Chapter 6: Parasitic diseases

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[1] should be hospitalised immediately:

- Impaired consciousness, including coma.
- Seizures: more than 2 episodes of generalised or focal (e.g. abnormal eye movements) seizures within 24 hours.
- Prostration: extreme weakness; in children: inability to sit or drink/suck.
- Respiratory distress: rapid, laboured breathing or slow, deep breathing.
- Shock: cold extremities, weak or absent pulse, capillary refill time ≥ 3 seconds, cyanosis.
- Jaundice: yellow discolouration of mucosal surfaces of the mouth, conjunctivae and palms.
- Haemoglobinuria: dark red urine.
- Abnormal bleeding: skin (petechiae), conjunctivae, nose, gums; blood in stools.
- Acute renal failure: oliguria (urine output < 12 ml/kg/day in children and < 400 ml/day in adults) despite adequate hydration.

Laboratory

Parasitological diagnosis[2]

Diagnosis of malaria should be confirmed, whenever possible. If testing is not available, treatment of suspected malaria should not be delayed.

Rapid diagnostic tests (RDTs)[a]
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[b]
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)[c] should be used instead[1]. 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)[c] given by the oral route for 3 days[1]. 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[b]

ACT	Presentation	Dosage
artemether/lumefantrine (AL)	**Coformulated tablets** of 20 mg artemether/120 mg lumefantrine	On D1, the first dose is given at 0 hour and the 2nd dose at 8-12 hours. Subsequent doses on D2 and D3 are given 2 times daily (morning and evening).
	Blister child 5 to < 15 kg, 6 tab/blister	==> 1 tab 2 times daily on D1, D2, D3
	Blister child 15 to < 25 kg, 12 tab/blister	==> 2 tab 2 times daily on D1, D2, D3
	Blister child 25 to < 35 kg, 18 tab/blister	==> 3 tab 2 times daily on D1, D2, D3
	Blister child ≥ 35 kg and adult, 24 tab/blister	==> 4 tab 2 times daily on D1, D2, D3
	Coformulated tablets of 80 mg artemether/ 480 mg lumefantrine	
	Blister child ≥ 35 kg and adult, 6 tab/blister	==> 1 tab 2 times daily on D1, D2, D3
artesunate/amodiaquine (AS/AQ)	**Coformulated tablets**	
	Blister child 4.5 to < 9 kg, tab of AS 25 mg/AQ base 67.5 mg, 3 tab/blister	==> 1 tab once daily on D1, D2, D3
	Blister child 9 to < 18 kg, tab of AS 50 mg/AQ base 135 mg, 3 tab/blister	==> 1 tab once daily on D1, D2, D3
	Blister child 18 to < 36 kg, tab of AS 100 mg/AQ base 270 mg, 3 tab/blister	==> 1 tab once daily on D1, D2, D3
	Blister child ≥ 36 kg and adult, tab of AS 100 mg/AQ base 270 mg, 6 tab/blister	==> 2 tab once daily on D1, D2, D3
dihydroartemisinin/piperaquine (DHA/PPQ)	**Coformulated tablets**	
	Blister child, tab of DHA 20 mg/PPQ 160 mg, 3 tab/blister	5 to < 8 kg: 1 tab 20/160 mg once daily on D1, D2, D3
	Blister child, tab of DHA 40 mg/PPQ 320 mg, 3 tab/blister	8 to < 11 kg: 1½ tab 20/160 mg once daily on D1, D2, D3
	Blister child, tab of DHA 40 mg/PPQ 320 mg, 6 tab/blister	11 to < 17 kg: 1 tab 40/320 mg once daily on D1, D2, D3
	Blister adolescent-adult, tab of DHA 40 mg/PPQ 320 mg, 9 tab/blister	17 to < 25 kg: 1½ tab 40/320 mg once daily on D1, D2, D3
	Blister adolescent-adult, tab of DHA 40 mg/PPQ 320 mg, 12 tab/blister	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[3] .

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[b]
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**[d] (10 mg/kg)
  - Children 2 months to < 3 years (≤ 10 kg): 1 rectal capsule (100 mg)
  - Children 3 to < 6 years (≤ 20 kg): 2 rectal capsules (200 mg)

or

- At dispensary level, for children and adults: the first dose of artesunate or, if unavailable, the first dose of artemether. For dosing information, see below.

In either case, provide patients, especially children, with some sugar prior to or during transfer.

Inpatient treatment

The drug of choice is artesunate, preferably IV, or if not possible IM.
For patients in shock: IM route is not appropriate, use artesunate IV only.

artesunate slow IV injection (3 to 5 minutes) or, if not possible, slow IM injection, into the anterior thigh:
Children under 20 kg: 3 mg/kg/dose
Children 20 kg and over and adults: 2.4 mg/kg/dose

- One dose on admission (H0)
- One dose 12 hours after admission (H12)
- One dose 24 hours after admission (H24)
- Then one dose once daily

Treat parenterally for at least 24 hours (3 doses), then, if the patient can tolerate the oral route, change to a complete 3-day course of an ACT. If not, continue parenteral treatment once daily until the patient can change to oral route (without exceeding 7 days of parenteral treatment).

If artesunate is not unavailable, artemether may be an alternative:
artemether IM into the anterior thigh (never administer by IV route)
Children and adults: 3.2 mg/kg on admission (D1) then 1.6 mg/kg once daily
Treat parenterally for at least 24 hours (2 doses), then, if the patient can tolerate the oral route, change to a complete 3-day course of an ACT. If not, continue parenteral treatment once daily until the patient can change to oral route (without exceeding 7 days of parenteral treatment).

