the patient to an intensive care unit for treatment of refractory status epilepticus.
  - If seizures stop after 1 or 2 second-line ASM(s), see [Postictal management](#) and [Maintenance ASM treatment](#).

### Patients with known epilepsy

- History taking:
  - ASM and dose taken, effectiveness.
  - Missed doses if any, and reason (e.g. forgetting, interruption due to adverse effects, shortage of medication).
- Management:
  - Administer the IV loading dose of the medication that the patient should usually take or see [Table 2](#).

- If seizures do not stop, continue treatment as for patients with no known epilepsy.
- If seizures stop after 1 or 2 second-line ASM(s), see [Postictal management](#) and [Maintenance ASM treatment](#).

## Step 3 - Maintenance ASM treatment

Some patients may require maintenance treatment after the loading dose.

- In children, maintenance treatment is indicated when:
  - a second-line ASM has been used to control seizures, unless a reversible cause of seizure can be quickly treated (e.g. hypoglycaemia, electrolyte disturbances),
  - 3 or more seizures occur within a 24-hour period,
  - focal signs and/or impaired consciousness persist beyond expected postictal period,
  - there is known or presumed traumatic brain injury (within 24 hours of injury),
  - there is known or presumed epilepsy.

Unless the child has already received a loading dose, start with a loading dose, see [Table 3](#).

- In adults, maintenance treatment is indicated for all patients, unless a reversible cause of seizure can be quickly treated (e.g. hypoglycaemia, electrolyte disturbances).
- If seizures do not recur, administer maintenance treatment for 48 to 72 hours and then reassess. Use oral route (or nasogastric tube). For maintenance doses to be administered, see [Table 3](#).
- For seizures in the context of head trauma, maintenance treatment should last 7 days.
- In case of epilepsy, start or resume long-term treatment. See [Epilepsy](#), Chapter 12.

## Postictal management

- Note time of end of seizure; keep patient in recovery position; maintain airway.
- Administer oxygen to all patients if available and especially to patients who received ASM(s). Maintain SpO<sub>2</sub> > 94%.
- Monitor vital signs and SpO<sub>2</sub> every 15 minutes until stable, then every hour.
- Closely monitor RR if the patient received BZD, PB or PHT; HR and BP (and ECG if available) if the patient received PHT.
- Observe for further seizures.
- As soon as possible, try to identify the underlying cause and treat it, even in patients with known epilepsy (see [Frequent causes of seizures](#)):
  - Take a detailed history and perform a full clinical examination, looking particularly for general status and focal signs.
  - Depending on assessment, perform the following tests if available:
    - ▷ capillary blood glucose, especially if not done during the seizure. Check regularly blood glucose if necessary.
    - ▷ rapid diagnostic test for malaria in endemic areas
    - ▷ CSF examination (lumbar puncture) and culture
    - ▷ white blood cell count, serum electrolytes and creatinine, liver enzymes and coagulation tests, blood culture
- Note if patient does not return to baseline status within 30 to 60 minutes of end of seizure.

## Frequent causes of seizures

- Febrile seizures: in young children with fever, usually in a context of a respiratory or gastrointestinal viral infection.
- CNS infections: e.g. any meningitis (for [Bacterial meningitis](#), see Chapter 7); severe malaria, neurocysticercosis, trypanosomiasis (see [Chapter 6](#)); cerebral toxoplasmosis, cryptococcal meningitis (see [HIV infection and AIDS](#), Chapter 8).
- Metabolic abnormalities: e.g. [hypoglycaemia](#) (Chapter 1), electrolyte disorders (hyponatremia, hypocalcaemia).
- Intoxications: e.g. psychoactive drugs and alcohol, methanol, medications, neurotoxic pesticides and venoms, carbon monoxide.

- Withdrawal from CNS depressants: e.g. alcohol (see [Agitation](#) and [Acute confusional state](#), Chapter 11), opioids, benzodiazepines, barbiturates.
- Use of seizure-provoking drugs: many drugs may be involved, e.g. antidepressants, antipsychotics, some antimicrobials.
- Vitamin B deficiencies (thiamine and pyridoxine), particularly in patients with chronic alcohol consumption.
- Epilepsy: undiagnosed epilepsy, poor adherence to treatment, ineffective treatment or abrupt stop of ASM.
- Head trauma, CNS tumour, stroke, sepsis, encephalopathy (e.g. hypertensive, hypoxic).

## Dosage of second-line antiseizure medications

**Table 3** - Second-line antiseizure medications (loading doses and maintenance doses)

ASMs	Loading dose	Maintenance dose
<b>levetiracetam</b> = <b>LEV</b> 500 mg in 5 ml vial (100 mg/ml)	<ul style="list-style-type: none"> <li>• Children ≥ 1 month: <ul style="list-style-type: none"> <li>▫ Use diluted solution: add 3 ml (300 mg) of LEV to 17 ml of 0.9% NaCl to obtain 20 ml of solution containing 15 mg of LEV per ml.</li> <li>▫ Administer 40 mg/kg (max. 3 g) over 10 minutes by IV infusion using a syringe pump or by very slow IV injection.</li> <li>▫ If seizures do not stop after the end of the first dose, readminister half-dose: 20 mg/kg (max. 1.5 g) as above.</li> <li>▫ Do not exceed the total dose of 60 mg/kg or 4.5 g.</li> <li>▫ Do not exceed an infusion rate of 5 mg/kg/minute.</li> </ul> </li> </ul>	12 hours after the loading dose: <ul style="list-style-type: none"> <li>• Children 1 to 5 months: 7 mg/kg every 12 hours PO</li> <li>• Children 6 months to 15 years: 10 mg/kg every 12 hours PO</li> </ul>
	<ul style="list-style-type: none"> <li>• Adults<sup>(1)</sup> : <ul style="list-style-type: none"> <li>▫ 60 mg/kg (max. 4.5 g) single dose over 15 minutes</li> <li>▫ Use diluted solution as above (15 mg/ml) if administered by IV infusion using a syringe pump.</li> <li>▫ Use undiluted solution if administered by IV infusion in a bag of 100 ml of 0.9% NaCl.</li> <li>▫ Do not exceed an infusion rate of 5 mg/kg/minute</li> </ul> </li> </ul>	12 hours after the loading dose: <ul style="list-style-type: none"> <li>• Adults: 1 to 1.5 g every 12 hours PO</li> </ul>
<b>phenobarbital</b> = <b>PB</b> 200 mg in 1 ml ampoule (200 mg/ml)	<ul style="list-style-type: none"> <li>• Children ≥ 1 month: <ul style="list-style-type: none"> <li>▫ Use diluted solution: add 1 ml (200 mg) of PB to 9 ml of 0.9% NaCl to obtain 10 ml of solution containing 20 mg of PB per ml.</li> <li>▫ Administer 20 mg/kg (max. 1 g) over 20 minutes by IV infusion using a syringe pump (or only if not available, using a pediatric infusion set).</li> <li>▫ If seizures do not stop after the end of the first dose, readminister half-dose: 10 mg/kg as above.</li> <li>▫ Do not exceed an infusion rate of 1 mg/kg/minute.</li> </ul> </li> </ul>	12 hours after the loading dose: <ul style="list-style-type: none"> <li>• Children 1 to 11 months: 5 to 6 mg/kg once daily PO</li> <li>• Children 1 to 5 years: 6 to 8 mg/kg once daily PO</li> <li>• Children 6 to 12 years: 4 to 6 mg/kg once daily PO</li> <li>• Children &gt; 12 years: 1 to 3 mg/kg once daily PO</li> </ul>

	<ul style="list-style-type: none"> <li>Adults: <ul style="list-style-type: none"> <li>15 mg/kg (max. 1 g) single dose over 15 minutes</li> <li>Use diluted solution as above (20 mg/ml) if administered by IV infusion using a syringe pump.</li> <li>Use undiluted solution if administered by IV infusion in a bag of 100 ml of 0.9% NaCl.</li> <li>Do not exceed an infusion rate of 100 mg/minute.</li> </ul> </li> </ul>	12 hours after the loading dose: <ul style="list-style-type: none"> <li>Adults: 60 to 180 mg once daily PO</li> </ul>
<b>phenytoin</b> <b>= PHT</b> 250 mg in 5 ml ampoule or vial (50 mg/ml)	<ul style="list-style-type: none"> <li>Children <math>\geq</math> 1 month and <math>\leq</math> 25 kg <ul style="list-style-type: none"> <li>Use diluted solution: add 1 ml (50 mg) of PHT to 9 ml of 0.9% NaCl to obtain 10 ml of solution containing 5 mg of PHT per ml.</li> <li>Administer 20 mg/kg (max. 2 g) single dose over 20 minutes by IV infusion using a syringe pump. Only if syringe pump is not available, use a paediatric infusion set.</li> <li>Do not exceed an infusion rate of 1 mg/kg/minute.</li> </ul> </li> </ul>	12 hours after the loading dose: <ul style="list-style-type: none"> <li>Children: 2.5 mg/kg every 12 hours PO</li> </ul>
<ul style="list-style-type: none"> <li>Use a large central or peripheral vein.</li> <li>Use a infusion set or line with a 0.2 micron filter.</li> <li>Before and after infusion, flush the catheter with 0.9% NaCl to limit venous irritation and potential incompatibility with other drugs.</li> <li><b>DO NOT DILUTE IN GLUCOSE.</b></li> <li>Do not use a line used for glucose solution.</li> </ul>	<ul style="list-style-type: none"> <li>Children <math>&gt;</math> 25 kg and adults<sup>(1)</sup> <ul style="list-style-type: none"> <li>Add undiluted solution to a 100 ml bag of 0.9% NaCl.</li> <li>Administer 20 mg/kg (max. 2 g) single dose by IV infusion at the following rate: <ul style="list-style-type: none"> <li><math>\leq</math> 1 g or <math>\leq</math> 50 kg: 20 minutes</li> <li><math>&gt;</math> 1 g and <math>\leq</math> 1.5 g or <math>&gt;</math> 50 kg and <math>\leq</math> 75 kg: 30 minutes</li> <li><math>&gt;</math> 1.5 g and <math>\leq</math> 2 g or <math>&gt;</math> 75 kg and <math>\leq</math> 100 kg: 40 minutes</li> </ul> </li> <li>Do not exceed an infusion rate of 50 mg/minute.</li> </ul> </li> </ul>	12 hours after the loading dose: <ul style="list-style-type: none"> <li>Adults: 3 to 4 mg/kg once daily PO</li> </ul>
	<ul style="list-style-type: none"> <li>Older patients (<math>\geq</math> 65 years) and adults with cardiac disorders <ul style="list-style-type: none"> <li>Add undiluted solution to a 100 ml bag of 0.9% NaCl.</li> <li>Administer 20 mg/kg (max. 2 g) single dose by IV infusion at the following rate: <ul style="list-style-type: none"> <li><math>\leq</math> 1 g or <math>\leq</math> 50 kg: 40 minutes</li> </ul> </li> </ul> </li> </ul>	12 hours after the loading dose: <ul style="list-style-type: none"> <li>Adults: 60 to 180 mg once daily PO</li> </ul>

	<ul style="list-style-type: none"> <li>▷ &gt; 1 g and ≤ 1.5 g or &gt; 50 kg and ≤ 75 kg: 60 minutes</li> <li>▷ &gt; 1.5 g and ≤ 2 g or &gt; 75 kg and ≤ 100 kg: 80 minutes</li> <li>▫ Do not exceed an infusion rate of 25 mg/minute.</li> </ul>	
<b>valproic acid</b> = VPA (or sodium valproate) <sup>(k)</sup> 400 mg in 4 ml ampoule (100 mg/ml)	<ul style="list-style-type: none"> <li>• Children ≥ 2 years: <ul style="list-style-type: none"> <li>▫ Use diluted solution: add 4 ml (400 mg) of VPA to 6 ml of 0.9% NaCl to obtain 10 ml of solution containing 40 mg of VPA per ml.</li> <li>▫ Administer 20 mg/kg (max. 1.5 g) over 5 minutes by IV infusion using a syringe pump or by slow IV injection.</li> <li>▫ If seizures do not stop after the end of the first dose, readminister the same dose: 20 mg/kg (max. 1.5 g) as above.</li> <li>▫ Do not exceed the total dose of 40 mg/kg or 3 g.</li> <li>▫ Do not exceed an infusion rate of 6 mg/kg/minute</li> </ul> </li> </ul>	6 to 8 hours after the loading dose: <ul style="list-style-type: none"> <li>• Children ≥ 2 years: <ul style="list-style-type: none"> <li>5 to 7.5 mg/kg (max. 600 mg) 2 times daily PO</li> </ul> </li> </ul>
	<ul style="list-style-type: none"> <li>• Adults<sup>(l)</sup> : <ul style="list-style-type: none"> <li>▫ 40 mg/kg (max. 3 g) single dose over 10 minutes</li> <li>▫ Use diluted solution as above (40 mg/ml) if administered by IV infusion using a syringe pump.</li> <li>▫ Use undiluted solution if administered by IV infusion in a bag of 100 ml of 0.9% NaCl.</li> <li>▫ Do not exceed an infusion rate of 6 mg/kg/minute.</li> </ul> </li> </ul>	12 hours after the loading dose: <ul style="list-style-type: none"> <li>• Adults: 1 g 2 times daily PO</li> </ul>

- (i) Reduce dosage in patients with renal impairment.
- (j) Reduce dosage in patients with hepatic impairment.
- (k) For a pregnant woman, if VPA is the only ASM available, use the lowest possible loading dose (an option could be to administer 20 mg/kg over 5 minutes, then repeat the same dose only if seizures do not stop by the end of the first dose).

## Footnotes

- (a) Thiamine should be administered at the same time as glucose because glucose may precipitate Wernicke's encephalopathy in patients with chronic alcohol consumption. Treatment should be continued for 3 to 5 days with thiamine PO (100 to 200 mg once daily) or IM (100 mg once daily).

## References

1. Lowenstein DH, Bleck T, Macdonald RL. It's Time to Revise the Definition of Status Epilepticus. *Epilepsia*. 1999;40(1):120-122. <https://doi.org/10.1111/j.1528-1157.1999.tb02000.x>
2. Brophy GM, Bell R, Claassen J, et al. Guidelines for the Evaluation and Management of Status Epilepticus. *Neurocrit Care*. 2012;17:3-23. [https://higherlogicdownload.s3.amazonaws.com/NEUROCRITICALCARE/b8b3b384-bfb9-42af-bb55-45973d5054a4/UploadedImages/Documents/Guidelines/SE\\_Guidelines\\_NCS\\_0412.pdf](https://higherlogicdownload.s3.amazonaws.com/NEUROCRITICALCARE/b8b3b384-bfb9-42af-bb55-45973d5054a4/UploadedImages/Documents/Guidelines/SE_Guidelines_NCS_0412.pdf)
3. Pottkämper JCM, Hofmeijer J, Van Waarde JA, Van Putten MJAM. The postictal state — What do we know? *Epilepsia*. 2020;61(6):1045-1061. <https://doi.org/10.1111/epi.16519>
4. Steering Committee on Quality Improvement and Management, Subcommittee on Febrile Seizures. Febrile Seizures: Clinical Practice Guideline for the Long-term Management of the Child With Simple Febrile Seizures. *Pediatrics*. 2008;121(6):1281-1286. <https://doi.org/10.1542/peds.2008-0939>

# Hypoglycaemia

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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)<sup>[1]</sup>

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)<sup>a</sup>
  - 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 acute 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.

## Footnotes

- (a) If ready-made 10% glucose solution is not available: remove 100 ml of 5% glucose from a 500 ml bottle or bag, then add 50 ml of 50% glucose to the remaining 400 ml of 5% glucose to obtain 450 ml of 10% glucose solution.

## References

1. American Diabetes Association. Standards of Care in Diabetes—2023 Abridged for Primary Care Providers. *Clinical Diabetes*. 2022;41(1):4-31.  
<https://doi.org/10.2337/cd23-as01>

# Fever

Last updated: December 2023

Fever is defined as an axillary temperature higher than 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

- Petechial or purpuric rash, meningeal signs, heart murmur, severe abdominal pain, dehydration.
- Signs of severe bacterial infection or sepsis: critically ill appearance<sup>a</sup>, hypothermia, altered level of consciousness, severe tachycardia, hypotension, tachypnoea, respiratory distress, seizures; a bulging fontanel in young children.
- Signs of circulatory impairment or shock: see [Shock](#), Chapter 1.

## Infectious causes of fever according to signs and symptoms

Signs or symptoms	Possible aetiology
Meningeal signs, seizures	Meningitis/meningoencephalitis/severe malaria
Abdominal pain or peritoneal signs	Appendicitis/peritonitis/enteric fevers/amebic liver abscess
Diarrhoea, vomiting	Gastroenteritis/enteric fevers
Jaundice, enlarged liver	Viral hepatitis
Cough	Pneumonia/measles/tuberculosis if persistent
Eyelid erythema, eye pain and oedema	Orbital cellulitis
Ear pain, red tympanic membrane	Otitis media
Tender swelling behind the ear	Mastoiditis
Sore throat, enlarged lymph nodes	Streptococcal pharyngitis/diphtheria/retropharyngeal or tonsillar abscess/epiglottitis
Multiple vesicles on the oral mucosa and lips	Oral herpes
Dysuria, urinary frequency, back pain	Urinary tract infection
Red, warm, painful skin	Erysipelas/cellulitis/necrotising infections of the skin and soft tissues/abscess
Limp, difficulty walking	Osteomyelitis/septic arthritis
Rash	Measles/dengue/viral haemorrhagic fevers/chikungunya
Bleeding (petechiae, epistaxis, etc.)	Dengue/viral haemorrhagic fevers/severe malaria
Joint pain	Rheumatic fever/chikungunya/dengue

- If the patient is ill appearing<sup>a</sup> and has a persistent fever, consider HIV infection and tuberculosis, according to clinical presentation.

## Laboratory and other examinations

- Malaria rapid diagnostic test in endemic areas.
- In case of circulatory impairment or shock: see [Shock](#), Chapter 1.
- Children 1 to 3 months with fever without a focus:
  - urine dipstick and urine culture, if available;
  - blood culture, if available;
  - full blood count (FBC), if available;

- lumbar puncture (LP) if meningeal signs or signs of severe bacterial infection or sepsis, or failure of prior antibiotic treatment;
  - chest x-ray, if available, in case of signs of respiratory disease or severe infection or sepsis.
- Children > 3 months to 2 years with fever without a focus:
  - urine dipstick and urine culture, if available;
  - LP if meningeal signs or signs of severe bacterial infection or sepsis;
  - chest x-ray, if available, if fever > 72 hours or signs of severe bacterial infection or sepsis;
  - blood culture, if available, if fever > 72 hours or signs of severe bacterial infection or sepsis;
  - FBC, if available, if fever > 72 hours or signs of severe bacterial infection or sepsis;
  - other: according to clinical presentation.
- Children over 2 years with fever without a focus:
  - urine dipstick and urine culture, if available, if history of urinary tract infection or fever > 72 hours or signs of severe bacterial infection or sepsis;
  - LP if meningeal signs or signs of severe bacterial infection or sepsis;
  - chest x-ray, if available, if fever > 72 hours or signs of severe bacterial infection or sepsis;
  - blood culture, if available, if fever > 72 hours or signs of severe bacterial infection or sepsis;
  - FBC, if available, if fever > 72 hours or signs of severe bacterial infection or sepsis;
  - other: according to clinical presentation.
- Adults: according to clinical presentation.

## Aetiological treatment

- Treat patients with a positive malaria test: see [Malaria](#), Chapter 6.
- If the source of infection has been found: administer antibiotic treatment accordingly.
- If severe infection, sepsis, circulatory impairment or shock: hospitalise and immediately administer an empiric antibiotic treatment (see [Shock](#), Chapter 1). Continue this treatment until the source of infection is found and adapt antibiotic treatment accordingly.
- If no source of infection is found, and there are no signs of severe infection, sepsis, circulatory impairment or shock, hospitalise for further investigations and monitoring:
  - Children 1 to 3 months;
  - Children > 3 months to < 2 years with negative urine dipstick (and negative urine culture if available).
- For malnourished children, see [Severe acute malnutrition](#), Chapter 1.
- For patients with sickle cell disease, see [Sickle cell disease](#), Chapter 12.

## 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 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 viral haemorrhagic fevers and dengue: acetylsalicylic acid and ibuprofen are contraindicated; use paracetamol with caution in the presence of hepatic dysfunction.

## **Footnotes**

- (a) Critically ill appearing child: weak grunting or crying, drowsiness, difficult to arouse, does not smile, disconjugate or anxious gaze, pallor or cyanosis, general hypotonia.

# Pain

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

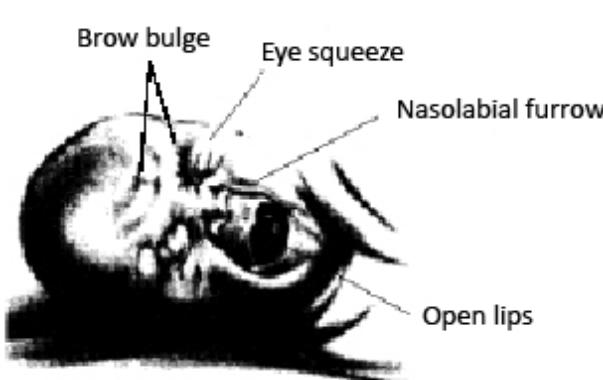
Each category is scored from 0 to 2, giving a final score between 0 and 10.

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

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

	<b>Analgesics</b>	<b>Children</b>	<b>Adults (except pregnant/breast-feeding women)</b>	<b>Remarks</b>
<b>Level 1</b>	<b>paracetamol</b> 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.
	<b>paracetamol</b> 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)	
	<b>acetylsalicylic acid (aspirin)</b> PO	–	300 mg to 1 g every 4 to 6 hours (max. 4 g daily)	Avoid in children less than 16 years.
	<b>diclofenac</b> IM	–	75 mg once daily	Treatment must be as short as possible. Respect contra-indications.
<b>Level 2</b>	<b>ibuprofen</b> 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)	
	<b>codeine</b> 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.
	<b>tramadol</b> 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.
<b>Level 3</b>	<b>tramadol</b> 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)	
	<b>morphine</b> PO immediate release (MIR)	> 6 months: 0.15 mg/kg every 4 hours, to be adjusted in relation to pain intensity	10 mg every 4 hours, to be adjusted in relation to pain intensity	• Reduce the dose by half in elderly patients and patients with renal or hepatic impairment.

			<ul style="list-style-type: none"> <li>• Add a laxative if treatment &gt; 48 hours.</li> </ul>
<b>morphine</b> 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 adjusted 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 adjusted in relation to pain intensity	<ul style="list-style-type: none"> <li>• Do not initiate treatment with the MSR in elderly patients and patients with renal or hepatic impairment. Begin treatment with MIR.</li> <li>• Add a laxative if treatment &gt; 48 hours.</li> </ul>
<b>morphine</b> SC, IM	> 6 months: 0.1 to 0.2 mg/kg every 4 hours	0.1 to 0.2 mg/kg every 4 hours	<ul style="list-style-type: none"> <li>• Reduce doses by half and administer less frequently, according to clinical response, in elderly patients and patients with severe renal or hepatic impairment.</li> </ul>
<b>morphine</b> 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	<ul style="list-style-type: none"> <li>• Add a laxative if treatment &gt; 48 hours.</li> </ul>

#### Notes on the use of morphine and derivatives:

- Morphine is an effective treatment for many types of severe pain. Its analgesic effect is dose-dependent. 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		<b>Breast-feeding</b>
		0-5 months	From 6 <sup>th</sup> month	
<b>Level 1</b>	<b>paracetamol</b>	first choice	first choice	first choice
	<b>aspirin</b>	avoid	contra-indicated	avoid
	<b>ibuprofen</b>	avoid	contra-indicated	possible
<b>Level 2</b>	<b>codeine</b>	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 third trimester. 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.
	<b>tramadol</b>	possible	The child may develop drowsiness when the mother receives tramadol 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.	
<b>Level 3</b>	<b>morphine</b>	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

Last updated: January 2024

Anaemia is defined as a haemoglobin (Hb) level below reference values<sup>[1][2]</sup>, which vary depending on age, sex, and pregnancy status (see [Table 2](#)).

Anaemia may be caused by:

- Decreased production of red blood cells: iron deficiency, nutritional deficiencies (folic acid, vitamin B<sub>12</sub>, vitamin A), depressed bone marrow function, certain infections (HIV, visceral leishmaniasis), renal failure;
- Loss of red blood cells: acute or chronic haemorrhage (gastrointestinal ulcer, 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, nitrofurantoin, etc.) in patients with G6PD deficiency.

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 of decompensation: cold extremities, altered mental status, oedema in the lower limbs, respiratory distress, elevated jugular venous pressure, cardiac/coronary failure, shock.
- Significant signs: cheilosis and glossitis (nutritional deficiency), jaundice, hepatosplenomegaly, dark coloured urine (haemolysis), bleeding (maelena, haematuria, etc.), signs of [malaria](#) (Chapter 6), etc.

## Laboratory

- Hb levels
- Rapid diagnostic test or thick and thin blood films in areas where malaria is endemic.
- Urinary dipstick: check for haemoglobinuria or haematuria.
- If sickle cell disease is suspected (to be done before blood transfusion): rapid diagnostic test (Sickle SCAN®) or, if not available, Emmel test.
- Full blood count (FBC) if available to guide diagnosis.

**Table 1** - Possible diagnoses with FBC

Characteristics	Main diagnoses
Macrocytic	Deficiency (folic acid, vitamin B <sub>12</sub> ), 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 <sub>12</sub> ), 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

**ferrous salts/folic acid** PO, or if not available, **ferrous salts** PO, for 3 months

Doses are expressed in elemental iron<sup>a</sup>:

- 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	60 or 65 mg tablet
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

- Helminthic infections: see [Schistosomiasis](#) and [Nematode infections](#) (Chapter 6).

- Folic acid deficiency (rarely isolated)

**folic acid** PO for 4 months:

- Children under 1 year: 0.5 mg/kg once daily
- Children 1 year and over and adults: 5 mg once daily

- Malaria: see [Malaria](#) (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<sup>b</sup>. For transfusion thresholds, see [Table 2](#).

### Volume to be transfused

If presence of haemorrhagic shock: see [Shock](#), Chapter 1. Otherwise:

- Children<sup>[3]</sup>:

Transfusion volume is based on presence or absence of fever at any point from the time of ordering blood to the time of transfusion:

- If no fever (axillary temperature  $\leq 37.5^{\circ}\text{C}$ )<sup>c</sup>: administer either 15 ml/kg of packed red blood cells (PRBC) over 3 hours or 30 ml/kg of whole blood over 4 hours
- If fever (axillary temperature  $> 37.5^{\circ}\text{C}$ )<sup>c</sup>: administer either 10 ml/kg of PRBC over 3 hours or 20 ml/kg of whole blood over 4 hours

- Adolescents and adults: start with an adult unit of PRBC or whole blood; 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.
- Pay attention to signs of transfusion reaction, fluid overload, decompensation or continuing blood loss.
- For children: measure Hb once between 8 and 24 hours after the end of the transfusion or if signs of decompensation or continuing blood loss.
- If signs of circulatory overload appear:
  - Stop temporarily the transfusion.
  - Sit the patient in an upright position.
  - Administer oxygen.
  - Administer **furosemide** by slow IV injection:
    - 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:  
**ferrous salts/folic acid** PO, or if not available, **ferrous salts** PO, as long as the risk of deficiency persists (e.g. pregnancy<sup>[4]</sup>, malnutrition).  
Doses are expressed in elemental iron<sup>a</sup>:
    - ▷ 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	60 or 65 mg tablet
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

- Nutritional supplements (if the basic diet is insufficient).
- In the event of sickle cell anaemia: see [Sickle cell disease](#) (Chapter 12).
- Early treatment of malaria, helminthic infections, etc.

**Table 2** - Definition of anaemia and transfusion thresholds

<b>Patients</b>	<b>Hb levels defining anaemia</b>	<b>Transfusion thresholds</b>
Children 2-6 months	< 9.5 g/dl	
Children 6 months-4 years	< 11 g/dl	
Children 5-11 years	< 11.5 g/dl	
Children 12-14 years	< 12 g/dl	
Men ( $\geq$ 15 years)	< 13 g/dl	Hb < 7 g/dl if there are signs of decompensation or ongoing blood loss or severe malaria or serious bacterial infection or pre-existing heart disease
Women ( $\geq$ 15 years)	< 12 g/dl	
Pregnant women	<p>&lt; 11 g/dl (1<sup>st</sup> and 3<sup>rd</sup> trimester)</p> <p>&lt; 10.5 g/dl (2<sup>nd</sup> trimester)</p>	<p><b>&lt; 36 weeks</b></p> <ul style="list-style-type: none"> <li>Hb <math>\leq</math> 5 g/dl, even if there are no signs of decompensation</li> <li>Hb &gt; 5 g/dl and &lt; 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</li> </ul> <p><b><math>\geq</math> 36 weeks</b></p> <ul style="list-style-type: none"> <li>Hb <math>\leq</math> 6 g/dl, even if there are no signs of decompensation</li> <li>Hb &gt; 6 g/dl and &lt; 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</li> </ul>

- (a) Immediate transfusion is not required in children 2 months to 12 years with Hb  $\geq$  4 g/dl and < 6 g/dl and no sign of decompensation or ongoing blood loss, provided that:
- they are closely monitored (including Hb measurements at 8, 24 and 48 hours), and
  - transfusion preparation (blood grouping, etc.) is carried out without delay in case the child needs to be transfused later on.

## Footnotes

- (a) A coformulated tablet of ferrous salts/folic acid contains 185 mg of ferrous fumarate or sulfate (equivalent to 60 mg of elemental iron) and 400 micrograms of folic acid.  
A 200 mg tablet of ferrous fumarate or sulfate contains 65 mg of elemental iron.  
A 140 mg/5 ml syrup of ferrous fumarate contains 45 mg/5 ml of elemental iron.
- (b) 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, hepatitis B and C, syphilis and, in endemic areas, malaria and Chagas disease.
- (c) Axillary temperature should be taken at the time of ordering blood and immediately prior to transfusion.

## References

1. World Health Organization. *Haemoglobin Concentrations for the Diagnosis of Anaemia and Assessment of Severity*. World Health Organization; 2011. [Accessed June 26, 2023]  
<https://apps.who.int/iris/handle/10665/85839>
2. World Health Organization. *Educational Modules on Clinical Use of Blood*. World Health Organization; 2021. [Accessed June 26, 2023]  
<https://apps.who.int/iris/handle/10665/350246>
3. Maitland K, Olupot-Olupot P, Kiguli S, et al. Transfusion Volume for Children with Severe Anemia in Africa. *N Engl J Med*. 2019;381(5):420-431.  
<https://doi.org/10.1056/NEJMoa1900100>
4. Word Health Organization. *Daily iron and folic acid supplementation in pregnant women*. Word Health Organization. Geneva, 2012. [Accessed June 26, 2023]  
<https://apps.who.int/iris/handle/10665/77770>

# Dehydration

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](#), Chapter 1) or in patients with severe burns (see [Burns](#), 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)<sup>[1][2]</sup>

	<b>Severe dehydration At least 2 of the following signs:</b>	<b>Some dehydration At least 2 of the following signs:</b>	<b>No dehydration No signs of "severe" or "some" dehydration.</b>
<b>Mental status</b>	Lethargic or unconscious	Restless or irritable	Normal
<b>Radial pulse</b>	Weak or absent	Palpable	Easily palpable
<b>Eyes<sup>(a)</sup></b>	Sunken	Sunken	Normal
<b>Skin pinch<sup>(b)</sup></b>	Goes back very slowly (> 2 seconds)	Goes back slowly (< 2 seconds)	Goes back quickly (< 1 second)
<b>Thirst</b>	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](#), Chapter 1).
- If able to drink, administer oral rehydration solution (ORS) PO whilst obtaining IV access. according to WHO Treatment Plan C, monitoring infusion rate closely:
- Insert peripheral IV line using large caliber catheter (22-24G in children or 18G in adults) or intraosseous needle.
- Administer **Ringer lactate** (RL)<sup>a</sup>

### WHO Treatment Plan C<sup>[1][2]</sup>

Age	First, give 30 ml/kg over <sup>(c)</sup> :	Then, give 70 ml/kg over:
Children < 1 year	1 hour	5 hours
Children ≥ 1 year and adults	30 minutes	2 ½ hours

(c) 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](#), Chapter 1).<sup>b</sup>
- 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](#), Chapter 1).
- develops muscle cramps/weakness and abdominal distension: treat for moderate hypokalaemia with **7.5% potassium chloride** syrup (1 mmol of K<sup>+</sup>/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 inpatient<sup>c</sup>.
- 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 B<sup>[1][d]</sup>

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<sup>[1][2]</sup>

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

## Treatment of diarrhoea

In addition to the WHO treatment plan corresponding to patient's degree of dehydration:

- Administer aetiological treatment if required.
- Administer zinc sulfate to children under 5 years (see [Acute diarrhoea](#), Chapter 3).

## Footnotes

- (a) If RL not available, 0.9% sodium chloride can be used.
- (b) 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.
- (c) If available, take blood tests to monitor urea and electrolyte levels.
- (d) 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](https://apps.who.int/iris/bitstream/handle/10665/81170/9789241548373_eng.pdf?sequence=1)

# Severe acute malnutrition

Last updated: February 2024

Severe acute malnutrition (SAM) results from insufficient energy (kilocalories), fat, protein and/or other nutrients (vitamins and minerals, etc.) to cover individual needs.

SAM is frequently associated with medical complications due to metabolic disturbances and compromised immunity. It is a major cause of morbidity and mortality in children globally.

The protocols below are focused on the diagnosis and management of SAM in children 6 to 59 months only. For further details regarding this age group, and guidance for other age groups, refer to national recommendations and/or specialised protocols.

## Clinical assessment

### Characteristic physical signs

- In marasmus: skeletal appearance resulting from significant loss of muscle mass and subcutaneous fat.
- In kwashiorkor:
  - Bilateral oedema of the lower limbs sometimes extending to other parts of the body (e.g. arms and hands, face).
  - Discoloured, brittle hair; shiny skin which may crack, weep, and become infected.

### Diagnostic and admission criteria

Diagnostic criteria for SAM are both anthropometric and clinical:

- Mid-upper arm circumference (MUAC)<sup>a</sup> measures the degree of muscle wasting. MUAC < 115 mm indicates SAM and significant mortality risk.
- Weight-for-height z-score (WHZ) indicates the degree of weight loss by comparing the weight of the child with the median weight of non-malnourished children of the same height and sex. SAM is defined as WHZ < -3 with reference to the WHO Child Growth Standards<sup>b</sup>.
- The presence of bilateral pitting oedema of the lower limbs (when other causes of oedema have been ruled out) indicates SAM, regardless of MUAC and WHZ.

Admission criteria for SAM treatment programmes vary with context. Refer to national recommendations.

### Medical complications

- Children with any of the following severe medical conditions should receive hospital-based medical management:
  - Pitting oedema extending from the lower limbs up to the face;
  - Anorexia (observed during appetite test);
  - Other severe complications: persistent vomiting, shock, altered mental status, seizures, severe anaemia (clinically suspected or confirmed), persistent hypoglycaemia, eye lesions due to vitamin A deficiency, frequent or abundant diarrhoea, dysentery, dehydration, severe malaria, pneumonia, meningitis, sepsis, severe cutaneous infection, fever of unknown origin, etc.
- In the absence of these conditions, children should be treated as outpatients with regular follow-up.

## Nutritional treatment

- All children with SAM should receive nutritional treatment.

- Nutritional treatment is based on the use of specialised nutritious foods enriched with vitamins and minerals: F-75 and F-100 therapeutic milks, and ready-to-use therapeutic food (RUTF).
- Nutritional treatment is organised into phases:
  - Phase 1 (inpatient) intends to restore metabolic functions and treat or stabilize medical complications. Children receive F-75 therapeutic milk. This phase may last 1 to 7 days, after which children usually enter transition phase. Children with medical complications generally begin with phase 1.
  - Transition phase (inpatient) intends to ensure tolerance of increased food intake and continued improvement of clinical condition. Children receive F-100 therapeutic milk and/or RUTF. This phase usually lasts 1 to 3 days, after which children enter phase 2.
  - Phase 2 (outpatient or inpatient) intends to promote rapid weight gain and catch-up growth. Children receive RUTF. This phase usually lasts 1 to 3 days when inpatient, after which children are discharged for outpatient care. Children without medical complications enter directly into this phase as outpatients. The outpatient component usually lasts several weeks.
- Breastfeeding should be continued in breastfed children.
- Drinking water should be given in addition to meals, especially if the ambient temperature is high, or the child has a fever or is receiving RUTF.

## Routine medical management

The following should be provided to all inpatients and outpatients with SAM:

<b>Antibiotic treatment</b>	From D1, unless specific signs of infection are present: <b>amoxicillin</b> PO: 50 mg/kg (max. 1 g) 2 times daily for 5 to 7 days
<b>Malaria</b>	On D1, rapid diagnostic test in endemic areas and treatment for malaria according to results or if testing is not available (see <u>Malaria</u> , Chapter 6).
<b>Intestinal parasites</b>	In transition phase or upon outpatient admission, <b>albendazole</b> PO: Children 12 to 23 months: 200 mg single dose Children 24 months and over: 400 mg single dose
<b>Vaccination</b>	<ul style="list-style-type: none"> <li>• In transition phase or upon outpatient admission, <b>measles vaccine</b> for children 6 months to 5 years, unless a document shows that the child received 2 doses of vaccine administered as follows: one dose at or after 9 months and one dose at least 4 weeks after the first dose. Children vaccinated between 6 and 8 months should be re-vaccinated as above (i.e. with 2 doses) once they reach 9 months of age, provided that an interval of 4 weeks from the first dose is respected.</li> <li>• Other vaccines included in the EPI: check vaccination status and refer the child to vaccination services at discharge.</li> </ul>
<b>Tuberculosis (TB)</b>	At D1 then regularly during treatment, screen for TB. For a child screening positive, perform complete diagnostic evaluation. For more information, refer to the guide <u>Tuberculosis</u> , MSF.
<b>HIV infection</b>	Perform HIV counselling and testing (unless the mother explicitly declines testing). <ul style="list-style-type: none"> <li>• Children under 18 months: test the mother with rapid diagnostic tests. For a mother testing positive, request PCR test for the child.</li> <li>• Children 18 months and over: test the child with rapid diagnostic tests.</li> </ul>

# Management of complications

## Infections

- Respiratory, cutaneous and urinary infections are common. However, classic signs of infection, such as fever, may be absent [1].
- Severe infection or sepsis should be suspected in children that are lethargic or apathetic or suffering from an acute complication such as hypothermia, hypoglycaemia, seizures, difficulty breathing, or shock. Immediately administer **ampicillin** IV 50 mg/kg every 8 hours + **gentamicin** IV 7.5 mg/kg once daily. Continue this treatment unless the source of infection is identified and different antibiotic treatment is required.
- If circulatory impairment or shock, immediately administer **ceftriaxone** IV, one dose of 80 mg/kg, then assess the source of infection to determine further antibiotic treatment. See also [Shock](#), Chapter 1. Transfuse urgently as for severe anaemia (see below) if haemoglobin (Hb) is < 6 g/dl.
- In less severe infections, assess the source of infection (see [Fever](#), Chapter 1) and treat accordingly.
- If fever is present and causes discomfort, undress the child. If insufficient, administer **paracetamol** PO in low dose: 10 mg/kg, up to 3 times maximum per 24 hours. Encourage oral fluids (including breast milk).
- If hypothermia is present, place the child skin-to-skin against the mother's body and cover with a warm blanket. Treat for infection as above. Check blood glucose level and treat for hypoglycaemia if necessary (see [Hypoglycaemia](#), Chapter 1).
- In children with kwashiorkor, infection of cutaneous lesions is common and may progress to soft tissue or systemic infection. If cutaneous infection is present, stop amoxicillin and start **amoxicillin/clavulanic acid** PO. Use formulations in a ratio of 8:1 or 7:1. The dose is expressed in amoxicillin: 50 mg/kg 2 times daily for 7 days.

## Severe anaemia

- Children with Hb < 4 or < 6 with signs of decompensation (such as respiratory distress) or ongoing blood loss require transfusion within the first 24 hours. See [Anaemia](#) (Chapter 1) for volume to be transfused and patient monitoring during and after transfusion.
- Preferably use packed red blood cells (PRBC), if available. Monitor closely for signs of fluid overload (see [box](#) below).

