# 10 Helminths

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Helminths (*helmins*: worm) are parasitic metazoans from the phyla Platyhelmintha (flatworms), Nematoda (roundworms), and Acanthocephala (thorny-headed worms). The organisms in this last phylum are of little significance as human parasites. Table 10.**1**, p. 545 provides a taxonomic overview of the groups covered in the text.

**Eggs and Larvae of Important Helminths**

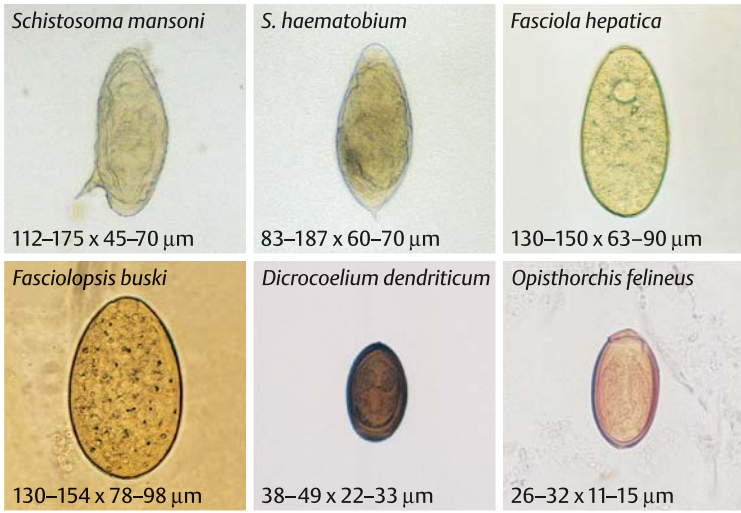


Fig. 10.**1** Differential diagnosis of the eggs of important helminths (trematodes, cestodes, and nematodes) and of the larvae of *Strongyloides stercoralis*. Note: images are not to the same scale! (Images of *Hymenolepis* and *Enterobius*: H. Mehlhorn, Düsseldorf.)