Note: if patient is still on parenteral treatment on Day 5, continue on the same treatment until Day 7. In this case it is not necessary to start an ACT.

Quinine IV is still recommended in some national protocols. It may be used in treatment of malaria with shock if artesunate IV is not available. The dose is expressed in quinine salt:

- Loading dose: 20 mg/kg to be administered over 4 hours, then, keep the vein open with an infusion of 5% glucose over 4 hours; then
- Maintenance dose: 8 hours after the start of the loading dose, 10 mg/kg every 8 hours (alternate quinine over 4 hours and 5% glucose over 4 hours).

For adults, administer each dose of quinine in 250 ml of glucose. For children under 20 kg, administer each dose of quinine in a volume of 10 ml/kg of glucose.
Do not administer a loading dose to patients who have received oral quinine, or mefloquine within the previous 24 hours: start with maintenance dose.
Treat parenterally for at least 24 hours, then, if the patient can tolerate the oral route, change to a complete 3-day course of an ACT (or if not available, oral quinine to complete 7 days of quinine treatment). If not, continue parenteral treatment until the patient can change to oral route (without exceeding 7 days of parenteral treatment).

Symptomatic treatment and management of complications

Hydration

Maintain adequate hydration. As a guide, for volume to be administered per 24 hours by oral or IV route, see Appendix 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[e].
- 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[4] .
- 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.

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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 hyperaesthesia), psychiatric disorders (apathy or agitation), disturbance of the sleep cycle (with daytime somnolence alternating with insomnia at night), impaired motor functions (paralysis, seizures, tics) and neuroendocrine disorders (amenorrhoea, impotence).
- In the absence of treatment: cachexia, lethargy, coma and death.

Rhodesiense HAT

The first stage is the same as above, but the incubation period is shorter (< 3 weeks), the disease evolves more rapidly and symptoms are more severe. Patients often die of myocarditis in 3 to 6 months without having developed signs of the meningo-encephalitic stage.

In practice, gambiense and rhodesiense HAT can be difficult to differentiate: e.g., there exist cases of acute gambiense infection and others of chronic rhodesiense infection.

Laboratory

- Diagnosis involves 3 steps for gambiense HAT (screening test, diagnostic confirmation and stage determination) and 2 steps for rhodesiense HAT (diagnostic confirmation and stage determination).
- The recommended screening test for *T.b. gambiense* infection is the CATT (Card Agglutination Test for Trypanosomiasis). It detects the presence of specific antibodies in the patient's blood or serum.
- Diagnostic confirmation: presence of trypanosomes in lymph node aspirates or in blood using concentration techniques: capillary tube centrifugation technique (Woo test), quantitative buffy coat (QBC), mini-anion exchange centrifugation technique (mAEC).
- Stage determination: detection of trypanosomes (after centrifugation) and white cell count in the cerebrospinal fluid (lumbar puncture):
  - Haemolymphatic stage: no trypanosomes AND ≤ 5 white cells/mm^3

- Meningoencephalitic stage: evidence of trypanosomes OR > 5 white cells/mm^3

Treatment (except in pregnant women)

- Due to the toxicity of trypanocides, detection of the parasite is essential before initiating treatment. In the absence of parasitological confirmation, treatment may nevertheless be justified in certain cases: very strong clinical suspicion, patients in life-threatening condition, strong serological suspicion (CATT 1:16 positive) in a population where the disease is highly prevalent (> 2%).
- Several treatment regimens exist. Check national recommendations and local resistance levels.
- Treatment must be administered under close medical supervision. Patients receiving pentamidine can be treated as outpatients but those receiving suramin, eflornithine (with or without nifurtimox) or melarsoprol should be hospitalised.
- After treatment, patients should be checked every 6 months (clinical examination, lumbar puncture and examination for trypanosomes) over 24 months, to look for relapse.

Haemolymphatic stage (Stage I)

Gambiense HAT

pentamidine isetionate deep IM
Children and adults: 4 mg/kg once daily for 7 to 10 days
Patients should receive a source of glucose (meal, sweet tea) one hour before injection (risk of hypoglycaemia); they should remain supine during administration and one hour after injection (risk of hypotension).

Rhodesiense HAT

suramin slow IV
Children and adults:
D1: test dose of 4 to 5 mg/kg
D3, D10, D17, D24, D31: 20 mg/kg (max. 1 g per injection)
Suramin may cause anaphylactic reactions, a test dose is recommended prior to starting treatment. In the event of an anaphylactic reaction after the test dose, the patients must not be given suramin again.

Meningoencephalitic stage (Stage II)

Before administrating trypanocides, the priority is to improve the patient's general condition (rehydration, treatment of malaria, intestinal worms, malnutrition, bacterial infections). It is nonetheless recommended not to postpone the trypanocidal treatment for more than 10 days.

Gambiense HAT

- First choice: nifurtimox-eflornithine combination therapy (NECT)
  nifurtimox PO
  Children and adults: 5 mg/kg 3 times daily for 10 days
  + **eflornithine** IV infusion over 2 hours
  Children and adults: 200 mg/kg every 12 hours for 7 days
  The catheter must be handled with great attention to avoid local or general bacterial infections: thoroughly disinfect the insertion site, ensure secure catheter fixation, protect the insertion site with a sterile dressing, systematically change the catheter every 48 hours or earlier in case of signs of phlebitis.
- Second choice:
  eflornithine IV infusion over 2 hours

Children under 12 years: 150 mg/kg every 6 hours for 14 days
Children 12 years and over and adults: 100 mg/kg every 6 hours for 14 days

- In the event of a relapse after NECT or eflornithine:
  melarsoprol slow IV
  Children and adults: 2.2 mg/kg once daily for 10 days
  Melarsoprol is highly toxic: reactive encephalopathy (coma, or recurrent or prolonged seizures) in 5 to 10% of treated patients, fatal in around 50% of cases; peripheral neuropathy, invasive diarrhoea, severe skin rash, phlebitis, etc.
  Prednisolone PO (1 mg/kg once daily) is frequently combined throughout the duration of treatment.