## Diarrhoea and dehydration

- Diarrhoea is common. Therapeutic foods facilitate the recovery of physiological function of the gastrointestinal tract. Amoxicillin administered as part of routine treatment reduces intestinal bacterial overgrowth. Diarrhoea generally resolves without additional treatment. If an aetiological treatment is necessary, see [Acute diarrhoea](#), Chapter 3.
- Zinc supplementation is not needed if children consume recommended amounts of therapeutic foods.
- The diagnosis of dehydration is based on history and clinical features.
- Clinical assessment is difficult in children with SAM as delayed skin pinch test and sunken eyes are often present even in the absence of dehydration.
- For classification of degree of dehydration adapted for children with SAM, see table below:

<b>Clinical features (2 or more of the following signs)</b>	<b>No dehydration</b>	<b>Some dehydration</b>	<b>Severe dehydration</b>
<b>Mental status</b>	Normal	Restless, irritability	Lethargic or unconscious
<b>Thirst</b>	No thirst, drinks normally	Thirsty, drinks eagerly	Unable to drink or drinks poorly
<b>Urine output</b>	Normal	Reduced	Absent for several hours
<b>Recent frequent watery diarrhoea and/or vomiting</b>	Yes	Yes	Yes
<b>Recent obvious rapid weight loss</b>	No	Yes	Yes

#### **Acute diarrhoea with no dehydration (Plan A SAM)**

- Stools are neither frequent nor abundant (outpatient): **oral rehydration solution (ORS)** PO: 5 ml/kg after each loose stool to prevent dehydration.
- Stools are frequent and/or abundant (inpatient): **ReSoMal<sup>c</sup>** PO or by nasogastric tube (NGT): 5 ml/kg after each loose stool to prevent dehydration.
- In all cases, continue feeding and breastfeeding, encourage oral fluids.

#### **Acute diarrhoea with some dehydration (Plan B SAM)**

- Determine the target weight (weight before the onset of diarrhoea) before starting rehydration. If not feasible (e.g. new admission), estimate target weight as current weight x 1.06.
- **ReSoMal<sup>c</sup>** PO or by NGT: 20 ml/kg/hour for 2 hours. In addition, administer 5 ml/kg of **ReSoMal** after each loose stool if tolerated.
- Assess after 2 hours (clinical evaluation and weight):
  - If improvement (diarrhoea and signs of dehydration regress):
    - ▷ Reduce **ReSoMal** to 10 ml/kg/hour until the signs of dehydration and/or weight loss (known or estimated) have been corrected.
    - ▷ Assess every 2 hours.
    - ▷ Once there are no signs of dehydration and/or the target weight is reached, change to Plan A SAM to prevent dehydration.
  - If no improvement after 2 to 4 hours or if oral rehydration cannot compensate for losses: change to Plan C SAM "with circulatory impairment".
- Continue feeding including breastfeeding.
- Monitor for signs of fluid overload (see [box](#) below). Regardless of the target weight, stop rehydration if signs of fluid overload appear.

#### **Acute diarrhoea with severe dehydration (Plan C SAM)**

- In all patients:
  - Assess for circulatory impairment (see [Shock](#), Chapter 1).
  - Estimate target weight as current weight x 1.1.

- Measure blood glucose level and treat [hypoglycaemia](#) (Chapter 1) if necessary.
- Monitor vital signs and signs of dehydration every 15 to 30 minutes.
- Monitor urine output.
- Monitor for signs of fluid overload (see [box](#) below).
- If there is no circulatory impairment:
  - **ReSoMal** PO or by NGT: 20 ml/kg over 1 hour
  - If the child is alert, continue feeding including breastfeeding.
  - Assess after 1 hour:
    - ▷ If improvement: change to Plan B SAM, but keep the same target weight.
    - ▷ If rehydration PO/NGT not tolerated (e. g. vomiting):
      - ▷ Stop ReSoMal. Administer **glucose 5%-Ringer lactate (G5%-RL)**<sup>d</sup> IV infusion: 10 ml/kg/hour for 2 hours.
      - ▷ Assess after 2 hours of IV fluids:
        - ▷ If improvement and/or not vomiting, stop G5%-RL IV infusion and change to Plan B SAM.
        - ▷ If no improvement or still vomiting, continue G5%-RL IV infusion: 10 ml/kg/hour for 2 hours.
      - ▷ If deterioration with circulatory impairment: see below.
  - If there is circulatory impairment:
    - Stabilize (see [Shock](#), Chapter 1).
    - Administer **ceftriaxone** IV, one dose of 80 mg/kg. Subsequent antibiotic treatment depends on assessment of underlying cause.
    - Administer **G5%-RL** IV infusion: 10 ml/kg/hour for 2 hours. Stop ReSoMal if the child was taking it.
    - Assess after 1 hour of IV fluids:
      - ▷ If improvement and no vomiting: stop IV fluid and change to Plan B SAM, but keep the same target weight.
      - ▷ If no improvement:
        - ▷ Continue **G5%-RL** IV infusion: 10 ml/kg/hour.
        - ▷ Prepare for blood transfusion.
    - Assess after 2 hours of IV fluids:
      - ▷ If improvement: change to Plan B SAM, but keep the same target weight.
      - ▷ If no improvement or deterioration:
        - ▷ Check Hb as baseline and administer blood transfusion using a separate IV line. See [Anaemia](#) (Chapter 1) for volume to be transfused and patient monitoring during and after transfusion.
        - ▷ While transfusing, continue **G5%-RL** IV infusion 10 ml/kg/hour for another 2 hours.



Signs of fluid overload include:

- RR ≥ 10 breaths/minute compared to initial RR, or
- HR ≥ 20 beats/minute compared to initial HR

Plus any one of the following:

- New or worsening hypoxia (decrease in SpO<sub>2</sub> by > 5%)
- New onset of rales and/or fine crackles in lung fields
- New galloping heart rhythm
- Increased liver size (must have marked liver border with pen before rehydration)
- New peripheral or eyelid oedema

## Other complications

For other complications (to be treated as inpatient), see:

- [Hypoglycaemia](#), [seizures](#), Chapter 1.
- [Acute pneumonia](#), Chapter 2.
- [Stomatitis](#), Chapter 3.
- [Xerophthalmia](#) (vitamin A deficiency), Chapter 5.

# Discharge criteria

In general:

- Children can be discharged from hospital and be treated as outpatients if the following criteria are met:
  - clinically well;
  - medical complications controlled;
  - able to eat RUTF (observed during appetite test);
  - reduction or absence of oedema;
  - caregiver feels able to provide care as outpatient;
  - vaccinations up to date or referral to vaccination service organised.
- Children can be discharged from nutritional treatment if the following criteria are met:
  - co-existing medical conditions stable and outpatient treatment organised if necessary (e.g. dressing changes, follow-up for chronic diseases);
  - vaccinations up to date or referral to vaccination service organised;
  - absence of oedema and WHZ > -2 or MUAC > 125 mm for at least 2 weeks.

Discharge criteria vary with context. Refer to national recommendations.

## Footnotes

- (a) MUAC is measured at the mid-point of the left upper arm. The arm should be relaxed. The measuring tape should be in contact with the skin all around the arm, without exerting pressure.
- (b) For WHZ, see WHO simplified field tables in z-scores for girls and for boys:  
<https://www.who.int/tools/child-growth-standards/standards/weight-for-length-height>
- (c) ReSoMal is a specific oral rehydration solution for malnourished children, containing less sodium and more potassium than standard ORS. It should be administered under medical supervision to avoid overdosing and hyponatremia.
- (d) Remove 50 ml of Ringer lactate (RL) from a 500 ml RL bottle or bag, then add 50 ml of 5% glucose to the remaining 450 ml of RL to obtain 500 ml of 5% glucose-RL solution.

## References

1. Jones KDJ, Berkley JA. Severe acute malnutrition and infection. *Paediatrics and International Child Health* 2014; 34(sup1): S1-S29.  
<https://www.tandfonline.com/doi/full/10.1179/2046904714Z.000000000218> [Accessed 24 August 2022]

# Chapter 2: Respiratory diseases

[Acute upper airway obstruction](#)

[Rhinitis and rhinopharyngitis \(common cold\)](#)

[Acute sinusitis](#)

[Acute pharyngitis](#)

[Diphtheria](#)

[Other upper respiratory tract infections](#)

[Croup \(laryngotracheitis and laryngotracheobronchitis\)](#)

[Epiglottitis](#)

[Bacterial tracheitis](#)

[Otitis](#)

[Acute otitis externa](#)

[Acute otitis media \(AOM\)](#)

[Chronic suppurative otitis media \(CSOM\)](#)

[Whooping cough \(pertussis\)](#)

[Bronchitis](#)

[Acute bronchitis](#)

[Chronic bronchitis](#)

[Bronchiolitis](#)

[Acute pneumonia](#)

[Pneumonia in children under 5 years of age](#)

[Pneumonia in children over 5 years and adults](#)

[Persistent pneumonia](#)

[Staphylococcal pneumonia](#)

[Asthma](#)

[Acute asthma \(asthma attack\)](#)

[Chronic asthma](#)

[Pulmonary tuberculosis](#)

# Acute upper airway obstruction

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	<ul style="list-style-type: none"><li>Respiratory distress followed by cardiac arrest</li></ul>	
Imminent complete	<ul style="list-style-type: none"><li>Severe respiratory distress with cyanosis or <math>\text{SpO}_2 &lt; 90\%</math></li><li>Agitation or lethargy</li><li>Tachycardia, capillary refill time &gt; 3 seconds</li></ul>	
Severe	<ul style="list-style-type: none"><li>Stridor (abnormal high pitched sound on inspiration) at rest</li><li>Severe respiratory distress:<ul style="list-style-type: none"><li>Severe intercostal and subcostal retractions</li><li>Nasal flaring</li><li>Substernal retractions (inward movement of the breastbone during inspiration)</li><li>Severe tachypnoea</li></ul></li></ul>	Yes
Moderate	<ul style="list-style-type: none"><li>Stridor with agitation</li><li>Moderate respiratory distress:<ul style="list-style-type: none"><li>Mild intercostal and subcostal retractions</li><li>Moderate tachypnoea</li></ul></li></ul>	No
Mild	<ul style="list-style-type: none"><li>Cough, hoarse voice, no respiratory distress</li></ul>	

## 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  $\text{SpO}_2$ , except in mild obstruction.
- Administer oxygen continuously:
  - to maintain the  $\text{SpO}_2$  between 94 and 98% if it is  $\leq 90\%$  <sup>a</sup> or if the patient has cyanosis or respiratory distress;
  - if pulse oximeter 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,  $\text{SpO}_2$  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 resuscitation. Tracheostomy if unable to ventilate.

## Differential diagnosis and management of airway obstructions of infectious origin

Infections	Symptoms	Appearance	Timing of symptoms
<b>Viral croup</b>	Stridor, cough and moderate respiratory difficulty	Prefers to sit	Progressive
<b>Epiglottitis</b>	Stridor, high fever and severe respiratory distress	Prefers to sit, drooling (cannot swallow their own saliva)	Rapid
<b>Bacterial tracheitis</b>	Stridor, fever, purulent secretions and severe respiratory distress	Prefers to lie flat	Progressive
<b>Retropharyngeal or tonsillar abscess</b>	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](#).
- Abscess: refer for surgical drainage.

## Management of other causes

- Anaphylactic reaction (angioedema): see [Anaphylactic shock](#) (Chapter 1)
- Burns to the face or neck, smoke inhalation with airway oedema: see [Burns](#) (Chapter 10).

## **Footnotes**

(a) If possible it is better to treat all patients with a SpO<sub>2</sub> < 95% with oxygen.

# Rhinitis and rhinopharyngitis (common cold)

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<sup>a</sup>.
  - Fever, throat soreness: paracetamol PO for 2 to 3 days ([Fever](#), Chapter 1).

## Footnotes

- (a) For a child: place him on his back, head turned to the side, and instil 0.9% sodium chloride into each nostril.

# Acute sinusitis

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](#)). 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](#) and [pain](#) (Chapter 1).
- Clear the nose with 0.9% sodium chloride<sup>a</sup>.

### 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<sup>b</sup>

Adults: 1 g 2 to 3 times daily

- In infants with ethmoiditis, see [Periorbital and orbital cellulitis](#) (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.

## Footnotes

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

(b) For dosage according to age or weight, see [erythromycin](#) in the guide Essential drugs, MSF.

# Acute pharyngitis

Last updated: November 2020

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<sup>[1][2]</sup>. 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](#), 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](#), 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](#), 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](#), Chapter 2).

## Treatment

- Symptomatic treatment (fever and pain): paracetamol or ibuprofen PO ([Fever](#), Chapter 1).
- Centor score  $\leq 1$ : viral pharyngitis, which typically resolves within a few days (or weeks, for IM): no antibiotic treatment.
- Centor score  $\geq 2$  or scarlet fever: antibiotic treatment for GAS infections <sup>[3]</sup> :
  - 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.  
**phenoxymethylenicillin (penicillin V)** PO for 10 days  
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  
Children under 1 year: 125 mg 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](#) (Chapter 9) and [syphilis](#) (Chapter 9).
- Diphtherial pharyngitis: see [Diphtheria](#) (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

Last updated: October 2022

Diphtheria is a bacterial infection due to *Corynebacterium diphtheriae*, spread from person to person through inhalation of infected respiratory droplets of symptomatic or asymptomatic individuals, or direct contact with contaminated objects or diphtheria skin lesions<sup>[1][2]a</sup>.

After infection, *C. diphtheriae* has an incubation period of 1 to 5 days (max. 10 days)<sup>[1]</sup> during which time it multiplies in the upper respiratory tract. The bacteria secretes a toxin which causes severe local as well as systemic effects. Death can occur from airway obstruction or as a result of systemic complications, including damage to the myocardium and nervous system, caused by the toxin.

Cases can remain infectious up to 8 weeks after initial infection<sup>[2]</sup>. Antibiotic treatment can reduce infectiousness to 6 days<sup>[3]</sup>.

Vaccination is the key to prevention and control of diphtheria. It protects individuals from severe disease (fewer and less severe symptoms) but does not prevent the spread of *C. diphtheriae*. Clinical disease does not confer protective immunity and vaccination is an integral part of case management.

## Clinical features

- During clinical examination respect standard, contact, and droplet precautions (handwashing, gloves, gown, mask, etc.). Conduct a careful examination of the throat.
- Signs of respiratory diphtheria<sup>a</sup> :
  - pharyngitis, rhinopharyngitis, tonsillitis or laryngitis with tough, greyish, firmly adherent pseudo-membranes of the pharynx, nasopharynx, tonsils, or larynx;
  - 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, larynx, trachea and bronchi;
  - fever is generally low-grade<sup>[2]</sup>.
- Generalised signs due to effects of the toxin:
  - cardiac dysfunction (tachycardia, arrhythmias), severe myocarditis with heart failure and possibly cardiogenic shock (see [Shock](#), Chapter 1) 3 to 7 days or 2 to 3 weeks after onset of the disease;
  - neuropathies in 2 to 8 weeks after the onset of disease leading to nasal voice and difficulty with swallowing (paralysis of the soft palate), vision (ocular motor paralysis), breathing (paralysis of respiratory muscles) and ambulation (limb paralysis);
  - oliguria, anuria and acute renal failure.
- Differential diagnoses: [Epiglottitis](#) and [Acute pharyngitis](#), Chapter 2, [Stomatitis](#), Chapter 3.

## Laboratory

- Diagnosis is confirmed by isolation of toxigenic *C. diphtheriae* by culture (and antibiotic susceptibility test) of swab specimens collected from the affected areas: throat (tonsils, pharyngeal mucosa, soft palate, exudate, ulcer, etc.), nasopharynx.
- The presence of the toxin is confirmed by PCR testing (detection of diphtheria toxin gene).

## Treatment

- Isolation of patients; standard, droplet, and contact precautions for medical staff.

- **Diphtheria antitoxin (DAT)<sup>b</sup>** derived from horse serum:

Administer DAT as soon as possible after disease onset. Do not wait for bacteriological confirmation<sup>[1]</sup>; administer DAT under close monitoring in a hospital setting, according to the Besredka method to assess possibility of allergy. Any delay can diminish efficacy.



There is a risk of 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 (see [Shock](#), Chapter 1).

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 cm 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
<b>Laryngitis or pharyngitis or duration &lt; 48 hours</b>	20 to 40 000	
<b>Rhinopharyngitis</b>	40 to 60 000	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.
<b>Severe disease (respiratory distress, shock), cervical oedema or duration ≥ 48 hours</b>	80 to 100 000	

- Antibiotic treatment (as soon as possible without waiting for bacteriological confirmation) for 14 days or according to length of treatment recommended by the national protocol:

- if the patient can swallow:

**azithromycin** PO (first-line)

Children: 10 to 12 mg/kg once daily (max. 500 mg daily)

Adults: 500 mg once daily

or

**erythromycin** PO

Children under 40 kg: 10 to 15 mg/kg (max. 500 mg) 4 times daily

Children 40 kg and over and adults: 500 mg 4 times daily

or

**phenoxycephalothin (penicillin V)** PO

Children under 40 kg: 10 to 15 mg/kg (max. 500 mg) 4 times daily

Children 40 kg and over and adults: 500 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

Children under 25 kg: 50 000 IU/kg (= 50 mg/kg) once daily (max. 1.2 MIU = 1.2 g daily)

Children 25 kg and over and adults: 1.2 MIU (= 1.2 g) once daily



Never administer procaine benzylpenicillin by IV injection or infusion.

In penicillin-allergic patients, use erythromycin IV<sup>c</sup>.

- Intubation/tracheotomy if necessary (airway obstruction, respiratory failure, etc.).
- If the event of shock, see [Shock](#), Chapter 1, for complementary treatment.
- Update every patient's vaccination status before hospital discharge (or during first visit, if receiving home-based care). If the patient has been administered DAT and can receive adequate home-based follow up after hospital discharge, wait 3 weeks after administration of DAT before vaccination.

# Management of close contacts

Close contacts include household members living under the same roof and people who were directly exposed (less than one metre) to nasopharyngeal secretions of the patient on a regular basis (e.g. family or close friends, children in the same class, medical personnel) during the 5 days or nights prior to onset of symptoms of the case<sup>[4]</sup>.

- Collect nasal and pharyngeal swabs for culture before starting antibiotic prophylaxis; temperature and throat examination daily (10 days); exclusion from school or work until 48 hours after starting antibiotic prophylaxis. If symptoms of respiratory infection appear: treat immediately as a case of diphtheria.
- Antibiotic prophylaxis:

## **benzathine benzylpenicillin IM**

Children under 30 kg: 600 000 IU single dose

Children 30 kg and over and adults: 1.2 MIU single dose



Benzathine benzylpenicillin should never be administered by IV route.

or azithromycin PO or erythromycin PO as above for 7 days.

- Check vaccination status:
  - if less than 3 injections received: complete vaccination schedule (see [Prevention](#) below);
  - if 3 injections received, with the last injection over one year ago: administer a booster dose immediately;
  - if 3 injections received, with the last injection less than one year ago: a booster dose is not immediately necessary.

# Outbreak surveillance measures

- A suspected case of diphtheria is defined as a person with:
  - pharyngitis, rhinopharyngitis, tonsillitis and/or laryngitisAND
  - an adherent pseudo-membrane of the pharynx, nose, tonsils and/or larynx<sup>[1]</sup>.
- Isolate and treat suspect cases without delay. Collect swab samples before starting antibiotic treatment. Submit case notification to the public health authorities within 24 hours<sup>[1]</sup>.

# Prevention

- Routine vaccination (EPI), for information: 3 doses of conjugate vaccine containing the higher potency (D) formulation of diphtheria toxoid as soon as possible as of 6 weeks of age and at 4 week intervals; D booster between 12 and 23 months, then between 4 and 7 years; booster with a vaccine containing a reduced dose (d) of diphtheria toxoid between 9 and 15 years<sup>[5]</sup>.
- Catch-up vaccination (individuals who have not received routine vaccination), for information:
  - children 1 to 6 years: 3 doses of conjugate vaccine containing the higher potency (D) formulation of diphtheria toxoid at least 4 weeks apart;
  - children 7 years and over and adults (including medical staff): 3 doses of conjugate vaccine containing a reduced dose (d) of diphtheria toxoid. Administer with a minimum interval of 4 weeks between first and second dose and an interval of at least 6 months between second and third dose (in the event of an outbreak this interval may be reduced to 4 weeks to achieve protection quicker).

Administer 2 subsequent booster doses containing d at least 4 weeks apart<sup>[5]</sup>.

## Footnotes

- (a) This guide focuses on respiratory diphtheria and signs due to the toxin. It should be noted that cutaneous diphtheria is still a significant reservoir of *C. diphtheriae*.

(b) DAT reduces mortality and should be given to all diphtheria patients. However, as supply is very limited, it may be necessary to define criteria and reserve DAT for the treatment of patients who will benefit the most from it. DAT can be administered to pregnant women.

(c) **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 20 kg and over and in adults. Do not dilute in glucose.

## References

1. World Health Organization. Diphtheria. Vaccine-Preventable Diseases Surveillance Standards. 2018. [https://www.who.int/immunization/monitoring\\_surveillance/burden/vpd/WHO\\_SurveillanceVaccinePreventable\\_04\\_Diphtheria\\_R2.pdf?ua=1](https://www.who.int/immunization/monitoring_surveillance/burden/vpd/WHO_SurveillanceVaccinePreventable_04_Diphtheria_R2.pdf?ua=1) [Accessed 11 August 2020]
2. Tiwari TSP, Wharton M. Chapter 19: Diphtheria Toxoid. In: Plotkin SA, Orenstein WA, Offit PA, editors. Vaccines. 7th ed. Philadelphia, PA: Elsevier; 2018. p. 261–275.
3. Truelove SA, Keegan LT, Moss WJ, Chaisson LH, Macher E, Azman AS, Lessler J. Clinical and Epidemiological Aspects of Diphtheria: A Systematic Review and Pooled Analysis. Clin Infect Dis. 2020 Jun 24;71(1):89–97. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7312233/> [Accessed 24 November 2020]
4. Pan American Health Organization, World Health Organization. Diphtheria in the Americas - Summary of the situation 2018. Epidemiological Update Diphtheria. 16 April 2018. [https://www.paho.org/hq/index.php?option=com\\_docman&view=download&category\\_slug=diphtheria-098968&alias=44497-16-april-2018-diphtheria-epidemiological-update-497&Itemid=270&lang=en](https://www.paho.org/hq/index.php?option=com_docman&view=download&category_slug=diphtheria-098968&alias=44497-16-april-2018-diphtheria-epidemiological-update-497&Itemid=270&lang=en) [Accessed 11 August 2020]
5. World Health Organization. Diphtheria vaccine: WHO position paper - August 2017. Weekly epidemiological record 2017; 92(31):417–436. [https://www.who.int/immunization/policy/position\\_papers/wer\\_31\\_diphtheria\\_updated\\_position\\_paper.pdf?ua=1](https://www.who.int/immunization/policy/position_papers/wer_31_diphtheria_updated_position_paper.pdf?ua=1) [Accessed 11 August 2020]

# Other upper respiratory tract infections

- [Laryngotracheitis and laryngotracheobronchitis \(croup\)](#)
- [Epiglottitis](#)
- [Bacterial tracheitis](#)

# Croup (laryngotracheitis and laryngotracheobronchitis)

Last updated: October 2024

Common viral respiratory infection with peak incidence amongst children between 6 months and 3 years.

## Clinical features

- Typical barking cough, hoarse voice or cry.
- Inspiratory stridor (abnormal high pitched sound on inspiration):
  - Croup is considered mild 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 intercostal, subcostal or sternal retractions, treat symptomatically: ensure adequate hydration, seek medical attention if symptoms worsen (e.g. respiratory difficulty, noisy breathing, inability to tolerate oral fluids).
- If stridor is only present with agitation (mild croup)<sup>[1]</sup>:
  - Assure adequate hydration.
  - Corticosteroids:
    - ▷ **dexamethasone** PO: 0.15 to 0.6 mg/kg (max. 16 mg)<sup>a</sup> single dose
    - ▷ or, if not available, **prednisolone** PO: 1 mg/kg single dose
  - Keep the child under observation at least 30 minutes after oral corticosteroid. Consider hospitalisation or longer observation (> 4 hours) if the child is less than 6 months old, or is dehydrated, or lives far from health facility.
- If danger signs are present (stridor at rest, respiratory distress, hypoxia) or the child is unable to drink, admit to hospital<sup>[1]</sup>:
  - Administer oxygen continuously if respiratory distress or SpO<sub>2</sub> < 92%: maintain SpO<sub>2</sub> between 94 and 98% (or if SpO<sub>2</sub> cannot be determined, at least 5 litres/minute).
  - Insert a peripheral IV line and provide IV hydration.
  - **Epinephrine (adrenaline)** via nebulizer<sup>[2]b</sup>: 0.5 mg/kg (max. 5 mg) to be repeated every 20 minutes if danger signs persist (see [table](#) below).  
Monitor heart rate during nebulization (if heart rate greater than 200, stop the nebulization).

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 (1 mg/ml, 1 ml ampoule)	3 ml	3.5 ml	4 ml	4.5 ml	5 ml
NaCl 0.9% <sup>(a)</sup>	1 ml	1 ml	-	-	-

(a) 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.

- Corticosteroids:
  - ▷ **dexamethasone<sup>c</sup>** PO (or IM or IV if the child is vomiting): 0.6 mg/kg (max. 16 mg) single dose (see [table below](#))
  - ▷ or, if not available, **prednisolone** PO: 1 mg/kg single dose

Weight	6-8 kg	9-11 kg	12-14 kg	15-17 kg
<b>Dose in mg</b>	4 mg	6 mg	8 mg	10 mg
<b>Dose in 2 mg tablet</b>	2 tab	3 tab	4 tab	5 tab
<b>Dose in ml (4 mg/ml, 1 ml ampoule)</b>	1 ml	1.5 ml	2 ml	2.5 ml

- Suspect bacterial tracheitis in a critically ill appearing child<sup>d</sup> with croup who does not improve with the above treatment.
- If the patient has a complete airway obstruction, intubation if possible or emergency tracheotomy.

## Footnotes

- (a) If children can easily return to hospital in case of deterioration or return of symptoms, administer 0.15 mg/kg of dexamethasone. Otherwise, the dose of 0.6 mg/kg should be used.
- (b) Although not licensed for this indication, epinephrine 1:1000 (1 mg/ml) should be used for nebulisation.
- (c) Administer orally if possible in order to avoid causing agitation in the child as this may worsen symptoms.
- (d) Critically ill appearing child: weak grunting or crying, drowsiness, difficult to arouse, does not smile, disconjugate or anxious gaze, pallor or cyanosis, general hypotonia.

## References

1. Pocket book of primary health care for children and adolescents: guidelines for health promotion, disease prevention and management from the newborn period to adolescence. Copenhagen: WHO Regional Office for Europe; 2022. Licence: CC BY-NCSA 3.0 IGO.  
<https://www.who.int/europe/publications/i/item/9789289057622>
2. Bjornson C, Russell K, Vandermeer B, Klassen TP, Johnson DW. Nebulized epinephrine for croup in children. Cochrane Acute Respiratory Infections Group, ed. Cochrane Database Syst Rev. Published online October 10, 2013.  
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# Epiglottitis

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<sup>a</sup>.



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)<sup>b</sup>. 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<sup>c</sup> 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)

## Footnotes

- (a) Critically ill appearing child: weak grunting or crying, drowsiness, difficult to arouse, does not smile, unconjugate or anxious gaze, pallor or cyanosis, general hypotonia.
- (b) For administration by IV route, ceftriaxone powder should 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.
- (c) Improvement criteria include: fever reduction, diminished respiratory distress, improved SpO<sub>2</sub>, improved appetite and/or activity.

# Bacterial tracheitis

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<sup>a</sup>.
- 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<sup>b</sup> (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<sup>c</sup> 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.

## Footnotes

- (a) Critically ill appearing child: weak grunting or crying, drowsiness, difficult to arouse, does not smile, unconjugate or anxious gaze, pallor or cyanosis, general hypotonia.
- (b) For administration by IV route, ceftriaxone powder should 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.
- (c) Improvement criteria include: fever reduction, diminished respiratory distress, improved SpO<sub>2</sub>, improved appetite and/or activity.

# Otitis

- [Acute otitis externa](#)
- [Acute otitis media \(AOM\)](#)
- [Chronic suppurative otitis media \(CSOM\)](#)

# Acute otitis externa

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](#)).
- 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  $\geq$  1 year: 3 drops 2 times daily  
Adults: 4 drops 2 times daily

# Acute otitis media (AOM)

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](#) and [pain](#): 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:
    - 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.
    - 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)

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 antibiotic therapy 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](#) (Chapter 7).

# Whooping cough (pertussis)

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, malnutrition, 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 antibioticotherapy.

	<b>Antibiotic</b>	<b>Children</b>	<b>Adults</b>
<b>First line</b>	<b>azithromycin</b> PO for 5 days	10 mg/kg once daily (max. 500 mg daily)	D1 500 mg D2 to D5 250 mg once daily
<b>Alternative<sup>(a)</sup></b>	<b>co-trimoxazole</b> 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

(a) 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.

- For hospitalised children:
  - Place the child in a semi-reclining position ( $\pm 30^\circ$ ).
  - 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.

# Bronchitis

- [Acute bronchitis](#)
- [Chronic bronchitis](#)

# Acute bronchitis

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](#)). In children under 2 years of age, consider bronchiolitis (see [Bronchiolitis](#)).

## 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:** 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

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](#)).
- Discourage smoking and other irritating factors.

# Bronchiolitis

Last updated: October 2023

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 signs of respiratory distress (exhaustion) and decline of respiratory rate (< 30/minute below the age of 1 year and < 20/minute below the age of 3 years). Exercise caution in interpreting these signs as indicators of clinical improvement.
  - SpO<sub>2</sub> persistently < 92%
  - 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 or longer.

Hospitalise children with one of the following criteria:

- Presence of any sign of severity
- Pre-existing pathology (cardiac or pulmonary disease, malnutrition, HIV infection, 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)<sup>a</sup>.
- Small, frequent feedings to reduce vomiting triggered by bouts of coughing.
- Increased fluids if fever and/or significant secretions are present.
- Treat fever (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 ( $\pm 30^\circ$ ).
  - 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 if respiratory distress or  $\text{SpO}_2 < 92\%$ .
  - 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 is not indicated but a trial treatment may be given in case of severe respiratory distress (**salbutamol** metered-dose inhaler, 100 micrograms/puff: 2 to 3 puffs with spacer, repeated 2 times 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.

## **Footnotes**

- (a) 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](#)
- [Pneumonia in children over 5 years and adults](#)
- [Persistent pneumonia](#)

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

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

## Clinical features

- Cough or difficulty breathing
- Fever often high ( $> 39^{\circ}\text{C}$ ), 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 severity.

- A child has tachypnoea (increased respiratory rate) if:
  - RR  $\geq 60$  breaths/minute in children under 1 months
  - RR  $\geq 50$  breaths/minute in children from 1 to 11 months
  - RR  $\geq 40$  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 severity (severe pneumonia):
  - Chest indrawing: the inferior thoracic wall depresses on inspiration as the superior abdomen expands
  - Cyanosis (lips, oral mucosa, fingernails) or  $\text{SpO}_2 < 90\%$
  - 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](#) in patients with empyema or painful abdominal swelling and diarrhoea.
- Pneumocystosis in children with confirmed or suspected HIV infection (see [HIV infection and AIDS](#), Chapter 8).
- Tuberculosis:
  - in a child with cough, fever and poor weight gain and a history of close contact with a tuberculous patient<sup>a</sup>. 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	<b>ampicillin</b> 50 mg/kg every 12 hours + <b>gentamicin</b> 3 mg/kg once daily
	≥ 2 kg	<b>ampicillin</b> 50 mg/kg every 8 hours + <b>gentamicin</b> 5 mg/kg once daily
Children 8 days - < 1 month		<b>ampicillin</b> 50 mg/kg every 8 hours + <b>gentamicin</b> 5 mg/kg once daily
Children 1 month - < 2 months		<b>ampicillin</b> 50 mg/kg every 6 hours + <b>gentamicin</b> 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](#), Chapter 7), or, as a last resort: **ceftriaxone** slow IV<sup>b</sup> (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<sup>c</sup> after 48 hours of well administered treatment, add **cloxacillin** IV for 10 to 14 days:

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

## Children from 2 months to 5 years

The first line treatment is:

**ceftriaxone** IM or slow IV<sup>b</sup> (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<sup>c</sup> 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](#)).

#### 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](#)).

### Adjvant therapy

- [Fever](#): 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  $\text{SpO}_2 \geq 90\%$  or, if pulse oximeter 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](#), Chapter 1).

## Pneumonia with no signs of severity

### Children under 2 months

Admit the child for inpatient care and treat for [severe pneumonia](#).

### 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<sup>c</sup>: continue with the same antibiotic to complete treatment.
- If there is no improvement after 3 days of correct administration: add azithromycin (see [Atypical pneumonia](#)).
- If the condition is deteriorating: hospitalise and treat as severe pneumonia.

### Footnotes

- (a) 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.
- (b) 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.
- (c) Improvement criteria include: fever reduction, diminished respiratory distress, improved  $\text{SpO}_2$ , improved appetite and/or activity.

# Pneumonia in children over 5 years and adults

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 severity (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 older patients, patients with 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<sup>a</sup> (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<sup>b</sup> 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<sup>b</sup> 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](#)).

## Adjvant therapy

- **Fever:** 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<sub>2</sub> ≥ 90% or, if pulse oximeter is not available, minimum 1 litre/minute.
- Maintain adequate hydration and nutrition.

## Pneumonia without signs of severity (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 patient's condition deteriorates:

- If the condition is improving<sup>b</sup>: continue with the same antibiotic to complete treatment.
- If there is no improvement after 3 days of correct administration: add azithromycin (see [Atypical pneumonia](#)).
- If the condition is deteriorating: hospitalise and treat as severe pneumonia.

## Footnotes

- (a) 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.
- (b) Improvement criteria include: fever reduction, diminished respiratory distress, improved SpO<sub>2</sub>, improved appetite and/or activity.

# Persistent pneumonia

Last update: November 2022

In patients not responding to therapy, consider atypical pneumonia, tuberculosis, pneumocystosis ([HIV infection and AIDS](#), 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 (max. 500 mg) once 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 (max. 500 mg) 4 times daily for 10 to 14 days

Adults: 500 mg 4 times daily for 10 to 14 days

or

**doxycycline** PO (except in pregnant or breastfeeding women)

Children under 45 kg: 2 to 2.2 mg/kg (max. 100 mg) 2 times daily for 10 to 14 days

Children 45 kg and over and adults: 100 mg 2 times daily for 10 to 14 days

# Staphylococcal pneumonia

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 distension.
- 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<sup>a</sup> (at least 3 minutes): 50 mg/kg once daily

+ **cloxacillin** IV infusion (60 minutes)<sup>b</sup>

Neonates 0 to 7 days (< 2 kg): 50 mg/kg every 12 hours

Neonates 0 to 7 days ( $\geq$  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 ( $\geq$  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<sup>c</sup>, 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: paracetamol (Chapter 1).
- Hydration by oral route or infusion or nasogastric tube depending on clinical condition.
- Oxygen at the flow rate required to maintain SpO<sub>2</sub>  $\geq$  90% or, if pulse oximeter 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.

## Footnotes

- (a) 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.
- (b) 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.
- (c) Improvement criteria include: fever reduction, diminished respiratory distress, improved SpO<sub>2</sub>, improved appetite and/or activity.

# Asthma

Last updated: June 2023

- [Acute asthma \(asthma attack\)](#)
- [Chronic asthma](#)

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. Symptoms are sometimes worse at night.

In children up to 5 years, 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.

# Acute asthma (asthma attack)

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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 [1][2][3]

Mild or moderate attack	Severe or life-threatening attack
<b>Able to talk in sentences</b>	<b>Cannot complete sentences in one breath</b> or <b>Too breathless to talk or feed</b>
Mild or moderate increase of <b>respiratory rate (RR)</b>	Very high <b>RR</b> Children 2-5 years: > 40/minute Children > 5 years and adults: > 30/minute
Normal or mild increase of <b>heart rate (HR)</b> Children 2-3 years: ≤ 180/minute Children 4-5 years: ≤ 150/minute Children > 5 years and adults: ≤ 120/minute	Very high <b>HR</b> Children 2-3 years: > 180/minute Children 4-5 years: > 150/minute Children > 5 years and adults: > 120/minute
<b>SpO<sub>2</sub> ≥ 90% (≥ 92% for children 2-5 years)</b>	<b>SpO<sub>2</sub> &lt; 90% (&lt; 92% for children 2-5 years)</b>
and <b>No criteria of severe or life-threatening attack</b>	<b>Signs of life-threatening attack:</b> Altered level of consciousness (drowsiness, confusion, coma) Exhaustion Silent chest Cyanosis Arrhythmia or hypotension in adults

## Treatment

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

### Mild to moderate attack

- Place the patient in a 1/2 sitting position.
- Administer:

- **salbutamol** metered-dose inhaler (MDI) 100 micrograms/puff: 2 to 10 puffs every 20 minutes during the first hour. In children, use a spacer<sup>a</sup> (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. A spacer can also be used in adults to increase effectiveness.
- **prednisolone** PO: one dose of 1 to 2 mg/kg (max. 50 mg) for children over 5 years and adults
- **oxygen** if SpO<sub>2</sub> < 94% <sup>b</sup>.
- If the attack is completely resolved:
  - Observe the patient for 1 hour (4 hours if they live far from the health centre) then give outpatient treatment: **salbutamol** MDI for 24 to 48 hours (2 to 4 puffs every 4 to 6 hours depending on clinical evolution) and **prednisolone** PO (same dose as above once daily) to complete 5 days of treatment.
  - Reassess after 1 to 2 days: address any identified risk factor, reassess need for salbutamol and long-term treatment. If the patient is already receiving long-term treatment, reevaluate the severity of the asthma (see [Chronic asthma](#)), review compliance and correct use of medications and adjust treatment if necessary.
- If the attack is only partially resolved, continue with **salbutamol** MDI (2 to 10 puffs every 1 to 4 hours) until symptoms subside. For children up to 5 years, administer one dose of **prednisolone** PO as above if symptoms recur within 3 to 4 hours. When the attack is completely resolved, proceed as above.
- If symptoms worsen or do not improve, treat as [severe attack](#).

## Severe attack

- Hospitalise<sup>c</sup>; place the patient in a 1/2 sitting position.
- Administer:
  - **oxygen** to maintain SpO<sub>2</sub> between 94 and 98% <sup>b</sup>.
  - **salbutamol + ipratropium** nebuliser solutions using a nebuliser (continue oxygen via nasal cannula during nebulisation):

Children < 5 years	<b>salbutamol</b> 2.5 mg (1.25 ml) + <b>ipratropium</b> 0.25 mg (1 ml) every 20 minutes for the first hour
Children 5 to 11 years	<b>salbutamol</b> 2.5 to 5 mg (1.25 to 2.5 ml) + <b>ipratropium</b> 0.5 mg (2 ml) every 20 minutes for the first hour
Children 12 years and over and adults	<b>salbutamol</b> 5 mg (2.5 ml) + <b>ipratropium</b> 0.5 mg (2 ml) every 20 minutes for the first hour

The two solutions should be mixed in the drug reservoir of the nebuliser. Assess symptoms at the end of each nebulisation.

If there is no nebuliser, use **salbutamol** MDI (same dose as for mild to moderate attack) and **ipratropium** MDI 20 micrograms/puff, 4 to 8 puffs every 20 minutes for the first hour.

- **prednisolone** PO: one dose of 1 to 2 mg/kg (max. 50 mg)
  - If prednisolone is not available, or if the patient cannot take oral treatment, administer:
    - ▷ Children: **dexamethasone** PO/IV/IM, one dose of 0.15 to 0.6 mg/kg (max. 16 mg)
    - ▷ Adults: **hydrocortisone** IV, 4 mg/kg (max. 100 mg) every 6 hours for 24 hours
- If symptoms do not improve after one hour:
  - transfer to intensive care unit
  - insert an IV line
  - **oxygen** to maintain SpO<sub>2</sub> between 94 and 98% <sup>b</sup>
  - continue **salbutamol** (solution for nebuliser) without ipratropium, and corticosteroids as above.
  - administer one dose of **magnesium sulfate** by IV infusion in 0.9% sodium chloride over 20 minutes, monitoring blood pressure:

- ▷ Children: 40 mg/kg (max. 2 g)
- ▷ Adults: 2 g
- If symptoms improve: continue **salbutamol** (solution for nebuliser) every 1 to 4 hours (depending on symptoms) and **oxygen** as above. Assess symptoms at the end of each nebulisation. When possible, switch to **salbutamol** MDI and continue as for mild to moderate attack.
- If the attack is completely resolved, observe the patient for at least 4 hours. Continue the treatment with **salbutamol** (MDI) and **prednisolone** PO and reassess as for a mild to moderate attack.

#### **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.

#### **Footnotes**

- (a) 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 patient breathes from the mouth of the bottle in the same way as they would with a spacer. The use of a plastic cup instead of a spacer is not recommended (ineffective).
- (b) If pulse oxymetry is not available, administer oxygen continuously in case of moderate, severe or life-threatening attack.
- (c) If signs of life-threatening attack, transfer to intensive care unit as soon as possible.