**Eggs and Larvae of Important Helminths**

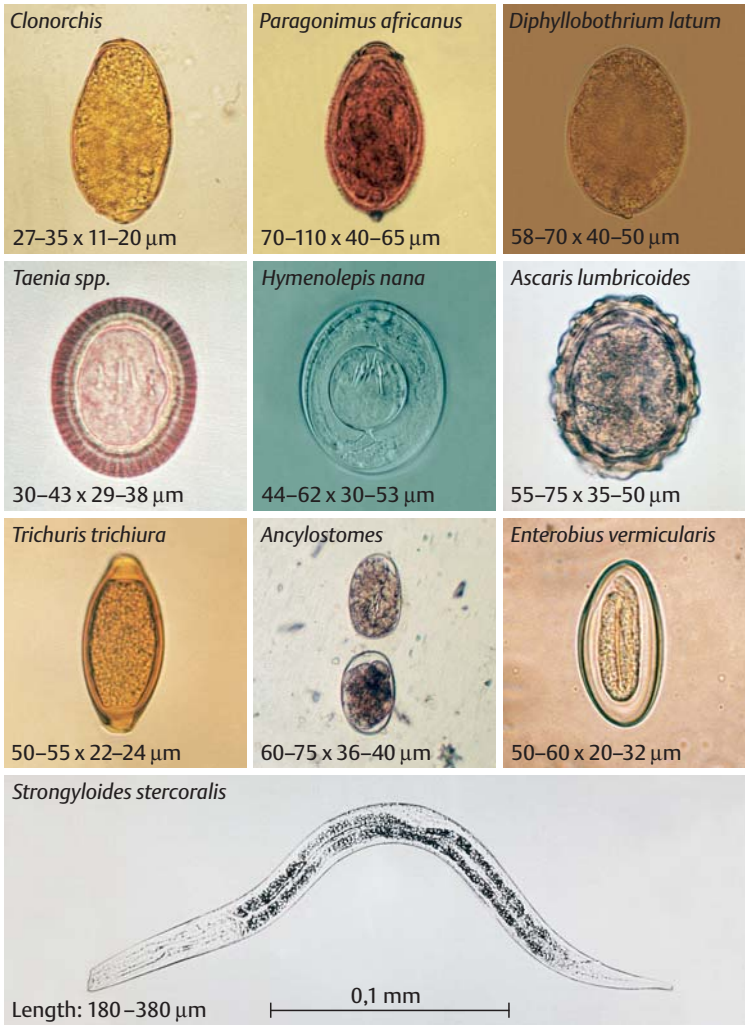


Fig. 10.**1** *Continued*

Table 10.1 Classification of Helminths Mentioned in the Text

| Phylum<br>■ Superclass***<br>■ Class**<br>■ Subclass* | Order<br>■ Superfamily | Genus |
|---|---|---|
| **Platyhelmintha** | | |
| ■ Trematoda*** | Strigeatida | *Schistosoma, Bilharziella, Trichobilharzia* |
| | Echinostomida | *Fasciola, Fasciolopsis, Echinostoma* |
| | Plagiorchiida | *Dicrocoelium, Paragonimus* |
| | Opisthorchiida | *Opisthorchis, Clonorchis, Heterophyes, Metagonimus* |
| ■ Cestoda** | Pseudophyllida | *Diphyllobothrium* |
| | Cyclophyllida | *Taenia, Echinococcus, Hymenolepis* |
| **Nematoda** | | |
| ■ Secernentia* | Rhabditida | *Strongyloides* |
| | Strongylida | *Ancylsotsoma, Necator, Trichostrongylus, Angiostrongylus (= Parastrongylus)* |
| | Oxyurida | *Enterobius* |
| | Ascaridida | *Ascaris, Toxocara, Baylisascaris, Anisakis, Phocanema, Contracaecum* |
| | Spirurida | |
| | ■ Filarioidea | *Wuchereria, Brugia, Loa, Onchocerca, Mansonella, Dirofilaria* |
| | ■ Dracunculoidea | *Dracunculus* |
| ■ Adenophoria | Enoplida | *Trichuris, Trichinella* |

# Platyhelmintha (syn. Platyhelminthes)

## Trematoda (Flukes)

**General.** Most of the trematode species that parasitize humans are dorsoventrally flattened with an oval to lancet shape, although others have different shapes such as the threadlike schistosomes. Suckers (*trema*: hole, opening) serve as attachment organs: an oral sucker around the mouth connected to the esophagus and the blind-ending intestine, and a ventral sucker. The body surface of adult trematodes is covered by a cellular tegument (composed of an outer annucleate, syncytial layer of cytoplasm connected by cytoplasmic strands to inner nucleated portions) through which substances can be absorbed from the environment. Most species are hermaphroditic, only the schistosomes have separate sexes. Snails are the first intermediate hosts; some species require arthropods or fish as second intermediate hosts.

### Schistosoma (Blood Flukes)

Causative agents of schistosomosis or bilharziosis

■ Schistosomosis (bilharziosis) is one of the most frequent tropical diseases with about 200 million infected persons. The occurrence of schistosomosis depends on the presence of suitable intermediate hosts (freshwater snails). Human infections result from contact with standing or slow-moving bodies of water (freshwater) when *Schistosoma* cercariae penetrate the skin. *Schistosoma hematobium* causes urinary schistosomosis; *S. mansoni*, *S. japonicum*, *S. intercalatum*, and *S. mekongi* are the causative agents of intestinal schistosomosis and other forms of the disease. Diagnosis can be made by detection of either *Schistosoma* eggs in stool or urine or of specific antibodies in serum. ■



**Parasite species and occurrence.** Schistosomosis is also known as bilharziosis after the German physician Th. Bilharz, who discovered *Schistosoma hematobium* in human blood vessels in 1851. Schistosomosis occurs endemically in 74 tropical and subtropical countries of Africa, South America, and Asia (Fig. 10.**2**). The number of persons infected with schistosomes is estimated at 200 million (WHO, 2004).

The most important species pathogenic to humans are *Schistosoma hematobium* (Africa, the Near East, and questionable occurrence in India), *S. mansoni* (Africa, the Caribbean, the north-east of South America), and *S. japoni-*

**Distribution of Schistosomes**

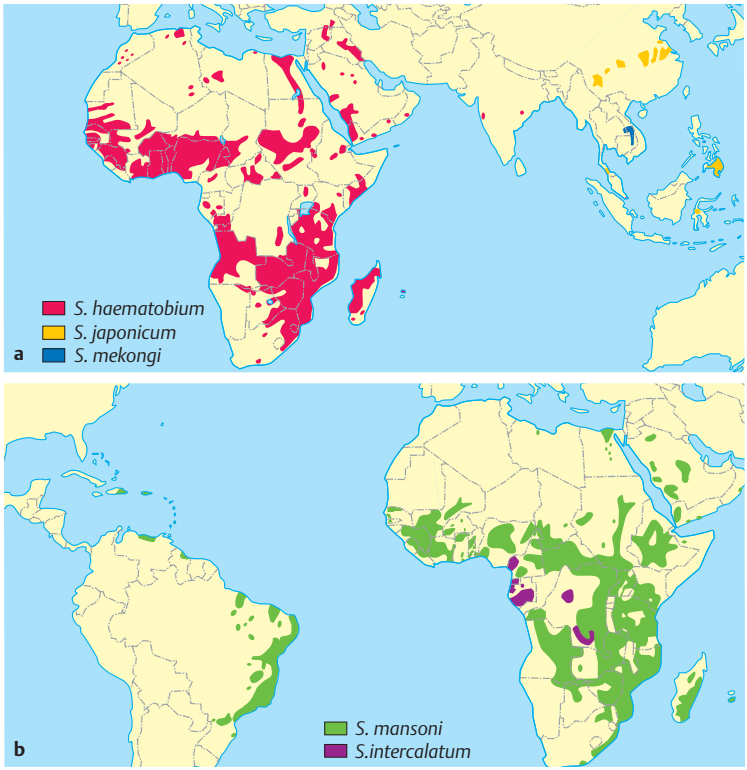


Fig. 10.**2** **a** *Schistosoma hematobium*, *S. japonicum*, and *S. mekongi*; **b** *S. mansoni* and *S. intercalatum* (according to *WHO Technical Report Series* No. 830. Geneva: World Health Organization; 1993).