Rhodesiense HAT

melarsoprol slow IV
Children and adults: 2.2 mg/kg once daily for 10 days
Prednisolone PO (1 mg/kg once daily) is frequently combined throughout the duration of treatment.

Treatment in pregnant women

All trypanocides are potentially toxic for the mother and the foetus (risk of miscarriage, malformation, etc.). However, due to the life-threatening risk for the mother and the risk of mother-to-child transmission, treatment must be initiated as follows:

- Haemolymphatic stage:
  pentamidine for gambiense HAT as of the second trimester and suramin for rhodesiense HAT.
- Meningoencephalitic stage: treatment depends on the mother's condition:
  - If in immediately life-threatening condition: treatment with NECT or eflornithine cannot be deferred until after delivery.
  - If not immediately life-threatening condition: pentamidine for gambiense HAT and suramin for rhodesiense HAT. Treatment with NECT or eflornithine is to be administered after delivery.

Prevention and control

- Individual protection against tsetse fly bites: long sleeves and trousers, repellents, keeping away from risk areas (e.g. near rivers).
- Disease control: mass screening and treatment of patients (*T.b. gambiense*), trypanocide treatment of cattle (*T.b. rhodesiense*), vector control using tsetse fly traps or insecticides.

American trypanosomiasis (Chagas disease)

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[a] . It is significantly underdiagnosed.[1]

Clinical features

Acute phase

- Most cases are asymptomatic.
- If transmitted through a break in the skin: a red swelling on the skin (chagoma) or unilateral painless purplish periorbital oedema (Romaña's sign) with local lymphadenopathy, headache and fever.
- Rarely: multiple lymphadenopathies, hepatosplenomegaly, myocarditis (chest pain, dyspnoea), meningoencephalitis (seizures, paralysis).

Chronic phase

- Many cases remain asymptomatic (indeterminate phase).
- Up to 30% of cases develop organ damage:[2]
  - cardiac lesions (conduction disorders, dilated cardiomyopathy): arrhythmia, dyspnoea, chest pain, heart failure;
  - gastrointestinal lesions (dilation of the oesophagus or colon i.e. megaoesophagus, megacolon): difficulty swallowing, severe constipation.
  - Individuals with immunosuppression have a higher risk of developing organ damage than the general population.

Diagnosis

Laboratory [1]

- Acute phase:
  - Identification of *Trypanosoma cruzi* by direct microscopy of fresh blood or blood concentrated by microhematocrit method.
  - In case of strong clinical suspicion despite no definitive diagnosis from direct microscopy, perform serologic tests after a delay of approximately 1 month (see "Chronic phase").
- Chronic phase:
  - Identification of anti-*Trypanosoma cruzi* antibodies by serologic tests, e.g. enzyme-linked immunosorbent assay (ELISA), hemagglutination inhibition assay (HAI), indirect immunofluorescence (IIF) or rapid diagnostic test (RDT).
  - For a definitive diagnosis, two different serological tests should be performed simultaneously; in case of conflicting results, a third test is recommended.[b]

Other investigations

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

Treatment

Aetiologic treatment

- Acute or chronic Chagas disease can be treated with either benznidazole or nifurtimox. However, treatment is not recommended if patient has already developed cardiac or digestive complications.
- Close clinical monitoring should be provided due to the frequent occurrence of adverse effects. Where available, blood tests (complete blood count, liver and renal function tests) should be performed before, during and after treatment.
- Protocols vary according to the country, follow national recommendations.
  For information:

	Age	Dose and duration
benznidazole PO[(a)]	2 to 12 years[3]	5 to 8 mg/kg daily in 2 divided doses for 60 days
	> 12 years and adults[4]	5 to 7 mg/kg daily in 2 divided doses for 60 days
nifurtimox PO[(b)] [3]	≤ 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

(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.

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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 pentavalant antimonial (20 mg/kg daily for 10 to 20 days) is restricted to severe cases and must be administered under close medical supervision.
- Miltefosine PO (as for visceral leishmaniasis) for 28 days is effective in many forms of cutaneous leishmaniasis.
- Ulcers are often secondarily infected with streptococci and staphylococci: administer suitable antibiotics.
- Mucocutaneous forms: as for visceral leishmaniasis.