#### **References**

1. British guideline on the management of asthma. A national clinical guideline First published 2003. Revised edition published July 2019.  
<https://www.sign.ac.uk/our-guidelines/british-guideline-on-the-management-of-asthma/> [Accessed 12 January 2023]
2. Global INitiative for Asthma. Global Strategy for Asthma Management and Prevention. 2022 update.  
<https://ginasthma.org/gina-reports/> [Accessed 12 January 2023]
3. WHO Pocket book of primary health care for children and adolescents: guidelines for health promotion, disease prevention and management from the newborn period to adolescence. WHO Regional Office for Europe; 2022.  
<https://www.who.int/europe/publications/i/item/9789289057622> [Accessed 12 January 2023]

# Chronic asthma

Last updated: June 2023

## Clinical features

- Asthma should be suspected in patients with recurrent 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.
- 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.
- Any identified asthma risk factor (e.g. allergen, pollution, tobacco smoke exposure) should be eliminated where possible. The assessment of the frequency of symptoms and limitations of daily activities determines the treatment.

## Treatment

The mainstay of long-term treatment are inhaled corticosteroids (ICS) and long-acting beta-2 agonists (LABA). LABAs should never be used alone but always in combination with an ICS. Combination inhalers are preferred, when available. In addition to long-term treatment, salbutamol (short-acting beta-2 agonist, SABA) and combination inhalers can be used to reduce bronchoconstriction if the patient is symptomatic.

Treatment is started at the step most appropriate to initial severity then, re-evaluated and adjusted according to clinical response. An intervening severe asthma attack or loss of control necessitates treatment reassessment. The inhaler is chosen according to age. In children, a spacer should be used. Instructions on inhaler technique and information on asthma attack symptoms should be provided.

**Long-term treatment of asthma according to severity in children 6 years and over and adults<sup>[1][2]</sup>**

Symptoms	Children 6 to 11 years	Children ≥ 12 years and adults
<b>Intermittent asthma</b> <ul style="list-style-type: none"><li>• Daytime symptoms &lt; 2 times monthly</li><li>• Normal daily activities</li></ul>	<b>salbutamol</b> when symptomatic	<b>beclometasone/formoterol</b> when symptomatic
		OR <b>beclometasone + salbutamol</b> when symptomatic <sup>(a)</sup>
<b>Mild persistent asthma</b> <ul style="list-style-type: none"><li>• Daytime symptoms ≥ 2 times monthly</li><li>• Symptoms may affect daily activities</li></ul>	<b>beclometasone</b> (low dose) daily AND <b>salbutamol</b> when symptomatic	<b>beclometasone/formoterol</b> when symptomatic
		OR <b>beclometasone</b> (low dose) daily AND <b>salbutamol</b> when symptomatic
<b>Moderate persistent asthma</b> <ul style="list-style-type: none"><li>• Daytime symptoms most days OR nighttime symptoms ≥ once weekly</li><li>• Symptoms affect daily activities</li></ul>	<b>beclometasone</b> (low dose) + <b>salmeterol</b> daily <sup>(b)</sup> AND <b>salbutamol</b> when symptomatic	<b>beclometasone/formoterol</b> (low dose) daily AND <b>beclometasone/formoterol</b> when symptomatic
	OR <b>budesonide/formoterol</b> (very low dose) daily AND <b>budesonide/formoterol</b> when symptomatic	OR <b>beclometasone</b> (low dose) + <b>salmeterol</b> daily <sup>(b)</sup> AND <b>salbutamol</b> when symptomatic
<b>Severe persistent asthma</b> <ul style="list-style-type: none"><li>• Daily daytime symptoms OR very frequent nighttime symptoms</li><li>• Daily activities very limited by symptoms</li></ul>	<b>beclometasone</b> (medium dose) + <b>salmeterol</b> daily AND <b>salbutamol</b> when symptomatic	<b>beclometasone/formoterol</b> (medium dose) daily AND <b>beclometasone/formoterol</b> when symptomatic
	OR <b>budesonide/formoterol</b> (low dose) daily AND <b>budesonide/formoterol</b> when symptomatic	OR <b>beclometasone</b> (medium dose) + <b>salmeterol</b> daily <sup>(c)</sup> AND <b>salbutamol</b> when symptomatic

(a) Salbutamol should be taken just before beclometasone, or together if a combination inhaler is available.

(b) If salmeterol is not available, use beclometasone medium-dose.

(c) If salmeterol is not available, use beclometasone high-dose.

The doses vary according to the severity of asthma. Find the lowest possible effective dose necessary to both relieve symptoms and avoid local and systemic adverse effects.

**beclometasone MDI (ICS):**

	<b>Children 6 to 11 years</b>	<b>Children ≥ 12 years and adults</b>
<b>When symptomatic</b>	–	200 to 500 micrograms
<b>Long-term treatment</b>		
Low dose	50 to 100 micrograms 2 times daily	100 to 250 micrograms 2 times daily
Medium dose	150 to 200 micrograms 2 times daily	300 to 500 micrograms 2 times daily
High dose	–	> 500 micrograms 2 times daily

In all cases, do not exceed 2000 micrograms daily.

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

**salbutamol MDI 100 micrograms/puff (SABA):**

- Children and adults: 2 to 4 puffs up to 4 times daily if necessary

**salmeterol MDI 25 micrograms/puff (LABA):**

- Children 6 to 11 years: 2 puffs 2 times daily (max. 4 puffs daily)
- Children 12 years and over and adults: 2 to 4 puffs 2 times daily (max. 8 puffs daily)

**budesonide/formoterol MDI 80/4.5 micrograms/puff (ICS/LABA combination):**

- Children 6 to 11 years:
  - when symptomatic: 1 puff
  - long-term treatment, very low-dose: 1 puff once daily
  - long-term treatment, low-dose: 1 puff 2 times daily

In all cases, do not exceed 8 puffs daily.

**beclometasone/formoterol MDI 100/6 micrograms/puff (ICS/LABA combination):**

- Children 12 years and over and adults:
  - when symptomatic: 1 puff
  - long-term treatment, low-dose: 1 puff 2 times daily
  - long-term treatment, medium-dose: 2 puffs 2 times daily

In all cases, do not exceed 8 puffs daily.

Do not restrict exercise. If exercise is a trigger for asthma attacks, administer 1 or 2 puffs of salbutamol or beclometasone/formoterol 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 should be continued under close monitoring.

If symptoms have not been well controlled for a period of 2 to 3 months, check inhalation technique and adherence before changing to a stronger treatment.

If symptoms have been well controlled for a period of at least 3 months (the patient is asymptomatic or the asthma attacks are well controlled): try a step-wise reduction in medication.

## References

1. Global INitiative for Asthma. Global Strategy for Asthma Management and Prevention. 2022 update.  
<https://ginasthma.org/gina-reports/> [Accessed 23 January 2023]
2. WHO Pocket book of primary health care for children and adolescents: guidelines for health promotion, disease prevention and management from the newborn period to adolescence. WHO Regional Office for Europe; 2022.  
<https://www.who.int/europe/publications/i/item/9789289057622> [Accessed 23 January 2023]

# Pulmonary tuberculosis

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<sup>[1]</sup>.

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](#), 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<sup>[2]</sup>.
- If HIV co-infection suspected or diagnosed: Xpert® MTB/RIF test and point-of-care, urine LF-LAM (lateral flow urine lipoarabinomannan assay)<sup>[2]</sup>.

## 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<sup>[3]</sup>.
- 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](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/](https://www.who.int/immunization/policy/position_papers/bcg/en/) [Accessed 21 October 2019]

# **Chapter 3: Gastrointestinal disorders**

[Acute diarrhoea](#)

[Shigellosis](#)

[Amoebiasis](#)

[Disorders of the stomach and duodenum](#)

[Gastro-oesophageal reflux](#)

[Gastric and duodenal ulcers in adults](#)

[Dyspepsia](#)

[Stomatitis](#)

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[Oral herpes](#)

[Other infectious causes](#)

[Stomatitis from scurvy \(vitamin C deficiency\)](#)

[Other lesions resulting from a nutritional deficiency](#)

# Acute diarrhoea

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](#), 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](#) and [Amoebiasis](#) (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](#)).
- 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](#), Chapter 1.

Adapted treatment protocols are recommended for children with malnutrition (see [Severe acute malnutrition](#), 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 ( $\frac{1}{2}$  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](#), 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](#) (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](#), 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<sup>[1]</sup>.

## **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

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<sup>a</sup>, 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	
<b>ciprofloxacin</b> PO for 3 days Children: 15 mg/kg 2 times daily (max. 1 g daily) Adults: 500 mg 2 times daily	<ul style="list-style-type: none"><li>• if the strain is sensitive</li><li>• if there is no antibiotic sensitivity test</li><li>• if oral administration is possible</li></ul>
<b>ceftriaxone</b> IM for 3 days Children: 50 to 100 mg/kg once daily (max. 1 g daily) Adults: 1 to 2 g once daily	<ul style="list-style-type: none"><li>• in patients with severe infection and/or oral administration is not possible</li><li>• in pregnant women<sup>b</sup></li></ul>

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<sup>\[1\]\[2\]</sup>](#).

- For pain and/or fever:

**paracetamol** PO (see [Pain](#), 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](#), Chapter 1).

▫ zinc supplement in children under 5 years (see [Acute diarrhoea](#), Chapitre 3).

- Never give loperamide or any other antidiarrhoeal.

- Management of complications: rectal prolapse reduction, septicaemia (see [Septic shock](#), 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).

## **Footnotes**

(a) 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.).

(b) 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. World 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](http://apps.who.int/iris/bitstream/handle/10665/81170/9789241548373_eng.pdf;jsessionid=CE5C46916607EF413AA9FCA89B84163F?sequence=1) [Accessed 20 September 2018]

# Amoebiasis

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

## Investigations

- Amoebic dysentery: identification of mobile trophozoites (*E. histolytica histolytica*) in fresh stool samples
- Amoebic liver abscess: indirect haemoagglutination and ELISA
- POCUS<sup>a</sup>: perform an EFAST (extended focused assessment with sonography for trauma) examination, with additional views of the liver and spleen to evaluate for signs of amoebic lesions. Contact an expert (local or via telemedicine services) to help interpret the images and differentiate amoebic abscesses from other pathologies with similar characteristics.

## 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](#). 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](#), Chapter 1).
- Amoebic liver abscess
  - **tinidazole** PO: same treatment for 5 days
  - **metronidazole** PO: same treatment for 5 to 10 days

## **Footnotes**

(a) POCUS should only be performed and interpreted by trained clinicians.

# **Disorders of the stomach and duodenum**

- [Gastro-oesophageal reflux](#)
- [Gastric and duodenal ulcers in adults](#)
- [Dyspepsia](#)

# Gastro-oesophageal reflux

## 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)<sup>a</sup> : 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°).

## Footnotes

- (a) 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

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\*](#).

## 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](#), 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](#), 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\*](#)).

### 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](#), 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<sup>a</sup>.

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.

### Footnotes

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

# Dyspepsia

Last updated: December 2020

## Clinical features

Epigastric pain or discomfort following meals, often accompanied by bloating, sensation of fullness and nausea. Dyspepsia is most commonly functional. The diagnosis of functional dyspepsia is based on clinical assessment after ruling out organic causes ([Gastro-oesophageal reflux](#), [Gastric and duodenal ulcers](#), drug-induced symptoms, gastric cancer). If possible, test for *Helicobacter pylori*.

## Treatment

In adults:

- In case of patients who test positive for *H. pylori*, see [Eradication of \*Helicobacter pylori\*](#)<sup>[1]</sup>.
- **Omeprazole** PO (10 mg once daily) for 4 weeks may help even in *H. pylori*-negative patients<sup>[2][3]</sup>.

**Note:** consider and treat possible intestinal parasites (see [Intestinal protozoan infections](#), [Cestodes](#), [Nematode infections](#), Chapter 6; [Amoebiasis](#), Chapter 3).

## References

1. Ford AC, Mahadeva S, Carbone MF, Lacy BE, Talley NJ. Functional dyspepsia. Lancet. 2020 Nov 21;396(10263):1689-1702.
2. Moayyedi PM, Lacy BE, Andrews CN, et al. ACG and CAG clinical guideline: management of dyspepsia. Am J Gastroenterol. 2017 Jul;112(7):988-1013.  
[http://www.cag-acg.org/images/publications/CAG\\_CPG\\_Dyspepsia\\_AJG\\_Aug2017.pdf](http://www.cag-acg.org/images/publications/CAG_CPG_Dyspepsia_AJG_Aug2017.pdf) [Accessed 24 November 2020]
3. National Institute for Health and Care Excellence. Gastro-oesophageal reflux disease and dyspepsia in adults: investigation and management. Sept 2014.  
<https://www.nice.org.uk/guidance/CG184/chapter/1-Recommendations#interventions-for-functional-dyspepsia> [Accessed 24 November 2020]

# Stomatitis

- [Oral and oropharyngeal candidiasis](#)
- [Oral herpes](#)
- [Other infectious causes](#)
- [Stomatitis from scurvy \(vitamin C deficiency\)](#)
- [Other lesions resulting from a nutritional deficiency](#)

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

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](#), Chapter 8.

# Oral herpes

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](#), Chapter 8).

## Treatment

### Primary herpetic gingivostomatitis

- Treat [pain](#): 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](#), 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](#) (Chapter 2), [Diphtheria](#) (Chapter 2), [Measles](#) (Chapter 8).

# Stomatitis from scurvy (vitamin C deficiency)

## 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 administered 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<sub>2</sub> (riboflavin), niacin (see [Pellagra](#), Chapter 4) or vitamin B<sub>6</sub> (pyridoxine) deficiencies.

Iron deficiency may also provoke angular stomatitis (see [Anaemia](#), Chapter 1).

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

# **Chapter 4: Skin diseases**

[Dermatology](#)

[Scabies](#)

[Lice \(pediculosis\)](#)

[Superficial fungal infections](#)

[Bacterial skin infections](#)

[Impetigo](#)

[Furuncles and carbuncles](#)

[Erysipelas and cellulitis](#)

[Cutaneous anthrax](#)

[Endemic treponematoses](#)

[Leprosy](#)

[Herpes simplex and herpes zoster](#)

[Herpes simplex](#)

[Herpes zoster \(shingles\)](#)

[Other skin disorders](#)

[Eczema](#)

[Seborrheic dermatitis](#)

[Urticaria](#)

[Pellagra](#)

# 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

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  $\geq 60^{\circ}\text{C}$  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](#)).

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.

	<b>Children &lt; 2 years</b>	<b>Children 2 to 12 years</b>	<b>Children &gt; 12 years and adults</b>	<b>Pregnant women</b>
<b>Dilution</b>	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
<b>Contact time</b>	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
<b>Number of applications</b>	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)<sup>a</sup>.

Administration of ivermectin to patients with loiasis carries a risk of severe neurological complications when significant *Loa loa* microfilaraemia is present (see [Filariasis, Chapter 6](#))<sup>b</sup>.

**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.

## Footnotes

- (a) Treatment with ivermectin in these patients is reserved for severe cases for which no alternative exists (see [Crusted scabies](#)).
- (b) 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)

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](#) (Chapter 7), typhus ([Eruptive rickettsioses](#), 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  $\geq 60^{\circ}\text{C}$ /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,  $> 1\text{ cm}$  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](#)); local treatment is applied later when tolerated.

# Superficial fungal infections

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](#), Chapter 3.
- Vulvovaginal candidiasis: see [Abnormal vaginal discharge](#), Chapter 9.

### Dermatophytoses

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

Anatomic site <sup>(a)</sup>	Clinical features	Treatment
<b>Scalp</b> Scalp ringworm <i>Tinea capitis</i>	<p>Common in children. Depending on the species:</p> <ul style="list-style-type: none"> <li>• One or more round, scaly, erythematous plaques with the ends of broken hairs.</li> <li>• Inflammation, suppuration, crusting and peripheral lymphadenopathy (kerion).</li> <li>• Permanent hair loss (favus).</li> </ul> <p>Some scalp ringworms are contagious: simultaneously examine (and treat) symptomatic contacts.</p>	<ul style="list-style-type: none"> <li>• Shave or cut hair short on and around the lesions.</li> <li>• Local treatment: 2 times daily, clean with soap and water, dry and apply <b>miconazole 2% cream</b> or <b>Whitfield's ointment</b> for 2 weeks or longer if necessary.</li> <li>• Administer systemic treatment as local treatment alone does not cure scalp ringworm: <b>griseofulvin</b> 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 <b>itraconazole</b> 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</li> <li>• Suppurative lesions: treat superinfection (see <u>Impetigo</u>) before applying local antifungal treatment.</li> <li>• For painful kerion: paracetamol PO. <i>In pregnant/lactating/breastfeeding women:</i> 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.</li> </ul>
<b>Glabrous skin</b> Ringworm of the body <i>Tinea corporis</i>	Erythematous, scaly, pruritic macule with a well-demarcated, raised, vesicular border and central healing.	<ul style="list-style-type: none"> <li>• For non widespread, localised tinea: Local treatment: 2 times daily, clean with soap and water, dry and apply <b>miconazole 2% cream</b> or <b>Whitfield's ointment</b> for 2 to 4 weeks or for 2 weeks after clinical resolution.</li> <li>• Reserve oral antifungals for particularly extensive lesions: griseofulvin PO for 4 to 6 weeks or itraconazole for 2 weeks.</li> </ul>
Folds	• Interdigital spaces ( <i>Tinea pedis</i> ):	Topical treatment as above. If oozing

<i>Tinea pedis</i> (athlete's foot)	Pruritus, fissure and whitish scales in the 3 <sup>rd</sup> and/or 4 <sup>th</sup> interdigital spaces <sup>(b)</sup> .	
<i>Tinea cruris</i>	<ul style="list-style-type: none"> <li>• Groin (<i>Tinea cruris</i>):</li> </ul> <p>Circumscribed, pruritic, erythematous plaque, with a pale centre surrounded by vesiculo- pustules, extending outward from the groin.</p>	lesions, use <b>miconazole 2%</b> cream only (do not use Whitfield's ointment).

(a) 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.

(b) In candidal intertrigo, lesions are usually located in the 1st and 2nd interdigital spaces.

# Bacterial skin infections

- [Impetigo](#)
- [Furuncles and carbuncles](#)
- [Erysipelas and cellulitis](#)

# Impetigo

Impetigo is a benign, contagious infection of the epidermis due to group A  $\beta$ -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 of 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<sup>a</sup>:  
**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, administer cloxacillin 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](#), [scabies](#), [eczema](#), [herpes](#), [scalp ringworm](#), or an ENT infection.
- Trace and treat contacts.
- Check for proteinuria (use urine dipstick) 3 weeks after the infection.

## Footnotes

- (a) 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

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<sup>a</sup>:  
**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.

## Footnotes

- (a) 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

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](#), Chapter 5. If the infection is perifollicular, see [Furuncles and carbuncles](#), 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](#), Chapter 10).
- Other complications: septicaemia (see [Septic shock](#), 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<sup>a</sup>.
  - Bed rest, elevation of affected area (e.g. leg).
  - Treatment of [pain](#) (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](#), 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 <sup>b</sup>, 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 antibiotic therapy <sup>c</sup> :

**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 antibiotic therapy <sup>d</sup> :

▫ First line therapy:

**cloxacillin** IV infusion over 60 minutes <sup>e</sup>

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 <sup>f</sup>

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.

## Footnotes

- The erythema will regress if the treatment is effective. If the erythema spreads consider a treatment failure (MRSA or a necrotising infection).
- 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.
- For penicillin-allergic patients, **clindamycin** PO for 7 to 10 days (children: 10 mg/kg 3 times daily; adults: 600 mg 3 times daily).
- For penicillin-allergic patients, **clindamycin** IV infusion (children: 10 mg/kg 3 times daily; adults: 600 mg 3 times daily).
- 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.

- (f) 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

Last updated: September 2022

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 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<sup>a</sup>: culture and drug 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.
- Antibiotic treatment for 7 to 10 days:
  - First-line antibiotics:  
**ciprofloxacin** PO (including in pregnant or breastfeeding women and children)  
Children: 15 mg/kg (max. 500 mg) 2 times daily  
Adults: 500 mg 2 times daily  
or  
**doxycycline** PO (except in pregnant or breastfeeding women)  
Children under 45 kg: 2 to 2.2 mg/kg (max. 100 mg) 2 times daily  
Children 45 kg and over and adults: 100 mg 2 times daily
  - Alternatives include:  
**clindamycin** PO (in patients allergic to first-line antibiotics)  
Children: 10 mg/kg (max. 600 mg) 3 times daily  
Adults: 600 mg 3 times daily  
or

**amoxicillin** PO, if penicillins are effective (documented susceptibility)

Children: 30 mg/kg (max. 1 g) 3 times daily

Adults: 1 g 3 times daily

## Severe cutaneous anthrax

- Combined antibiotic treatment for 14 days:



Do not mix the two antibiotics in the same infusion bag (incompatibility).

- First-line:

**ciprofloxacin** IV infusion over 60 minutes<sup>b</sup>

Children: 10 mg/kg (max. 400 mg) every 8 hours

Adults: 400 mg every 8 hours

+ **clindamycin** IV infusion over 30 minutes<sup>b</sup>

Children 1 month and over: 10 to 13 mg/kg (max. 900 mg) every 8 hours

Adults: 900 mg every 8 hours

- Alternative, if penicillins are effective (documented susceptibility):

**ampicillin** IV infusion over 30 minutes<sup>b</sup>

Children 1 month and over: 50 mg/kg (max. 3 g) every 6 hours or 65 mg/kg (max. 4 g) every 8 hours

Adults: 3 g every 6 hours or 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 uncomplicated cutaneous anthrax.

- Intensive care: symptomatic treatment of shock (see [Shock](#), 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 uncomplicated cutaneous anthrax.
- Livestock vaccination; burial or burning of animal carcasses.

## Footnotes

(a) Samples can be stored (including transport time) for 7 days max. in cold chain (if not available, at a temperature < 30 °C).

(b) Dilute each dose of ciprofloxacin, clindamycin or ampicillin 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 above and in adults. Administer ciprofloxacin more slowly than clindamycin or ampicillin.

# **Endemic treponematoses**

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](#), Chapter 9.

## **Clinical features**

	<b>Yaws</b>	<b>Pinta</b>	<b>Bejel</b>
<b>Pathogen</b>	<i>Treponema pertenue</i>	<i>Treponema carateum</i>	<i>Treponema pallidum</i> type M
<b>Geographic distribution</b>	Tropical and humid forests	Tropical zones of Latin America	Arid areas, semi-desert of the Middle East and Africa
<b>Population</b>	Children between 4 and 14 years	Children and adults	Nomadic populations, particularly children
<b>First stage</b>	<p>Yaws chancre: skin coloured lesion, non-indurated, itchy, on the lower limbs in 95% of cases, with peripheral adenopathy.</p> <p>Spontaneous healing or development of a large yaw surrounded by smaller yaws.</p>	<p>Annular, erythematous, scaly plaques, usually on uncovered body parts (face, extremities), resemble dermatophytes.</p> <p>Lesions heal spontaneously leaving scars.</p>	<p>Discrete chancre: moist papule, most commonly on the mucous membranes or in dermal folds, with peripheral adenopathy.</p>
<b>Second stage</b>	<p>Lesions appear 3 weeks after the initial chancre, occur in crops and heal spontaneously:</p> <ul style="list-style-type: none"> <li>• Frambesioma (papillomatous lesion, vegetal, very contagious)</li> <li>• Isolated or associated with yaws (round, squamous papules, not very contagious)</li> <li>• Osteoperiostitis of the long bones (phalanges, nasal process of the maxilla, tibia)</li> </ul>	<p>Pintids: plaques of various colours (bluish, reddish, whitish). May occur anywhere on the body.</p>	<ul style="list-style-type: none"> <li>• 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</li> <li>• Condyloma in the anogenital region (rare)</li> <li>• Cutaneous lesions are rare: vegetal aspect, in dermal folds</li> <li>• Bone destruction identical to that of yaws, in the legs and forearms</li> </ul>
<b>Late stage</b>	<p>After some years of latency:</p> <ul style="list-style-type: none"> <li>• Periostitis; painful, debilitating osteitis</li> <li>• Ulcerating and disfiguring rhinopharyngitis</li> <li>• Juxta-articular nodules</li> </ul>	<p>Symmetrical white patches on the limbs. The depigmentation is permanent, remaining after treatment.</p>	<p>After several years of latency:</p> <ul style="list-style-type: none"> <li>• Gummatus lesions of skin and long bones</li> <li>• Plantar and palmar keratosis</li> <li>• Juxta-articular nodules</li> <li>• Hyper- and hypo-pigmented patches (as in pinta)</li> </ul>

# Treatment

## Yaws

### **azithromycin PO<sup>[1]</sup>**

Children and adults: 30 mg/kg single dose (max. 2 g)

or, if not available,

### **benzathine benzylpenicillin IM<sup>[2][3]</sup>**

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 [Accessed 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> [Accessed 15 May 2018]

# Leprosy

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.<sup>[1]</sup>

## 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, deformities 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 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	<b>rifampicin</b> PO: 450 mg once monthly + <b>clofazimine</b> PO: 150 mg once monthly and 50 mg on alternate days + <b>dapsone</b> PO: 50 mg once daily	<b>rifampicin</b> PO: 450 mg once monthly + <b>clofazimine</b> PO: 150 mg once monthly and 50 mg on alternate days + <b>dapsone</b> PO: 50 mg once daily
Children 15 years and over and adults	<b>rifampicin</b> PO: 600 mg once monthly + <b>clofazimine</b> PO: 300 mg once monthly and 50 mg once daily + <b>dapsone</b> PO: 100 mg once daily	<b>rifampicin</b> PO: 600 mg once monthly + <b>clofazimine</b> PO: 300 mg once monthly and 50 mg once daily + <b>dapsone</b> PO: 100 mg once daily
Duration	<b>12 months</b>	<b>6 months</b>

**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.<sup>[2]</sup>

For example, for an adult:<sup>[3]</sup>

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.<sup>[2]</sup>
  - Fever: paracetamol PO (see [Fever](#), 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](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](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](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](#)
- [Herpes zoster \(shingles\)](#)

# **Herpes simplex**

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](#), Chapter 3), genital ([Genital ulcers](#), 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](#).

# **Herpes zoster (shingles)**

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](#), 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](#), Chapter 8).

# Other skin disorders

- [Eczema](#)
- [Seborrheic dermatitis](#)
- [Urticaria](#)
- [Pellagra](#)

# 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](#).
- For patients with intense pruritus, antihistamines for a few days (see [Urticaria](#)).

# Seborrheic dermatitis

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](#)).

# Urticaria

Last updated: July 2022

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, strongyloidiasis, 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

- In the event of anaphylactic reaction, see [Shock](#) (Chapter 1).

# Pellagra

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<sup>[1]</sup>**

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](http://www.who.int/nutrition/publications/en/pellagra_prevention_control.pdf) [Accessed 23 May 2018]

# Chapter 5: Eye diseases

[Xerophthalmia \(vitamin A deficiency\)](#)

[Conjunctivitis](#)

[Neonatal conjunctivitis](#)

[Viral epidemic keratoconjunctivitis](#)

[Trachoma](#)

[Periorbital and orbital cellulitis](#)

[Other pathologies](#)

[Onchocerciasis \(river blindness\)](#)

[Loiasis](#)

[Pterygium](#)

[Cataract](#)

# Xerophthalmia (vitamin A deficiency)

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 <sup>(a)</sup>
Children < 6 months <sup>(b)</sup>	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<sup>a</sup>, routine supplementation of **retinol** PO:

<b>Age</b>	<b>200 000 IU capsule<sup>(c)</sup></b>
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

(c) 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.

## Footnotes

- (a) 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](#)
- [Viral epidemic keratoconjunctivitis](#)

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 conjunctivitis 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](#)).
- 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](#), Chapter 4).

**Note:** in the event of a foreign body, check tetanus immunisation status.

# Neonatal conjunctivitis

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.
- Antibiotic treatment:
  - 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
<b>First line</b>	<b>ceftriaxone</b> IM: 50 mg/kg single dose (max. 125 mg)	<b>ceftriaxone</b> IM: 50 mg/kg single dose (max. 125 mg) + <b>azithromycin</b> PO: 20 mg/kg once daily for 3 days
<b>Alternatives</b>	If ceftriaxone contra-indicated: <b>cefotaxime</b> IM: 100 mg/kg single dose	If azithromycin unavailable: <b>erythromycin</b> 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](#), Chapter 9).
- Azithromycin and erythromycin are associated with an increased risk of pyloric stenosis in neonates. The risk is higher with erythromycin<sup>[1][2][3]</sup>. Adverse effects should be monitored.

## Prevention

Apply as soon as possible and preferably within one hour after birth:

**1% tetracycline eye ointment:** application of 1 cm in each eye.

## References

1. Lund M et al. Use of macrolides in mother and child and risk of infantile hypertrophic pyloric stenosis: nationwide cohort study. *BMJ*. 2014; 348: g1908.  
<https://www.bmjjournals.org/content/348/bmj.g1908> [Accessed 16 April 2021]
2. Murchison L et al. Post-natal erythromycin exposure and risk of infantile hypertrophic pyloric stenosis: a systematic review and meta-analysis. *Pediatr Surg Int*. 2016 Dec; 32(12): 1147-1152.  
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5106491/> [Accessed 16 April 2021]
3. Almaramhy HH et al. The association of prenatal and postnatal macrolide exposure with subsequent development of infantile hypertrophic pyloric stenosis: a systematic review and meta-analysis. *Ital J Pediatr*. 2019 Feb 4; 45(1)20.  
<https://ijponline.biomedcentral.com/articles/10.1186/s13052-019-0613-2> [Accessed 16 April 2021]

# 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](#).

# Trachoma

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<sup>[1][2]</sup> :

- Stage 1: 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 2: 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 3: trachomatous scarring (TS)  
Follicles disappear, leaving scars: scars are white lines, bands or patches in the tarsal conjunctiva.
- Stage 4: trachomatous trichiasis (TT)  
Due to multiple scars the margin of the eyelid, usually the upper lid, turns inwards (entropion); the eyelashes rub against the cornea and cause ulcerations and chronic inflammation.
- Stage 5: corneal opacity (CO)  
Cornea gradually loses its transparency, leading to visual impairment and blindness.

## Treatment

- Stages 1 and 2:
  - Clean eyes and face several times per day.
  - Antibiotic treatment<sup>[3]</sup> :  
The treatment of choice is **azithromycin PO**:  
Children: 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, or, as a last resort, **erythromycin PO**: 20 mg/kg (max. 1 g) 2 times daily for 14 days.
- Stage 3: no treatment
- Stage 4: 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 a 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 5: no treatment

## Prevention

Cleaning of the eyes, face and hands with clean water reduces direct transmission and the development of secondary bacterial infections.

## References

1. Solomon AW et al. The simplified trachoma grading system, amended. Bull World Health Organ. 2020;98(10):698-705.  
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7652564/> [Accessed 20 April 2021]
2. Thylefors B et al. A simple system for the assessment of trachoma and its complications. Bull World Health Organ. 1987;65(4):477–83.  
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2491032/> [Accessed 20 April 2021]
3. Evans JR et al. Antibiotics for trachoma. Cochrane Database Syst Rev. 2019 Sep 26;9:CD001860.  
<https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD001860.pub4/full> [Accessed 20 April 2021]

# Periorbital and orbital cellulitis

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<sup>a</sup>, 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<sup>b</sup>:

**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<sup>c</sup>:

**ceftriaxone** slow IV<sup>d</sup> (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)<sup>e</sup>

Neonates 0 to 7 days (< 2 kg): 50 mg/kg every 12 hours

Neonates 0 to 7 days ( $\geq 2$  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 ( $\geq 2$  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  $\geq 40$  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)<sup>f</sup>

Neonates 0 to 7 days (< 2 kg): 5 mg/kg every 12 hours

Neonates 0 to 7 days ( $\geq 2$  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 ( $\geq 2$  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.

## Footnotes

- (a) 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.
- (b) For penicillin-allergic patients, **clindamycin** PO for 7 to 10 days:  
Children: 10 mg/kg 3 times daily; adults: 600 mg 3 times daily
- (c) For penicillin-allergic patients, **clindamycin** IV infusion (doses as above).
- (d) For administration by IV route, ceftriaxone powder should 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.
- (e) 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.
- (f) 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](#)
- [Loiasis](#)
- [Pterygium](#)
- [Cataract](#)

# 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](#), 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](#), 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 [Loiasis](#), 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](#)

[Human African trypanosomiasis \(sleeping sickness\)](#)

[American trypanosomiasis \(Chagas disease\)](#)

[Leishmaniases](#)

[Intestinal protozoan infections \(parasitic diarrhoea\)](#)

[Flukes](#)

[Schistosomiases](#)

[Cestodes](#)

[Nematode infections](#)

[Filariasis](#)

[Onchocerciasis \(river blindness\)](#)

[Loiasis](#)

[Lymphatic filariasis \(LF\)](#)

# Malaria

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<sup>[1]</sup> 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  $\geq$  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<sup>[2]</sup>

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)<sup>a</sup>

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](#), Chapter 1).

## **Treatment of malaria due to *P. vivax*, *P. ovale*, *P. malariae*, *P. knowlesi***

### **chloroquine (CQ) PO<sup>b</sup>**

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)<sup>c</sup> should be used instead<sup>[1]</sup>. For dosing information, see [Treatment of uncomplicated falciparum malaria](#).

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](#).

Treatment is an artemisinin-based combination therapy (ACT)<sup>c</sup> given by the oral route for 3 days<sup>[1]</sup>. 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<sup>b</sup>

ACT	Presentation	Dosage
artemether/lumefantrine (AL)	Coformulated tablets of 20 mg artemether/120 mg lumefantrine  Blister child 5 to < 15 kg, 6 tab/blister Blister child 15 to < 25 kg, 12 tab/blister Blister child 25 to < 35 kg, 18 tab/blister Blister child ≥ 35 kg and adult, 24 tab/blister  Coformulated tablets of 80 mg artemether/ 480 mg lumefantrine Blister child ≥ 35 kg and adult, 6 tab/blister	On D1, the first dose is given at 0 hour and the 2 <sup>nd</sup> dose at 8-12 hours. Subsequent doses on D2 and D3 are given 2 times daily (morning and evening).  ==> 1 tab 2 times daily on D1, D2, D3 ==> 2 tab 2 times daily on D1, D2, D3 ==> 3 tab 2 times daily on D1, D2, D3 ==> 4 tab 2 times daily on D1, D2, D3  ==> 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 Blister child 9 to < 18 kg, tab of AS 50 mg/AQ base 135 mg, 3 tab/blister Blister child 18 to < 36 kg, tab of AS 100 mg/AQ base 270 mg, 3 tab/blister Blister child ≥ 36 kg and adult, tab of AS 100 mg/AQ base 270 mg, 6 tab/blister	  ==> 1 tab once daily on D1, D2, D3  ==> 1 tab once daily on D1, D2, D3  ==> 1 tab once daily on D1, D2, D3  ==> 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 Blister child, tab of DHA 40 mg/PPQ 320 mg, 3 tab/blister Blister child, tab of DHA 40 mg/PPQ 320 mg, 6 tab/blister Blister adolescent-adult, tab of DHA 40 mg/PPQ 320 mg, 9 tab/blister Blister adolescent-adult, tab of DHA 40 mg/PPQ 320 mg, 12 tab/blister	  5 to < 8 kg: 1 tab 20/160 mg once daily on D1, D2, D3 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 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 36 to < 60 kg: 3 tab 40/320 mg once daily on D1, D2, D3 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<sup>[3]</sup>.

### 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<sup>b</sup>

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](#), Chapter 1).

## Treatment of severe malaria

The patient must be hospitalised.

## Antimalarial treatment

During pregnancy, see [Antimalarial treatment in pregnant women](#).

## 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<sup>d</sup>** (10 mg/kg)
  - Children 2 months to < 3 years ( $\leq 10$  kg): 1 rectal capsule (100 mg)
  - Children 3 to < 6 years ( $\leq 20$  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 1](#).

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](#), Chapter 1).

## Severe anaemia

For treatment, see [Anaemia](#), Chapter 1.

## Hypoglycaemia

For treatment, see [Hypoglycaemia](#), 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<sup>e</sup>.
- 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](#), Chapter 7).
- Reposition the patient every 2 hours; ensure eyes and mouth are kept clean and moist, etc.

## Seizures

See [Seizures](#), 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](#), 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](#), 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](#) can be used in all trimesters.

If ACTs are not available, quinine PO (for dosing, see [Treatment of uncomplicated falciparum malaria](#)) 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<sup>[4]</sup>.
- 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.

## Footnotes

(a) 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.

(b) 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](#).

- (c) ACT: a combination of artemisinin or one of its derivatives (e.g. artesunate, artemether) with another antimalarial of a different class.
- (d) 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).
- (e) 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](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 *Plasmodium falciparum* malaria control in highly seasonal transmission areas of the Sahel sub-region in Africa. 2012.  
[https://www.who.int/malaria/publications/atoz/smcpolicy\\_recommendation\\_en\\_032012.pdf?ua=1](https://www.who.int/malaria/publications/atoz/smcpolicy_recommendation_en_032012.pdf?ua=1)

# Human African trypanosomiasis (sleeping sickness)

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 hyperesthesia), 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  $\leq 5$  white cells/mm<sup>3</sup>

- Meningoencephalitic stage: evidence of trypanosomes OR  $> 5$  white cells/mm<sup>3</sup>

## 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)

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<sup>a</sup>. It is significantly underdiagnosed.<sup>[1]</sup>

## 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:<sup>[2]</sup>
  - 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<sup>[1]</sup>

- 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.<sup>b</sup>

### Other investigations

- ECG may demonstrate conduction disorders.
- Chest or abdominal x-ray may demonstrate cardiomegaly, megaoesophagus or megacolon.

## Treatment

## Aetiological 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 <sup>(a)</sup>	2 to 12 years <sup>[3]</sup>	5 to 8 mg/kg daily in 2 divided doses for 60 days
	> 12 years and adults <sup>[4]</sup>	5 to 7 mg/kg daily in 2 divided doses for 60 days
nifurtimox PO <sup>(b)[3]</sup>	≤ 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](#) (Chapter 1), [Pain](#) (Chapter 1) and [Heart failure](#) (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.