Visceral leishmaniasis

Visceral leishmaniasis in East Africa

- First-line treatment:
  a **pentavalent antimonial** IM or slow IV: 20 mg/kg daily for 17 days
  + **paromomycin** IM: 15 mg (11 mg base)/kg daily for 17 days
- Second-line treatment for relapse and for specific vulnerable groups: severe disease, pregnant women, patients over 45 years:
  liposomal amphotericin B IV infusion: 3 to 5 mg/kg once daily for 6 to 10 days up to a total dose of 30 mg/kg
- Treatment in HIV co-infected patients:
  liposomal amphotericin B IV infusion: 3 to 5 mg/kg once daily for 6 to 10 days up to a total dose of 30 mg/kg
  + **miltefosine** PO for 28 days:
  Children 2 to 11 years: 2.5 mg/kg once daily
  Children ≥ 12 years and < 25 kg: 50 mg once daily
  Children ≥ 12 years and adults 25 to 50 kg: 50 mg 2 times daily
  Adults > 50 kg: 50 mg 3 times daily

Visceral leishmaniasis in South Asia

- First-line treatment:
  liposomal amphotericin B IV infusion: 3 to 5 mg/kg once daily for 3 to 5 days up to a total dose of 15 mg/kg
  or
  liposomal amphotericin B IV infusion: 10 mg/kg single dose
- Second-line treatment for relapse:
  liposomal amphotericin B IV infusion: 3 to 5 mg/kg once daily for 5 to 8 days up to a total dose of 25 mg/kg

For all patients with visceral leishmaniasis, hydration, nutritional support and treatment of intercurrent infections (malaria, dysentery, pneumonia, etc.) are essential.
Tuberculosis and/or HIV infection may also be present and should be suspected if relapse occurs more than once or in the event of treatment failure.

Post-kala azar dermal leishmaniasis (PKDL)

Only patients with severe or disfiguring disease or with lesions remaining for > 6 months, and young children with oral lesions that interfere with feeding, are treated.

PKDL in East Africa

a **pentavalent antimonial** IM or slow IV: 20 mg/kg daily for 17 to 60 days
+ **paromomycin** IM: 15 mg (11 mg base)/kg daily for 17 days
or
liposomal amphotericin B IV infusion: 2.5 mg/kg once daily for 20 days
or
miltefosine PO for 28 days (as for visceral leishmaniasis) may be beneficial in HIV co-infected patients

PKDL in South Asia

liposomal amphotericin B IV infusion: 5 mg/kg 2 times weekly up to a total dose of 30 mg/kg

Prevention

- Insecticide-treated mosquito nets.
- Vector control and elimination of animal reservoir hosts.

Intestinal protozoan infections (parasitic diarrhoea)

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:

Giardiasis	**tinidazole** PO single dose Children: 50 mg/kg (max. 2 g) Adults: 2 g or **metronidazole** PO for 3 days Children: 30 mg/kg once daily Adults: 2 g once daily
Cryptosporidiosis	In immunocompetent patients, no aetiological treatment; spontaneous resolution in 1 to 2 weeks.
Cyclosporiasis	**co-trimoxazole** PO for 7 days Children: 25 mg SMX + 5 mg TMP/kg 2 times daily Adults: 800 mg SMX + 160 mg TMP 2 times daily In immunocompetent patients, symptoms usually resolve spontaneous in 1 to 3 weeks. Treatment is given in case of severe or prolonged symptoms.
Isoporiasis	**co-trimoxazole** PO for 7 to 10 days Adults: 800 mg SMX + 160 mg TMP 2 times daily In immunocompetent patients, symptoms usually resolve spontaneous in 2 to 3 weeks. Treatment is given in case of severe or prolonged symptoms.

- If reliable stool examination cannot be carried out: parasitic diarrhoeas cannot be differentiated on clinical grounds, nor is it possible to distinguish these from non- parasitic diarrhoeas. An empirical treatment (using tinidazole or metronidazole and co-trimoxazole as above, together or in succession) may be tried in the case of prolonged diarrhoea or steatorrhoea. In patients with HIV infection, see empirical treatment (HIV infections and AIDS, Chapter 8).
- In patients with advanced HIV disease, cryptosporidiosis, cyclosporiasis and isosporiasis are opportunistic infections; the most effective intervention is the treatment of the underlying HIV infection with antiretrovirals. Patients remain at high risk for dehydration/death until immunity is restored.

Flukes

Infection/Epidemiology	Clinical features/Diagnosis	Treatment
Lung flukes *Paragonimus* sp *Distribution*: South-East Asia, China, parts of Cameroon, Nigeria, Gabon, Congo, Colombia, Peru *Transmission*: eating raw freshwater crustaceans	The two most prominent symptoms are prolonged (> 2 weeks) productive cough and intermittent haemoptysis (rusty-brown sputum). In endemic areas, paragonimosis should be considered whenever pulmonary tuberculosis is suspected as the clinical and radiological features overlap. Paragonimosis is confirmed when eggs are detected in sputum (or possibly in stools).	**praziquantel** PO Children 4 years and over and adults: 25 mg/kg 3 times daily for 2 days
Hepatobiliary flukes *Fasciola hepatica* and *gigantica* *Distribution*: worldwide, in areas where sheep and cattle are raised *Transmission*: eating uncooked aquatic plants	*During migration phase*: asthenia, prolonged fever, myalgia, right upper quadrant pain, mild hepatomegaly; sometimes, allergic signs (e.g. pruritus). At this stage, the diagnosis is rarely considered and can only be confirmed through serology; parasitological examination of stools is always negative. *Once adult flukes are present in the biliary tract*: presentation resembles cholelithiasis: right upper quadrant pain, recurrent episodes of obstructive jaundice/ febrile cholangitis. The diagnosis is confirmed when parasite eggs are detected in stools (or flukes are seen in the biliary tract with sonography).	**triclabendazole** PO Children and adults: 10 mg/kg single dose May repeat in 24 hours in the event of severe infection
Opisthorchis felineus (Asia, Eastern Europe) *Opisthorchis viverrini* (Cambodia, Laos, Vietnam, Thailand) *Clonorchis sinensis* (China, Koera, Vietnam) *Transmission*: eating raw/undercooked freshwater fish	Abdominal pain and diarrhoea. With heavy infection, hepatobiliary symptoms: hepatomegaly, right upper quadrant pain, jaundice or episodes of febrile cholangitis. The diagnosis is confirmed when parasite eggs are detected in stools.	**praziquantel** PO Children 4 years and over and adults: 25 mg/kg 3 times daily for 2 days
Intestinal flukes *Fasciolopsis buski* (India, Bangladesh, South-East Asia) *Heterophyes heterophyes* (South-East Asia, Nile delta) *Metagonimus yokogawai* (Siberia, China, Korea) *Transmission*: eating uncooked aquatic plants (*F. buski*),	Symptoms are limited to diarrhoea and epigastric or abdominal pain. With massive infection, *F. buski* can cause oedematous allergic reactions (including ascites, anasarca). The diagnosis is confirmed when parasite eggs are detected in stools.	**praziquantel** PO Children 4 years and over and adults: 25 mg/kg 3 times daily, 1 day