## Footnotes

(a) For more information on geographical distribution of cases of *T. cruzi* infection:  
[http://gamapserver.who.int/mapLibrary/Files/Maps/Global\\_chagas\\_2009.png](http://gamapserver.who.int/mapLibrary/Files/Maps/Global_chagas_2009.png)

(b) 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](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

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 pentavalent 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)

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](#), 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](#), Chapter 1).
- If the causal agent has been identified in the stool:

<b>Giardiasis</b>	<b>tinidazole</b> PO single dose Children: 50 mg/kg (max. 2 g) Adults: 2 g or <b>metronidazole</b> PO for 3 days Children: 30 mg/kg once daily Adults: 2 g once daily
<b>Cryptosporidiosis</b>	In immunocompetent patients, no aetiological treatment; spontaneous resolution in 1 to 2 weeks.
<b>Cyclosporiasis</b>	<b>co-trimoxazole</b> 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 spontaneously in 1 to 3 weeks. Treatment is given in case of severe or prolonged symptoms.
<b>Isosporiasis</b>	<b>co-trimoxazole</b> PO for 7 to 10 days Adults: 800 mg SMX + 160 mg TMP 2 times daily In immunocompetent patients, symptoms usually resolve spontaneously 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](#), 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
<b>Lung flukes</b> <i>Paragonimus</i> sp <i>Distribution:</i> South-East Asia, China, parts of Cameroon, Nigeria, Gabon, Congo, Colombia, Peru <i>Transmission:</i> 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).	<b>praziquantel</b> PO Children 4 years and over and adults: 25 mg/kg 3 times daily for 2 days
<b>Hepatobiliary flukes</b> <i>Fasciola hepatica</i> and <i>gigantica</i> <i>Distribution:</i> worldwide, in areas where sheep and cattle are raised <i>Transmission:</i> eating uncooked aquatic plants	<p><i>During migration phase:</i> 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.</p> <p><i>Once adult flukes are present in the biliary tract:</i> 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).</p>	<b>triclabendazole</b> PO Children and adults: 10 mg/kg single dose May repeat in 24 hours in the event of severe infection
<i>Opisthorchis felineus</i> (Asia, Eastern Europe) <i>Opisthorchis viverrini</i> (Cambodia, Laos, Vietnam, Thailand) <i>Clonorchis sinensis</i> (China, Korea, Vietnam) <i>Transmission:</i> 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.	<b>praziquantel</b> PO Children 4 years and over and adults: 25 mg/kg 3 times daily for 2 days
<b>Intestinal flukes</b> <i>Fasciolopsis buski</i> (India, Bangladesh, South-East Asia) <i>Heterophyes heterophyes</i> (South-East Asia, Nile delta) <i>Metagonimus yokogawai</i> (Siberia, China, Korea) <i>Transmission:</i> eating uncooked aquatic plants ( <i>F. buski</i> ),	<p>Symptoms are limited to diarrhoea and epigastric or abdominal pain. With massive infection, <i>F. buski</i> can cause oedematous allergic reactions (including ascites, anasarca).</p> <p>The diagnosis is confirmed when parasite eggs are detected in stools.</p>	<b>praziquantel</b> PO Children 4 years and over and adults: 25 mg/kg 3 times daily, 1 day

raw/undercooked fish  
(other species)

# 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 to *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

	<b>Parasite/Epidemiology<sup>a</sup></b>	<b>Clinical features/Diagnosis (established infection)</b>
<b>Genito-urinary schistosomiasis</b>	<p><b><i>S. haematobium</i></b>  <i>Distribution:</i> Africa, Madagascar and the Arabian peninsula</p>	<ul style="list-style-type: none"> <li>• Urinary manifestations: <ul style="list-style-type: none"> <li>▫ 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).</li> <li>▫ 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 indispensable.</li> <li>▫ Presumptive treatment is recommended in the presence of macro- or microscopic haematuria, when parasitological confirmation (parasite eggs detected in urine) cannot be obtained.</li> </ul> </li> <li>• 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).</li> <li>• 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.</li> <li>• 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 a history of haematuria).</li> </ul>
<b>Intestinal schistosomiasis</b>	<p><b><i>S. mansoni</i></b>  <i>Distribution:</i> tropical Africa, Madagascar, the Arabian peninsula, South America (especially Brazil)</p> <p><b><i>S. japonicum</i></b>  <i>Distribution:</i> China, Indonesia, the Philippines</p> <p><b><i>S. mekongi</i></b>  <i>Distribution:</i> parts of Lao PDR, Cambodia (along the Mekong River)</p> <p><b><i>S. intercalatum</i></b>  <i>Distribution:</i> parts of DRC, Congo, Gabon, Cameroon, Chad</p>	<ul style="list-style-type: none"> <li>• Non-specific digestive symptoms (abdominal pain; diarrhoea, intermittent or chronic, with or without blood) and hepatomegaly.</li> <li>• For <i>S. intercalatum</i>: digestive symptoms only (rectal pain, tenesmus, rectal prolapse, bloody diarrhoea).</li> <li>• If left untreated: risk of hepatic fibrosis, portal hypertension, cirrhosis, gastrointestinal haemorrhage (hematemesis, melena, etc.), except with <i>S. intercalatum</i> (less pathogenic than other intestinal schistosomes, no severe hepatic lesions).</li> <li>• The diagnosis is confirmed when parasite eggs are detected in stools.</li> <li>• 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.</li> </ul>

# Treatment

## **praziquantel PO<sup>[1][2]</sup>**

Children 4 years and over and adults<sup>b</sup> :

- *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

## **Footnotes**

(a) For more information on geographic distribution of schistosomiasis:  
[https://www.who.int/schistosomiasis/Schistosomiasis\\_2012-01.png?ua=1](https://www.who.int/schistosomiasis/Schistosomiasis_2012-01.png?ua=1)

(b) For the treatment of schistosomiasis, praziquantel may be 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](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](https://www.cdc.gov/parasites/schistosomiasis/health_professionals/index.html#tx) [Accessed 25 May 2020]

# Cestodes

## Cestodes (adult forms)

Parasites	Clinical features/Laboratory	Treatment	Transmission/Prevention
<b>Taeniasis</b> <i>Taenia saginata</i> <i>Taenia solium</i> (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	<b>praziquantel</b> PO <sup>(a)</sup> Children 4 years and over and adults: 5 to 10 mg/kg single dose	<b>Transmission</b> by eating raw or under-cooked meat: <ul style="list-style-type: none"><li>• beef for <i>T. saginata</i></li><li>• pork for <i>T. solium</i></li></ul> <b>Prevention:</b> <ul style="list-style-type: none"><li>• individual: cook meat thoroughly</li><li>• collective: slaughterhouse monitoring</li></ul>
<b>Diphyllobothriasis</b> <i>Diphyllobothrium latum</i> (temperate or cold lake areas)	Often asymptomatic In the event of heavy infection: mild gastrointestinal disturbances, anaemia due to vitamin B <sub>12</sub> deficiency associated with (rare) neurological sequelae Laboratory: eggs in stools	<b>praziquantel</b> PO <sup>(a)</sup> Children 4 years and over and adults: 5 to 10 mg/kg single dose If anaemia: <b>vitamin B<sub>12</sub></b> + <b>folic acid</b>	<b>Transmission</b> by eating raw or under-cooked freshwater fish <b>Prevention:</b> <ul style="list-style-type: none"><li>• individual: cook fish thoroughly</li></ul>
<b>Hymenolepiasis</b> <i>Hymenolepis nana</i> (worldwide)	Often asymptomatic In the event of heavy infection: gastrointestinal disturbances (epigastric pain) Laboratory: eggs in stools	<b>praziquantel</b> PO <sup>(a)</sup> Children 4 years and over and adults: 15 to 25 mg/kg single dose	<b>Transmission</b> by faecal-oral route or auto-infection <b>Prevention:</b> <ul style="list-style-type: none"><li>• individual: hand washing, nail cutting</li><li>• collective: hygiene and sanitation (water, latrines, etc.)</li></ul>

(a) Praziquantel may be administered to pregnant women with *T. solium* taeniasis. For the other indications, treatment can usually be deferred until after delivery.

## Cestodes (larvae)

Parasites	Clinical features/Laboratory	Treatment	Transmission/Prevention
<b>Cysticercosis</b> <i>Taenia solium</i> (worldwide)	<ul style="list-style-type: none"> <li>Muscular: asymptomatic or myalgia</li> <li>Subcutaneous: nodules</li> <li>Neurological (neurocysticercosis): headache, convulsions, coma, etc.</li> <li>Ocular: exophthalmia, strabismus, iritis, etc.</li> </ul> <p>Laboratory: hypereosinophilia in blood and cerebrospinal fluid</p>	<p>Neurological and ocular cysticercosis should be managed in specialized facilities.</p> <p>Antiparasitic treatment without diagnosis of location by computerised tomography and/or magnetic resonance imaging can worsen the symptoms even threaten the life. Neurosurgical treatment can be required.</p>	<p><b>Transmission:</b> by eating food contaminated with <i>T. solium</i> eggs or auto-infection</p> <p><b>Prevention:</b></p> <ul style="list-style-type: none"> <li>individual: treat <i>T. solium</i> carriers, hygiene, cook meat thoroughly</li> </ul>
<b>Hydatid cyst</b> <i>Echinococcus granulosus</i> (South America, North, East and South Africa, Western Europe)	<p>Cysts located in the liver (60% of cases); lungs (30% of cases), and, less frequently, in other sites including the brain.</p> <p>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.).</p>	<p>First-line treatment: surgical excision</p> <p><b>albendazole PO<sup>(b)</sup></b> is useful in addition to, or instead of, surgery:</p> <p>Children over 2 years and adults under 60 kg: 7.5 mg/kg 2 times daily</p> <p>Adults over 60 kg: 400 mg 2 times daily</p> <p>Treatment duration:</p> <p>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.</p> <p>Inoperable cases: 28-day courses with drug-free intervals of 14 days, for 3 to 6 months (on average), possibly up to 1 year.</p>	<p><b>Transmission:</b></p> <ul style="list-style-type: none"> <li>direct: contact with dogs</li> <li>indirect: water and food contaminated by dog faeces</li> </ul> <p><b>Prevention:</b></p> <ul style="list-style-type: none"> <li>individual: avoid contact with dogs</li> <li>collective: eliminate stray dogs, monitor slaughterhouses</li> </ul>

(b) Albendazole is contra-indicated during the first trimester of pregnancy.

# **Nematode infections**

Infection/Epidemiology	Clinical features/Diagnosis	Treatment
<b>Ascariasis</b> (roundworms) <sup>(a)</sup> <i>Ascaris lumbricoides</i> <i>Distribution:</i> worldwide, mainly in tropical and subtropical <i>Transmission:</i> ingestion of ascaris eggs	<ul style="list-style-type: none"> <li>• <i>During larval migration</i> Loeffler's syndrome: transient pulmonary symptoms (dry cough, dyspnoea, wheezing) and mild fever.</li> <li>• <i>Once adult worms are present in the intestine</i> 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.</li> <li>• <i>Complications</i> Ascariasis is usually benign, but massive infestation may cause intestinal obstruction (abdominal pain, vomiting, constipation), especially in children &lt; 5 years. Worms may accidentally migrate to gall bladder, liver or peritoneum, causing jaundice, liver abscess, or peritonitis.</li> <li>• Ascaris eggs may be detected through parasitological examination of stools.</li> </ul>	<b>albendazole</b> PO single dose Children > 6 months and adults: 400 mg (200 mg in children > 6 months but < 10 kg) or <b>mebendazole</b> 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)
<b>Trichuriasis</b> (whipworms) <sup>(a)</sup> <i>Trichuris trichiura</i> <i>Distribution and transmission:</i> as for <i>A. lumbricoides</i>	<ul style="list-style-type: none"> <li>• In heavy infection: abdominal pain and diarrhoea.</li> <li>• 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.</li> <li>• Trichuris eggs may be detected through parasitological examination of stools.</li> </ul>	<b>albendazole</b> 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 <b>mebendazole</b> PO for 3 days, as for ascariasis. A single dose of albendazole or mebendazole is often insufficient.
<b>Ankylostomiasis</b> <sup>(a)</sup> <i>Ancylostoma duodenale</i> <i>Necator americanus</i> <i>Distribution:</i> tropical and subtropical regions <i>Transmission:</i> larval skin penetration following contact (feet, hands) with contaminated soil	<ul style="list-style-type: none"> <li>• <i>During larval penetration/migration</i> Cutaneous signs (pruritic papulo-vesicular rash at the site of penetration, usually the feet) and pulmonary symptoms (similar to ascariasis).</li> <li>• <i>Once adult worms are present in the intestine</i> 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).</li> <li>• Hookworm eggs may be detected through parasitological examination of stools.</li> </ul>	<b>albendazole</b> single dose (as for ascariasis) is much more effective than mebendazole single dose. When using <b>mebendazole</b> , a 3-day treatment (as for ascariasis) is recommended. Treatment of <u>anaemia</u> (Chapter 1).
<b>Strongyloidiasis</b>	<ul style="list-style-type: none"> <li>• <i>Acute strongyloidiasis</i></li> </ul>	First line treatment is:

<p><b>Strongyloides stercoralis</b></p> <p><i>Distribution:</i> humid tropical regions</p> <p><i>Transmission:</i> larval skin penetration and auto-infection</p>	<ul style="list-style-type: none"> <li>▫ 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).</li> <li>▫ Once larvae are present in the intestine: gastrointestinal symptoms (bloating, abdominal and epigastric pain, vomiting, diarrhoea).</li> </ul> <ul style="list-style-type: none"> <li>• <i>Chronic strongyloidiasis</i> 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 (<i>larva currens</i>), 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.</li> <li>• <i>Complications</i> 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).</li> <li>• Strongyloides larvae may be detected through parasitological examination of stools.</li> </ul>	<p><b>ivermectin</b> PO<sup>(b)</sup> single dose Children &gt; 15 kg and adults: 200 micrograms/kg, on an empty stomach</p> <p>While less effective, a 3-day treatment with <b>albendazole</b> PO (as for trichuriasis) may be an alternative.</p> <p>Hyperinfections are refractory to conventional therapy. Prolonged or intermittent multiple-dose regimens are required.</p>
<p><b>Enterobiasis</b> (pinworms)</p> <p><i>Enterobius vermicularis</i></p> <p><i>Distribution:</i> worldwide</p> <p><i>Transmission:</i> faecal-oral route or auto-infection</p>	<ul style="list-style-type: none"> <li>• 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.</li> <li>• Pinworm eggs may be collected from the anal area (scotch tape method) and detected under the microscope.</li> </ul>	<p><b>albendazole</b> PO single dose, as for ascariasis</p> <p>or</p> <p><b>mebendazole</b> PO single dose Children &gt; 6 months and adults: 100 mg (50 mg in children &gt; 6 months but &lt; 10 kg) A second dose may be given after 2 to 4 weeks.</p>
<p><b>Trichinellosis</b></p> <p><i>Trichinella</i> sp</p> <p><i>Distribution:</i> worldwide, particularly frequent in Asia (Thailand, Laos, China, etc.)</p>	<ul style="list-style-type: none"> <li>• <i>Enteric phase</i> (1 to 2 days after ingestion of infected meat) Self-limited episode of diarrhoea and abdominal pain lasting several days.</li> </ul>	<p><b>albendazole</b> PO for 10 to 15 days</p> <p>Children &gt; 2 years: 5 mg/kg 2 times daily</p> <p>Adults:</p>

<p><i>Transmission:</i> consumption of raw or undercooked meat containing trichinella larvae (pork, wart-hog, bear, dog, etc.)</p>	<ul style="list-style-type: none"> <li>• <b>Muscular phase</b> (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 &gt; 39 °C and myalgia and facial oedema) in several individuals who have shared the same meal (e.g. ceremony) or hypereosinophilia &gt; 1000/mm<sup>3</sup>, reinforce the clinical suspicion.</li> <li>• Definitive diagnosis: muscle biopsy; serology (ELISA, Western Blot).</li> </ul>	<p>400 mg 2 times daily or <b>mebendazole</b> PO for 10 to 15 days Children &gt; 2 years: 2.5 mg/kg 2 times daily Adults: 200 mg 2 times daily <i>plus, regardless of which antihelminthic is chosen:</i> <b>prednisolone</b> PO 0.5 to 1 mg/kg once daily for the duration of treatment</p>
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- (a) Roundworms, whipworms and hookworms frequently co-infect the same host. This should be taken into account when prescribing antihelminthic treatment.
- (b) 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 \(river blindness\)](#)
- [Loiasis.](#)
- [Lymphatic filariasis \(LF\)](#)

Filiases 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 <i>Wolbachia</i>
<b><i>Onchocerca volvulus</i></b> (onchocerciasis)	Subcutaneous nodules	Skin and eye	Microfilariae	Yes
<b><i>Loa loa</i></b> (loiasis)	Subcutaneous tissue	Blood	Macrofilariae	No
<b><i>Wuchereria bancrofti, Brugia malayi</i> and <i>Brugia timori</i></b> (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)

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 onchodermititis: papular rash, sometimes diffuse but often confined to the buttocks or lower extremities, intensely itchy, associated with scratch marks, often superinfected ("filarial scabies")<sup>a</sup>. 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](#), 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<sup>b</sup>. 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 2<sup>nd</sup> 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<sup>c</sup>. 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 microfilaremia. Administer the appropriate treatment according to the microfilarial load (see [Loiasis](#)).
  - 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](#)), 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 loiasis and if onchocerciasis has a significant clinical impact, administer ivermectin under close supervision (see [Loiasis](#)) 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](#)) 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.

## **Footnotes**

- Differential diagnosis is sarcoptic scabies ([Scabies](#), Chapter 4).
- Elimination of *Wolbachia* reduces the longevity and fertility of the macrofilariae, and thus the production of new microfilariae within the organism.
- 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

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 trace<sup>a</sup>. 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 micrograms/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<sup>b</sup>. 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<sup>c</sup>. 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](#), Chapter 5.

## Footnotes

(a) For differential diagnosis, see [cutaneous larva migrans](#).

(b) 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).

(c) 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)

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)<sup>a</sup>; 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](#) 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<sup>b</sup>, 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.

## **Footnotes**

- (a) 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 ».
- (b) 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](#)

[Tetanus](#)

[Enteric \(typhoid and paratyphoid\) fevers](#)

[Brucellosis](#)

[Plague](#)

[Leptospirosis](#)

[Relapsing fever \(borreliosis\)](#)

[Louse-borne relapsing fever \(LBRF\)](#)

[Tick-borne relapsing fever \(TBRF\)](#)

[Eruptive rickettsioses](#)

# Bacterial meningitis

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*, *Pseudomonas 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 <sup>3</sup> )	Protein	Other tests
<b>Normal CSF</b>		Clear	< 5	Pandy- < 40 mg/dl	-
<b>Bacterial meningitis</b>	++++	Cloudy, turbid	100-20 000 mainly neutrophiles In neonates: > 20 In immunocompromised, the WBC may be < 100	Pandy+ 100-500 mg/dl	Gram stain +
<b>Viral meningitis</b>	Normal to +	Clear	10-700 mainly lymphocytes	Pandy-	-
<b>TB meningitis</b>	+++	Clear or yellowish	< 500 mainly lymphocytes	Pandy+	AFB
<b>Cryptococcal meningitis</b>	++++	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

### Antibiotic therapy

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	<b>ampicillin IV</b> 100 mg/kg every 12 hours + <b>cefotaxime IV</b> 50 mg/kg every 12 hours	<b>ampicillin IV</b> 100 mg/kg every 12 hours + <b>gentamicin IV</b> 3 mg/kg once daily	<b>cloxacillin IV</b> 50 mg/kg every 12 hours + <b>cefotaxime IV</b> 50 mg/kg every 12 hours	<b>cloxacillin IV</b> 50 mg/kg every 12 hours + <b>gentamicin IV</b> 3 mg/kg once daily
0 to 7 days ≥ 2 kg	<b>ampicillin IV</b> 100 mg/kg every 8 hours + <b>cefotaxime IV</b> 50 mg/kg every 8 hours	<b>ampicillin IV</b> 100 mg/kg every 8 hours + <b>gentamicin IV</b> 5 mg/kg once daily	<b>cloxacillin IV</b> 50 mg/kg every 8 hours + <b>cefotaxime IV</b> 50 mg/kg every 8 hours	<b>cloxacillin IV</b> 50 mg/kg every 8 hours + <b>gentamicin IV</b> 5 mg/kg once daily
8 days to < 1 month ≥ 2 kg	<b>ampicillin IV</b> 100 mg/kg every 8 hours + <b>cefotaxime IV</b> 50 mg/kg every 8 hours	<b>ampicillin IV</b> 100 mg/kg every 8 hours + <b>gentamicin IV</b> 5 mg/kg once daily	<b>cloxacillin IV</b> 50 mg/kg every 6 hours + <b>cefotaxime IV</b> 50 mg/kg every 8 hours	<b>cloxacillin IV</b> 50 mg/kg every 6 hours + <b>gentamicin IV</b> 5 mg/kg once daily
1 to 3 months	<b>ampicillin IV</b> 100 mg/kg every 8 hours + <b>ceftriaxone IV</b> 100 mg/kg on D1 then starting on D2: 100 mg/kg once daily or 50 mg/kg every 12 hours	<b>ampicillin IV</b> 100 mg/kg every 8 hours + <b>gentamicin IV</b> 2.5 mg/kg every 8 hours	<b>cloxacillin IV</b> 50 mg/kg every 6 hours + <b>ceftriaxone IV</b> 100 mg/kg on D1 then starting on D2: 100 mg/kg once daily or 50 mg/kg every 12 hours	<b>cloxacillin IV</b> 50 mg/kg every 6 hours + <b>gentamicin IV</b> 2.5 mg/kg every 8 hours

> 3 months	<b>ceftriaxone IV</b> 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)	<b>cloxacillin IV</b> Children < 40 kg: 50 mg/kg every 6 hours Children ≥ 40 kg: 2 g every 6 hours + <b>ceftriaxone IV</b> 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	<b>ceftriaxone IV:</b> 4 g once daily or 2 g every 12 hours	<b>cloxacillin IV:</b> 2 g every 6 hours + <b>ceftriaxone IV:</b> 4 g once daily or 2 g every 12 hours

Duration of antibiotic therapy:

1) According to the pathogen:

- *Haemophilus influenzae*: 7 days
- *Streptococcus pneumoniae*: 10-14 days
- Group B streptococcus and *Listeria*: 14-21 days
- Gram-negative bacilli: 21 days
- *Neisseria meningitidis*: see antibiotic therapy 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**<sup>[1][2]</sup>

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 (Chapter 1).
- Coma: prevention of bed sores, care of the mouth and eyes, etc.

## Treatment in an epidemic context

### Antibiotic therapy

In this context, *N. meningitidis* is the most likely pathogen.

Age	Treatment <sup>[3]</sup>
Children < 2 months	<b>ceftriaxone</b> IV <sup>(a)</sup> or IM <sup>(b)</sup> for 7 days 100 mg/kg once daily
Children ≥ 2 months and adults	<b>ceftriaxone</b> IV <sup>(a)</sup> or IM <sup>(b)</sup> or 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

(a) 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.

(b) For IM administration, divide the dose into 2 injections if needed, half-dose in each buttock.

#### 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<sup>a</sup>**

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 (Chapter 1).
- Coma: prevention of bed sores, care of the mouth and eyes, etc.
- Dexamethasone is not indicated.

## Footnotes

(a) For IM administration, divide the dose into 2 injections if needed, half-dose in each buttock.

## 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](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](https://apps.who.int/iris/bitstream/handle/10665/154595/WHO_HSE_GAR_ERI_2010.4_Rev1_eng.pdf?sequence=1)

# Tetanus

Last updated: August 2022

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<sup>a</sup>** 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 ( $\geq 2$  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 spasms 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 ( $\text{SpO}_2$ ) 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.

<b>Neonates</b>	<p><b>diazepam emulsion</b> for injection (10 mg ampoule, 5 mg/ml, 2 ml)</p> <ul style="list-style-type: none"> <li>• 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 <math>\geq 30</math>.</li> <li>• 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 <math>\geq 30</math>.</li> <li>• 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 <math>\geq 30</math>.</li> <li>• Diluted diazepam emulsion does not keep for more than 6 hours.</li> </ul> <p>Example:</p> <p>Neonate weighing 3 kg (administration by electric syringe)</p> $0.1 \text{ mg/kg/hour} \times 3 \text{ kg} = 0.3 \text{ mg/hour}$ <p>Dilute one 10 mg ampoule of <b>diazepam emulsion</b> for injection in 50 ml of 10% glucose to obtain a solution containing 0.2 mg of diazepam per ml.</p> <p>Administer 1.5 ml/hour [dose (in mg/hour) <math>\div</math> dilution (in mg/ml) = dose in ml/hour i.e. 0.3 (mg/hour) <math>\div</math> 0.2 (mg/ml) = 1.5 ml/hour].</p> <p>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.</p>
<b>Children &gt; 1 month and adults</b>	<p>Same doses and protocol as in neonates but:</p> <ul style="list-style-type: none"> <li>• Use <b>diazepam solution</b> for injection 5 mg/ml: (10 mg ampoule, 5 mg/ml, 2 ml). <sup>(a)</sup></li> <li>• These doses can be administered as long as the RR is: <ul style="list-style-type: none"> <li><math>\geq 30</math> in children under 1 year</li> <li><math>\geq 25</math> in children 1 to 4 years</li> <li><math>\geq 20</math> in children 5 to 12 years</li> <li><math>\geq 14</math> in children over 12 years</li> <li><math>\geq 12</math> in adults</li> </ul> </li> </ul> <p>Examples:</p> <ul style="list-style-type: none"> <li>• Child weighing 6 kg (continuous IV infusion using a pediatric infusion set; 1 ml = 60 drops) <math display="block">0.1 \text{ mg/kg/hour} \times 6 \text{ kg} = 0.6 \text{ mg/hour}</math> <p>Dilute one 10 mg ampoule of <b>diazepam solution</b> for injection in 50 ml of 5% glucose (10% glucose if child <math>&lt; 3</math> months) to obtain a solution containing 0.2 mg of diazepam per ml.</p> <p>Administer 3 ml/hour [dose (in mg/hour) <math>\div</math> dilution (in mg/ml) = dose in ml/hour i.e. 0.6 (mg/hour) <math>\div</math> 0.2 (mg/ml) = 3 ml/hour] or 3 drops/minute (in a paediatric infusion set ml/hour = drops/minute).</p> </li> <li>• Adult weighing 60 kg (standard adult infusion set, 1 ml = 20 drops) <math display="block">0.1 \text{ mg/kg/hour} \times 60 \text{ kg} = 6 \text{ mg/hour}</math> <p>Dilute 5 ampoules of 10 mg of <b>diazepam solution</b> (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.</p> <p>Administer 30 ml/hour [dose (in mg/hour) <math>\div</math> dilution (in mg/ml) = dose in ml/hour e.g. 6 (mg/hour) <math>\div</math> 0.5 (mg/ml) = 30 ml/hour] or 10 drops/minute.</p> </li> </ul>

(a) Administer the first dose rectally if an IV cannot be placed immediately.

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)<sup>b</sup> 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<sup>c</sup> 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 spasms.

## **Treatment of pain**

**morphine** PO (via nasogastric tube) if necessary (see [Pain](#), 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](#)).

## **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)<sup>d</sup> 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 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 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
<b>TV1</b>	On first contact with the health care system or as soon as possible during pregnancy	No protection
<b>TV2</b>	At least 4 weeks after TV1	80% 1 to 3 years
<b>TV3</b>	6 months to 1 year after TV2 or during the following pregnancy	95% 5 years
<b>TV4</b>	1 to 5 years after TV3 or during the following pregnancy	99% 10 years
<b>TV5</b>	1 to 10 years after TV4 or during the following pregnancy	99% Throughout the reproductive years

## Footnotes

- (a) Clindamycin IV for 7 days is an alternative (for doses, see [Periorbital and orbital cellulitis](#), Chapter 5).
- (b) 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.
- (c) Withdrawal signs: excessive irritability, tremors, increased muscle tone, frequent yawning, poor feeding, watery stools and sweating.
- (d) Tetanus-containing vaccine, such as Td or DTP or DTP + HepB or DTP + HepB + Hib according to availability and patient's age.

# Enteric (typhoid and paratyphoid) fevers

Last updated: March 2024

Enteric fevers include typhoid fever, due to *Salmonella enterica* serotype Typhi (*S. Typhi*) and paratyphoid fever, due to *Salmonella enterica* serotype Paratyphi A, B or C (*S. Paratyphi*).

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 in South, Central and Southeast Asia, sub-Saharan Africa, Oceania and, to a lesser extent, in Latin America.

Effective treatment significantly reduces the risk of complications and death.

## Clinical features

Clinical manifestations of typhoid and paratyphoid fevers are the same. Enteric fevers have insidious onset and vary from mild to severe.

- The characteristic sign is prolonged fever, which gradually increases during the first week, plateaus the second week then decreases between the third and fourth week.
- Non-specific signs and symptoms are frequently associated: gastrointestinal disturbances (abdominal pain, constipation or diarrhoea, vomiting), headache, malaise, chills, fatigue, non productive cough and/or hepatosplenomegaly.
- Erythematous maculopapular rash on the trunk extreme fatigue and/or relative bradycardia (heart rate-temperature dissociation) may be present.
- Serious complications affect about 27% of hospitalised patients<sup>[1]</sup> and usually occur during the second or third week of illness. These may include decreased level of consciousness, intestinal haemorrhage or perforation or peritonitis, shock, or nephritis. In pregnant women, severe infection may lead to foetal complications (miscarriage, preterm delivery, intrauterine death).
- Relapse may occur 2 to 3 weeks after recovery. It is usually not due to antibiotic resistance, and re-treatment is required.

Clinical diagnosis is difficult as enteric fevers resembles other infections present in regions where they are endemic. The main differential diagnoses are: [malaria](#), [brucellosis](#), [leptospirosis](#), [typhus](#), [rickettsiosis](#), [sepsis](#) and [dengue](#).

## Laboratory

- Culture of *S. Typhi* or Paratyphi and drug susceptibility test (blood and stool specimens).
- In all cases, rapid test for malaria in endemic regions (and antimalarial treatment if needed, see [Malaria](#), Chapter 6).
- Widal agglutination test, other serologic tests, and rapid diagnostic tests are not recommended (low sensitivity and specificity).

## Treatment

### In all cases

- Hydrate and treat [fever](#) (Chapter 1). Fever usually resolves 4 to 5 days after starting effective antibiotic treatment.
- Choice of antibiotic treatment depends on the susceptibility of the strain, or when susceptibility is unknown, on recent data on susceptibility of strains in the region. Check national recommendations. For information:

- Strains resistant to chloramphenicol, ampicillin/amoxicillin and co-trimoxazole (multidrug-resistant, MDR strains) are present in most parts of the world.
- Ciprofloxacin is used as first-line treatment in some countries, however fluoroquinolone resistance is endemic in Asia and is increasing in several parts of the world<sup>[2]</sup>.
- Ceftriaxone resistance has been identified in several regions<sup>[2]</sup>.
- MDR strains also resistant to fluoroquinolones and third-generation cephalosporins (extensively drug-resistant, XDR strains) have developed<sup>[3]</sup>.

## **Uncomplicated cases (outpatients)**

Uncomplicated cases (the vast majority of cases) can be treated with an oral antibiotic treatment.

- First-line antibiotics:
  - azithromycin** PO for 7 days (including for MDR and XDR cases, and pregnant women)
    - Children: 10 to 20 mg/kg (max. 1 g) once daily
    - Adults: 500 mg to 1 g once daily or 1 g on D1 then 500 mg once daily
    - or
    - cefixime** PO for 10 to 14 days (except for third-generation cephalosporin resistance and XDR cases)
      - Children: 10 mg/kg (max. 200 mg) 2 times daily
      - Adults: 200 mg 2 times daily
  - Alternatives include, only if recent data show susceptibility of strains to these antibiotics in the region:
    - amoxicillin** PO for 14 days
      - Children: 30 mg/kg (max. 1 g) 3 times daily
      - Adults: 1 g 3 times daily
      - or
      - co-trimoxazole** PO for 14 days
        - Children: 20 mg SMX + 4 mg TMP/kg (max. 800 mg SMX + 160 mg TMP) 2 times daily
        - Adults: 800 mg SMX + 160 mg TMP 2 times daily

## **Severe cases (inpatients)**

- Severe cases include:
  - toxic appearance or decreased level of consciousness or medical or surgical complication;
  - oral administration not possible due to persistent vomiting.
- These cases should be treated under close monitoring. Antibiotic treatment is initially parenteral, then oral when there is decreasing fever, clinical improvement and the patient can tolerate oral treatment.
- Start with **ceftriaxone IV<sup>a</sup>** (including for pregnant women)
  - Children: 50 to 100 mg/kg (max. 4 g) once daily
  - Adults: 2 g once daily or 2 times daily
- Then change to azithromycin PO (as above) to complete at least 7 days of treatment.
- For suspected or confirmed ceftriaxone resistance or XDR stains, use meropenem IV, including for pregnant women, then change to azithromycin PO to complete at least 7 days of treatment.

## **Additional measures**

- In case of decreased level of consciousness or shock, **dexamethasone IV**: a loading dose of 1 mg/kg followed by 0.25 mg/kg every 6 hours for 48 hours (total of 8 doses).
- Treat in intensive care unit patients with shock, significant intestinal haemorrhage or suspected perforation/peritonitis. If suspected perforation/peritonitis, get urgent surgical review and add metronidazole to ceftriaxone for anaerobic bacterial coverage<sup>b</sup>.

## **Prevention**

- Hygiene measures common to all diarrhoeas: handwashing; consumption of treated water (chlorinated, boiled, bottled, etc.); washing/cooking of food, etc.
- In hospitals: for patients with watery diarrhoea, consider disinfection of excreta with chlorinated solution, if stools are collected in buckets.
- Vaccination with the typhoid conjugate vaccine in endemic regions<sup>c</sup>. This vaccine can be used to control typhoid outbreaks. It does not protect against paratyphoid fever.

## Footnotes

- (a) 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.
- (b) Do not add metronidazole if the patient receives meropenem (meropenem already covers anaerobic bacteria).
- (c) For more information, see Typhoid vaccines: WHO position paper:  
<http://apps.who.int/iris/bitstream/handle/10665/272272/WER9313.pdf?ua=1>

## References

1. Cruz Espinoza LM, McCready E, Holm M, et al. Occurrence of typhoid fever complications and their relation to duration of illness preceding hospitalization: a systematic literature review and meta-analysis. Clin Infect Dis 2019;69(Suppl 6):S435-48. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6821330/> [Accessed 28 June 2022]
2. Browne AJ, Hamadani BHK, Kumaran EAP, Rao P, et al. Drug-resistant enteric fever worldwide, 1990 to 2018: a systematic review and meta-analysis. BMC Medicine 2020;18:1+22. <https://doi.org/10.1186/s12916-019-1443-1> [Accessed 23 February 2022]
3. Klemm EJ, Shakoor S, Page AJ, Qamar FN, et al. Emergence of an Extensively Drug-Resistant *Salmonella enterica* Serovar Typhi Clones Harboring a Promiscuous Plasmid Encoding Resistance to Fluoroquinolones and Third-Generation Cephalosporins. mBio. 2018 Jan-Feb; 9(1): e00105-18. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5821095/> [Accessed 26 June 2022]

# Brucellosis

Last updated: September 2022

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).

### 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:

<b>Children under 8 years</b>	co-trimoxazole + rifampicin or co-trimoxazole + gentamicin
<b>Children 8 years and over</b>	doxycycline + rifampicin or doxycycline + gentamicin
<b>Adults</b>	doxycycline + rifampicin or doxycycline + streptomycin or gentamicin
<b>Pregnant/breast-feeding women</b>	rifampicin

### **co-trimoxazole** PO for 6 weeks

Children < 8 years: 20 mg SMX + 4 mg TMP/kg (max. 800 mg SMX + 160 mg TMP) 2 times daily

### **doxycycline** PO for 6 weeks

Children ≥ 8 years and < 45 kg: 2 to 2.2 mg/kg (max. 100 mg) 2 times daily

Children ≥ 45 kg and adults: 100 mg 2 times daily

### **rifampicin** PO for 6 weeks

Children: 15 to 20 mg/kg (max. 600 mg) once 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

Last updated: September 2022

Plague is a zoonosis caused by the Gram-negative bacillus *Yersinia pestis* that affects many wild and domestic mammals, particularly rodents.

Plague is transmitted to man by infected animals (direct contact or inhalation of their respiratory secretions), the bite of a flea of infected animals, or inhalation of respiratory secretions of individuals with pneumonic plague.

Natural foci of infection include Africa, Asia, North and South America, and parts of Europe.

Bubonic plague is the most common form, usually resulting from the bite of an infected flea. Without prompt treatment, the bacteria may be disseminated by haematogenous route, producing a more severe form (see below) with a high mortality rate.

The following forms of plague may be primary or secondary to bubonic plague:

- Pneumonic plague can rapidly progress to respiratory distress, shock, and death without prompt treatment.
- Septicaemic plague is a fulminant illness that can progress to disseminated intravascular coagulation, respiratory distress, shock, and death.
- Plague meningitis is a rare but very severe form of plague.

## Clinical features

See [table](#) below.

Main differential diagnoses include:

- Other causes of lymphadenitis (e.g. some [bacterial skin infections](#), tularemia, [lymphogranuloma venereum, chancroid](#))
- [Acute pneumonia](#) (Chapter 2)
- Other causes of septicaemia (see [Shock](#), Chapter 1) or meningitis (see [Bacterial meningitis](#), Chapter 7)

## Laboratory

- Collect pre-treatment specimens: lymph node aspirate (bubonic plague), sputum (pneumonic plague), blood (septicaemic plague), or cerebrospinal fluid (plague meningitis).
- Send specimens<sup>a</sup> to reference laboratory for:
  - Rapid diagnostic test for detection of F1 capsular antigen of *Y. pestis*
  - PCR
  - Culture of *Y. pestis* and drug susceptibility test
- In all cases, rapid test for malaria in endemic regions (and antimalarial treatment if needed, see [Malaria](#), Chapter 6).

## Management

- Start empiric antibiotic treatment for 10 to 14 days as soon as plague is suspected, before results of diagnosis tests are available.
- A combination of 2 antibiotics from different classes is recommended in severe disease, plague meningitis, and pregnant women.
- Follow national recommendations according to antibiotic resistance patterns if known. For information: see [table](#) below.

## **Treatment of suspected cases**

Forms of plague	Clinical features	Antibiotic treatment <sup>[1]</sup>
<b>Bubonic</b>	<ul style="list-style-type: none"> <li>• Fever, chills, malaise, headache</li> </ul> <p>AND</p> <ul style="list-style-type: none"> <li>• Lymph node (bubo), painful, usually inguinal, (one or more)</li> </ul>	<p>Children (including &lt; 8 years) and adults:</p> <p><b>doxycycline</b> PO:</p> <ul style="list-style-type: none"> <li>• Under 45 kg: 4.4 mg/kg (max. 200 mg) on D1, then 2.2 mg/kg (max. 100 mg) 2 times daily</li> <li>• 45 kg and over: 200 mg on D1, then 100 mg 2 times daily</li> </ul> <p>or</p> <p><b>gentamicin</b> IM or IV:<sup>(a)</sup></p> <ul style="list-style-type: none"> <li>• Children: 4.5 to 7.5 mg/kg once daily</li> <li>• Adults: 5 mg/kg once daily</li> </ul> <p>or</p> <p><b>ciprofloxacin</b> PO:</p> <ul style="list-style-type: none"> <li>• Children: 15 mg/kg 2 to 3 times daily (max. 750 mg 2 times daily or 500 mg 3 times daily)</li> <li>• Adults: 750 mg 2 times daily</li> </ul>
<b>Pneumonic</b>	<ul style="list-style-type: none"> <li>• Fever, chills, malaise, headache</li> </ul> <p>AND</p> <ul style="list-style-type: none"> <li>• Dyspnea, chest pain, productive cough with purulent or blood-stained sputum</li> <li>• Respiratory distress or failure and sepsis in severe or advanced, untreated disease</li> </ul>	<p>Children and adults:</p> <p>If mild disease:</p> <p><b>gentamicin</b> IM or IV<sup>(a)</sup> (as above)</p> <p>or</p> <p><b>ciprofloxacin</b> PO (as above) or IV<sup>(b)</sup></p> <p>If severe disease:</p> <p><b>gentamicin + ciprofloxacin</b> (as above)</p> <p>or, if not available, <b>gentamicin + doxycycline</b> (as above)</p> <p>After clinical improvement, change to ciprofloxacin or doxycycline PO (as above).</p>
<b>Septicaemic</b>	<ul style="list-style-type: none"> <li>• Frequently no localizing symptoms or signs</li> <li>• Gastrointestinal disturbances (abdominal pain, vomiting, diarrhoea, etc.) often present</li> </ul>	As severe pneumonic plague
<b>Meningitis<sup>(c)</sup></b>	Signs of <u>meningitis</u> .	<p>Children and adults:</p> <p><b>chloramphenicol</b> IV:</p> <ul style="list-style-type: none"> <li>• Children 1 to 12 years: 25 mg/kg (max. 1 g) every 8 hours</li> <li>• Children 13 years and over and adults: 1 g every 8 hours</li> </ul> <p>+ <b>ciprofloxacin</b> PO or IV (as above)</p> <p>or, if not available,</p> <p><b>gentamicin + ciprofloxacin</b> (as above)</p>

- (a) **Streptomycin** IM may be an alternative to gentamicin (except in pregnant women):
  - Children: 15 mg/kg (max. 1 g) every 12 hours
  - Adults: 1 g every 12 hours
- (b) Use **ciprofloxacin** IV when oral route is not possible:
  - Children: 10 mg/kg (max. 400 mg) every 8 or 12 hours
  - Adults: 400 mg every 8 hours
- (c) If plague meningitis develops, add chloramphenicol to the existing regimen, and continue the combined regimen for an additional 10 days.

## Treatment in pregnant women

- Bubonic, pneumonic, and septicaemic plague: **gentamicin** IM or IV (as above) + **ciprofloxacin** PO (500 mg 3 times daily) or IV (as above)
- Plague meningitis: **chloramphenicol** IV + **ciprofloxacin** PO (500 mg 3 times daily) or IV (as above)

## Infection prevention and control (in hospitals)

- Bubonic plague: no isolation, standard precautions (handwashing, gowns, gloves, eye protection, etc.) with respect to lymph node aspiration or discharge and other body fluids.
- Pneumonic plague: isolation (in single room if possible), standard precautions, plus, for 48 hours after the start of antibiotic treatment, droplet precautions (medical mask for healthcare workers and for patients during contact). Only for aerosol-generating procedures, airborne precautions (FFP2 or N95 respirators) for health workers exposed to aerosols.
- Elimination of fleas (e.g. bedding, clothing, corpse): refer to the guide [Public health engineering](#), MSF.

## Post-exposure prophylaxis of contacts

In the event of contact (distance less than 2 meters without appropriate personal protective equipment) with a pneumonic plague patient or direct contact with infected body fluids or tissues of any plague patient and within one week after the end of exposure:

**doxycycline** PO for 7 days

Children: 2.2 mg/kg (max. 100 mg) 2 times daily

Adults (including pregnant women): 100 mg 2 times daily

or

**ciprofloxacin** PO for 7 days

Children: 20 mg/kg (max. 750 mg) 2 times daily

Adults: 500 to 750 mg 2 times daily

Pregnant women: 500 mg 3 times daily

## Prevention

- Flea vector control, sanitation and rodent reservoir control, refer to the guide [Public health engineering](#), MSF.
- Vaccination against plague is indicated for laboratory technicians handling rodents or working with *Y. pestis* and is not a method for controlling an epidemic.

## Footnotes

- (a) Transportation of specimens in 0.9% sodium chloride requires a cold chain (failing that, a temperature below 30 °C), triple packaging and UN3373 label.

## **References**

1. Nelson CA, Meaney-Delman D, Fleck-Derderian S, Cooley KM, et al. Antimicrobial treatment and prophylaxis of plague: recommendations for naturally acquired infection and bioterrorism response. MMWR Recomm Rep 2021;70(No. RR-3):1-27. [https://www.cdc.gov/mmwr/volumes/70/rr/rr7003a1.htm?s\\_cid=rr7003a1\\_w](https://www.cdc.gov/mmwr/volumes/70/rr/rr7003a1.htm?s_cid=rr7003a1_w) [Accessed 25 January 2022]

# Leptospirosis

Last update: October 2022

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 (spirochetes) 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 asymptomatic or mild with a favourable outcome. 5 to 15% of cases present a severe form with multiple organ dysfunction and a high mortality rate without prompt treatment.

### Mild form

- Acute phase (septicaemic):
  - Sudden onset of high fever with chills, headache, myalgia (especially calf and lumbar pain), photophobia, ocular pain. Bilateral conjunctival suffusion affecting the bulbar conjunctiva (redness without discharge) is a characteristic sign, but not always present.
  - May be associated with: gastrointestinal symptoms (anorexia, abdominal pain, nausea, vomiting), non-productive cough, lymphadenopathy, hepatomegaly, and sometimes, skin rash.
- 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.
  - Signs of meningitis (thought to be of immune origin) are however very common during this phase.

### Severe or icterohaemorrhagic 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<sup>[1]</sup>:

- abrupt onset of fever, chills, conjunctival suffusion, headache, myalgia and jaundice and
- one or more risk factors for infection: exposure to contaminated freshwater (e.g. swimming, fishing, rice fields, flooding) or infected animals (e.g. crop and livestock farmers, veterinarians, butchers and slaughterhouse workers).

Other conditions to consider include a wide range of acute febrile illnesses, e.g.:

- [Viral haemorrhagic fevers](#), [dengue](#), chikungunya, Zika, influenza, [measles](#), [viral hepatitis](#), other causes of [meningitis](#)

- [Malaria](#)
- [Typhoid fever, brucellosis, rickettsioses](#)

## Laboratory

### Diagnosis

- Collect pre-treatment specimens and send them to reference laboratory:
  - Acute phase (first week of illness): blood and/or serum for IgM screening, PCR, and acute specimen for microscopic agglutination test (MAT);
  - Immune phase (second week of illness): serum for IgM screening and convalescent specimen for MAT, and urine for PCR.
- In all cases, rapid test for malaria in endemic regions (and antimalarial treatment if needed, see [Malaria](#), Chapter 6).

### Other investigations

(if available)

- Serum creatinine: elevated if renal dysfunction.
- Full blood count: possible neutrophilia and thrombocytopenia (acute phase), or anaemia secondary to haemorrhage (immune phase).
- Cerebrospinal fluid (immune phase): features of aseptic meningitis in CSF (see [viral meningitis](#), Chapter 7).
- Urine: mild proteinuria, leukocyturia, possible microscopic haematuria (acute phase).

## Treatment

Start empiric antibiotic treatment as soon as leptospirosis suspected, before results of diagnosis tests are available.

### Mild form (outpatients)

#### Symptomatic treatment

- Rest and treatment of pain and [fever](#): paracetamol PO (Chapter 1).
- Acetylsalicylic acid (aspirin) is contra-indicated (risk of haemorrhage).

#### Antibiotic treatment

- **doxycycline** PO for 7 days

Children under 45 kg: 2 to 2.2 mg/kg (max. 100 mg) 2 times daily

Children 45 kg and over and adults: 100 mg 2 times daily

or, particularly in pregnant women:

- **azithromycin** PO for 3 days

Children: 10 mg/kg (max. 500 mg) on D1 then 5 mg/kg (max. 250 mg) once daily on D2 and D3

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 (max. 1 g) 2 times daily

Adults: 1 g 2 times daily



Antibiotic treatment 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 (inpatients)

#### Symptomatic treatment

- Specific management according to organs affected. Oliguria generally responds to correction of hypovolaemia.
- Rest and treatment of pain and **fever**: paracetamol PO (Chapter 1). Avoid or use paracetamol with caution in patients with hepatic involvement.

#### **Antibiotic treatment**

- **ceftriaxone** IV for 7 days<sup>a</sup>

Children: 80 to 100 mg/kg (max. 2 g) once daily

Adults: 2 g once daily

or

- **benzylpenicillin** IV for 7 days

Children: 50 000 IU (30 mg)/kg (max. 2 MIU or 1200 mg) every 6 hours

Adults: 1 to 2 MIU (600 to 1200 mg) every 6 hours

## **Prevention**

- Avoid bathing in freshwater in endemic areas.
- Disinfect laundry and objects soiled by urine of infected animal or patient.
- Vaccination and protective clothing (only for professionals at risk of exposure).

#### **Footnotes**

- (a) For IV administration of ceftriaxone, dilute with water for injection only.

## **References**

1. World Health Organization. Human leptospirosis: guidance for diagnosis, surveillance and control. World Health Organization, 2003.  
[https://apps.who.int/iris/bitstream/handle/10665/42667/WHO\\_CDS\\_CSR\\_EPH\\_2002.23.pdf?%20sequence=1&isAllowed=y](https://apps.who.int/iris/bitstream/handle/10665/42667/WHO_CDS_CSR_EPH_2002.23.pdf?%20sequence=1&isAllowed=y)  
[Accessed 5 September 2022]

# Relapsing fever (borreliosis)

- [Louse-borne relapsing fever \(LBRF\)](#)
- [Tick-borne relapsing fever \(TBRF\)](#)

Relapsing fever (FR) is caused by spirochetes of the genus *Borrelia*, transmitted to humans by arthropod vectors.

# Louse-borne relapsing fever (LBRF)

Last updated: October 2022

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](#)). 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 recurs; 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 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

- Antibiotic treatment (suspect or confirmed cases and close contacts):

**doxycycline PO**

Children: 4 mg/kg (max. 100 mg) single dose

Adults: 200 mg single dose

or

**erythromycin PO**

Children under 5 years: 250 mg single dose

Children 5 years and over and adults: 500 mg single dose

or

**azithromycin PO**

Children: 10 mg/kg (max. 500 mg) single dose

Adults: 500 mg single dose

- Treatment of pain and [fever](#) (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](#), Chapter 4).

# Tick-borne relapsing fever (TBRF)

Last update: October 2022

TBRFs are caused by different *Borrelia* species. They are endemic in temperate and warm regions of the world, 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 central nervous system (CNS) involvement (particularly lymphocytic meningitis) is 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.
- In all cases, rapid test for malaria in endemic regions (and antimalarial treatment if needed, see [Malaria](#), Chapter 6).

## Treatment

- Antibiotic treatment:

**doxycycline** PO for 7 to 10 days

Children under 45 kg: 2.2 mg/kg (max. 100 mg) 2 times daily

Children 45 kg and over and adults: 100 mg 2 times daily

or

**azithromycin** PO for 7 to 10 days (if doxycycline is contra-indicated or not available)

Children: 10 mg/kg (max. 500 mg) once daily

Adults: 500 mg once daily

or

**ceftriaxone** IV<sup>a</sup> for 10 to 14 days (for pregnant women or in case of CNS involvement)

Children: 50 to 75 mg/kg (max. 2 g) once daily

Adults: 2 g once daily

- Treatment of pain and [fever](#) (paracetamol PO) and prevention or treatment of dehydration in the event of associated diarrhoea.



Antibiotic treatment 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.

## **Footnotes**

(a) For IV administration of ceftriaxone, dilute with water for injection only.

# Eruptive rickettsioses

Last update: October 2022

Rickettsioses are 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
<b>Form</b>	Epidemic typhus	Murine typhus	Mediterranean spotted fever	Rocky Mountain spotted fever	Other Old-World tick-borne fevers	Scrub typhus
<b>Pathogen</b>	<i>R. prowasekii</i>	<i>R. typhi</i>	<i>R. conorii</i>	<i>R. rickettsii</i>	<i>R. sibirica</i> , <i>R. australis</i>	<i>O. tsutsugamushi</i>
<b>Vector</b>	body lice	rat fleas	ticks	ticks	ticks	mites
<b>Reservoir</b>	<b>man</b>	rats	dogs	rodents	rodents, dogs, etc.	rodents
<b>Occurrence</b>	<b>epidemic</b>	endemic	endemic	endemic	endemic	sporadic
<b>Geographical distribution</b>	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
<b>Rash</b>	maculopapular	maculopapular	maculopapular	purpural	maculopapular	macular
<b>Eschar</b>	0	0	<b>black necrotic area</b>	rare	<b>black necrotic area</b>	<b>black necrotic area</b>
<b>Typhoid state</b>	+++	+++	+/-	+/-	+/-	+++
<b>Extra-cutaneous signs</b>	cough, myalgia, meningeal signs	gastrointestinal signs	meningeal signs	gastrointestinal and neurological signs, hypotension	variables	meningeal signs
<b>Case fatality (%)</b>	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: paracetamol PO (Chapter 1). Acetylsalicylic acid (aspirin) is contra-indicated due to the risk of haemorrhage.
- Antibiotic<sup>a</sup> for 5 to 7 days or until 3 days after the fever has disappeared:  
**doxycycline** PO

Children under 45 kg: 2.2 mg/kg (max. 100 mg) 2 times daily  
Children 45 kg and over and adults: 100 mg 2 times daily  
In severe infections, a loading dose of doxycycline is recommended:  
Children under 45 kg: 4.4 mg/kg (max. 200 mg) on D1 then 2.2 mg /kg (max. 100 mg) 2 times daily  
Children 45 kg and over and adults: 200 mg on D1 then 100 mg 2 times daily
- In a context of epidemic typhus, **doxycycline** PO is the choice treatment, but there is a risk of recurrence:

Children: 4 mg/kg (max. 100 mg) single dose  
Adults: 200 mg single dose

# Prevention

- Epidemic typhus: control of body lice (see [Pediculosis](#), 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).

## Footnotes

- (a) 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](#)).

# **Chapter 8: Viral diseases**

[Measles](#)

[Poliomyelitis](#)

[Rabies](#)

[Viral hepatitis](#)

[Dengue](#)

[Viral haemorrhagic fevers](#)

[HIV infection and AIDS](#)

# Measles

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<sub>2</sub> < 90%)
  - Acute laryngotracheobronchitis (croup)<sup>a</sup>
  - 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](#), 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-blown 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](#), 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](#), Chapter 1).
- Insert a nasogastric tube for a few days if oral lesions prevent the child from drinking.

### Treatment of complications

	<b>Treatment of complications</b>
<b>Severe pneumonia</b>	<b>ceftriaxone IV or IM + cloxacillin IV</b> then change to <b>amoxicillin/clavulanic acid PO</b> (see <a href="#">Chapter 2</a> ) + <b>oxygen</b> if cyanosis or SpO <sub>2</sub> < 90% + <b>salbutamol</b> if expiratory wheezing and sibilant rales on auscultation In all cases, close monitoring.
<b>Pneumonia without severe signs</b>	<b>amoxicillin PO</b> for 5 days
<b>Croup</b>	Inpatient monitoring (risk of worsening). Keep the child calm. Agitation and crying exacerbate the symptoms. For severe croup: <b>dexamethasone IM</b> : 0.6 mg/kg single dose + nebulized <b>epinephrine (adrenaline)</b> , 1 mg/ml ampoule): 0.5 ml/kg (max. 5 ml) + <b>oxygen</b> if cyanosis or SpO <sub>2</sub> < 90% Intensive monitoring until symptoms resolve.
<b>Acute otitis media</b>	See <a href="#">Otitis</a> , Chapter 2.
<b>Dehydration</b>	Per oral route or IV depending on the degree of dehydration.
<b>Oral candidiasis</b>	See <a href="#">Stomatitis</a> , Chapter 3.
<b>Purulent conjunctivitis</b>	See <a href="#">Conjunctivitis</a> , Chapter 5.
<b>Keratitis/keratoconjunctivitis</b>	<b>tetracycline 1% eye ointment</b> 2 times daily for 7 days + <b>retinol PO</b> one dose on D1, D2 and D8 (see <a href="#">Xerophthalmia</a> , Chapter 5) + eye protection and pain management (see <a href="#">Pain</a> , Chapter 1). No topical corticosteroids.
<b>Xerophthalmia</b>	See <a href="#">Xerophthalmia</a> , Chapter 5.
<b>Febrile seizures</b>	See <a href="#">Seizures</a> , 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.

## **Footnotes**

- (a) 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

Poliomyelitis is an acute viral infection due to a poliovirus (serotypes 1, 2 or 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, poliomyelitis mainly affect children under 5 years not (or not fully) vaccinated, but the infection can affect persons of any age, especially in areas where population immunity is low.

## Clinical features

- Up to 90% of cases are asymptomatic or present mild symptoms<sup>[1]</sup>.
- **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 24-48 hours, and within 14 days of onset of symptoms<sup>[2]</sup>. Send the 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.

## 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.

## Outbreak control in case of acute flaccid paralysis (AFP)

- Consider any patient with AFP as a suspected case of poliomyelitis.
- Send stool samples to a reference laboratory to confirm the diagnosis.
- Organize vaccination of all children under 5 years living in the area (from the same village or neighbouring villages) irrespective of their vaccination status, within 14 days of laboratory confirmation and with the available vaccine (round 0)<sup>[3]</sup>.
- Organize two mass vaccination campaigns within 8 weeks of the laboratory confirmation. The type of vaccine, the area and the age groups are determined by epidemiological data.
- Organize a mop-up (door-to-door) vaccination campaign wherever monitoring suggests that children have been missed, to ensure interruption of transmission.
- 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

- 3 types of vaccines exist:
  - a trivalent injectable inactivated poliovirus vaccine (IPV),
  - a bivalent oral live attenuated poliovirus vaccine (bOPV), containing serotypes 1 and 3,
  - a monovalent oral type 2 vaccine (mOPV or nOPV) exclusively used for responding to epidemics.
- 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 <sup>(a)</sup>	Other zones
<b>Birth</b>	1 dose bOPV <sup>(b)</sup>	-
<b>6 weeks</b>	1 dose bOPV	1 dose bOPV
<b>10 weeks</b>	1 dose bOPV	1 dose bOPV
<b>14 weeks</b>	1 dose bOPV + 1 dose IPV	1 dose bOPV + 1 dose IPV

(a) Countries where poliomyelitis is endemic or zones at high risk of importation and subsequent spread of the virus.

(b) The first 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 first dose of bOPV, followed by 2 doses of bOPV alone administered 4 weeks apart.

There is also an 'IPV only' schedule: 3 doses administered at least 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.

## References

1. World Health Organization. Poliomyelitis (polio). [https://www.who.int/health-topics/poliomyelitis#tab=tab\\_1](https://www.who.int/health-topics/poliomyelitis#tab=tab_1) [Accessed 08 June 2021]
2. Centers for Disease Control and Prevention. Poliomyelitis. 2020. <https://www.cdc.gov/vaccines/pubs/pinkbook/polio.html> [Accessed 08 June 2021]
3. Global Polio Eradication Initiative. Standard operating procedures: responding to a poliovirus event or outbreak, version 3.1. World Health Organization. 2020. <https://www.who.int/publications/i/item/9789240002999> [Accessed 08 June 2021]

# Rabies

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<sup>[1]</sup>.

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)

<b>Category I</b>	Contact with animal, or licks on intact skin	<b>No exposure</b>
<b>Category II</b>	Nibbles on exposed skin Minor bite(s) or scratch(es) without bleeding	<b>Minor exposure</b>
<b>Category III</b>	Transdermal bite(s) or scratch(es) Licks on broken skin Contamination of mucous membranes by animal's saliva (licks) Direct contact with bats <sup>a</sup>	<b>Severe exposure</b>

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](#));
- Category II and III exposures in immunocompromised patients<sup>b</sup> (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.<sup>[1]</sup>

## **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<sup>c</sup>. 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<sup>[1]</sup>

Date	No pre-exposure prophylaxis or unknown prophylaxis status or incomplete pre-exposure prophylaxis or complete pre-exposure prophylaxis with an NTV		
	IM route <sup>(a)</sup> <b>1 dose = 0.5 or 1 ml depending on the manufacturer</b>	ID route <sup>(b)</sup> <b>1 dose = 0.1 ml</b>	
D0	2 doses <sup>(c)</sup> (1 dose in each arm or thigh)	1 dose <sup>(c)</sup>	2 doses <sup>(c)</sup> (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 <sup>(d)</sup>	
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.<sup>[1]</sup>
- In patients that have received a full course of pre-exposure prophylaxis (see [Prevention](#)), 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<sup>[2]</sup>

Infection present	No infection and	No infection and
<ul style="list-style-type: none"> <li>local: redness, oedema, serosanguinous or purulent drainage</li> <li>locoregional or general: lymphangitis, lymphadenopathy, localised cellulitis, bone or joint infection, fever</li> </ul>	<ul style="list-style-type: none"> <li>wounds on the face or hands or genital region</li> <li>wounds involving joint, tendon, ligament or fracture</li> <li>deep puncture wounds</li> <li>wounds with crush injury</li> <li>wounds very contaminated or requiring debridement</li> <li>wounds where correct debridement is not possible</li> <li>immunocompromised patients</li> </ul>	<ul style="list-style-type: none"> <li>no criteria requiring antibiotic prophylaxis</li> <li>wounds more than 24-48 hours old</li> </ul>
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<sup>d</sup>**

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](#), 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.

## Footnotes

(a) In the event of direct contact with bats, check national recommendations.

(b) For example, for HIV-infected patients: CD4 < 25% in children < 5 years and < 200 cells/mm<sup>3</sup> in children ≥ 5 years and adults. (<http://apps.who.int/iris/bitstream/handle/10665/272371/WER9316.pdf?ua=1>)

(c) 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.

(d) 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. No 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: October 2021

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
<b>Age group most at risk</b>	Children	Children	Young adults	Young adults	Young adults
<b>Transmission</b>	Faecal-oral Contaminated food and water  Transfusion (rare)	Vertical <sup>(a)</sup>  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 <sup>(a)</sup>	Exposure to blood (transfusion; material contaminated with blood)  Sexual  Possibly vertical <sup>(a)</sup>	Faecal-oral Contaminated food and water
<b>Incubation period</b>	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
<b>Fulminant forms</b>	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
<b>Prognosis</b>	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

<b>Individual prevention</b>	Polyvalent immunoglobulin  Safe sex (condoms)	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)
<b>Vaccination</b>	Anti-hepatitis A	Anti-hepatitis B	Does not exist	Anti-hepatitis B	Does not exist
<b>Collective prevention</b>	Hygiene, sanitation	Limit transfusion, screen blood prior to transfusion  Single use of disposable material			Hygiene, sanitation

- (a) 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.

## 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):  $[(\text{patient's AST level}/\text{normal AST level}) \times 100]/\text{platelet count}$  ( $10^9$  platelets/litre). An APRI score  $> 1$  indicates probable severe fibrosis.
- HIV test.

## Other investigations

Elastography (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<sup>[1]</sup>

Genotypes 1, 2, 3, 4, 5, 6 without cirrhosis or with compensated cirrhosis	<b>sofosbuvir/velpatasvir</b> 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	<b>sofosbuvir/daclatasvir</b> PO (400 mg SOF/60 mg DCV tablet) 1 tablet once daily for 12 weeks
Genotype 3 with compensated cirrhosis	<b>sofosbuvir/daclatasvir</b> PO (400 mg SOF/60 mg DCV tablet) 1 tablet once daily for 24 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<sup>[2]</sup> (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<sup>a</sup>
  - 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<sup>a</sup>
- 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

## Footnotes

(a) 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.

## 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

Last update: October 2022

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<sup>a</sup>, 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 or occasionally severe 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): at the end of the febrile phase, temperature decreases. 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) at this stage. These patients are at higher risk for developing 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 PAHO <sup>[1]</sup> )	
Dengue without warning signs	Fever + 2 of the following symptoms: <ul style="list-style-type: none"><li>• Nausea, vomiting</li><li>• Rash resembling measles</li><li>• Generalized aches (headache, retro-orbital pain, myalgias, arthralgias)</li><li>• Benign mucocutaneous bleeding (petechiae, positive tourniquet test<sup>(a)</sup>, epistaxis, gingival bleeding)</li><li>• Leucopenia</li></ul>
Dengue with warning signs	Presence of at least one of these symptoms: <ul style="list-style-type: none"><li>• Intense abdominal pain</li><li>• Persistent vomiting</li><li>• Fluid accumulation (ascites, pleural effusion)</li><li>• Mucosal bleeding</li><li>• Hepatomegaly (&gt; 2 cm)</li><li>• Postural hypotension</li><li>• Agitation or lethargy</li><li>• Increasing haematocrit</li></ul>
Severe dengue	<ul style="list-style-type: none"><li>• Severe fluid accumulation (ascites, pleural effusion) with respiratory distress and/or shock</li><li>• Severe mucocutaneous bleeding</li><li>• Severe organ involvement (e.g.: transaminases &gt; 1000 IU/litre, myocarditis, altered mental status)</li></ul>

(a) 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.

## Major differential diagnoses

Other conditions to consider include a wide range of acute febrile illnesses, e.g.:

- Chikungunya, Zika, influenza, mononucleosis, [measles](#), rubella, [viral haemorrhagic fevers](#)
- [Malaria](#)
- Meningococcemia, [typhoid fever](#), [leptospirosis](#), [rickettsioses](#), other causes of sepsis
- Leukaemia

## Laboratory

### Diagnosis

- NS-1 antigen detection during febrile phase with rapid diagnostic test or ELISA (serum, plasma or blood).
- Antibody detection (complex interpretation):
  - IgM detection 5 to 6 days after onset of illness may support (but does not confirm) a diagnosis of recent infection;
  - IgG detection may indicate prior infection by, or vaccination against, dengue virus or a closely related virus (e.g. chikungunya, Zika, Japanese encephalitis, yellow fever).
- PCR may also be available in reference laboratories.
- In all cases, rapid test for malaria in endemic regions (and antimalarial treatment if needed, see [Malaria](#), Chapter 6).

## Monitoring disease course

- Haematocrit (Hct) or if available full blood count (FBC) at baseline, then daily if possible.
  - A progressive increase in Hct is a warning sign. It indicates haemoconcentration due to increased vascular permeability (plasma leakage). Hct should be monitored frequently (before and after fluid administration) in patients with warning signs up to the end of the fluid treatment.
  - Leukopenia and thrombocytopenia are common and improve as the recovery phase begins. Leukocytosis may occur with severe bleeding.
- Liver function tests if possible at baseline, then according to results.

## Treatment

### Patients in Group A (outpatients)

Patients with no warning signs, able to drink sufficiently and with a normal urine output.

- Bed rest and good hydration.
- Fever and pain: **paracetamol** PO at the usual doses (see [Fever](#), Chapter 1), maintaining a 6 to 8 hour interval between doses. Do not prescribe acetylsalicylic acid, ibuprofen or other NSAIDs.
- 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 (inpatients)

Patients with any of the following:

- Warning sign(s)
- Acute (e.g. severe dehydration or malaria) or chronic (e.g. diabetes, cardiovascular, renal or haemolytic disease, obesity) co-morbidities
- Risk factors for bleeding (e.g. anticoagulation, coagulopathy, peptic ulcer or gastritis, treatment with NSAIDs)
- Pregnant women, patients under 1 year or 65 years and over or patients with difficulty drinking

#### In all cases:

- Place the patient under a mosquito net; encourage oral fluid intake (including oral rehydration solution (ORS) if needed).
- Avoid invasive procedures (nasogastric tube, IM injections) to minimize the risk of bleeding.
- Fever and pain: **paracetamol** PO<sup>[2]</sup> with caution and without exceeding:
  - children: 10 mg/kg every 6 to 8 hours
  - adults: 500 mg every 6 to 8 hours
- In case of elevated transaminases  $\geq 10$  times the upper limit of normal, do not administer paracetamol. Use tepid sponging for reducing fever.
- Monitor vital signs, fluid intake (infusion and oral) and urine output every 4 hours<sup>b</sup>.

#### If poor oral intake:

- Place an intravenous line and administer:
  - children: **5% glucose + Ringer lactate** solution<sup>c</sup> as maintenance fluids, according to the Holliday-Segar formula, i.e. 4 ml/kg/hour for first 10 kg of body weight + 2 ml/kg/hour for next 10 kg + 1 ml/kg/hour for each additional kg above 20 kg.
  - adults: **Ringer lactate**, 2 to 3 ml/kg/hour
- Encourage oral intake as soon as possible.

#### If warning signs:

- Monitor clinical status (warning signs, general symptoms, vital signs, capillary refill time), IV and oral fluid intake, urine output, hourly for at least 4 hours, then every 4 hours while the patient is on IV fluid treatment.
- Place an intravenous line and administer a bolus of Ringer lactate:
  - children and adults: 10 ml/kg over one hour
  - patients 65 years and over or with co-morbidities : 5 ml/kg over one hour
- Re-assess the patient:
  - If no improvement after first bolus: administer a second bolus as above. If necessary, a total of 3 boluses can be administered. If still no improvement after 3 bolus, consider as severe dengue (patients in Group C) and transfer to intensive care unit.
  - If improvement after the first, second, or third bolus, reduce Ringer lactate:
    - ▷ children and adults: 5 to 7 ml/kg/hour over 2 to 4 hours
    - ▷ patients 65 years and over or with co-morbidities: 5 ml/kg/hour over 2 to 4 hours
  - If continuing improvement, reduce Ringer lactate (then stop as soon as possible to reduce the risk of fluid overload):
    - ▷ children and adults: 3 to 5 ml/kg/hour over 2 to 4 hours, then 2 to 4 ml/kg/hour over 24 to 48 hours
    - ▷ patients 65 years and over or with co-morbidities: 3 ml/kg/hour over 2 to 4 hours, then 2 ml/kg/hour over 24 to 48 hours
  - If the patient deteriorates after initial improvement, resume the bolus therapy with Ringer lactate (up to 3 bolus) as above.

## **Patients in Group C (intensive care unit)**

Patients with severe dengue requiring emergency treatment for managing shock and other complications (e.g. severe bleeding, acidosis, coagulopathy).

## **Prevention**

- Individual protection: long sleeves and trousers, repellents, mosquito net (*Aedes* bites during the day).
- Elimination of mosquito breeding sites (small collections of water in discarded tires, flower pots, and other containers).

## **Footnotes**

- (a) For more information:  
[http://gamapserver.who.int/mapLibrary/Files/Maps/Global\\_DengueTransmission\\_ITHRiskMap.png?ua=1](http://gamapserver.who.int/mapLibrary/Files/Maps/Global_DengueTransmission_ITHRiskMap.png?ua=1)
- (b) Adequate urine output: 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.
- (c) Remove 50 ml of Ringer lactate (RL) from a 500 ml RL bottle or bag, then add 50 ml of 50% glucose to the remaining 450 ml of RL to obtain 500 ml of 5% glucose-RL solution.

## **References**

1. Pan American Health Organization. Dengue: guidelines for patient care in the Region of the Americas, 2nd edition. Washington, D.C.: PAHO, 2016.  
<https://iris.paho.org/bitstream/handle/10665.2/31207/9789275118900-eng.pdf?sequence=1&isAllowed=y> [Accessed 23 Aug 2022]
2. Pan American Health Organization. Guidelines for the Clinical Diagnosis and Treatment of Dengue, Chikungunya, and Zika.

Washington, D.C. : PAHO; 2022.

<https://iris.paho.org/handle/10665.2/55867> [Accessed 16 Aug 2022]

# Viral haemorrhagic fevers

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](#), 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.

	<b>Reservoir/ Vector <i>Geographical distribution</i></b>	<b>Isolation of patients</b>	<b>Clinical features</b>	<b>Estimated case fatality rate</b>
<b>Ebola<sup>(a)</sup> Marburg</b>	Bats (?) <i>Africa</i>	Strict isolation	CS + sudden onset general malaise, vomiting and diarrhoea	60-80%
<b>Lassa<sup>(a)</sup></b>	Rodents <i>West Africa<sup>(b)</sup></i>	Strict isolation	CS + general malaise, headache, muscle pain, facial oedema, pharyngitis, proteinuria on reagent strip	15-20%
<b>Junin and Machupo<sup>(a)</sup></b>	Rodents <i>South America</i>	Isolation	CS + vomiting, erythema of the face and, depending on the aetiology: <ul style="list-style-type: none"> <li>• periorbital oedema, cervical adenopathy, pharyngitis</li> <li>• pharyngitis, reddened conjunctivae</li> <li>• oedema of the soft palate, generalised petechial rash</li> <li>• proteinuria on reagent strip</li> </ul>	15-30%
<b>Omsk</b>	Ticks <i>Europe, Asia</i>	None		2-5%
<b>Crimean Congo<sup>(a)</sup></b>	Livestock/Ticks <i>Africa, Asia</i>	Strict isolation		5-20%
<b>FHSR (hantavirus)<sup>(a)</sup></b>	Rodents <i>Asia and Europe</i>	None		< 1%
<b>Kyasanur</b>	Small mammals/Ticks <i>India</i>	None	CS + headache, muscle pain, prostration	2-10%
<b>Rift Valley<sup>(a)</sup></b>	Livestock/Mosquitoes <i>Africa</i>	Mosquito nets	Clinical signs: <ul style="list-style-type: none"> <li>• isolated fever</li> <li>• SC</li> <li>• encephalitis</li> <li>• retinitis and blindness</li> </ul>	30-50%
<b>Yellow fever<sup>(a)</sup></b>	Primates/Mosquitoes <i>Africa, South America</i>	Mosquito nets	CS + jaundice, proteinuria on reagent strip, oliguria, headache	10-30%

(a) Viral haemorrhagic fever with epidemic potential.

(b) For more information on geographic distribution of Lassa fever:

<https://www.who.int/emergencies/diseases/lassa-fever/geographic-distribution.png?ua=1>

## Laboratory

- A sample of whole blood must be sent 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).  
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:
  - two pairs of gloves,
  - double gown or coverall suit,
  - surgical cap or hood, mask, protective glasses,
  - impermeable apron,
  - rubber boots.
- 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: paracetamol (Chapter 1). Acetylsalicylic acid (aspirin) is contra-indicated.
  - Pain: mild (paracetamol), moderate (tramadol), severe (sublingual morphine): see Pain, Chapter 1.
  - Dehydration: oral rehydration salts and/or IV rehydration with Ringer lactate, see Dehydration, Chapter 1.
  - Seizures (Chapter 1).
  - Vomiting: **ondansetron** PO<sup>[1]</sup>
    - 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<sup>[2]</sup>:
 

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.

## References

1. World Health Organization. Clinical management of patients with viral haemorrhagic fever. A pocket guide for front-line health workers. Interim emergency guidance for country adaptation, February 2016.  
[http://apps.who.int/iris/bitstream/handle/10665/205570/9789241549608\\_eng.pdf;jsessionid=15E17DE39631519C2051413DDCBBC8A7?sequence=1](http://apps.who.int/iris/bitstream/handle/10665/205570/9789241549608_eng.pdf;jsessionid=15E17DE39631519C2051413DDCBBC8A7?sequence=1) [Accessed 11 January 2019]
2. Weekly epidemiological record-Relevé épidémiologique hebdomadaire 5 july 2013, 88th year / 5 juillet 2013, 88e 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

Last updated: January 2024

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<sup>3</sup>. 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.<sup>[1]</sup>

## 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<sup>3</sup> 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<sup>3</sup>, 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<sup>3</sup> regardless of symptoms).

## Treatment of HIV infection

### Antiretroviral (ARV) treatment<sup>a</sup>

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.

### 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<sup>3</sup>. 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](#)). 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](#), Chapter 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](#)).

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	<b>co-trimoxazole</b> PO
Cerebral toxoplasmosis	Children: 50 mg SMX + 10 mg TMP/kg once daily
Isosporiasis	Adults: 800 mg SMX + 160 mg TMP once daily
Various bacterial infections	
Malaria	

## 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		Alternative <b>dapsone</b> PO Children: 2 mg/kg once daily (max. 100 mg daily) Adults: 100 mg once daily
Toxoplasmosis	<b>co-trimoxazole</b> PO Children: 50 mg SMX + 10 mg TMP/kg once daily Adults: 800 mg SMX + 160 mg TMP once daily	Alternative Adults: <b>dapsone</b> PO: 200 mg once weekly or 50 mg once daily + <b>pyrimethamine</b> PO: 75 mg once weekly + <b>folinic acid</b> PO: 25 to 30 mg once weekly
Isosporiasis		—
Penicilliosis Histoplasmosis	<b>itraconazole</b> PO Adults: 200 mg once daily	—
Cryptococcal meningitis	<b>fluconazole</b> PO Children: 6 mg/kg once daily Adults: 200 mg once daily	—
Oral or oesophageal candidiasis	<b>fluconazole</b> PO Children: 3 to 6 mg/kg once daily Adults: 100 to 200 mg once daily	Only for frequent and severe recurrences
<i>Herpes simplex</i>	<b>aciclovir</b> 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
<b>Diarrhoea</b> with or without blood (also see <u>Chapter 3</u> )	Diarrhoea is defined as at least 3 liquid stools per day. Aetiologies: <b>Parasitic infections</b> <ul style="list-style-type: none"> <li>• <i>Isospora belli</i></li> <li>• <i>Cryptosporidium</i></li> <li>• <i>Microsporidium</i></li> <li>• <i>Giardia lamblia</i></li> <li>• <i>Entamoeba histolytica</i></li> </ul> <b>Bacterial infections</b> <ul style="list-style-type: none"> <li>• <i>Shigella</i></li> <li>• <i>Salmonella enteritis</i></li> <li>• <i>Campylobacter enteritis</i></li> </ul> <b>Mycobacterial infections</b> <ul style="list-style-type: none"> <li>• <i>Mycobacterium tuberculosis</i>            (gastrointestinal TB)</li> <li>• <i>Mycobacterium avium</i> complex</li> </ul> <b>Helminthiasis</b> <ul style="list-style-type: none"> <li>• <i>Strongyloides stercoralis</i></li> </ul> <b>Viral infections</b> <ul style="list-style-type: none"> <li>• Cytomegalovirus (CMV)</li> </ul> <b>Other causes</b> <ul style="list-style-type: none"> <li>• Kaposi sarcoma</li> <li>• Lymphoma</li> <li>• Idiopathic (HIV infection)</li> <li>• Antiretrovirals (especially lopinavir and ritonavir)</li> </ul>	1. History and clinical examination 2. Microscopic examination of stool for ova and parasites (2 to 3 samples) <b>Note:</b> <i>I. belli, Cryptosporidium, Microsporidium, MAC and CMV are unlikely if CD4 count &gt; 200 cells.</i>	<ul style="list-style-type: none"> <li>• Persistent (&gt; 2 weeks) or chronic (&gt; 4 weeks) diarrhoea is often associated with weight loss and dehydration.</li> <li>• Prevention or treatment of dehydration is critical (<u>Dehydration</u>, Chapter 1).</li> <li>• Depending on the results of the stool examinations: give appropriate treatment.</li> <li>• If there is no laboratory support:  <b>Acute bloody diarrhoea</b>  <ul style="list-style-type: none"> <li>• First-line treatment:            Children: <b>azithromycin</b> PO: 20 mg/kg once daily for 5 days or <b>ciprofloxacin</b> PO: 15 mg/kg 2 times daily for 7 days            Adults: <b>ciprofloxacin</b> PO: 500 mg 2 times daily for 7 days</li> <li>• If amoebiasis suspected: <b>tinidazole</b> or <b>metronidazole</b> PO (<u>Amoebiasis</u>, Chapter 3).</li> </ul> </li> </ul>

***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, Chapter 6).

- If no improvement (and no contraindications such as bloody diarrhoea), symptomatic treatment with **loperamide** PO:

Adults: initial dose 4 mg then 2 mg after each liquid stool (max. 16 mg daily)

			<p><b>Nutrition ++++</b></p> <p>Children: continue to breastfeed; increase daily calorie intake:</p> <p>6-11 months: add 150 kcal daily</p> <p>12-23 months: add 200 kcal daily</p> <p>2-5 years: add 250 kcal daily</p> <p>6-9 years: add 350 kcal daily</p> <p>10-14 years: add 400 kcal daily</p> <p>Eliminate fresh milk, give porridge prepared with rice water or soup or yoghurts. Give 2.5 ml of oil per meal.</p> <p>Any child 0-5 years should receive zinc sulfate (<u>Acute diarrhoea</u>, Chapter 3).</p> <p>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.</p>
<b>Oral and oesophageal lesions</b>	<p><b>Fungal infections</b></p> <ul style="list-style-type: none"> <li>• Oral candidiasis: see <u>Stomatitis</u>, Chapter 3.</li> <li>• Oesophageal candidiasis: pain on swallowing, dysphagia. May result in weight loss.</li> </ul> <p><b>Viral infections</b></p> <ul style="list-style-type: none"> <li>• Oral hairy leukoplakia (keratosis on the lateral sides of the tongue due to the Epstein-Barr virus)</li> <li>• Oral and oesophageal herpes</li> </ul> <p><b>Aphthous ulcers</b></p>	<p>Clinical examination is enough to make a diagnosis.</p> <p>Consider all severe oral candidiasis (if the pharynx is involved) as oesophageal candidiasis even in the absence of dysphagia.</p>	<ul style="list-style-type: none"> <li>• Mild oral candidiasis</li> </ul> <p><b>nystatin PO</b></p> <p>Children and adults: 100 000 IU (= 1 ml) 4 times daily</p> <p>or <b>miconazole oral gel</b></p> <p>Children 6 months-2 years: 1.25 ml 4 times daily</p> <p>Children over 2 years and adults: 2.5 ml 4 times daily</p> <p>The treatment lasts 7 to 14 days.</p> <ul style="list-style-type: none"> <li>• Moderate to severe oral candidiasis and oesophageal candidiasis</li> </ul> <p><b>fluconazole PO</b></p> <p>Children: 3 to 6 mg/kg once daily</p> <p>Adults: 50 to 200 mg once daily up to 400 mg daily if necessary</p> <p>The treatment lasts 7 to 14 days for oral candidiasis and 14 to 21 days for oesophageal candidiasis.</p> <p><i>Candidiasis is an indication for prophylaxis with co-trimoxazole.</i></p> <ul style="list-style-type: none"> <li>• Oral hairy leukoplakia: no treatment</li> </ul>

			<ul style="list-style-type: none"> <li>• Oral herpes: Analgesics (paracetamol, ibuprofen). For recurrent or extensive forms affecting the oesophagus, add: <b>aciclovir</b> 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 <i>Secondary prophylaxis only for patients with frequent recurrences.</i></li> </ul>
<b>Respiratory problems</b> (also see <u>Chapter 2</u> )	<p>Cough and/or thoracic pain and/or dyspnoea in a symptomatic HIV infected patient.</p> <p>Aetiologies:</p> <p><b>Bacterial infections</b></p> <ul style="list-style-type: none"> <li>• <i>Streptococcus pneumoniae</i></li> <li>• <i>Haemophilus influenzae</i></li> <li>• <i>Staphylococcus aureus</i></li> </ul> <p><b>Mycobacterial infections</b></p> <ul style="list-style-type: none"> <li>• <i>M. tuberculosis</i>, MAC</li> </ul> <p><b>Protozoal infections</b></p> <ul style="list-style-type: none"> <li>• <i>Pneumocystis jiroveci</i> (PCP)</li> </ul> <p><b>Fungal infections</b></p> <ul style="list-style-type: none"> <li>• <i>Cryptococcus neoformans</i></li> <li>• <i>Histoplasma capsulatum</i></li> <li>• <i>Coccidioides immitis</i></li> <li>• <i>Aspergillus</i> spp</li> <li>• <i>Penicillium marneffei</i></li> </ul> <p><b>Viral infections</b></p> <ul style="list-style-type: none"> <li>• CMV</li> </ul> <p><b>Neoplasms</b></p> <ul style="list-style-type: none"> <li>• Kaposi sarcoma</li> <li>• Non-Hodgkin's lymphoma</li> </ul>	<p>1. History and clinical examination: Blood in the sputum? If fever &lt; 7 days, dyspnoea: unlikely TB. If cough &gt; 21 days, weight loss, thoracic pain &gt; 15 days, no dyspnoea: likely TB. Pulmonary auscultation: bilateral lobar pneumonia?</p> <p>2. If possible:</p> <ol style="list-style-type: none"> <li>a) Look for AFB in sputum</li> <li>b) Chest x-ray</li> </ol> <ul style="list-style-type: none"> <li>• PCP: bilateral interstitial infiltrates</li> <li>• TB: miliary shadowing, large heart, pleural effusion, enlarged lymph nodes inside the chest.</li> </ul> <p><i>Notes</i></p> <ul style="list-style-type: none"> <li>• MAC, PCP, CMV and fungal infections are unlikely in patients with a CD4 count &gt; 200 cells/mm<sup>3</sup>.</li> <li>• Staphylococcal pneumonia is often associated with a pyomyositis or an abscess.</li> </ul>	<ul style="list-style-type: none"> <li>• For the diagnosis and treatment of upper respiratory tract infections, particularly pneumonia: see <u>Chapter 2</u>.</li> <li>• If the chest x-ray is consistent with staphylococcal pneumonia: Children: see <u>Staphylococcal pneumonia</u>, Chapter 2.</li> <li>• Adults: <b>ceftriaxone</b> IM or slow IV 1 g once daily + <b>cloxacillin</b> IV 2 g every 6 hours</li> <li>• If the sputum examination is AFB+, treat for TB.</li> </ul>