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 *S. mansoni, S. japonicum, S. mekongi* and *S. intercalatum*.

The severity of the disease depends on the parasite load. Heavily infected patients are prone to visceral lesions with potentially irreversible sequelae. Children aged 5 to 15 years are particularly at risk: prevalence and parasite load are highest in this age group.

An antiparasitic treatment should be administered to reduce the risk of severe lesions, even if there is a likelihood of re-infection.

Clinical features

	Parasite/Epidemiology[a]	Clinical features/Diagnosis (established infection)
Genito-urinary schistosomiasis	***S. haematobium*** *Distribution*: Africa, Madagascar and the Arabian peninsula	• Urinary manifestations: ▫ In endemic areas, urinary schistosomiasis should be suspected in any patients who complain of macroscopic haematuria (red coloured urine throughout, or at the end of, micturition). Haematuria is frequently associated with polyuria/dysuria (frequent and painful micturition). ▫ In patients, especially children and adolescents, with urinary symptoms, visual inspection of the urine (and dipstick test for microscopic haematuria if the urine appears grossly normal) is indispensible. ▫ Presumptive treatment is recommended in the presence of macro- or microscopic haematuria, when parasitological confirmation (parasite eggs detected in urine) cannot be obtained. • Genital manifestations: In women, symptoms of genital infection (white-yellow or bloody vaginal discharge, itching, lower abdominal pain, dyspareunia) or vaginal lesions resembling genital warts or ulcerative lesions on the cervix; in men, haematospermia (blood in the semen). • If left untreated: risk of recurrent urinary tract infections, fibrosis/calcification of the bladder and ureters, bladder cancer; increased susceptibility to sexually transmitted infections and risk of infertility. • In endemic areas, genito-urinary schistosomiasis may be a differential diagnosis to the genito-urinary tuberculosis, and in women, to the sexually transmitted infections (especially in women with an history of haematuria).
Intestinal schistosomiasis	***S. mansoni*** *Distribution*: tropical Africa, Madagascar, the Arabian peninsula, South America (especially Brazil) ***S. japonicum*** *Distribution*: China, Indonesia, the Philippines ***S. mekongi*** *Distribution*: parts of Lao PDR, Cambodia (along the Mekong River) ***S. intercalatum*** *Distribution*: parts of DRC, Congo, Gabon, Cameroon, Chad	• Non-specific digestive symptoms (abdominal pain; diarrhoea, intermittent or chronic, with or without blood) and hepatomegaly. • For *S. intercalatum*: digestive symptoms only (rectal pain, tenesmus, rectal prolapse, bloody diarrhoea). • If left untreated: risk of hepatic fibrosis, portal hypertension, cirrhosis, gastrointestinal haemorrhage (hematemesis, melena, etc.), except with *S. intercalatum* (less pathogenic than other intestinal schistosomes, no severe hepatic lesions). • The diagnosis is confirmed when parasite eggs are detected in stools. • In the absence of reliable parasitological diagnosis: in areas where intestinal schistosomiasis is common, diarrhoea (especially bloody diarrhoea) with abdominal pain and/or hepatomegaly may be a basis for presumptive diagnosis and treatment.

Treatment

praziquantel PO[1][2]

Children 4 years and over and adults[b] :

- *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

(b) For the treatment of schistosomiasis, praziquantel may me administered to pregnant women.

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Cestodes

Cestodes (adult forms)

Parasites	Clinical features/Laboratory	Treatment	Transmission/Prevention
Taeniasis *Taenia saginata* *Taenia solium* (worldwide)	Often asymptomatic Segments expelled in the stools, sometimes gastrointestinal disturbances (epigastric or abdominal pain, nausea, diarrhoea) Laboratory: eggs in stools or collected from perianal skin (scotch tape method), segments in stools	**praziquantel** PO[(a)] Children 4 years and over and adults: 5 to 10 mg/kg single dose	**Transmission** by eating raw or under-cooked meat: • beef for *T. saginata* • pork for *T. solium* **Prevention**: • individual: cook meat thoroughly • collective: slaughterhouse monitoring
Diphyllobothriasis *Diphyllobothrium latum* (temperate or cold lake areas)	Often asymptomatic In the event of heavy infection: mild gastrointestinal disturbances, anaemia due to vitamin B_{12} deficiency associated with (rare) neurological sequelae Laboratory: eggs in stools	**praziquantel** PO[(a)] Children 4 years and over and adults: 5 to 10 mg/kg single dose If anaemia: **vitamin B_{12}** + **folic acid**	**Transmission** by eating raw or under- cooked freshwater fish **Prevention**: • individual: cook fish thoroughly
Hymenolepiasis *Hymenolepis nana* (worldwide)	Often asymptomatic In the event of heavy infection: gastrointestinal disturbances (epigastric pain) Laboratory: eggs in stools	**praziquantel** PO[(a)] Children 4 years and over and adults: 15 to 25 mg/kg single dose	**Transmission** by faecal-oral route or auto-infection **Prevention**: • individual: hand washing, nail cutting • collective: hygiene and sanitation (water, latrines, etc.)