	<p><b>Others</b></p> <ul style="list-style-type: none"> <li>• Lymphoid interstitial pneumonia</li> <li>• Pleural effusion (often TB)</li> <li>• Pericardial effusion (often TB)</li> <li>• Pneumothorax (may be due to PCP)</li> </ul>	<ul style="list-style-type: none"> <li>• If the sputum examination is negative and the chest x-ray is consistent with PCP: <b>co-trimoxazole</b> PO for 21 days Children: 50 mg SMX + 10 mg TMP/kg 2 times daily Adults: 1600 SMX + 320 TMP 3 times daily</li> </ul> <p><b>Note:</b> the symptoms may become worse during the first phase of treatment, effectiveness can only be evaluated after one week of treatment.</p> <p>Add <b>prednisolone</b> 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</p> <p><i>Secondary prophylaxis is recommended.</i></p> <ul style="list-style-type: none"> <li>• Fungal infections (cryptococcosis, penicilliosis, histoplasmosis): Adults: <b>amphotericin B</b> IV: 0.7 to 1 mg/kg once daily for 2 weeks (cryptococcosis, penicilliosis) or 1 to 2 weeks (histoplasmosis), then: <b>fluconazole</b> PO: 400 mg daily for 8 weeks (cryptococcosis) <b>itraconazole</b> PO: 200 mg 2 times daily for 10 weeks (penicilliosis) <b>itraconazole</b> PO: 200 mg 3 times daily for 3 days then 200 to 400 mg daily for 12 weeks (histoplasmosis)</li> </ul> <p><i>Secondary prophylaxis is recommended.</i></p>
<b>Lymphadenopathy</b>	Enlarged lymph nodes in a symptomatic HIV-infected patient	<ol style="list-style-type: none"> <li>1. Clinical examination: look for a local cause (skin or dental infection etc.); TB or syphilis.</li> </ol> <ul style="list-style-type: none"> <li>• Treat according to the aetiology or empirical treatment with, for example <b>doxycycline</b> PO.</li> <li>• TB: see the guide <u><a href="#">Tuberculosis</a></u>, MSF.</li> </ul>

	<p>Persistent generalised lymphadenopathy (PGL):</p> <ul style="list-style-type: none"> <li>• 2 or more extra-inguinal sites</li> <li>• lymph nodes &gt; 1.5 cm</li> <li>• enlarged for 3 or more months PGL is usually due to HIV infection.</li> </ul> <p>Aetiologies:</p> <p><b>HIV infection</b></p> <p><b>Infections</b></p> <ul style="list-style-type: none"> <li>• TB</li> <li>• Syphilis</li> <li>• Histoplasmosis</li> <li>• Toxoplasmosis</li> <li>• CMV</li> </ul> <p><b>Neoplasms</b></p> <ul style="list-style-type: none"> <li>• Kaposi sarcoma</li> <li>• Lymphoma</li> </ul>	<p>2. Suspected TB: lymph node aspiration, look for AFB, chest x-ray  <i>Note:</i> in HIV infected patients, TB is often extrapulmonary.</p> <p>3. Suspected syphilis: serology</p> <p>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).</p>	<ul style="list-style-type: none"> <li>• Early syphilis:  <b>benzathine benzylpenicillin IM</b>            Adults: 2.4 MIU single dose (1.2 MIU in each buttock)            or, if not available:  <b>azithromycin PO</b>            Adults: 2 g single dose  <i>Note:</i> in patients in stage 1, no further investigation (other than 1, 2 and 3 in this table) or treatment are required.</li> </ul>
<p><b>Skin lesions</b>            (also see  <u>Chapter 4</u>)</p>	<p><b>Bacterial infections</b></p> <ul style="list-style-type: none"> <li>• Furunculosis</li> <li>• Impetigo and pyoderma</li> <li>• Axillary hidradenitis</li> <li>• Pyomyositis</li> <li>• Syphilis</li> </ul> <p><b>Viral infections</b></p> <ul style="list-style-type: none"> <li>• Herpes zoster</li> <li>• Herpes simplex</li> <li>• Genital warts</li> <li>• <i>Molluscum contagiosum</i></li> </ul> <p><b>Fungal infections</b></p> <ul style="list-style-type: none"> <li>• Candidiasis, dermatophytoses and deep mycoses (penicilliosis, cryptococcosis, histoplasmosis, etc.)</li> </ul> <p><b>Neoplasms</b></p> <ul style="list-style-type: none"> <li>• Kaposi sarcoma</li> </ul>		<p><b>Bacterial infections</b></p> <ul style="list-style-type: none"> <li>• Furunculosis, impetigo, chronic folliculitis: see <u>Bacterial skin infections</u>, Chapter 4.</li> <li>• Suppurative axillary hidradenitis: local treatment + <b>doxycycline PO</b>: 200 mg once daily for 6 weeks (in adults)</li> <li>• Pyomyositis: antibiotics and surgical drainage, see <u>Pyomyositis</u>, Chapter 10.</li> <li>• Primary and secondary syphilis: see <u>Genital ulcers</u>, Chapter 9.</li> </ul>

	<p><b>Other skin infections</b></p> <ul style="list-style-type: none"> <li>• Chronic prurigo or urticaria</li> <li>• Severe seborrhoeic dermatitis</li> <li>• Psoriasis</li> <li>• Scabies</li> <li>• Diffuse cutaneous xerosis</li> </ul> <p><b>Rash caused by medication</b></p> <p><b>Bed sores</b></p>	<p><b>Viral infections</b></p> <ul style="list-style-type: none"> <li>• Herpes zoster: see <a href="#">Herpes simplex and herpes zoster</a>, Chapter 4.</li> </ul> <p>For necrotic, extensive forms, eruption on the face, ophthalmic zoster, add <b>aciclovir</b> within 48 hours of the onset of lesions:</p> <p>Children (IV route): 5 to 10 mg/kg every 8 hours for 7 days</p> <p>Adults (oral route): 800 mg 5 times daily for 7 days</p> <ul style="list-style-type: none"> <li>• Herpes simplex: see <a href="#">Herpes simplex and herpes zoster</a>, Chapter 4.</li> <li>• Genital warts: see <a href="#">Venereal warts</a>, Chapter 9.</li> </ul> <p><b>Fungal infections</b></p> <ul style="list-style-type: none"> <li>• Candidiasis: <b>2% miconazole</b> cream, one application 2 times daily</li> <li>• Dermatophytoses: see <a href="#">Superficial fungal infections</a>, Chapter 4.</li> </ul> <p><b>Treatment of Kaposi sarcoma (KS)</b></p> <ul style="list-style-type: none"> <li>• Start promptly ART.</li> <li>• KS tumours with oedema or ulceration or presence of extensive oral or gastrointestinal or pulmonary KS +/- systemic illness: chemotherapy</li> </ul> <p><b>Other skin infections</b></p> <ul style="list-style-type: none"> <li>• Prurigo, urticaria: see <a href="#">Other skin disorders</a>, Chapter 4.</li> <li>• Seborrhoeic dermatitis: <b>Whitfield's</b> ointment or <b>2% miconazole</b>, one application 2 times daily. For severe inflammation, use a topical corticosteroid in combination with miconazole.</li> <li>• Xerosis: <b>zinc oxide</b> ointment or <b>calamine</b> lotion</li> <li>• Psoriasis: <b>corticosteroids</b> and <b>zinc oxide</b> ointment</li> <li>• Scabies: local treatment. For crusted or profuse scabies, add <b>ivermectin</b> PO (see <a href="#">Scabies</a>, Chapter 4).</li> </ul>	
<b>Neurological</b>	Aetiologies:	History and clinical	Positive malaria test: see <a href="#">Malaria</a> ,

<b>disorders in adults</b>	<p><b>Infections</b></p> <ul style="list-style-type: none"> <li>• TB meningitis</li> <li>• Cryptococcal meningitis</li> <li>• Cerebral toxoplasmosis</li> <li>• Neurosyphilis</li> <li>• CMV encephalitis</li> <li>• HIV encephalopathy</li> <li>• Progressive multifocal leuko- encephalopathy</li> <li>• Cerebral malaria</li> </ul> <p><b>Neoplasms</b></p> <ul style="list-style-type: none"> <li>• Primary CNS lymphoma</li> </ul> <p><b>Common causes of headache unrelated to HIV infection:</b> sometimes more frequent in HIV infected patients (sinusitis, problems with accommodation etc.)</p> <p><b>Adverse effects of ARVs</b></p>	<p>examination:</p> <ul style="list-style-type: none"> <li>• Change in mental state</li> <li>• Focal deficits</li> <li>• Seizures</li> <li>• Signs of meningeal irritation</li> <li>• Raised intracranial pressure</li> <li>• Motor problems, ataxia</li> </ul> <p>In settings where cryptococcal infection is common, screen all adults with CD4 &lt; 100 prior to initiation of ART, using a rapid CrAg test on serum or plasma.</p> <p>In endemic areas: check for malaria (if febrile). Lumbar puncture (LP) if not contra-indicated.</p> <p>Elements in favour of neurosyphilis:</p> <ul style="list-style-type: none"> <li>• VDRL positive in blood and/or CSF</li> <li>• cells in the CSF</li> <li>• high protein in the CSF</li> </ul>	<p>Chapter 6.</p> <p>If focal signs, treat for toxoplasmosis:</p> <p><b>co-trimoxazole</b> PO: 25 mg SMX + 5 mg TMP/kg 2 times daily for 4 to 6 weeks</p> <p>or</p> <p><b>pyrimethamine</b> PO: 100 mg morning and evening on D1, then 75 to 100 mg daily + <b>sulfadiazine</b> PO: 2 g 2 to 3 times daily + <b>folic acid</b> PO: 15 mg once daily, for 6 weeks</p> <p><i>A secondary prophylaxis is recommended.</i></p>
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			<p>If the LP is positive:</p> <ul style="list-style-type: none"> <li>• <u>Bacterial meningitis</u>: see Chapter 7.</li> <li>• TB meningitis: see the guide <u>Tuberculosis</u>, MSF.</li> <li>• Cryptococcal meningitis<sup>[2]</sup> : <b>amphotericin B</b> IV: 1 mg/kg once daily + <b>flucytosine</b> PO: 25 mg/kg 4 times daily for 1 week then <b>fluconazole</b> PO: 1200 mg once daily for 1 week then 800 mg once daily for 8 weeks or, if not available <b>amphotericin B</b> IV: 1 mg/kg once daily + <b>fluconazole</b> PO: 1200 mg once daily for 2 weeks then <b>fluconazole</b> PO alone: 800 mg once daily for 8 weeks or <b>fluconazole</b> PO: 1200 mg once daily + <b>flucytosine</b> PO: 25 mg/kg 4 times daily for 2 weeks then <b>fluconazole</b> 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. <i>A secondary prophylaxis is recommended.</i> <i>Note:</i> 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. <b>Neurosphylis:</b> <b>benzylpenicillin</b> IV: 2 to 4 MIU (1.2 to 2.4 g) every 4 hours for 14 days or <b>ceftriaxone</b> 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 <u>Pain</u>, Chapter 1).</li> </ul>
<b>Neurological</b>	Aetiologies:	Good history taking as	Positive malaria test: see <u>Malaria</u> ,

<b>disorders in children</b>	<ul style="list-style-type: none"> <li>• Bacterial meningitis</li> <li>• TB meningitis</li> <li>• Cryptococcal meningitis</li> <li>• Cerebral toxoplasmosis</li> <li>• CMV meningo-encephalitis</li> <li>• Cerebral malaria</li> </ul>	<p>only patients with acute episodes benefit from specific aetiological treatment (seizures, meningeal syndrome, focal signs).</p> <p>In endemic areas, check for malaria (if febrile). Lumbar puncture (LP) if not contra-indicated.</p>	<p>Chapter 6.</p> <p>If LP is not possible:</p> <ul style="list-style-type: none"> <li>• Treat for <b>bacterial meningitis</b> if patient febrile and/or meningeal syndrome (see Chapter 7).</li> <li>• If focal signs, treat for toxoplasmosis:</li> </ul> <p><b>co-trimoxazole</b> PO: 25 mg SMX + 5 mg TMP/kg 2 times daily for 4 to 6 weeks</p> <p>or</p> <p><b>pyrimethamine</b> PO: 1 mg/kg 2 times daily for 2 days then 1 mg/kg once daily + <b>sulfadiazine</b> PO: 40 mg/kg 2 times daily + <b>folinic acid</b> PO: 10 mg once daily, for 8 weeks</p> <p><i>A secondary prophylaxis is recommended.</i></p>
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			<p>If the LP is positive:</p> <ul style="list-style-type: none"> <li>• <b>Bacterial meningitis</b>: see Chapter 7.</li> <li>• TB meningitis: see the guide <b>Tuberculosis</b>, MSF.</li> <li>• Cryptococcal meningitis (in order of preference)<sup>[2]</sup>:</li> </ul> <p><b>amphotericin B IV</b>: 1 mg/kg once daily + <b>flucytosine</b> PO: 25 mg/kg 4 times daily for 1 week then <b>fluconazole</b> 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 <b>amphotericin B IV</b>: 1 mg/kg once daily + <b>fluconazole</b> PO: 12 mg/kg once daily (max. 800 mg daily) for 2 weeks then <b>fluconazole</b> PO alone: 6-12 mg/kg once daily for 8 weeks (max. 800 mg daily) or <b>fluconazole</b> PO: 12 mg/kg once daily (max. 800 mg daily) + <b>flucytosine</b> PO: 25 mg/kg 4 times daily for 2 weeks then <b>fluconazole</b> 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.</p> <p><i>A secondary prophylaxis is recommended.</i></p>
<b>Persistent or recurrent fever</b>	<p>Temperature &gt; 38 °C, chronic (lasting more than 5 days) or recurrent (multiple episodes in a period of more than 5 days)</p> <p>Aetiologies:</p>	<ol style="list-style-type: none"> <li>1. History and clinical examination: look for a ENT or urinary infection, TB, skin infection, enlarged lymph nodes etc.</li> <li>2. In endemic areas, check for malaria.</li> <li>3. Suspected TB: look for AFB.</li> </ol>	<p>Positive malaria test: see <b>Malaria</b>, Chapter 6.</p> <p>If testing is not available: in endemic areas, treat malaria.</p> <p>Suspected meningitis: treat according to the results of the LP.</p> <p>If LP is not available, treat for <b>bacterial meningitis</b>, see Chapter 7.</p>

<p><b>Infections</b></p> <ul style="list-style-type: none"> <li>• Common childhood diseases</li> <li>• Severe bacterial infections (TB, pneumonia, typhoid fever, septicaemia, meningitis, endocarditis, etc.)</li> <li>• Occult bacterial infections (sinusitis, otitis, urinary tract infections)</li> <li>• Opportunistic infections (TB, mycosis, toxoplasmosis)</li> <li>• Malaria</li> </ul> <p><b>Neoplasms</b></p> <ul style="list-style-type: none"> <li>• Non-Hodgkin's lymphoma</li> </ul> <p><b>HIV infection</b></p> <p><b>Fever caused by medication</b></p>	<p>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.</p>	<p>Identified or suspected focus of infection:</p> <ul style="list-style-type: none"> <li>• ENT: see <u>Chapter 2</u>; urinary: see <u>Chapter 9</u>, etc.</li> <li>• TB: see the guide <u>Tuberculosis</u>, MSF.</li> </ul>
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## Footnotes

- (a) 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=1](http://apps.who.int/iris/bitstream/10665/208825/1/9789241549684_eng.pdf?ua=1)

## 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](#)

[Urolithiasis](#)

[Acute cystitis](#)

[Acute pyelonephritis](#)

[Acute prostatitis](#)

[Genital infections](#)

[Urethral discharge](#)

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[Lower abdominal pain in women](#)

[Upper genital tract infections \(UGTI\)](#)

[Venereal warts](#)

[Major genital infections \(summary\)](#)

[Abnormal uterine bleeding \(in the absence of pregnancy\)](#)

# Nephrotic syndrome in children

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](#), 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](#) and [HIV infection](#) (Chapter 8), [Malaria](#) and [Schistosomiases](#) (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<sup>a</sup>. NS is excluded if heavy proteinuria is not consistently present.
  - In case of macroscopic haematuria, or microscopic haematuria  $\geq +$ , 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.

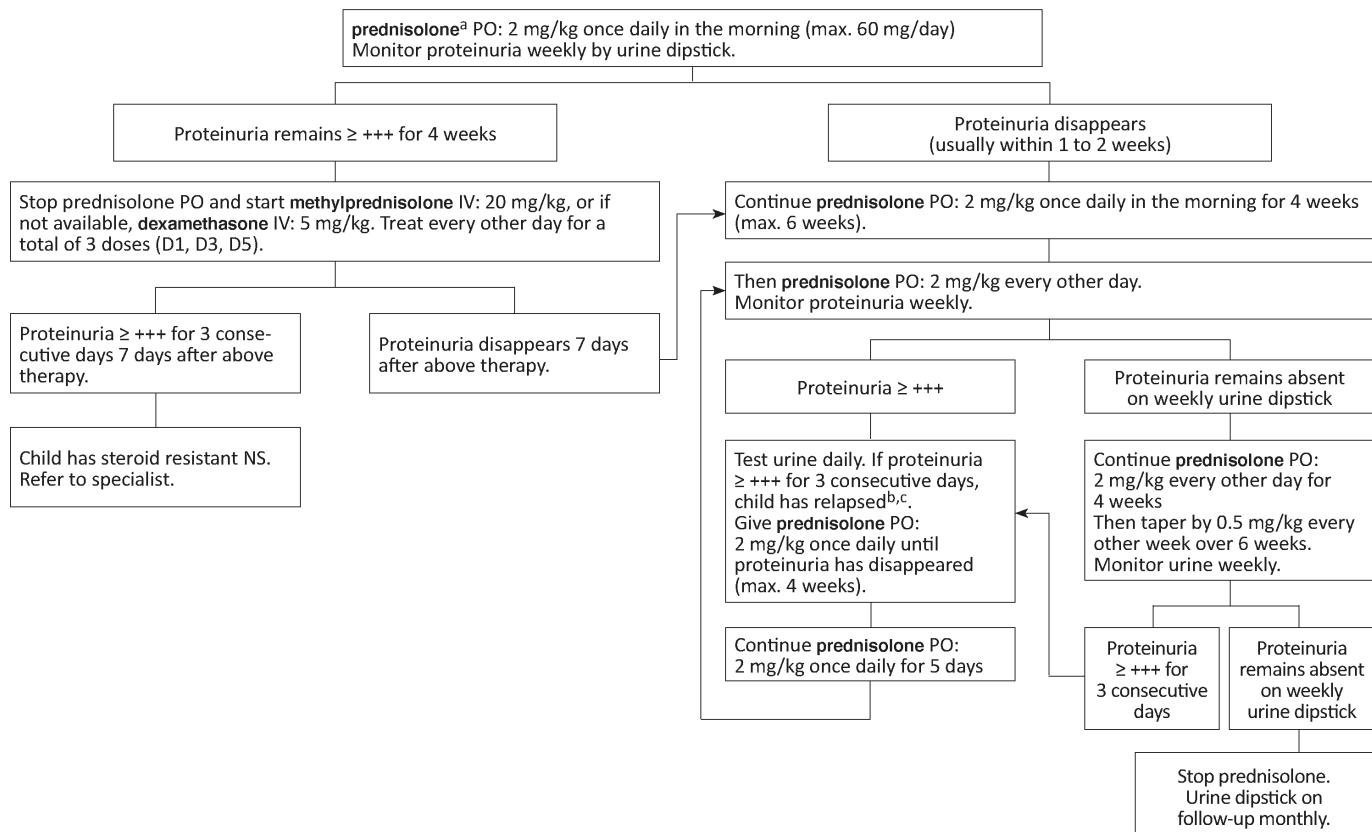
## Treatment

- 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  $\geq$  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](#), 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.

## Footnotes

- (a) 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

Last updated: December 2020

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](#), 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 (see [Pain](#), Chapter 1).
- In case of secondary infection: antibiotic treatment as for [pyelonephritis](#). 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.

# Acute cystitis

Last updated: July 2021

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](#).

The symptom 'burning pain on urination' alone is insufficient to make the diagnosis. See [Abnormal vaginal discharge](#).

## Investigations

- 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 positive for nitrites and/or leukocytes, a urinary infection is likely.
  - In women, if dipstick analysis is negative for both nitrites and leukocytes, a urinary infection is excluded.
- 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 antibiotic therapy should be administered to patients with typical signs of cystitis and positive dipstick urinalysis (leukocytes 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.

- POCUS<sup>a</sup>: in cases of recurrent cystitis, perform FAST views to evaluate for signs of urinary tract pathologies.

## 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 young, nonpregnant 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 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 3 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

**nitrofurantoin** PO (contraindicated in the last month of pregnancy): 100 mg 3 times daily for 7 days

or

**cefixime** PO: 200 mg 2 times daily for 5 days

## Footnotes

(a) POCUS should only be performed and interpreted by trained clinicians.

# Acute pyelonephritis

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](#), 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](#), Chapter 9.

## Treatment

- Criteria for hospital admission:
  - Patients at risk of complications: children, pregnant women, men<sup>a</sup>, 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 antibiotic therapy 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 ( $\geq$  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 ( $\geq 2$  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 ( $\geq 2$  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<sup>b</sup> (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  $\geq 40$  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<sup>[1]</sup>

▫ **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<sup>b</sup> : 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](#), Chapter 1).
- Maintain proper hydration (1.5 litres daily in adults), especially in children (risk of dehydration); treat dehydration if present (see [Dehydration](#), Chapter 1).
- Management of septic shock if needed.

## Footnotes

- (a) Pyelonephritis is rare in men; bacterial prostatitis should be suspected in the event of febrile urinary tract infection.

(b) 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. 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

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.<sup>[1]</sup>
- Symptomatic treatment:
  - Ensure adequate hydration (1.5 litres daily).
  - Treat fever (Chapter 1) and pain (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

Last updated: August 2021

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; sexual partners need to be treated simultaneously in case of sexually transmitted infections<sup>a</sup> 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<sup>b</sup> that may cause each syndrome.

Look for a GI if a patient complains of:	See
Urethral discharge Painful or difficult urination (dysuria)	<u>Urethral discharge</u>
Abnormal vaginal discharge Vulvar itching/burning Pain with intercourse (dyspareunia) Painful or difficult urination (dysuria)	<u>Abnormal vaginal discharge</u>
Genital blisters or sores Burning sensation in the vulva or perineum	<u>Genital ulcers</u>
Skin growths in the genital (or anal) area	<u>Venereal warts</u>
Lower abdominal pain (in women)	<u>Lower abdominal pain</u> <u>Upper genital tract infections</u>

## 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](#), Chapter 8);
  - ▷ b) the risk of pregnancy resulting from rape. Administer emergency contraception as soon as possible, ideally within 72 hours after the rape<sup>c</sup> :  
**levonorgestrel** PO, one 1.5 mg tablet single dose (including in women receiving HIV post-exposure prophylaxis); double the dose (3 mg) only if the patient was already taking an enzyme-inducing drug (e.g. rifampicin, carbamazepine, certain antiretrovirals) before the rape;  
or **ulipristal** PO, one 30 mg tablet single dose;  
or a **copper intrauterine device** (except in case of active genital infection);
- prevention of sexually transmitted infections: a single dose of **azithromycin** PO 2 g + **ceftriaxone** IM 500 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](#), Chapter 7) if there are any wounds;
- vaccination against hepatitis B (accelerated vaccination schedule, see [Viral hepatitis](#), Chapter 8).

- **Curative treatment:**

- of any related pathologies/infections if the assault is not recent.
- of wounds,

**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](#).

## Footnotes

- (a) GI may be sexually transmitted (e.g. gonorrhoea, chlamydia) or not (e.g. most cases of candidiasis).
- (b) Keep in mind that in *Schistosoma haematobium* endemic areas, genital symptoms may also be due to, or associated with, genitourinary schistosomiasis (see [Schistosomiasis](#), Chapter 6).
- (c) Nevertheless, between 72 and 120 hours (5 days) after the rape, emergency contraception is still sufficiently effective to be administered.

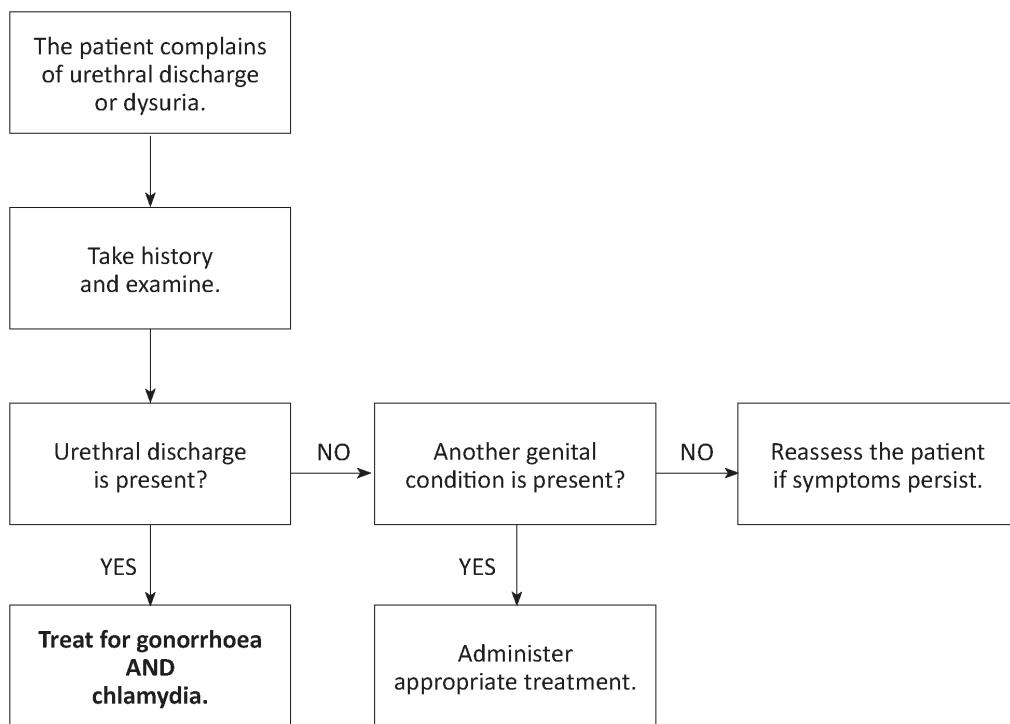
# Urethral discharge

Last updated: August 2022

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<sup>a</sup>. 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](#).
- 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:

<b>Treatment for chlamydia</b>		<b>Treatment for gonorrhoea</b>
<b>azithromycin</b> PO: 1 g single dose or <b>doxycycline</b> PO: 100 mg 2 times daily for 7 days	<b>PLUS</b>	<b>ceftriaxone</b> IM: 500 mg single dose or, if ceftriaxone is not available, <b>cefixime</b> PO: 400 mg 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 reinfection.

## Treatment of the partner

The sexual partner receives the same treatment as the patient, whether or not symptoms are present.

### Footnotes

- (a) 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

Last updated: August 2022

Abnormal vaginal discharge is defined as discharge that is different 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.

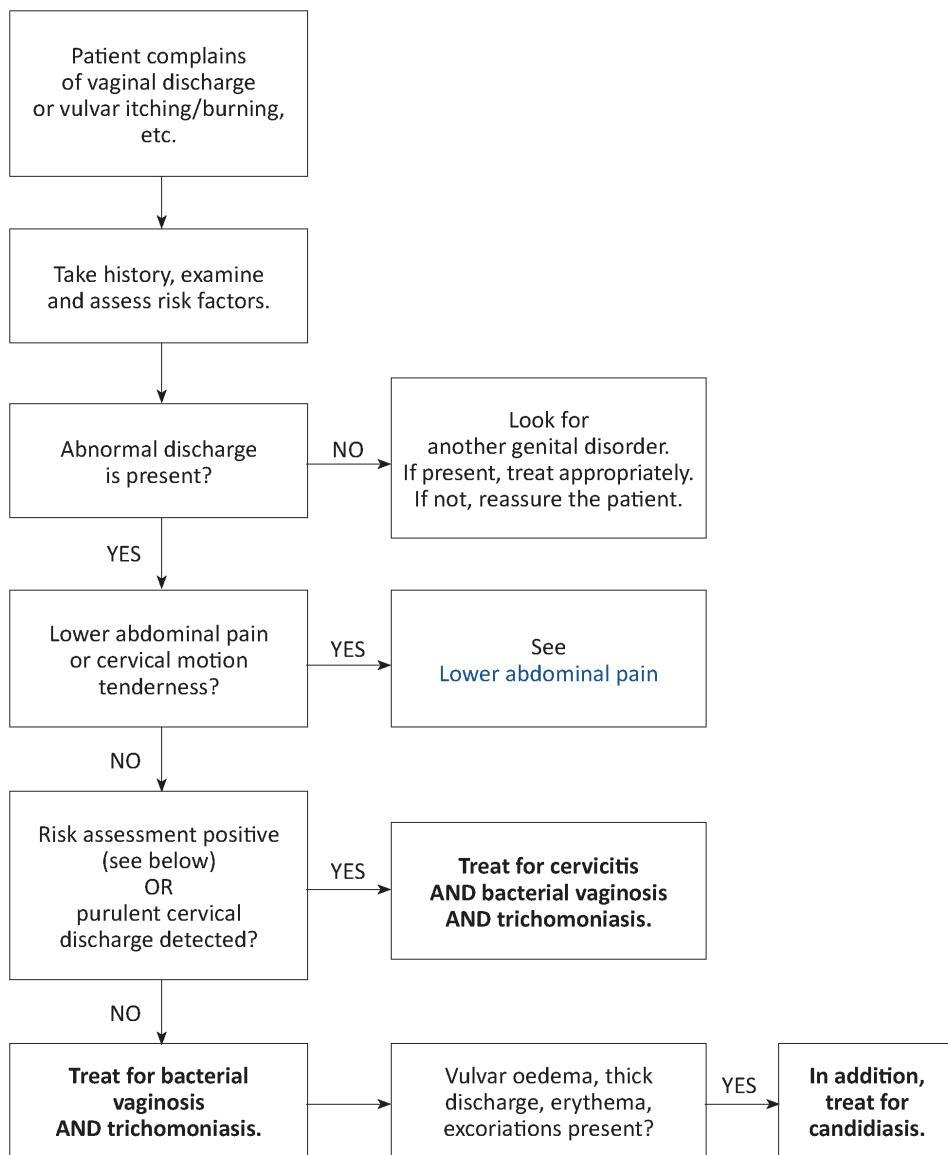
Abnormal discharge must be clinically confirmed: inspection of the vulva, speculum exam checking for cervical/vaginal inflammation or discharge.

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 [Upper genital tract infections](#).

## 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

- Xpert molecular (PCR) tests are recommended for the detection of *C. trachomatis* and *N. gonorrhoea*.
- 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.

Treatment for chlamydia		Treatment for gonorrhoea
<b>Non-pregnant women</b>		
<b>azithromycin</b> PO: 1 g single dose or <b>doxycycline</b> PO: 100 mg 2 times daily for 7 days	<b>PLUS</b>	<b>ceftriaxone</b> IM: 500 mg single dose or, if not available, <b>cefixime</b> PO: 400 mg single dose
<b>Pregnant women</b>		
<b>azithromycin</b> PO: 1 g single dose or <b>erythromycin</b> PO: 1 g 2 times daily or 500 mg 4 times daily for 7 days	<b>PLUS</b>	<b>ceftriaxone</b> IM: 500 mg single dose or, if not available, <b>cefixime</b> 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.

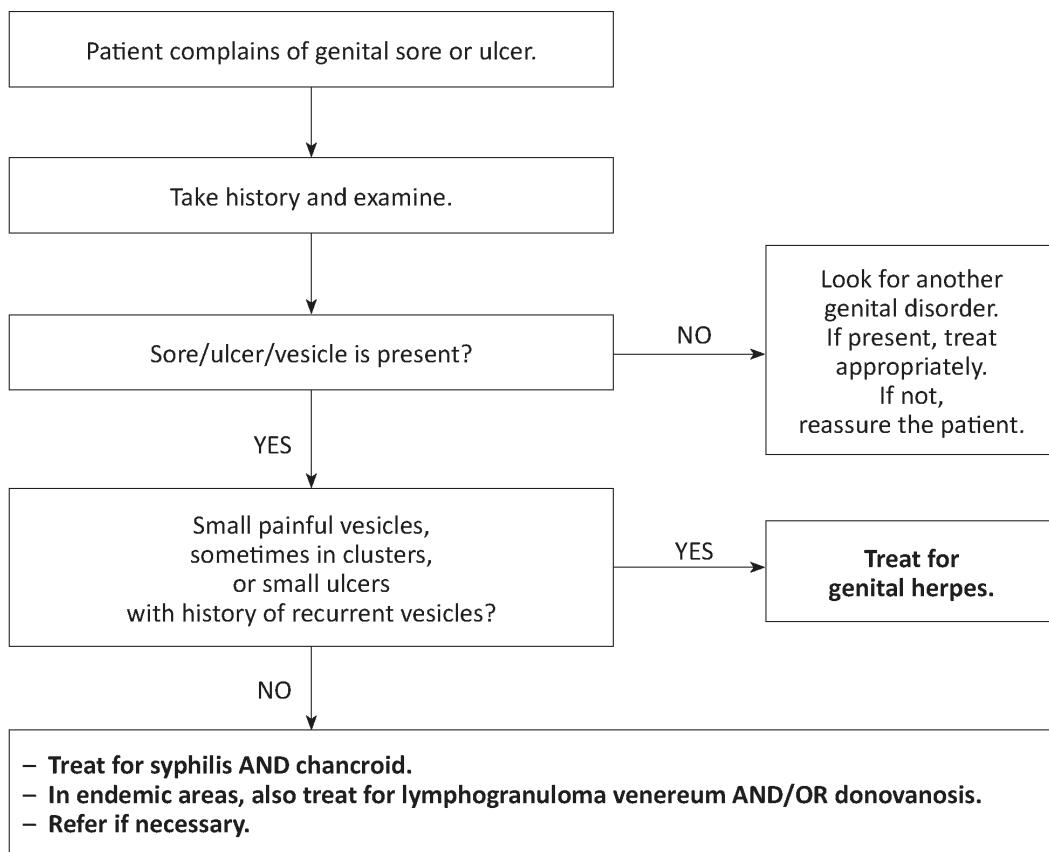
In the case of vulvovaginal candidiasis, the partner is treated only if symptomatic (itching and redness of the glans/prepuce): **miconazole 2%** cream, one application 2 times daily for 7 days.

# Genital ulcers

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)<sup>a</sup> 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 symptoms 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 per year), see [HIV infection and AIDS](#), Chapter 8.

- Treatment of [pain](#): paracetamol PO (Chapter 1).

## Syphilis

**benzathine benzylpenicillin** IM: 2.4 MUI per injection (half the dose in each buttock)<sup>[1]</sup>.

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)<sup>b</sup>

or

**azithromycin** PO: 2 g single dose (only in cases of early syphilis and only if the strain is sensitive)<sup>[2]</sup>

## 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<sup>b</sup>

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<sup>b</sup>

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).

## Footnotes

- (a) 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.
- (b) Doxycycline is contra-indicated in pregnant and breast-feeding women.

## 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

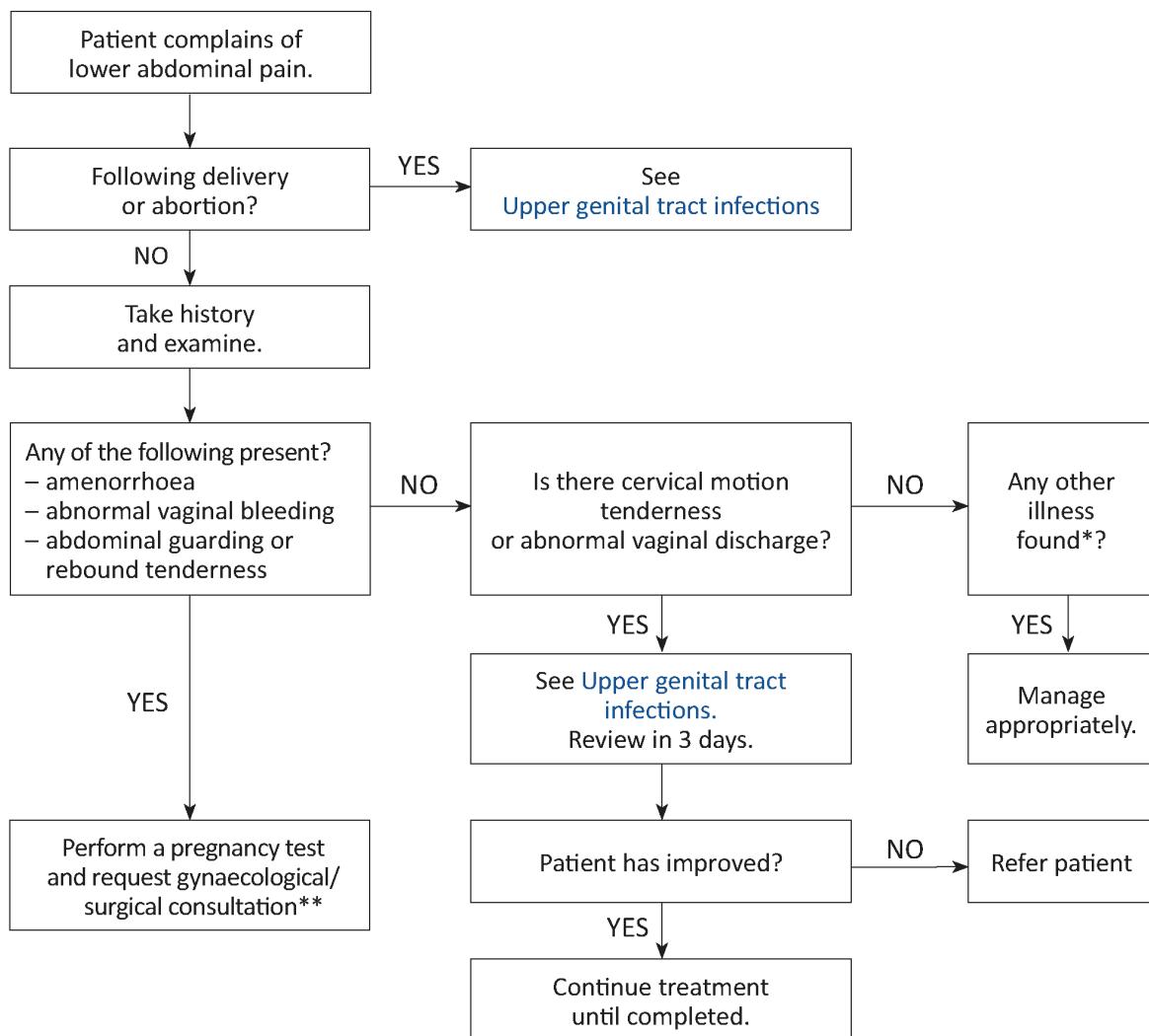
Upper genital tract infection should be suspected in women with lower abdominal pain (see [Upper genital tract infections](#)).

Gynaecological examination should be routinely performed:

- Inspection of the vulva, speculum examination: check for purulent discharge or inflammation.
- Abdominal exam and bimanual pelvic exam: check for pain on mobilising the cervix.

If available, POCUS<sup>a</sup>: perform FAST views to evaluate for free fluid and urological abnormalities. Perform pelvic views to evaluate for uterine and adnexal pathologies. Consult a gynaecologist (local or via telemedicine services).

## 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).

## Footnotes

- (a) POCUS should only be performed and interpreted by trained clinicians.

# Upper genital tract infections (UGTI)

Last update: March 2023

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: 500 mg single dose

- + **doxycycline** PO: 100 mg 2 times daily for 14 days<sup>a</sup>
- + **metronidazole** PO: 500 mg 2 times daily for 14 days
- Treatment in hospital:
  - ceftriaxone** IM or IV<sup>b</sup>: 1 g once daily
  - + **doxycycline** PO: 100 mg 2 times daily for 14 days<sup>a</sup>
  - + **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), 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.

## Footnotes

- (a) 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.
- (b) 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.

# Venereal warts

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<sup>a</sup>.

## 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%<sup>b</sup>** 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<sup>c</sup> 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.

## Footnotes

- (a) 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).
- (b) **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.
- (c) 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)**

Last updated: July 2021

Pathogens/ Infections	Clinical features	Investigations	Treatment
<i>Neisseria gonorrhoeae</i> (gonorrhoea)	<ul style="list-style-type: none"> <li>In women: <ul style="list-style-type: none"> <li>vaginal discharge, cervicitis (mucopurulent cervical discharge), dysuria (50% of infections are asymptomatic);</li> <li>UGTI (salpingitis, endometritis).</li> </ul> </li> <li>In men: purulent urethral discharge and sometimes dysuria (5 to 50% of infections are asymptomatic).</li> </ul>	<ul style="list-style-type: none"> <li>Best method is PCR (Xpert), if available.</li> <li>In men (not sensitive enough in women): Gram or methylene blue stain: intracellular diplococci and polymorphonuclear leukocytes (more than 4 per field).</li> </ul>	<b>ceftriaxone</b> IM: 500 mg single dose or, if not available, <b>cefixime</b> PO: 400 mg single dose Treat also for chlamydia. In case of upper genital tract infection, see <u>UGTI</u> .
<i>Chlamydia trachomatis</i> (chlamydia)	<ul style="list-style-type: none"> <li>In women: <ul style="list-style-type: none"> <li>vaginal discharge, cervicitis, and rarely dysuria (&gt; 50% of infections are asymptomatic);</li> <li>UGTI (salpingitis, endometritis).</li> </ul> </li> <li>In men: mild urethral discharge and/or dysuria but up to 90% of infections are asymptomatic.</li> </ul>	<ul style="list-style-type: none"> <li>The best method is PCR (Xpert), if available.</li> </ul>	<b>azithromycin</b> PO: 1 g single dose or <b>doxycycline</b> PO <sup>(a)</sup> : 200 mg daily for 7 days Treat also for gonococcal infection (except when a Gram stain in males or PCR shows no <i>N. gonorrhoeae</i> ). In case of upper genital tract infection, see <u>UGTI</u> .
<i>Trichomonas vaginalis</i> (trichomoniasis)	<ul style="list-style-type: none"> <li>In women: yellow-green vaginal discharge, sometimes foul smelling, vulvar irritation (10 to 50% of infections are asymptomatic).</li> <li>In men: most infections are asymptomatic. Can produce balanitis, urethritis with mild discharge and sometimes dysuria.</li> </ul>	<ul style="list-style-type: none"> <li>Wet mount of fresh vaginal fluid shows motile trichomonas (low sensitivity).</li> <li>pH of urethral/vaginal fluid &gt; 4.5.</li> </ul>	<b>tinidazole</b> or <b>metronidazole</b> PO: 2 g single dose
Bacterial vaginosis ( <i>Gardnerella vaginalis</i> and other associated bacteria)	<p>Diagnosis is made in the presence of 3 of the following 4 signs:</p> <ul style="list-style-type: none"> <li>Homogenous grey-white adherent vaginal discharge</li> <li>pH of vaginal fluid &gt; 4.5</li> <li>Vaginal fluid has an amine (fishy) odour, especially when mixed with 10% KOH</li> <li>Presence of clue cells in wet mount or Gram stain of vaginal fluid</li> </ul>		<b>tinidazole</b> or <b>metronidazole</b> PO: 2 g single dose
<i>Candida albicans</i> (candidiasis)	<ul style="list-style-type: none"> <li>Mainly seen in women: pruritus and vulvovaginitis, frequently creamy-white vaginal discharge, sometimes dysuria.</li> </ul>	<ul style="list-style-type: none"> <li>Saline of KOH wet mount of fresh vaginal fluid shows budding yeast cells and pseudohyphae.</li> </ul>	<ul style="list-style-type: none"> <li>In women: <b>clotrimazole</b> 500 mg: one vaginal tablet single dose</li> </ul>

	<ul style="list-style-type: none"> <li>In men: balanitis/balanoposthitis (inflammation of the glans/prepucce, erythema, pruritus, white pustules) and rarely urethritis</li> </ul>	<ul style="list-style-type: none"> <li>pH of vaginal fluid: normal</li> </ul>	<ul style="list-style-type: none"> <li>In men:</li> </ul> <p><b>miconazole 2%</b> cream: 1 application 2 times daily for 7 days</p>
<i>Herpes simplex</i> 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.	<p>Analgesics, local disinfection. If available, <b>aciclovir</b> PO:</p> <ul style="list-style-type: none"> <li>Primary episode: 1200 mg daily for 7 days, given within 5 days after onset of lesions.</li> <li>Recurrent infections: same dose for 5 days, given within 24 hours after onset of lesions.</li> </ul>
<i>Treponema pallidum</i> (syphilis)	Single firm painless genital ulcer, often unnoticed.	RPR/VDR 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.	<p><b>benzathine benzylpenicillin IM:</b> 2.4 MIU per injection, single dose (syphilis &lt; 12 months) or once weekly for 3 weeks (syphilis &gt; 12 months or unknown duration) or <b>azithromycin</b> PO: 2 g single dose or <b>erythromycin</b> PO: 2 g daily for 14 days or <b>doxycycline</b> PO<sup>(a)</sup> : 200 mg daily for 14 days Treat also for chancroid.</p>
<i>Haemophilus ducreyi</i> (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.	<i>H. ducreyi</i> bacillus is difficult to identify on microscopy or by culture.	<p><b>azithromycin</b> PO: 1 g single dose or <b>ceftriaxone</b> IM: 250 mg single dose or <b>ciprofloxacin</b> PO<sup>(b)</sup> : 1 g daily for 3 days or <b>erythromycin</b> PO: 2 g daily for 7 days Treat also for syphilis.</p>

<i>Human papillomavirus (venereal warts)</i>	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 is 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).	<ul style="list-style-type: none"> <li>External warts &lt; 3 cm and vaginal warts: <b>podophyllotoxin 0.5%</b></li> <li>External warts &gt; 3 cm; cervical, intra-urethral, rectal and oral warts; warts in pregnant or breastfeeding women: surgical excision or cryotherapy or electrocoagulation.</li> </ul>
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- (a) Doxycycline is contra-indicated in pregnant women. It should not be administered to breast-feeding women if the treatment exceeds 7 days (use erythromycin).
- (b) Ciprofloxacin should be avoided in pregnant women.

# Abnormal uterine bleeding (in the absence of pregnancy)

Last updated: October 2021

- Heavy menstrual bleeding or intermenstrual genital bleeding
- In women of childbearing age:
  - assess if the bleeding is pregnancy-related;
  - perform a pregnancy test.

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.
- Perform a pelvic examination:
  - speculum examination: determine the origin (vagina, cervix, uterine cavity) and cause of the bleeding; appearance of the cervix; amount and intensity of bleeding;
  - bimanual examination: look for cervical motion tenderness, uterine enlargement or irregularity.
- Assess for recent trauma or surgical history.
- Measure haemoglobin, if possible, to prevent or treat anaemia.
- In the event of signs of shock, see [Shock](#), Chapter 1.
- In the event of heavy bleeding:
  - start an IV infusion of Ringer lactate;
  - monitor vital signs (heart rate, blood pressure);
  - administer<sup>[1]</sup> :
    - tranexamic acid** IV: 10 mg/kg (max. 600 mg) every 8 hours. When bleeding has been reduced, switch to **tranexamic acid** PO: 1 g 3 times daily, until bleeding stops (max. 5 days).
    - if bleeding persists and/or in case of contraindication to tranexamic acid, administer one of the following two drugs (except if suspicion of cervical or endometrial cancer):
      - ethinylestradiol/levonorgestrel** PO (0.03 mg/0.15 mg tab): one tablet 3 times daily for 7 days
      - or **medroxyprogesterone acetate** PO: 20 mg 3 times daily for 7 days
- In case of massive haemorrhage and/or lack of response to medical management: surgical management (dilation and curettage, intrauterine balloon, and as a last resort, hysterectomy).
- In the event of referral to a surgical facility, difficult transport conditions may aggravate the bleeding: the patient should have an IV line and/or be accompanied by family members who are potential blood donors.
- If available, POCUS<sup>a</sup> : perform FAST to evaluate for free fluid and/or urological abnormalities; perform pelvic views to evaluate for uterine and/or adnexal pathologies.

## According to clinical examination

- Friable, hard, ulcerated, hypertrophic mass on the cervix: possible cervical cancer; surgical treatment, chemotherapy, radiation therapy or palliative care is required depending on the stage of the cancer. While waiting for appropriate treatment, **tranexamic acid** PO (1 g 3 times daily for 5 days max.) 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](#)) or salpingitis (see [Upper genital tract infections](#)).

- Enlarged, irregular uterus: uterine fibroids. In case of failure to respond to medical treatment, surgical management is required. While waiting for surgery or if surgery is not indicated, treat as for functional uterine bleeding.
- Normal uterus and cervix: possible functional uterine bleeding: **tranexamic acid** PO as above. In case of repeated bleeding, it can be combined with an NSAID (**ibuprofen** PO for 3 to 5 days, see [Pain](#), Chapter 1) and/or one of the following long-term treatments:
  - **levonorgestrel intrauterine device**
  - or **ethinylestradiol/levonorgestrel** PO (0.03 mg/0.15 mg tab): one tablet daily
  - or **medroxyprogesterone acetate** IM: 150 mg every 3 months
  - or **medroxyprogesterone acetate** PO<sup>b</sup>: 10 mg once daily (up to 30 mg once daily if necessary) for 21 days monthly.

**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](#), Chapter 6).

## Footnotes

- (a) POCUS should only be performed and interpreted by trained clinicians.
- (b) Unlike the other treatments, this drug has no contraceptive effect.

## References

1. American College of Obstetricians and Gynecologists. Management of acute abnormal uterine bleeding in nonpregnant reproductive-aged women. *Obstet Gynecol*. 2013 Apr;121(4):891-6.  
<https://www.acog.org/-/media/project/acog/acogorg/clinical/files/committee-opinion/articles/2013/04/management-of-acute-abnormal-uterine-bleeding-in-nonpregnant-reproductive-aged-1.pdf>

# **Chapter 10: Medical and minor surgical procedures**

[Dressings](#)

[Treatment of a simple wound](#)

[Burns](#)

[Cutaneous abscess](#)

[Pyomyositis](#)

[Leg ulcers](#)

[Necrotising infections of the skin and soft tissues](#)

[Venomous bites and stings](#)

[Dental infections](#)

# Dressings

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

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,
  - a wound close to a major artery may be an arterial wound even if it is no longer bleeding.
- 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](#), 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



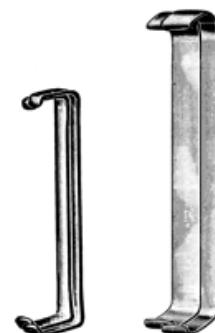
**Figure 1b**

Kelly forceps,  
curved, non-toothed



**Figure 1c**

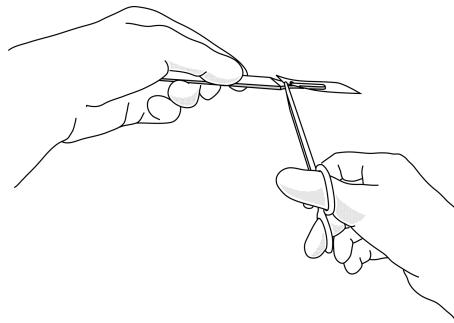
Small artery forceps,  
curved, non-toothed



**Figure 1d**

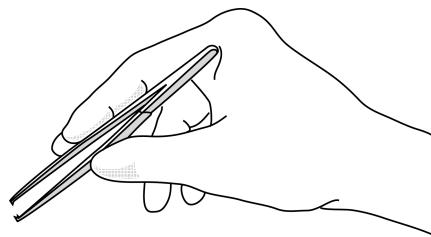
Farabeuf retractors

**Figures 2 : How to hold instruments**



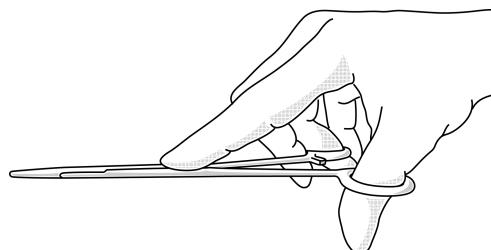
**Figure 2a**

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.

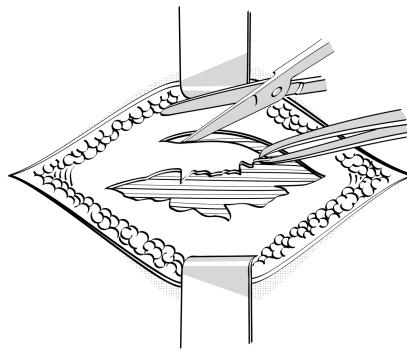
### **Figures 3 : Wound debridement**

This should be done sparingly, limited to excision of severely contused or lacerated tissue that is clearly becoming necrotic.



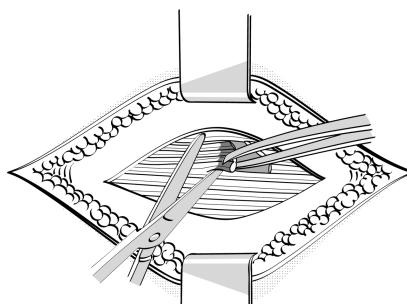
**Figure 3a**

Debridement of a contused, ragged wound: straightening of the wound edges with a scalpel. Be conservative in facial wounds.



**Figure 3b**

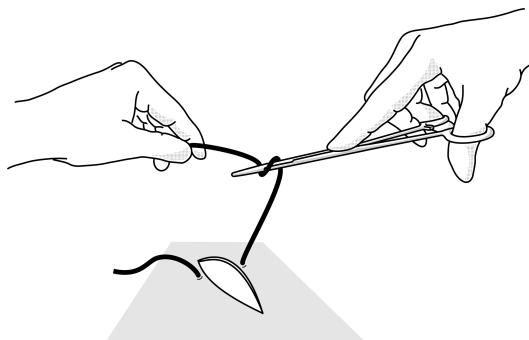
Excision of edges of the aponeurosis to prevent necrosis.



**Figure 3c**

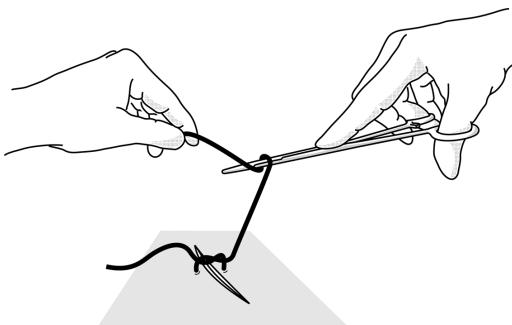
Excision of contused muscle.

**Figures 4 :** Practising making knots using forceps



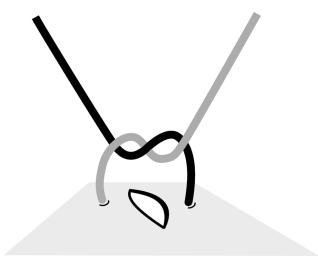
**Figure 4a**

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.



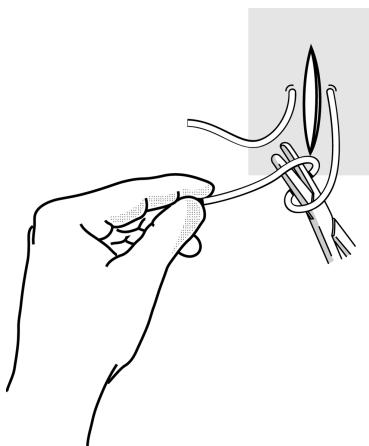
**Figure 4c**

In principle the first knot lies flat.

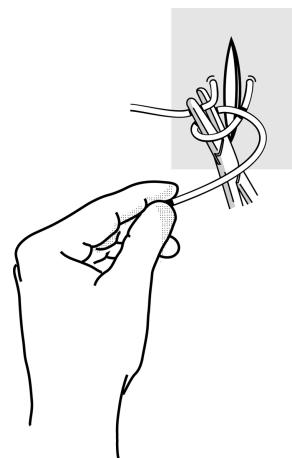


**Figure 4d**

Second knot in the opposite direction.

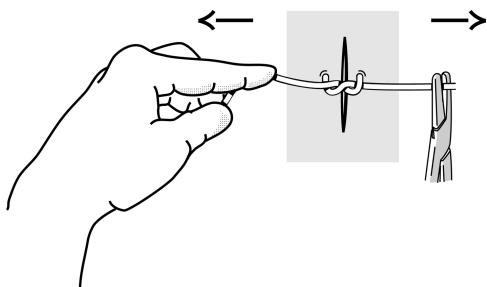


**Figure 4e**



**Figure 4f**

Grasp the loose end with the needle holder.

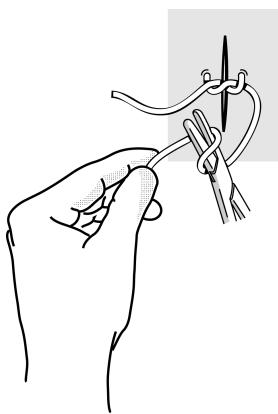


**Figure 4g**

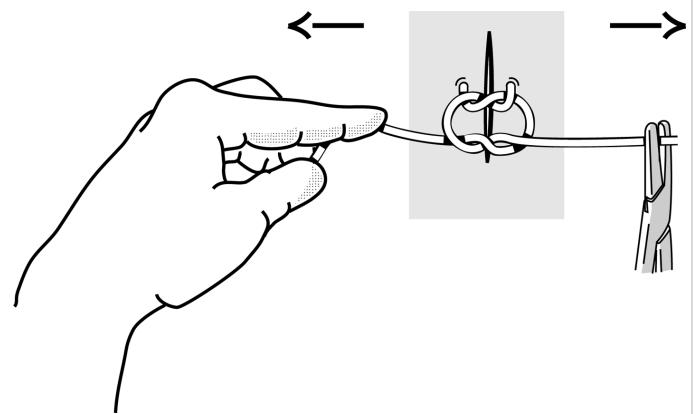
Fist flat knot.

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.



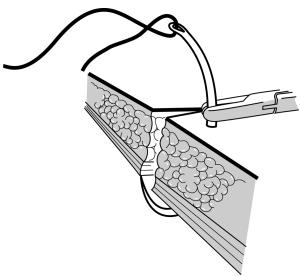
**Figure 4h**



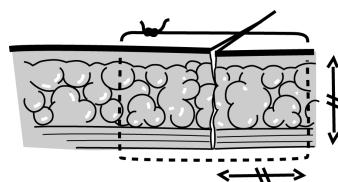
**Figure 4i**

Second knot in the opposite direction.

## **Figures 5 : Particular problems**

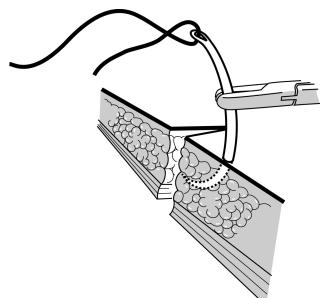


**Figure 5a**

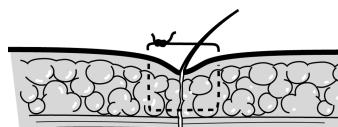


**Figure 5b**

The suture should be as deep as it is wide.

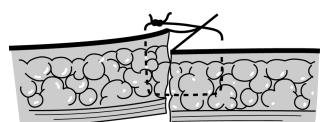


**Figure 5c**



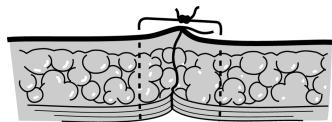
**Figure 5d**

The suture is too shallow, the edges are invaginated.



**Figure 5e**

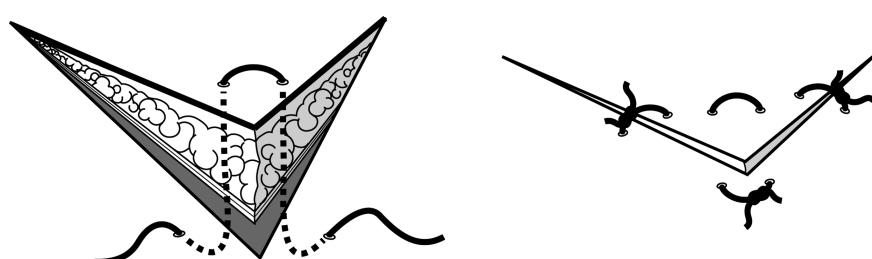
Poor lining of the edges.



**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

Last updated: August 2022

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
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.

	<b>Superficial burn on D8-D10</b>	<b>Deep burn on D8-D10</b>
<b>Sensation</b>	Normal or pain	Insensitive or diminished sensation
<b>Colour</b>	Pink, blanches with pressure	White, red, brown or black Does not blanch with pressure
<b>Texture</b>	Smooth and supple	Firm and leathery
<b>Appearance</b>	Minimal fibrinous exudate Granulation tissue evident Bleeds when incised	Covered with fibrinous exudate Little or no bleeding when incised
<b>Healing</b>	Heals spontaneously within 5-15 days	<ul style="list-style-type: none"> <li>Very deep burn: always requires surgery (no spontaneous healing)</li> <li>Intermediate burn: may heal spontaneously in 3 to 5 weeks; high risk of infection and permanent sequelae</li> </ul>

### 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<sub>2</sub> 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<sub>2</sub>, 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 of 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

	<b>Children &lt; 12 years</b>	<b>Children ≥ 12 years and adults</b>
0 - 8 h	2 ml/kg x % BSA of RL + maintenance fluid <sup>(a)</sup> per hour x 8 h	2 ml/kg x % BSA of RL
8 - 24 h	2 ml/kg x % BSA of RL + maintenance fluid <sup>(a)</sup> per hour x 16 h	2 ml/kg x % BSA of RL
24 - 48 h	Daily maintenance IV fluid requirements <sup>(a)</sup> 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).

(a) 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 $\geq$ 60	SAP 70 to 90 + (2 x age)	SAP $\geq$ 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](#)

## 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 ( $\geq$  7 days from burn).
- Do not administer antibiotic therapy 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 antibiotic therapy:

#### **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](#), Chapter 7).

- **Thromboprophylaxis**: low molecular weight heparin SC beginning 48 to 72 hours post-injury.

- **Physiotherapy** from D1 (prevention of contractures), analgesia is necessary.

- **Intentional burns** (suicide attempt, aggression): appropriate psychological follow-up.

## **III. Local treatment**

Regular dressing changes<sup>a</sup> 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](#), 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](#), Chapter 1)
- Moderate to severe pain:  
**paracetamol** PO + **sustained release morphine** PO (see [Pain](#), 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](#), 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<sub>2</sub>, 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](#), 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.

## **Footnotes**

- (a) Open technique « naked burn patient under a mosquito net » and water immersion therapy are obsolete and should no longer be used.

# Cutaneous abscess

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](#), Chapter 4).
- Regional adenopathy and fever may be present.
- Complications: osteomyelitis, septic arthritis, septic shock (see [Shock](#), 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](#), 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).

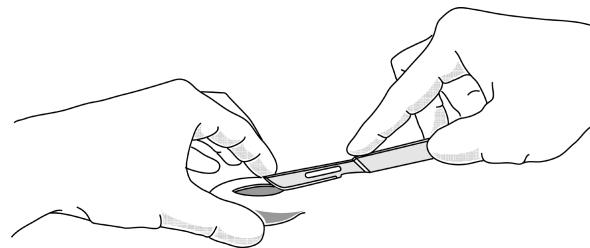
For analgesia, see [Pain](#), Chapter 1.

## 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

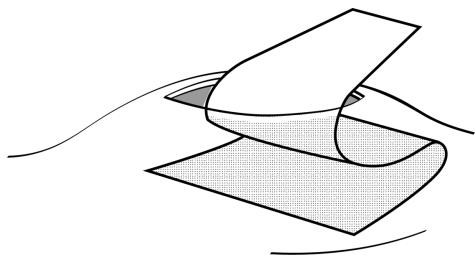
Abundant washing of the cavity using a syringe filled with 0.9% sodium chloride.

## 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

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](#), Chapter 1).

## Paraclinical investigations

- POCUS<sup>a</sup>: 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](#), Chapter 4).
- Adapt analgesics to the pain level (see [Pain](#), 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](#), 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

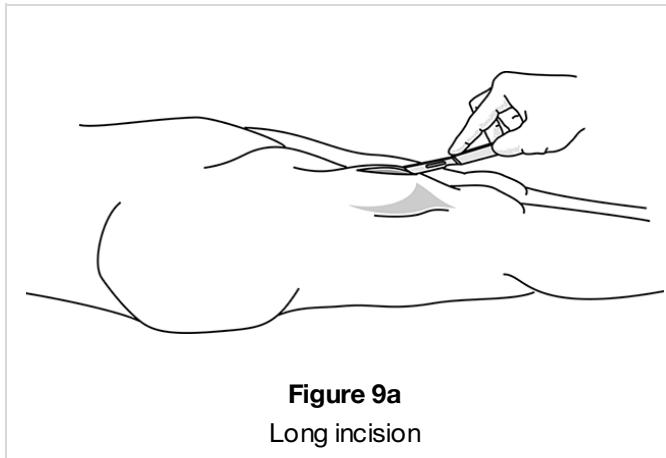
As for [Cutaneous abscess](#), Chapter 10.

## Technique

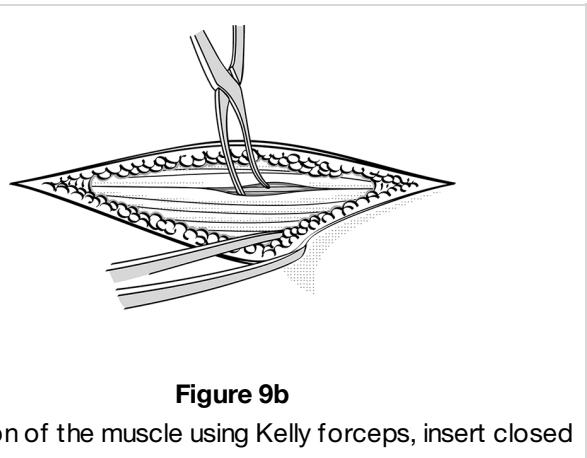
- Generous incision along the axis of the limb, over the site of the abscess and avoiding underlying neurovascular structures; incise the skin, subcutaneous tissues and muscular fascia with a scalpel (Figure 9a).
- Dissect the muscle fibres with non-toothed forceps (Kelly type) or round tipped scissors. 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 5<sup>th</sup> day (Figure 9d).

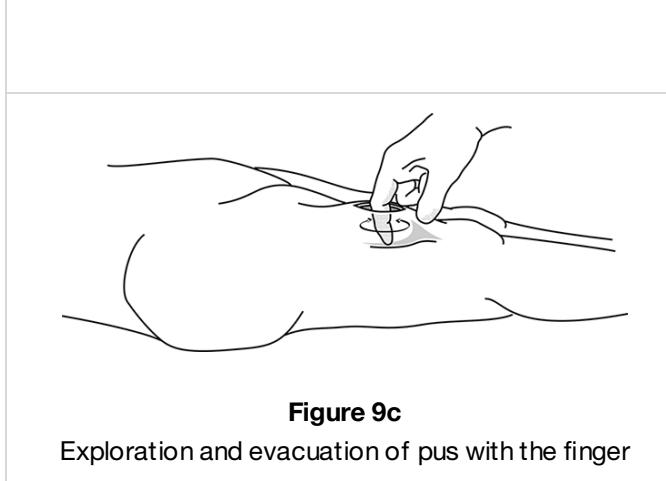
**Figures 9:** Surgical incision-drainage of a pyomyositis



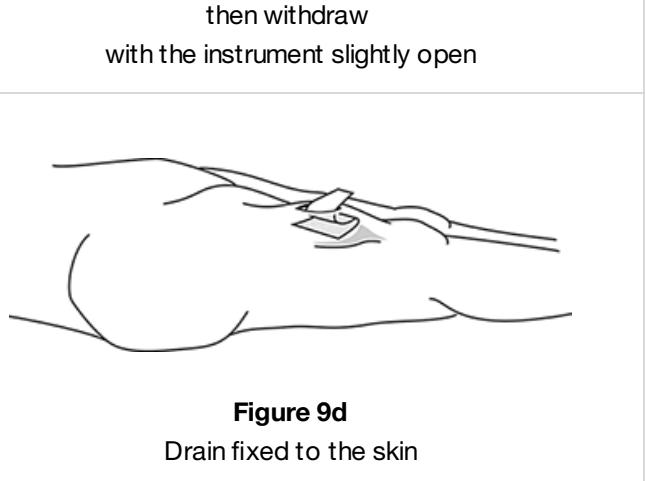
**Figure 9a**  
Long incision



**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

## Footnotes

(a) POCUS should only be performed and interpreted by trained clinicians.

# Leg ulcers

- 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](#), Chapter 1).
- Give systemic antibiotics in case of:
  - Secondary infection (see [Bacterial skin infections](#), 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, antibiotic therapy 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](#), 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

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](#), 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 hypoesthetic macules).
- Signs of late infection: crepitus on palpation and fetid odour (gas gangrene) with signs of severe systemic infection (see [Shock](#), Chapter 1).

## Laboratory

- If available, the following tests can help identify an early necrotising infection: white blood cell count  $> 15\,000/\text{mm}^3$  or  $< 4000/\text{mm}^3$ ; serum creatinine  $> 141 \mu\text{mol/litre}$ ; serum glucose  $> 10 \text{ mmol/litre}$  ( $180 \text{ mg/dl}$ ) or  $< 3.3 \text{ mmol/litre}$  ( $60 \text{ mg/dl}$ ). 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](#), 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)<sup>a</sup>

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)<sup>b</sup>

Children 1 month and over: 100 mg/kg once daily

Adults: 2 g once daily

**clindamycin** IV infusion (30 minutes)<sup>c</sup>

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)<sup>d</sup>

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](#), Chapter 1);
- Early nutritional support.

## Footnotes

- (a) 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.
- (b) For administration by IV route, ceftriaxone powder should 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.
- (c) 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.
- (d) 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

- 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](#) 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 bleeding<sup>a</sup>

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
<b>Bite</b>			
0	Fang marks Pain at the site of bite	?	Strict rest, immobilisation of the limb with a splint to slow the diffusion of venom <sup>(a)</sup> . Wound cleansing. Tetanus prophylaxis ( <u>Tetanus</u> , Chapter 7). Observe for manifestations of envenomation. At the dispensary level, prepare patient evacuation to a referral centre.
<b>Envenomation</b>			
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 <sup>(b)</sup> . IV or PO <sup>(b)</sup> anti-inflammatories.
30 minutes-5 hours	Cobra syndrome: bilateral eyelid drooping, trismus, respiratory muscle paralysis  Shock	Elapids	Intubation and assisted ventilation. See <u>Shock</u> , Chapter 1.
30 minutes-48 hours	Haemorrhagic syndrome: 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 <u>Shock</u> , 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](#), 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](#), Chapter 1).

## Spider bites and envenomation

- Treatment is usually limited to wound cleansing, strict rest, analgesics PO and tetanus prophylaxis (see [Tetanus](#), 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 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

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](#), Chapter 1).

## Footnotes

- (a) 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

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](#), 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 antibiotic therapy, 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](#), 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](#)).
  - extraction of the tooth.

# **Chapter 11: Mental disorders in adults**

[Anxiety](#)

[Insomnia](#)

[Agitation](#)

[Acute confusional state \(delirium\)](#)

[Post-traumatic stress disorder](#)

[Depression](#)

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# Anxiety

Last updated: November 2021

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](#), [post-traumatic stress disorder](#) and [psychosis](#). It can also occur in isolation, not associated with any other mental disorders. Anxiety symptoms 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<sup>a</sup>.

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. 2 or 3 weeks) of:

**diazepam** PO: 2.5 to 5 mg 2 times daily; reducing the dose by half in the last few days of treatment

Moderate anxiety lasting more than 2 weeks, administer as first-line treatment:

**hydroxyzine** PO: 25 to 50 mg 2 times daily (max. 100 mg daily)

or, only if there is no improvement after 1 week, **diazepam** PO: 2.5 to 5 mg 2 times daily for max. 2 weeks.

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 that lasts more than 2 months, and does not improve with psychosocial interventions, an antidepressant should be prescribed (**fluoxetine** or **paroxetine** PO: 20 mg once daily), to be continued for 2 to 3 months after symptoms resolve then, stop gradually over 2 weeks.

## Footnotes

- (a) 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

Last updated: November 2021

Complaints may be: difficulty falling or remaining asleep, waking up too early in the morning, nightmares, or fatigue. Symptoms occur at least three times a week for at least one month.

## Management

If insomnia is related to an organic cause, treat the cause (e.g. administer analgesics for pain).

If insomnia is related to the use of alcohol, drugs or a medication<sup>a</sup>, management depends on the substance involved.

If insomnia is related to a particular life event (e.g. bereavement), a short term treatment with a sedative may be useful:  
**promethazine** PO: 25 mg once daily at bedtime for 7 to 10 days

or, if promethazine is not available, **hydroxyzine** PO: 25 mg once daily at bedtime for 7 to 10 days

or, as a last resort (risk of addiction), **diazepam** PO: 2 to 5 mg once daily at bedtime for 7 days max.

If insomnia persists, re-evaluate the patient. Insomnia is a common feature in depression ([Depression](#)), post-traumatic stress disorder ([Post-traumatic stress disorder](#)) and anxiety disorders ([Anxiety](#)). In such cases, the underlying disorder should be addressed.

## Footnotes

- (a) The main drugs known to cause sleep problems are corticosteroids, beta blockers, levodopa/carbidopa, fluoxetine, levothyroxine, etc.

# Agitation

Last updated: November 2021

People who have recently experienced violent events, or with anxiety, depression, psychotic disorders or delirium, 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, violent or fleeing behaviour.

## 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 delirium. If present, the priority is to identify the cause and treat it (see [Acute confusional state](#)).

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 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 should only be used in certain circumstances, strictly following the procedure in place.

Avoid diazepam if agitation is related to acute alcohol intoxication or in case of delirium (risk of respiratory depression). Use haloperidol (see [Acute confusional state](#)).

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 symptoms 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 or very slow IV (100 mg 3 times daily for at least 3 days)

If the agitation is associated with anxiety, see [Anxiety](#); if associated with psychotic disorders, see [Psychotic disorders](#).

# Acute confusional state (delirium)

Last updated: July 2022

## 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 be associated symptoms.

## Management

Delirium almost always has an organic cause:

- Infectious: meningitis, severe malaria, encephalitis, septicaemia, syphilis, AIDS, etc.
- Metabolic: hyper/hypoglycaemia, electrolyte imbalance, niacin (vitamin PP or B<sub>3</sub>) or thiamine (vitamin B<sub>1</sub>) 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 delirium (opioid analgesics, psychotropic drugs, fluoroquinolones, etc.), use of toxic substances (alcohol/drugs), or withdrawal from these substances.

Delirium requires hospitalisation.

- Treat the underlying cause.
- Provide supportive care (i.e. nutrition, fluid, electrolyte balance); ensure bladder function.
- Ensure that the patient receives only medications appropriate to their needs.
- Treat pain if needed (see [Pain](#), Chapter 1);
- Ensure adequate sensory environment: low lightening, limit noise.

The administration of diazepam may increase delirium. If it is absolutely necessary to sedate an agitated patient, use low dose haloperidol for a short time (7 days or less):

**haloperidol** PO: 0.5 to 1 mg 2 times daily

or **haloperidol** IM: 0.5 to 1 mg, to be repeated if the patient is still agitated 30 to 60 minutes after the first injection.

If necessary, administer additional doses every 4 hours, do not exceed a total dose of 5 mg daily.

In case of delirium related to alcohol withdrawal (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 adjusted according to the clinical progress.

- IV hydration: 2 to 4 litres **0.9% sodium chloride** per 24 hours.
- Administer **thiamine** IM or very slow IV (over 30 minutes): 100 mg 3 times daily for 3 to 5 days.
- Monitor vital signs and blood glucose levels.

# Post-traumatic stress disorder

Last updated: November 2021

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). Exposure to one or several of these events causes feelings of helplessness and horror.

Immediate, transitory symptoms (disorientation, anxiety, sadness, fleeing, etc.) are to be distinguished from secondary, long-lasting problems that appear and/or last several weeks or months after the event: post-traumatic stress, often associated with depression ([Depression](#)), or sometimes acute psychosis ([Psychotic disorders](#)), even in people with no history of psychotic symptoms.

Post-traumatic stress disorder is characterized by three types of psychological response, generally seen in combination<sup>[1]</sup>.

- **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.

- **Persistent perceptions of heightened current threat**

Hypervigilance (constant state of alert), exaggerated startle reaction, anxiety, insomnia, poor concentration; sometimes somatic symptoms (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 their symptoms are a normal response to an abnormal event. Sessions should be conducted with tact. The patient should be listened to. Avoid intensely questioning the patient about their emotions: leave it to the patient to decide how far they want to go.

Associated symptoms (anxiety or insomnia), if persistent, can be relieved by symptomatic treatment (see [Anxiety](#) and [Insomnia](#)) for no more than two weeks.

If the patient has severe symptoms (obsessive thoughts, pronounced hypervigilance, comorbid depression etc.), the pharmacological treatment is **fluoxetine** PO (20 mg once daily) or **paroxetine** PO (10 to 20 mg once daily) or **sertraline** PO (50 mg once daily), to be continued for 2 to 3 months after symptoms resolve then, stop gradually.

## **References**

1. World Health Organization. Post traumatic stress disorder. International Classification of Diseases for Mortality and Morbidity Statistics, Eleventh Revision (ICD-11).  
<https://icd.who.int/browse11/l-m/en#/http://id.who.int/icd/entity/2070699808> [Accessed 26 January 2021]

# Depression

Last updated: July 2022

Depression is characterised by a set of symptoms that have been present at least two weeks and represent a change from previous functioning.

The standard criteria for diagnosis of major depressive disorder 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 change in 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
  - Feelings of guilt or worthlessness, loss of self-confidence or self-esteem
  - Feelings of despair
  - Thoughts of death, suicidal ideation or attempt

The features of depression can vary according to the patient's culture<sup>a</sup>. 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. sexual violence, recent childbirth and post-partum depression).

Depressive disorders are the most common mental disorders in patients with severe chronic infectious diseases such as HIV infection or tuberculosis. These disorders should not be neglected, especially as they have a negative impact on adherence to treatment.

Symptoms of depression are common after a major loss (bereavement, forced displacement, etc.). They gradually subside, in most cases, with social support. Psychological support may be useful.

Pharmacological treatment should always be offered, along with counseling, to patients with severe depression (Patient Health Questionnaire-9 (PHQ-9) score > 19; severe functional impairment, psychotic symptoms, and/or suicidal risk).

In patients with moderately severe depression (PHQ-9 score 15-19), pharmacological treatment should be considered if there is no improvement after 3 counselling sessions, or from the outset if patients express a personal preference for it.

Before prescribing, make sure that 9-month treatment and follow-up (psychological support, adherence and response) are possible.

Preferably use a serotonin reuptake inhibitor (SRI), particularly in older patients. Preferably use fluoxetine, except during pregnancy when sertraline is preferred.

**fluoxetine** PO: 20 mg on alternate days for one week, then once daily for 3 weeks, then increase the dose if necessary (max. 40 mg daily); use with caution in patients with severe anxiety disorders or who are immobilised (e.g. wounded) or

**paroxetine** PO: 10 mg once daily for 3 days, then 20 mg once daily for 3 weeks, then increase the dose if necessary (max. 40 mg daily), especially if the depression is accompanied by severe anxiety

or

**sertraline** PO: 25 mg once daily for 3 days, then 50 mg once daily for 3 weeks, then increase the dose if necessary (max. 100 mg daily)

Assess tolerance and response every week for 4 weeks. If the response is inadequate after 4 weeks at optimal dose or if the SRI is poorly tolerated, replace with another SRI (there is no need for a medication-free interval between the two).

If SRIs 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 older 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 may increase, especially with fluoxetine. **Hydroxyzine** PO (25 to 50 mg 2 times daily, max 100 mg daily) or **promethazine** PO (25 to 50 mg once daily at bedtime) may be given for the first 2 weeks of treatment. If there is no improvement after 1 week, change to **diazepam** PO (2.5 to 5 mg 2 times daily) for 2 weeks max.

During the first 2 to 4 weeks, 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.

Severe 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 improved after a month of treatment, increase to the maximum dose and assess after 2 weeks. If there is no improvement, 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:**

Re-evaluate the need to continue treatment. If treatment is still necessary, it is best to continue a treatment that has been effective rather than switching to a different antidepressant. Nevertheless, if the woman plans to breastfeed and is taking fluoxetine, consider switching to another SRI at least 3 weeks before expected delivery to reduce adverse effects in the neonate during breastfeeding. Monitor the neonate the first few days of life for signs of toxicity or withdrawal symptoms.