(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
Cysticercosis *Taenia solium* (worldwide)	• Muscular: asymptomatic or myalgia • Subcutaneous: nodules • Neurological (neurocysticercosis): headache, convulsions, coma, etc. • Ocular: exophthalmia, strabismus, iritis, etc. Laboratory: hypereosinophilia in blood and cerebrospinal fluid	Neurological and ocular cysticercosis should be managed in specialized facilities. Antiparasitic treatment without diagnosis of location by computerirsed tomography and/or magnetic resonance imaging can worsen the symptoms even threat the life. Neurosurgical treatment can be required.	**Transmission** by eating food contaminated with *T. solium* eggs or auto-infection **Prevention**: • individual: treat *T. solium* carriers, hygiene, cook meat thoroughly
Hydatid cyst *Echinococcus granulosus* (South America, North, East and South Africa, Western Europe)	Cysts located in the liver (60% of cases); lungs (30% of cases), and, less frequently, in other sites including the brain. Long asymptomatic period. The cyst becomes symptomatic when complications develop (biliary obstruction; anaphylactic shock in the event of rupture into peritoneal cavity, vessels or an organ; febrile painful jaundice in the event of rupture into the biliary tree, etc.).	First-line treatment: surgical excision **albendazole** PO[(b)] is useful in addition to, or instead of, surgery: Children over 2 years and adults under 60 kg: 7.5 mg/kg 2 times daily Adults over 60 kg: 400 mg 2 times daily Treatment duration: In addition to surgery (pre-operatively or post- operatively): continuous course of minimum 2 months or at least two 28-day courses with a drug-free interval of 14 days. Inoperable cases: 28-day courses with drug-free intervals of 14 days, for 3 to 6 months (on average), possibly up to 1 year.	**Transmission**: • direct: contact with dogs • indirect: water and food contaminated by dog faeces **Prevention**: • individual: avoid contact with dogs • collective: eliminate stray dogs, monitor slaughterhouses

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

Nematode infections

Infection/Epidemiology	Clinical features/Diagnosis	Treatment
Ascariasis (roundworms)[(a)] *Ascaris lumbricoides* *Distribution*: worldwide, mainly in tropical and subtropical *Transmission*: ingestion of ascaris eggs	• *During larval migration* Loeffler 's syndrome: transient pulmonary symptoms (dry cough, dyspnoea, wheezing) and mild fever. • *Once adult worms are present in the intestine* Abdominal pain and distension. In general, the diagnosis is made when adult worms are expelled from the anus (or occasionally from the mouth). Ascaris are large (15-30 cm), cylindrical worms, pinkish-white, with slightly tapered ends. • *Complications* Ascariasis is usually benign, but massive infestation may cause intestinal obstruction (abdominal pain, vomiting, constipation), especially in children < 5 years. Worms may accidentally migrate to gall bladder, liver or peritoneum, causing jaundice, liver abscess, or peritonitis. • Ascaris eggs may be detected through parasitological examination of stools.	**albendazole** PO single dose Children > 6 months and adults: 400 mg (200 mg in children > 6 months but < 10 kg) or **mebendazole** PO for 3 days Children > 6 months and adults: 100 mg 2 times daily (50 mg 2 times daily in children > 6 months but < 10 kg)
Trichuriasis (whipworms)[(a)] *Trichuris trichiura* *Distribution and transmission*: as for *A. lumbricoides*	• In heavy infection: abdominal pain and diarrhoea. • In massive infection: chronic bloody diarrhea, tenesmus, rectal prolapse due to frequent attempts to defecate, especially in children. Worms may sometimes be seen on the rectal mucosa when prolapsed: these are grayish-white, 3-5 cm in length, in the shape of a whip, with a thickened body and a long, threadlike extremity. • Trichuris eggs may be detected through parasitological examination of stools.	**albendazole** PO for 3 days Children > 6 months and adults: 400 mg once daily (200 mg once daily in children > 6 months but < 10 kg) or **mebendazole** PO for 3 days, as for ascariasis. A single dose of albendazole or mebendazole is often insufficient.
Ankylostomiase[(a)] *Ancylostoma duodenale* *Necator americanus* *Distribution*: tropical and subtropical regions *Transmission*: larval skin penetration following contact (feet, hands) with contaminated soil	• *During larval penetration/migration* Cutaneous signs (pruritic papulo-vesicular rash at the site of penetration, usually the feet) and pulmonary symptoms (similar to ascariasis). • *Once adult worms are present in the intestine* Mild abdominal pain. Attachment of the parasite to the mucosa leads to chronic blood loss and anaemia (in endemic areas, antihelminthic treatment is recommended for patients with iron-deficiency anaemia). • Hookworm eggs may be detected through parasitological examination of stools.	**albendazole** single dose (as for ascariasis) is much more effective than mebendazole single dose. When using **mebendazole**, a 3-day treatment (as for ascariasis) is recommended. Treatment of anaemia (Chapter 1).
Strongyloidiasis	• *Acute strongyloidiasis*	First line treatment is:

Strongyloides stercoralis *Distribution*: humid tropical regions *Transmission*: larval skin penetration and auto-infection	▫ During larval penetration/migration: cutaneous signs (erythema and pruritus at the site of penetration, which may persist several weeks) and pulmonary symptoms (similar to ascariasis). ▫ Once larvae are present in the intestine: gastrointestinal symptoms (bloating, abdominal and epigastric pain, vomiting, diarrhoea). • *Chronic strongyloidiasis* Intestinal larvae may re-infect their host (auto-infection) by penetrating through the intestinal wall or by migrating transcutaneously from perianal skin. Chronic infections result in prolonged or recurrent pulmonary and gastrointestinal symptoms. Transcutaneous migration of intestinal larvae gives rise to a typical rash (larva currens), mainly in the anal region and on the trunk: sinuous, raised, linear, migrating lesion, intensely pruritic, moving rapidly (5 to 10 cm/hour) and lasting several hours or days. • *Complications* Hyperinfection (massive infestation) results in exacerbation of pulmonary and gastrointestinal symptoms, and possible dissemination of larvae to atypical locations, (CNS, heart, etc.). This form occurs mainly in patients receiving immunosuppressive therapy (e.g. corticosteroids). • Strongyloides larvae may be detected through parasitological examination of stools.	**ivermectin** PO[(b)] single dose Children > 15 kg and adults: 200 micrograms/kg, on an empty stomach While less effective, a 3-day treatment with **albendazole** PO (as for trichuriasis) may be an alternative. Hyperinfections are refractory to conventional therapy. Prolonged or intermittent multiple-dose regimens are required.
Enterobiasis (pinworms) *Enterobius vermicularis* *Distribution*: worldwide *Transmission*: faecal-oral route or auto-infection	• Anal pruritus, more intense at night, vulvovaginitis in girls (rare). In practice, the diagnosis is most often made when worms are seen on the perianal skin (or in the stool in heavy infestation). Pinworms are small (1 cm), mobile, white, cylindrical worms with slightly tapered ends. • Pinworm eggs may be collected from the anal area (scotch tape method) and detected under the microscope.	**albendazole** PO single dose, as for ascariasis or **mebendazole** PO single dose Children > 6 months and adults: 100 mg (50 mg in children > 6 months but < 10 kg) A second dose may be given after 2 to 4 weeks.
Trichinellosis *Trichinella* sp *Distribution*: worldwide, particularly frequent in Asia (Thailand, Laos, China, etc.)	• *Enteric phase* (1 to 2 days after ingestion of infected meat) Self-limited episode of diarrhoea and abdominal pain lasting several days.	**albendazole** PO for 10 to 15 days Children > 2 years: 5 mg/kg 2 times daily Adults:

Transmission: consumption of raw or undercooked meat containing trichinella larvae (pork, wart-hog, bear, dog, etc.)	• *Muscular phase* (about 1 week after ingestion) High fever; muscular pain (ocular [pain on eye movement], masseters [limitation of mouth opening], throat and neck [pain with swallowing and speech], trunk and limbs); facial or bilateral peri-orbital oedema; conjunctival haemorrhage, subungual haemorrhage; headache. Typical features are not always present and the patient may present with a non-specific flu-like syndrome. Other features, such as dietary habits (consuming pork/raw meat), suggestive symptoms (fever > 39 °C and myalgia and facial oedema) in several individuals who have shared the same meal (e.g. ceremony) or hypereosinophilia > 1000/mm^3, reinforce the clinical suspicion. • Definitive diagnosis: muscle biopsy; serology (ELISA, Western Blot).	400 mg 2 times daily or **mebendazole** PO for 10 to 15 days Children > 2 years: 2.5 mg/kg 2 times daily Adults: 200 mg 2 times daily *plus, regardless of which anti-helminthic is chosen:* **prednisolone** PO 0.5 to 1 mg/kg once daily for the duration of treatment

[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)

Filariases are helminthiases due to tissue-dwelling nematode worms (filariae). Human to human transmission takes place through the bite of an insect vector.

The most important pathogens are outlined in the table below. Mixed infections are common in co-endemic regions.

Each filarial species is found in 2 principal developmental stages: macrofilariae (adult worms) and microfilariae (larval offspring). The treatment depends on the pathogenic stage of the species considered and targets microfilariae for *O. volvulus* and macrofilariae for the other species.

Species/Infections	Location of macrofilariae	Location of microfilariae	Pathogenic stage	Presence of *Wolbachia*
Onchocerca volvulus (onchocerciasis)	Subcutaneous nodules	Skin and eye	Microfilariae	Yes
Loa loa (loiasis)	Subcutaneous tissue	Blood	Macrofilariae	No
Wuchereria bancrofti, ***Brugia malayi*** and ***Brugia timori*** (lymphatic filariasis)	Lymph vessels	Blood	Macrofilariae	Yes

Classical antifilarial agents include diethylcarbamazine (DEC), ivermectin and albendazole. Doxycycline is used solely in the treatment of *O. volvulus* and lymphatic filarial worms, which harbour an endosymbiotic bacterium (*Wolbachia*) sensitive to doxycycline.

Onchocerciasis (river blindness)

The distribution of onchocerciasis is linked to that of its vector (*Simulium*), which reproduces near rapidly flowing rivers in intertropical Africa (99% of cases), Latin America (Guatemala, Mexico, Ecuador, Colombia, Venezuela, Brazil) and Yemen.

Clinical features

In endemic areas, the following signs, alone or in combination, are suggestive of onchocerciasis:

- Onchocercomas: painless subcutaneous nodules containing adult worms, usually found over a bony prominence (iliac crest, trochanters, sacrum, rib cage, skull, etc.), measuring several mm or cm in size, firm, smooth, round or oval, mobile or adherent to underlying tissue; single, or multiple and clustered.
- Acute papular onchodermatitis: papular rash, sometimes diffuse but often confined to the buttocks or lower extremities, intensely itchy, associated with scratch marks, often superinfected ("filarial scabies")[a] . 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[b] . It is contraindicated in children < 8 years and pregnant or breast-feeding women.
- **Ivermectin** PO is the drug of choice: 150 micrograms/kg single dose; a 2nd dose should be administered after 3 months if clinical signs persist. Repeat the treatment every 6 or 12 months to maintain the parasite load below the threshold at which clinical signs appear[c] . Ivermectin is not recommended in children < 5 years or < 15 kg and pregnant women.
- In case of co-infection with *Loa loa* or in regions where loiasis is co-endemic, ivermectin should be administered with caution (risk of severe adverse reactions in patients with high *L. loa* microfilarial load):
  - If it is possible to test for *Loa loa* (thick blood film):
    Confirm and quantify the microfilaraemia. Administer the appropriate treatment according to the microfilarial load (see Loiasis).
  - 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 loiaisis 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

(a) Differential diagnosis is sarcoptic scabies (Scabies, Chapter 4).

(b) Elimination of *Wolbachia* reduces the longevity and fertility of the macrofilariae, and thus the production of new microfilariae within the organism.

(c) 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[a] . 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[b] . 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[c] . 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)[a] ; 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[b], 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

Meningitis is an acute bacterial infection of the meninges, which may affect the brain and lead to irreversible neurological damage and auditory impairment.
Bacterial meningitis is a medical emergency. The treatment is based on early parenteral administration of antibiotics that penetrates well into the cerebrospinal fluid (CSF). Empiric antibiotic therapy is administered if the pathogen cannot be identified or while waiting for laboratory results.
The main bacteria responsible vary depending on age and/or context:

Meningitis in a non-epidemic context

- Children 0 to 3 months:
  - Children ≤ 7 days: Gram-negative bacilli (*Klebsiella spp*, *E. coli*, *S. marcescens*, *Pseudomona spp*, *Salmonella spp*) and group B streptococcus
  - Children > 7 days: *S. pneumoniae* accounts for 50% of all bacterial meningitis

  L. monocytogenes is occasionally responsible for meningitis during this period.
- Children 3 months-5 years: *S. pneumoniae*, *H. influenza B* and *N. meningitidis*
- Children > 5 years and adults: *S. pneumoniae* and *N. meningitidis*

Special conditions:
- Immunodepressed patients (HIV, malnourished): high percentage of Gram- negative bacilli (specially *Salmonella spp*) and also *M. tuberculosis*.
- Sickle cell anaemia: *Salmonella spp* and *Staphylococcus aureus* are frequent causes.
- Meningitis may be related to *S. aureus* when associated with skin infection or skull fracture.

Meningitis in an epidemic context

In the Sahelian region (but not exclusively, e.g. Rwanda, Angola, Brazil), during the dry season, epidemics of meningococcal meningitis (*Neisseria meningitidis* A or C or W135) affect children from 6 months of age, adolescents and adults. In these regions, whether during epidemics or not, all the above pathogens can be found, especially in young children.

Clinical features

The clinical presentation depends on the patient's age.

Children over 1 year and adults

- Fever, severe headache, photophobia, neck stiffness
- Brudzinski's sign (neck flexion in a supine patient results in involuntary flexion of the knees) and Kernig's sign (attempts to extend the knee from the flexed-thigh position are met with strong passive resistance).
- Petechial or ecchymotic purpura (usually in meningococcal infections)
- In severe forms: coma, seizures, focal signs, purpura fulminans

Children under 1 year

The classic signs of meningitis are usually absent.
- The child is irritable, appears sick with fever or hypothermia, poor feeding or vomiting.
- Other features include: seizures, apnoea, altered consciousness, bulging fontanelle (when not crying); occasionally, neck stiffness and purpuric rash.

Laboratory

- Lumbar puncture (LP):
  - Macroscopic examination of CSF: antibiotic therapy should be initiated immediately if the LP yields a turbid CSF.
  - Microscopic examination: Gram stain (but a negative examination does not exclude the diagnosis) and white blood cell count (WBC).
  - In an epidemic context, once the meningococcal aetiology has been confirmed, there is no need for routine LP for new cases.

	Pressure	Aspect	WBC (leucocytes/mm^3)	Protein	Other tests
Normal CSF		Clear	< 5	Pandy– < 40 mg/dl	–
Bacterial meningitis	++++	Cloudy, turbid	100-20 000 mainly neutrophiles In neonates: > 20 In immunocompromised, the WBC may be < 100	Pandy+ 100-500 mg/dl	Gram stain +
Viral meningitis	Normal to +	Clear	10-700 mainly lymphocytes	Pandy–	–
TB meningitis	+++	Clear or yellowish	< 500 mainly lymphocytes	Pandy+	AFB
Cryptococcal meningitis	++++	Clear	< 800 mainly lymphocytes	Pandy–	India ink

- Rapid test for detection of bacterial antigens.

Note: in an endemic area, it is essential to test for severe malaria (rapid test or thin/thick films).

Treatment in a non-epidemic context

Antibiotic therapy

For the choice of antibiotic therapy and dosages according to age, see table below.