- Depression occurring 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 sertraline as first-line option, or if not available, use paroxetine: do not administer fluoxetine. In case of severe depression during pregnancy: use sertraline, avoid paroxetine.

### **Footnotes**

- (a) 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](#)
- [Chronic psychoses](#)
- [Bipolar disorder](#)

**Last updated: July 2022**

Psychoses are characterised by delusions (the patient is convinced of things that are not real and not accounted for by the person's cultural background), or hallucinations (the patient hears voices that do not exist) and behavioural symptoms (e.g. strange behaviour, agitation, mutism, opposition, fleeing).

Management includes psychosocial support and antipsychotic medication.

Treatment efficacy and prognosis depend largely on the quality of the therapeutic relationship established with the patient and their family.

Keeping the patient at home with outpatient follow-up is preferred if there is no risk of self-harm or harm to others, and if the family is capable of managing the disorder.

Interpretation of psychotic symptoms vary according to the cultural context<sup>a</sup>. For example, psychotic disorders may be attributed to charms or to ancestor intervention. Therapeutic approach should take those beliefs into account.

Patients are usually already under “traditional” treatments, this should not be seen as an obstacle to conventional medical treatment.

## Footnotes

- (a) Hence the importance of working with an “informant” (in the anthropological sense of the word) when dealing with unfamiliar cultural contexts.

# Acute psychotic episode

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An acute psychotic episode can be a one-time occurrence, usually of sudden onset, or can occur repeatedly, or it may be the early phase of chronic psychosis. It can occur following an adverse life event (e.g. loss, acute stress or trauma). In postpartum psychosis, delusions are frequently related to the mother-child relationship.

Before prescribing antipsychotic medication, consider the possibility of an underlying organic cause (see [Acute confusional state \(delirium\)](#)) or substance use; check and record blood pressure, heart rate, weight.

Antipsychotic treatment is the same as for [chronic psychoses](#) (haloperidol or risperidone) 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. If the acute episode lasted more than 3 months, continue antipsychotic treatment for at least 2 years.

For severe anxiety or agitation, a [short-course anxiolytic](#) or sedative treatment may be added to the antipsychotic treatment, at the beginning of treatment.

# Chronic psychoses

Last updated: July 2022

Chronic psychoses (schizophrenia, paranoid psychosis, etc.) are defined by specific clinical characteristics and their long-term nature.

Schizophrenia is characterized by delusions, disorganized thinking, hallucinations, depersonalisation, loss of motivation, diminished emotional expression, impaired cognition, abnormal behaviour and neglected hygiene. Such patients are often very anxious.

The goal of treatment is to reduce symptoms and improve social and occupational functioning. It offers real benefits, even if chronic symptoms persist (tendency toward social isolation, possible relapses and periods of increased behavioural problems, etc.).

Before prescribing antipsychotic medication, consider the possibility of an underlying organic cause (see [Acute confusional state \(delirium\)](#)) and use of substances. Check and record blood pressure, heart rate and weight.

Treatment should last at least one year, possibly for life, particularly in patients with schizophrenia. 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 older patients, reduce the dose by half, whichever medication is used.

Haloperidol is the first-line antipsychotic. 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. patients with schizophrenia).

**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. After 2 weeks, assess if the treatment is well tolerated and effective. If it is not effective, check adherence; if necessary increase to 5 mg 2 times daily (max. 15 mg daily).

If haloperidol is not available, contraindicated or poorly tolerated, possible alternative are:

**risperidone** PO: 1 mg 2 times daily for one week, then 2 mg 2 times daily for one week; if necessary, 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 50 mg once daily in the evening for one week; if necessary, increase to 50 mg in the morning and 100 mg in the evening for one week; if necessary, 100 mg 3 times daily as of the third week.

or

**olanzapine** PO: 10 mg once daily; if necessary, increase by 5 mg every week (max. 20 mg daily).

In case of extrapyramidal symptoms, 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 **trihexyphenidyl** PO at the same dosage).

For severe anxiety, it is possible to add a short-course anxiolytic treatment (for a few days to max. 2 to 3 weeks) to the antipsychotic treatment:

**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, to be repeated after 60 minutes if necessary. After a further 60 minutes, if necessary administer **promethazine** IM 50 mg.

In case of hostile or aggressive behaviour, use IM route (same dose), to be repeated after 30 minutes if necessary; after a further 30 minutes, if necessary, administer **promethazine** IM 50 mg.

High doses of haloperidol can induce extrapyramidal symptoms, 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. patients with schizophrenia) a long-acting antipsychotic drug can be used once the patient has been stabilised on oral treatment. The dosage depends on the oral dose the patient is taking. The switch from oral to a long-acting antipsychotic should be gradual, according to a specific protocol. For information, at the end of the transition period from oral to long-acting antipsychotic, the dose of haloperidol decanoate IM administered every 3 to 4 weeks is approximately:

Daily dose of haloperidol PO	Monthly dose of haloperidol decanoate IM <sup>(a)</sup>
2.5 mg	25 mg
5 mg	50 mg
10 mg	100 mg
15 mg	150 mg

(a) If haloperidol decanoate is not available, **fluphenazine** IM: 12.5 to 50 mg/injection every 3 to 4 weeks.

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.
- First symptoms of psychosis during pregnancy: start with the lowest dose of haloperidol and only increase slowly if necessary.
- Post-partum psychosis: if the woman is breast-feeding, haloperidol should be preferred.
- Long-acting antipsychotics should not be administered.

# Bipolar disorder

Last updated: July 2022

Bipolar disorder is characterised by alternating manic and depressive episodes<sup>a</sup>, 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.

Look for family history of similar symptoms (particularly suicide), very frequent in bipolar patients.

Pharmacological treatment:

- Episodes of mania are treated with **haloperidol** PO: 5 mg once daily for 3 days, then 7.5 mg for one week; if necessary, increase by increments of 2.5 mg per week (max. 15 mg daily).

Possible alternatives:

**risperidone** PO: 2 mg once daily; if necessary, increase in increments of 1 mg per week (max. 6 mg daily).

or

**olanzapine** PO: 10 mg once daily for 3 days; if necessary, increase in increments of 5 mg per week (max. 20 mg daily).

If there is improvement after one week of treatment, continue with the same dose for at least 8 weeks after remission of symptoms.

- **Diazepam** PO (5 to 10 mg daily) can be added during the first 2 to 3 weeks.

- If symptoms do not resolve after 2 weeks of antipsychotic treatment at maximum tolerated dose (and 2 different antipsychotics have been tried), add a mood stabiliser:

**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).

- Treatment should be continued until at least 8 weeks after complete remission of symptoms. Assess together with the patient the benefits and risks of pursuing long-term treatment.

- If it is decided to discontinue antipsychotic treatment, medication should be stopped gradually, monitoring for possible relapse.

- Depressive episodes are treated as for depression (see [Depression](#)).

- 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.

Long-term treatment for bipolar disorder is based on continuation of the treatment that led to the remission of the manic episode: antipsychotic, mood stabilizer, or a combination of both.

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 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.

## **Footnotes**

- (a) "Unipolar forms" are characterized by recurring episodes of depression.

# **Chapter 12: Other conditions**

[Sickle cell disease](#)

[Epilepsy](#)

[Diabetes type 2 in adults](#)

[Essential hypertension in adults](#)

[Heart failure in adults](#)

[Chronic heart failure](#)

[Acute heart failure \(acute pulmonary oedema\)](#)

[Endemic goitre and iodine deficiency](#)

# Sickle cell disease

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 preceded 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
<b>Haemoglobin</b>	<ul style="list-style-type: none"> <li>• At the time of diagnosis and annually (frequently 7 to 9 g/dl).</li> <li>• In case of VOC, fever, acute anaemia (<math>\leq 5</math> g/dl or drop in Hb <math>\geq 2</math> g/dl below the patient's baseline), stroke, ACS.</li> <li>• For monitoring of transfused patients.</li> </ul>
<b>Platelets</b>	<ul style="list-style-type: none"> <li>• At the time of diagnosis and annually.</li> <li>• In case of acute anaemia (thrombocytopenia - platelet count <math>\leq 100\,000/\text{mm}^3</math> if splenic sequestration).</li> </ul>
<b>Urine dipstick</b>	<ul style="list-style-type: none"> <li>• In case of fever: look for a urinary tract infection.</li> <li>• In case of acute severe anaemia: look for haemoglobinuria.</li> </ul>
<b>Malaria test</b>	In case of VOC, fever, acute anaemia or stroke.
<b>Lumbar puncture</b>	In case of fever with meningeal signs or unexplained coma.
<b>Other (if available)</b>	<ul style="list-style-type: none"> <li>• Complete blood count and reticulocyte count.</li> <li>• Blood culture in case of fever.</li> <li>• X-ray if suspicion of pneumonia, osteomyelitis, ACS.</li> </ul>

## 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):
  - PO hydration (as above); if the patient is unable to drink sufficiently, IV hydration ([Appendix 1](#)); in the event of dehydration, treat according to the degree of dehydration (see [Dehydration](#), Chapter 1);
  - 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](#) (Chapter 1).

## Fever and infection

- Admit to hospital:
  - All children less than 2 years;
  - Children with fever  $\geq 38.5^{\circ}\text{C}$  and adults with fever  $\geq 39.5^{\circ}\text{C}$ ; patients who are critically ill appearing<sup>a</sup> or have acute anaemia.
- PO or IV hydration ([Appendix 1](#)).
- 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<sup>b</sup> injection (3 minutes) or IV infusion (30 minutes)

Children < 40 kg: 50 mg/kg every 12 hours

Children  $\geq 40$  kg and adults: 2 g every 12 hours

+ **cloxacillin** IV infusion (60 minutes)<sup>c</sup>

Children < 40 kg: 50 mg/kg every 6 hours

Children  $\geq 40$  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  $\geq 35$  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<sup>b</sup> injection (3 minutes) or IV infusion (30 minutes)

Children < 20 kg: 50 mg/kg once daily (max. 2 g/day)

Children  $\geq 20$  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 <sup>de</sup> 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<sub>2</sub> 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 1](#)).

## **Acute chest syndrome**

- Admit to hospital.
- Measure SpO<sub>2</sub> and administer oxygen as in stroke.
- PO hydration as for a VOC; if the patient is unable to drink sufficiently, IV hydration ([Appendix 1](#)) while monitoring for fluid overload; in the event of fluid overload, administer one dose of furosemide IV (see [Dehydration](#), Chapter 1).
- Antibiotics:
  - ceftriaxone** slow IV<sup>b</sup> 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](#), Chapter 1).

## **Priapism**

- PO hydration as for a VOC; IV hydration if necessary ([Appendix 1](#)) and treat dehydration if present (see [Dehydration](#), Chapter 1).
- 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

<ul style="list-style-type: none"> <li>Disease</li> <li>Treatment</li> <li>Monitoring</li> </ul>	<p>Chronic, necessarily transmitted by both parents, non-contagious.</p> <p>Routine (see below) and symptomatic (pain).</p> <p>Size of the spleen, temperature, baseline Hb.</p>
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## Major precipitating factors of a painful crisis and how to prevent them

<ul style="list-style-type: none"> <li>Cold</li> <li>Excessive heat</li> <li>Tight clothing</li> <li>Dehydration</li> <li>Excessive effort</li> <li>Infections</li> </ul>	<p>Wear warm clothing, avoid bathing in cold water.</p> <p>For example, avoid going out at mid-day.</p> <p>Wear wide comfortable clothing without elastics.</p> <p>Drink plenty of fluids.</p> <p>Moderate physical activity is beneficial.</p> <p>Follow routine treatments (including vaccination).</p>
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## 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

**phenoxyethylpenicillin (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:

<b>Children &lt; 5 years</b>	<ul style="list-style-type: none"> <li>DTP, hepatitis B, polio, measles, <i>H. influenzae</i> type B vaccines</li> <li>Pneumococcal conjugate vaccine (PCV13 or, if not available, PCV10)</li> <li>Meningococcal conjugate vaccine in endemic areas</li> <li>At 2 years: pneumococcal 23-valent polysaccharide vaccine, at least 8 weeks after the last PCV13 or 10</li> </ul>
<b>Children &gt; 5 years</b>	<ul style="list-style-type: none"> <li>DTP or Td, hepatitis B, polio, measles, <i>H. influenzae</i> type B vaccines</li> <li>Pneumococcal conjugate vaccine PCV13 (or PCV10)</li> <li>Meningococcal conjugate vaccine in endemic areas</li> </ul>

- To support red blood cell production

**folic acid** PO<sup>f</sup> (life-long treatment)

Children < 1 year: 2.5 mg once daily

Children  $\geq$  1 year and adults: 5 mg once daily

- Malaria chemoprophylaxis (if malaria prevalence  $\geq$  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  $\geq$  5 years and adults: every 3 to 6 months.

- After a crisis: as often as necessary, according to the clinical course.

## Footnotes

- (a) 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.
- (b) For administration by IV route, ceftriaxone powder should 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.
- (c) 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.
- (d) Always inquire how many transfusions a patient has previously received (risk of iron overload).
- (e) Do not transfuse whole blood if possible (risk of fluid overload).
- (f) Iron is contraindicated in patients who have received multiple transfusions. Avoid combined preparations of iron and folic acid.

# Epilepsy

Last updated: October 2024

Epilepsy is a chronic neurological disorder characterized by recurrent seizures.

People with epilepsy frequently face discrimination and stigma as well as social and economic difficulties. They are also at risk of mental, behavioural or cognitive disorders as well as seizure-related injuries. Management of comorbidities and patient/family education and support are essential.

Seizures are usually short episodes. A seizure lasting longer than 5 minutes (or 2 or more seizures in 5 minutes without complete restoration of baseline consciousness between seizures) is a medical emergency, see [Generalised tonic-clonic seizures and convulsive status epilepticus](#), Chapter 1.

## Clinical features

Manifestations of epilepsy (i.e. seizures) are varied. It is critical to recognize the type of seizure to determine patient management.

Seizures are classified as follows<sup>[1]</sup>:

### Generalized onset seizures

- Tonic-clonic seizures: contraction of muscles, including respiratory muscles (tonic phase), followed by rhythmic jerking of the arms and legs (clonic phase) and loss of consciousness;
- Myoclonic seizures: sudden and brief contractions of a muscle or group of muscles;
- Atonic seizures: sudden loss of muscle tone, frequently resulting in falls;
- Absence seizures: brief (a few seconds) impairment of consciousness and cessation of activity; most common in children from 4 years of age.

### Focal onset seizures

- Start with localised symptoms (e.g. jerking movements of one body part or repetitive lips smacking) and sometimes spread to the rest of the body, becoming generalised.

Epilepsy is clinically diagnosed when 2 or more "unprovoked" seizures (i.e. seizures not caused by a temporary reversible condition) of any type occur more than 24 hours apart<sup>[2][3]</sup>.

## Treatment principles

- Once the diagnosis of epilepsy (or seizures requiring long-term treatment) has been made, an antiseizure medication (ASM) is prescribed to prevent the occurrence of new seizures.
  - The treatment prescribed should be a monotherapy (i.e. a single ASM).
  - For choosing an ASM, see [Choice of an antiseizure medication](#). The likelihood of continued ASM availability should also be considered when making the choice.
  - Treatment should be taken daily without interruption for the long term. Abruptly stopping or reducing an ASM dose is likely to provoke seizures.
  - Long-term patient follow-up is required, see [Patient follow-up](#). Any change in treatment (dose increments, ASM substitution or discontinuation) requires close clinical monitoring.
- Rarely, ASMs may cause a paradoxical increase in seizure frequency, mainly at the start of treatment or after an increase in dose.
- If seizures are not controlled, assess adherence to treatment, consider increasing the dose if tolerated, up to the maximum dose if necessary.

- If seizures are still not controlled or treatment is not tolerated, gradually change to another ASM (slowly increase the dose of the new ASM then slowly decrease the dose of the first ASM until complete substitution).
- Combination therapy should be considered only if two different ASMs used in monotherapy have failed.
- Stopping an antiseizure treatment may be considered when the patient has been seizure-free for at least 2 years<sup>[4]</sup>. The benefits/risks of stopping the ASM should be discussed with the patient (seizures may recur after stopping treatment). The dose should be slowly tapered (e.g. by 10% every 2 weeks) over a period of at least 3 months. Patients should seek medical attention if seizures recur during or after stopping treatment.
- Patient and family education is essential. Provide information about epilepsy as a disease, the benefits of treatment, ways to maximize control (including adherence to treatment) and first aid for seizures. Explain that people with epilepsy can lead normal lives when certain safety measures are taken (e.g. not swimming alone, not cooking over open flames)<sup>[4][5]</sup>.

## Choice of an antiseizure medication

An ASM is selected according to:

- the type of seizure: some ASMs may exacerbate some symptoms,
- the patient's characteristics: age, sex, pregnancy or breastfeeding status, comorbidities, and related treatments,
- the ASM's adverse effect profile: in general, newer ASMs (e.g. levetiracetam) are safer, better tolerated, and have fewer drug interactions than older ASMs (e.g. carbamazepine, phenobarbital, phenytoin, valproic acid).

Age/Type of seizures	First choice	Second choice	Third choice
<b>Children 1 month to &lt; 2 years</b>			
Motor, generalised (tonic-clonic, myoclonic <sup>(a)</sup> , atonic <sup>(b)</sup> )	levetiracetam (LEV)	phenobarbital (PB)	carbamazepine (CBZ) or phenytoin (PHT)
Non-motor, generalised (absence)	-	-	-
Focal (partial)	LEV or CBZ	PB or PHT	-
<b>Girls 2 to &lt; 10 years, boys ≥ 2 years and men</b>			
Motor, generalised (tonic-clonic, myoclonic <sup>(a)</sup> , atonic <sup>(b)</sup> )	LEV or valproic acid (VPA)	CBZ or PB or PHT	-
Non-motor, generalised (absence <sup>(c)</sup> )	LEV or VPA	-	-
Focal (partial)	LEV or CBZ	VPA	PB or PHT
<b>Girls ≥ 10 years and women</b>			
Motor, generalised (tonic-clonic, myoclonics <sup>(a)</sup> , atonic <sup>(b)</sup> )	LEV	CBZ or PHT	PB
Non-motoras, generalised (absence <sup>(c)</sup> )	LEV	-	-
Focal (partial)	LEV	CBZ or PHT	PB

- (a) For myoclonic seizures: CBZ and PHT are not recommended (risk of worsening symptoms).
- (b) For atonic seizures: CBZ is not recommended (risk of worsening symptoms).
- (c) For absence seizures: CBZ, PB and PHT are not recommended (risk of worsening symptoms).

## **Children**

- VPA is contraindicated in children less than 2 years (increased risk of hepatotoxicity).

## **Patients over 65 years**

LEV is preferred in older patients<sup>[6]</sup>.

## **Pregnant women and girls**

- The risk of major congenital malformations (MCM) is lower with monotherapy than with combined therapy<sup>[7]</sup>.
- ASMs that can be used during pregnancy include:
  - LEV: first-line, safest ASM with the lowest risk of MCM<sup>[7][8]</sup>.
  - ASMs other than LEV (only if LEV is not available):
    - ▷ CBZ and PHT: associated with an intermediate risk of MCM<sup>[7][8]</sup>;
    - ▷ PB: associated with a high risk of MCM<sup>[7][8]</sup> and small for gestational age.
- If taking ASM treatment before pregnancy:
  - LEV: continue treatment under closer monitoring.
  - ASMs other than LEV:
    - ▷ The benefits/risks of substitution for a safer ASM should be discussed with patients.
    - ▷ Substitution may be beneficial for the foetus but may also be a risk for the mother and the foetus if it results in loss of seizure control. The term of pregnancy should be taken into account. For substitution with a safer ASM, see Treatment principles. A substitution frequently takes 2 to 3 months.
- VPA must not be prescribed in pregnant women and girls. It is associated with the highest risk of MCM and neurodevelopmental disorders in children exposed in utero<sup>[7][8]</sup>. In situations where VPA would be the only option, divide doses over the day to minimize peaks in VPA plasma concentrations.

In all cases:

- The parents should be informed of current knowledge in terms of risks for the unborn child, in particular when the risk of foetotoxicity is high.
- Administer the lower effective dose (foetal harms are mainly dose-dependent).
- ASM plasma concentrations may decrease during pregnancy. If the dose needs to be increased antepartum, start reducing it from D3-D4 postpartum to gradually return to the dose effective before pregnancy.
- Start taking high dose folic acid to reduce the risk of MCM (5 mg daily for the first trimester<sup>[9][a]</sup>).
- After pregnancy, the benefits of breastfeeding are considered to outweigh the risk of adverse effects of ASMs<sup>[10]</sup>.

## **Women and girls of childbearing age**

- The choice of an ASM is based on the same criteria as per pregnant women and girls due to the possibility of undiagnosed or future pregnancies.
- Preconception and/or contraception counselling should be offered.
- If considering pregnancy, depending on the ASM currently taken, consider a safer ASM.
- When planning pregnancy, start taking folic acid before conception to reduce the risk of MCM.
- If no pregnancy is planned, effective contraception should be provided:
  - Patient taking CBZ, PB or PHT: injectable medroxyprogesterone (DMPA) or levonorgestrel-containing or copper intrauterine device<sup>[7]</sup>.
  - Patient taking LEV or VPA: as above, but contraceptive implants and oral contraceptives can also be used<sup>[7]</sup>.

- In situations where VPA would be the only effective option (i.e. after confirmation that other ASMs are ineffective or poorly tolerated), a blood pregnancy test should be performed before starting the treatment, then regularly if the patient is not on effective contraception.
- If pregnancy occurs, see [Pregnant women and girls](#).

## Dosage of antiseizure medications

Start with a low dose then increase gradually based on patient's response (seizure control) and tolerance (occurrence of adverse effects). The following doses are given as a guide and should be adjusted individually.

### **carbamazepine PO:**

- Children 1 month to 11 years: start with 5 mg/kg once daily or 2.5 mg/kg 2 times daily; increase the daily dose by increments of 2.5 to 5 mg/kg every 3 to 7 days, up to 5 mg/kg 2 or 3 times daily if necessary (max. 20 mg/kg daily).
- Children 12 years and over: start with 100 to 200 mg once daily or 50 to 100 mg 2 times daily; increase the daily dose by increments of 100 to 200 mg every week, up to 200 to 400 mg 2 or 3 times daily if necessary (max. 1800 mg daily).
- Adults: start with 100 to 200 mg once daily or 50 to 100 mg 2 times daily; increase the daily dose by increments of 100 to 200 mg every week, up to 400 mg 2 or 3 times daily if necessary (max. 2 g daily).

### **levetiracetam PO:**

- Children 1 to 5 months: start with 7 mg/kg once daily; increase to 7 mg/kg 2 times daily after 2 weeks, then by increments of 7 mg/kg 2 times daily every 2 weeks if necessary (max. 21 mg/kg 2 times daily).
- Children 6 months to 17 years (< 50 kg): start with 10 mg/kg once daily; increase to 10 mg/kg 2 times daily after 2 weeks, then by increments of 10 mg/kg 2 times daily every 2 weeks if necessary (max. 30 mg/kg 2 times daily).
- Children 50 kg and over and adult: start with 250 mg 2 times daily; increase to 500 mg 2 times daily after 2 to 4 weeks, then by increments of 500 mg 2 times daily every 2 to 4 weeks if necessary (max. 1.5 g 2 times daily).

### **phenobarbital PO:**

- Children 1 month to 11 years: start with 2 to 3 mg/kg once daily at bedtime or 1 to 1.5 mg/kg 2 times daily for 2 weeks; increase the daily dose by increments of 1 to 2 mg/kg every week, up to 2 to 6 mg/kg once daily if necessary.
- Children 12 years and over and adults: start with 1 mg/kg (max. 60 mg) once daily at bedtime for 2 weeks; increase the daily dose by increments of 15 to 30 mg every week, up to 3 mg/kg once daily if needed (max. 180 mg daily).

### **phenytoin PO:**

- Children 1 month to 11 years: start with 1.5 to 2.5 mg/kg 2 times daily; increase the daily dose by increments of 5 mg/kg every 3 to 4 weeks, up to 2.5 to 5 mg/kg 2 times daily if necessary (max. 7.5 mg/kg 2 times daily or 300 mg daily).
- Children 12 years and over: start with 75 to 150 mg 2 times daily; increase the daily dose by increments of 25 mg every 3 to 4 weeks, up to 150 to 200 mg 2 times daily if necessary (max. 300 mg 2 times daily).
- Adults: start with 150 to 300 mg once daily or 75 to 150 mg 2 times daily; increase the daily dose by increments of 50 mg every 3 to 4 weeks, up to 200 to 400 mg once daily or 100 to 250 mg 2 times daily if necessary (max. 400 mg once daily or 300 mg 2 times daily).

### **valproic acid (sodium valproate) PO:**

- Children 2 to 11 years: start with 10 to 15 mg/kg once daily or 5 to 7.5 mg/kg 2 times daily; increase the daily dose by increments of 5 to 10 mg/kg every week, up to 12.5 to 15 mg/kg 2 times daily if necessary (max. 600 mg 2 times daily).
- Children 12 years and over and adults: start with 500 to 600 mg once daily; increase the daily dose by increments of 200 mg every 3 days, up to 500 mg to 1 g 2 times daily if necessary (max. 2.5 g daily).

## Patient follow-up

The initial follow-up schedule is guided by titration of the prescribed ASM. Once seizures are controlled for at least 1 month, follow-up can be spaced out to 3 months, then every 6 months if the patient is stable.

Encourage maintaining a seizure diary if possible.

At each consultation:

- Assess:
  - Growth and development in children.
  - Treatment :
    - ▷ response (seizure frequency) and tolerance (adverse effects),
    - ▷ impact on daily life (e.g. time off school or work).
  - Adherence to treatment.
  - Co-morbidities, including associated anxiety or depression.
- Adjust the dose of the ASM if necessary. In this case, review patient as needed but in any case within one month following any change in dose.
- Provide treatment until the next consultation or the facility's dispensing schedule.
- Answer questions, discuss problems, and try to find solutions with the patient.

## Footnotes

- (a) The optimal dose of folic acid to prevent MCM is not established. After the first trimester, the dose should be reduced (use the fixed-dose combination 60 mg of elemental iron/400 micrograms folic acid).

## References

1. Fisher RS, Cross JH, French JA, et al. Operational classification of seizure types by the International League Against Epilepsy: Position Paper of the ILAE Commission for Classification and Terminology. *Epilepsia*. 2017;58(4):522-530.  
<https://doi.org/10.1111/epi.13670>
2. World Health Organization. Pocket book of primary health care for children and adolescents: guidelines for health promotion, disease prevention and management from the newborn period to adolescence. Copenhagen: WHO Regional Office for Europe; 2022.  
<https://www.who.int/europe/publications/i/item/9789289057622>
3. Fisher RS, Acevedo C, Arzimanoglou A, et al. ILAE Official Report: A practical clinical definition of epilepsy. *Epilepsia*. 2014;55(4):475-482.  
<https://doi.org/10.1111/epi.12550>
4. World Health Organization. mhGAP Intervention Guide for Mental, Neurological and Substance Use Disorders in Non-Specialized Health Settings: Mental Health Gap Action Programme (mhGAP). version 2.0. World Health Organization; 2016.  
<https://www.who.int/publications/i/item/9789241549790>
5. NICE. Epilepsies in children, young people and adults. Published online April 27, 2022.  
<https://www.nice.org.uk/guidance/ng217>
6. Piccenna L, O'Dwyer R, Leppik I, et al. Management of epilepsy in older adults: A critical review by the ILAE Task Force on Epilepsy in the elderly. *Epilepsia*. 2023;64(3):567-585.  
<https://doi.org/10.1111/epi.17426>
7. American College of Obstetricians and Gynecologists. Gynecologic management of adolescents and young women with seizure disorders. ACOG Committee Opinion No. 806. *Obstet Gynecol*/2020;135:e213–20.  
<https://www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2020/05/gynecologic-management-of-adolescents-and-young-women-with-seizure-disorders>
8. Meador KJ. Effects of Maternal Use of Antiseizure Medications on Child Development. *Neurol Clin*. 2022 Nov;40(4):755-768.  
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9589915/>

9. Royal College of Obstetricians and Gynaecologists (UK). Epilepsy in Pregnancy. Published online June 2016.  
[https://www.rcog.org.uk/media/rzldnacf/gtg68\\_epilepsy.pdf](https://www.rcog.org.uk/media/rzldnacf/gtg68_epilepsy.pdf)
10. Pennell PB. Use of Antiepileptic Drugs During Pregnancy: Evolving Concepts. *Neurotherapeutics*. 2016 Oct;13(4):811-820.  
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5081129/>

# Diabetes type 2 in adults

Last update: November 2023

Diabetes is a metabolic disorder that leads to hyperglycaemia.

Type 2 diabetes usually occurs in adults and accounts for 90 to 95% of diabetes cases worldwide.<sup>[1]</sup>

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<sup>a[1][2]</sup>:

Tests	Symptomatic patient	Asymptomatic patient
<b>Fasting blood glucose<sup>(a)</sup></b>	1 fasting blood glucose ≥ 7 mmol/litre (≥ 126 mg/dl)	2 fasting blood glucose ≥ 7 mmol/litre (≥ 126 mg/dl)
<b>Random blood glucose<sup>(b)</sup></b>	1 random blood glucose ≥ 11 mmol/litre (≥ 200 mg/dl)	See tablenote <sup>(b)</sup>
<b>Post-load blood glucose<sup>(c)</sup></b>	1 post-load blood glucose: <ul style="list-style-type: none"><li>▫ on venous blood ≥ 11 mmol/litre (≥ 200 mg/dl)</li></ul>	2 post-load blood glucose: <ul style="list-style-type: none"><li>▫ on venous blood ≥ 11 mmol/litre (≥ 200 mg/dl)</li></ul>
	or <ul style="list-style-type: none"><li>▫ on capillary blood ≥ 12.2 mmol/litre (≥ 220 mg/dl)</li></ul>	or <ul style="list-style-type: none"><li>▫ on capillary blood ≥ 12.2 mmol/litre (≥ 220 mg/dl)</li></ul>
<b>Glycated Hb (HbA1c)<sup>(d)</sup></b>	1 HbA1c ≥ 6.5%	2 HbA1c ≥ 6.5%

(a) Fasting blood glucose test: performed on patient that has fasted at least 8 hours. Values are the same for venous and capillary blood.

(b) Random blood glucose test: performed at any moment of the day. Values are for venous blood only.  
For asymptomatic patients, it is not recommended to perform 2 random blood glucose tests. If the first test is a random blood glucose, the second test should be a fasting blood glucose.

(c) Post-load blood glucose test: performed 2 hours after oral ingestion of 75 g glucose (one sachet of 75 g anhydrous glucose powder dissolved in 200 to 300 ml of water, to be drunk within 10 minutes).

(d) Glycated haemoglobin (HbA1c): reflects average glycaemia over around 3 months.

- Perform urine dipstick analysis for ketones if:
  - fasting blood glucose  $\geq 15$  mmol/litre ( $\geq 270$  mg/dl) and symptoms of hyperglycemia, or
    - fasting or random blood glucose  $\geq 18$  mmol/litre ( $\geq 325$  mg/dl) even without symptoms.
- Refer the patient if acute complications (such as hyperosmolar hyperglycaemia or ketoacidosis) are present.

## Treatment

### Glycaemic targets

Fasting blood glucose  $\leq 7$  mmol/litre ( $\leq 126$  mg/dl) or HbA1c of 7%.<sup>[3]</sup>

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 (older patient, history of severe hypoglycaemia or long-standing poorly controlled diabetes), HbA1c  $\leq 8\%$  <sup>[2]</sup> is acceptable.

Blood glucose should not fall  $< 4.5$  mmol/litre (or  $< 80$  mg/dl) or HbA1c  $< 6.5\%$ .

### Lifestyle and dietary advice<sup>b</sup>

- 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  $\geq 25$ , try to reduce weight by 5 to 10%.
- Stop smoking.

### Pharmacological treatment

First-line treatment **metformin PO<sup>c</sup>**.

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).

If glycaemic control is not achieved, 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 achieved 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)	<ul style="list-style-type: none"> <li>Treat hypoglycaemia (see <u>Hypoglycaemia</u>, Chapter 1).</li> <li>Reduce daily dose of insulin by 2 to 4 units.</li> <li>Maintain new dose for 4 days.</li> <li>Check blood glucose after 4 days, readjust dose if glycaemic target has not been reached.</li> <li>Check blood glucose again after 4 days and repeat the process until glycaemic target is reached.</li> </ul>
≥ 4 and < 7.2 mmol/litre (≥ 70 and < 130 mg/dl)	Do not change dose.
≥ 7.2 and < 11 mmol/litre (≥ 130 and < 200 mg/dl)	<ul style="list-style-type: none"> <li>Increase daily dose of insulin by 2 units.</li> <li>Check blood glucose after 4 days, readjust dose if glycaemic target has not been reached.</li> <li>Check blood glucose again after 4 days and repeat the process until glycaemic target is reached.</li> </ul>
≥ 11 mmol/litre (≥ 200 mg/dl)	<ul style="list-style-type: none"> <li>Increase daily dose of insulin by 4 units.</li> <li>Check blood glucose after 4 days, readjust dose if glycaemic target has not been reached.</li> <li>Check blood glucose again after 4 days and repeat the process until glycaemic target is reached.</li> <li>Perform urine dipstick analysis for ketones according to the criteria defined in the <u>Diagnosis</u> section.</li> </ul>

Example for a man weighing 79 kg:

Start with 16 IU per day ( $79 \text{ kg} \times 0.2 \text{ IU}$ ).

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. 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<sup>b</sup>

- 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.
- Patients on insulin therapy or presenting hypoglycaemic episodes<sup>[3]</sup>: self-monitoring of blood glucose and adjustment of doses at home using a glucometer.
- Patients with sensory neuropathy or peripheral arterial disease: autoexamination of feet; prevention of foot lesions.

## Footnotes

- (a) Even in symptomatic patients, it is preferable to perform a second blood glucose test to confirm the result.
- (b) These measures concern all patients regardless of medication prescribed. They can be sufficient alone to normalize blood glucose levels in certain patients.
- (c) If metformin is contraindicated or not tolerated, replace with a sulfonylurea.

## References

1. World Health Organization. *Classification of Diabetes Mellitus*. World Health Organization; 2019 [Accessed October 19, 2023]. <https://iris.who.int/handle/10665/325182>
2. HEARTS D: diagnosis and management of type 2 diabetes [Accessed October 19, 2023]. <https://www.who.int/publications-detail-redirect/who-ucn-ncd-20.1>
3. Type 2 diabetes in adults: management | Guidance | NICE. Published December 2, 2015 [Accessed October 19, 2023]. <https://www.nice.org.uk/guidance/ng28>

# Essential hypertension in adults

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%.<sup>[1]</sup>

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.

## 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/vomiting, 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;<sup>a</sup>
  - 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  $\geq$  140 and/or DBP  $\geq$  90) without associated cardiovascular disorders or stroke or diabetes, start with lifestyle and dietary advice.
- Pharmacological treatment is indicated in the following cases:
  - SBP  $\geq$  160 and/or DBP  $\geq$  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  $\geq$  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<sup>b</sup>:

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  $\geq 220$  and/or DBP  $\geq 120$  (in this event administer labetalol).
- Acute pulmonary oedema: see [Acute heart failure](#).

### Footnotes

- 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.
- 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](#)
  - [Acute heart failure \(acute pulmonary oedema\)](#)

# Chronic heart failure

## 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 distension, 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<sup>[1]</sup>:

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  $\geq$  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 contraindications (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)

Last updated: April 2021

## Clinical features

- Sudden onset or exacerbation of dyspnoea
- Fatigue, increased time to recover after exercise
- Bilateral peripheral oedema
- Cold extremities
- Elevated jugular venous pressure
- On auscultation: bilateral pulmonary crepitations and/or extra heart sound (gallop rhythm)

Signs of severity:

- Severe respiratory distress (intercostal retractions, nasal flaring, see-saw breathing,  $\text{SpO}_2 < 90\%$ , etc.), cyanosis, profuse sweating, confusion
- Systolic blood pressure  $< 90 \text{ mmHg}$  (cardiogenic shock)
- Rapid and excessive increase in arterial blood pressure (hypertensive emergency)
- Heart rate (HR)  $> 130/\text{minute}$  or  $< 40/\text{minute}$
- Respiratory rate (RR)  $> 30/\text{minute}$  or  $< 12/\text{minute}$
- 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 and pleural effusion. Can exclude other lung disease, such as pulmonary infection.
- POCUS<sup>a</sup>:
  - Perform 12-zone lung exam to evaluate for signs of bilateral pulmonary oedema and/or pleural effusions.
  - Perform 5-view cardiac exam to evaluate for signs of acute volume overload and/or decreased cardiac function.
- Monitoring: full blood count, electrolytes, serum creatinine; cardiac troponins if available.

## Treatment

### Systolic blood pressure is $< 90 \text{ mmHg}$

See [Shock](#), Chapter 1.

### Systolic blood pressure is $\geq 90 \text{ mmHg}$ <sup>[1][2]</sup>

- The patient must be hospitalised.
- Place patient in semi-seated position, legs down.
- In patients with  $\text{SpO}_2 < 90\%$ , administer oxygen with a mask at the necessary flow rate to maintain  $\text{SpO}_2 \geq 95\%$ . If pulse oximetry is not available, administer oxygen at a flow rate of 6 to 10 litres/minute to patients with signs of

- hypoxia.
- Insert an IV line.
  - If there are signs of volume overload (and/or in case of hypertensive emergency): **furosemide** IV, 40 to 80 mg, may be repeated if necessary according to urine output, signs of respiratory distress and SpO<sub>2</sub>. If the patient was already taking furosemide at doses of > 40 mg, administer pre-existing dose by IV route.
  - Add a short-acting nitrate (vasodilator) if systolic blood pressure is > 100 mmHg. The aim is to gradually lower systolic blood pressure to near-baseline value. If the patient's baseline value is unknown, for information, lower systolic blood pressure to 120-150 mmHg and the diastolic pressure to under 110 mmHg.

**isosorbide dinitrate** sublingual (5 mg tablet)

5 mg per dose; if necessary up to 2 doses taken 10 minutes apart

or

**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 pump

or

**glyceryl trinitrate** sublingual (0.5 mg tablet)

0.5 mg per dose; if necessary up to 3 doses taken 5 minutes apart

- Non-invasive ventilation using continuous positive airway pressure (CPAP) is recommended in patients with persistent hypoxaemia, unless contraindicated (e.g. impaired consciousness) and on condition that appropriate monitoring is available.
- Monitoring: HR, RR, BP, SpO<sub>2</sub>, mental status, urine output.

Subsequent treatment depends on the underlying pathology ([chronic heart failure](#), [hypertension](#), acute coronary syndrome, etc.).

## Footnotes

- (a) POCUS should only be performed and interpreted by trained clinicians.

## References

1. Ponikowski P et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur J Heart Fail. 2016;18(8):891-975.  
<https://academic.oup.com/eurheart/article/37/27/2129/1748921> [Accessed 23 March 2021]
2. Ezekowitz, Justin A. et al. 2017 Comprehensive Update of the Canadian Cardiovascular Society Guidelines for the Management of Heart Failure. Can J Cardiol 2017;33:1342-1433.  
<https://www.onlinejc.ca/action/showPdf?pii=S0828-282X%2817%2930973-X> [Accessed 23 March 2021]

# Endemic goitre and iodine deficiency

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 iodine-deficient 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 1. Normal daily maintenance IV fluids in children > 1 month](#)

# Appendix 1. Normal daily maintenance IV fluids in children > 1 month

Last updated: January 2021

## Indications

Basic hydration needs<sup>a</sup> 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 <sup>(*)</sup> (paediatric infusion set 1 ml = 60 drops)
3 to < 4 kg	350 ml/24 h	15 drops/min
4 to < 5 kg	450 ml/24 h	19 drops/min
5 to < 6 kg	550 ml/24 h	23 drops/min
6 to < 7 kg	650 ml/24 h	27 drops/min
7 to < 8 kg	750 ml/24 h	31 drops/min
8 to < 9 kg	850 ml/24 h	35 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

<b>Weight</b>	<b>Volume /24 hours</b>	<b>Rate<sup>(*)</sup> (paediatric infusion set 1 ml = 60 drops)</b>	<b>Rate (standard infusion set 1 ml = 20 drops)</b>
<b>20 to &lt; 22 kg</b>	1500 ml/24 h	63 drops/min	21 drops/min
<b>22 to &lt; 26 kg</b>	1600 ml/24 h	67 drops/min	22 drops/min
<b>26 to &lt; 30 kg</b>	1700 ml/24 h	71 drops/min	24 drops/min
<b>30 to &lt; 35 kg</b>	1800 ml/24 h	75 drops/min	25 drops/min
<b>≥ 35 kg</b>	2000 ml/24 h	83 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

## Footnotes

- (a) 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

# Main references

## Websites consulted between June 2019 and December 2022

*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.cbjp.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/>