*cum* (Southeast Asia and the western Pacific, especially China, Indonesia, the Philippines, but no longer in Japan). *S. intercalatum* occurs focally in central and western Africa, *S. mekongi* in Laos and Cambodia.

**Morphology and life cycle.** The various *Schistosoma* species can be differentiated morphologically (Table 10.**2**).

The relatively thick male forms a tegumental fold, the ventral groove (or canalis gynaecophorus) in which the threadlike female is enclosed. The male thus appears to be slit longitudinally (*schizein*: to split, *soma*: body) (Fig. 10.**3**).

Table 10.**2** Schistosoma Species that Commonly Infect Humans[1]

| ***Schistosoma* species and length (mm)** | **Main location of adult stages[2]** | **Eggs: characteristics, dimensions, and excretion (E)** | **I: Intermediate hosts (snails), R: Animal reservoir hosts[3]** |
|---|---|---|---|
| ***S. haematobium***<br>♂♂: 7–15<br>♀♀: 9–20 | Venous plexus in minor pelvis (draining urinary bladder, etc.) | Ovoid, with terminal spine,<br>83–187 × 60–70 µm<br>E: urine, rarely stool | I: *Bulinus* species<br>R: (Monkeys) |
| ***S. intercalatum***<br>♂♂: 11–14<br>♀♀: 13–24 | Mesenteric veins (draining colon) | Ovoid, with terminal spine,<br>140–240 × 50–85 µm<br>E: stool[3] | I: *Bulinus* species<br>R: (sheep, goats) |
| ***S. mansoni***<br>♂♂: 6–10<br>♀♀: 7–15 | Mesenteric veins (draining colon) | Ovoid, with lateral spine,<br>112–175 × 45–70 µm<br>E: stool | I: *Biomphalaria* species.<br>R: (monkeys, dog, rodents) |
| ***S. japonicum***<br>♂♂: 7–20<br>♀♀: 10–26 | Mesenteric veins (draining intestine) | Elliptical, lateral spine tiny or lacking<br>70–100 × 50–65 µm<br>E: stool | I: *Oncomelania* species.<br>R: Cattle, buffalo, pig, dog, rodents, etc. |
| ***S. mekongi***<br>♂♂: 10–18<br>♀♀ : 14–20 | Mesenteric veins (draining small intestine) | Elliptical, lateral spine tiny or lacking<br>50–65 × 30–55 µm<br>E: stool | I: *Neotricula* species.<br>R: dog |

[1] Location not strictly specific; adult stages also found in vessels of liver, lungs, and, less frequently, in other organs.
[2] In parentheses: of secondary or local significance only.
[3] Stainable with Ziehl-Neelsen stain, in contrast to *S. hematobium*.

***Schistosoma mansoni* Pair**


Fig. 10.**3** The threadlike female is enclosed in a groove in the body of the male.

The adult parasites live in the lumen of veins. Table 10.**2** summarizes data on various *Schistosoma* species. Fig. 10.**4** (p. 550) shows their life cycle.

Sexually mature *Schistosoma* females lay about 100–3500 eggs a day, depending on the species, each containing an immature miracidium (= ciliate larva), which matures in the host within six to 10 days and remains viable for about three weeks (Fig. 10.**4**).

At the site of their deposition, the eggs lie in chainlike rows within small veins. Some penetrate through the vascular wall and surrounding tissue to reach the lumen of the urinary bladder or intestine (regarding the eggs that remain in the body see section on pathogenesis). Enzymes produced by the miracidium and secreted through micropores in the eggshell and granuloma formation (see below) contribute to the penetration process. The eggs are shed by the definitive host in stool or urine within a few weeks post infection (p.i.) (see below). If the eggs are deposited into freshwater, the miracidia hatch from the eggshell and begin their search for a suitable intermediate host (Fig. 10.**4**).

Various genera and species of freshwater snails serve as intermediate hosts (Table 10.**2**) in which the invading miracidia reproduce asexually, producing mother and daughter sporocysts, and finally numerous cercariae, which begin to swarm into the water three to six weeks p.i. at the earliest. A characteristic feature of the approximately 340–520 µm long cercariae is their forked tail. The cercariae swim freely about or cling to the surface of the water. Upon contact with a human host, enzyme secretion and vigorous movements enable them to penetrate the skin within a few minutes, or less frequently the mucosa when ingested with drinking water. During the infection process, the cercaria loses its tail, sheds the surface glycocalyx, forms a new tegument, and transforms into the schistosomulum.

***Schistosoma mansoni:* Life Cycle**

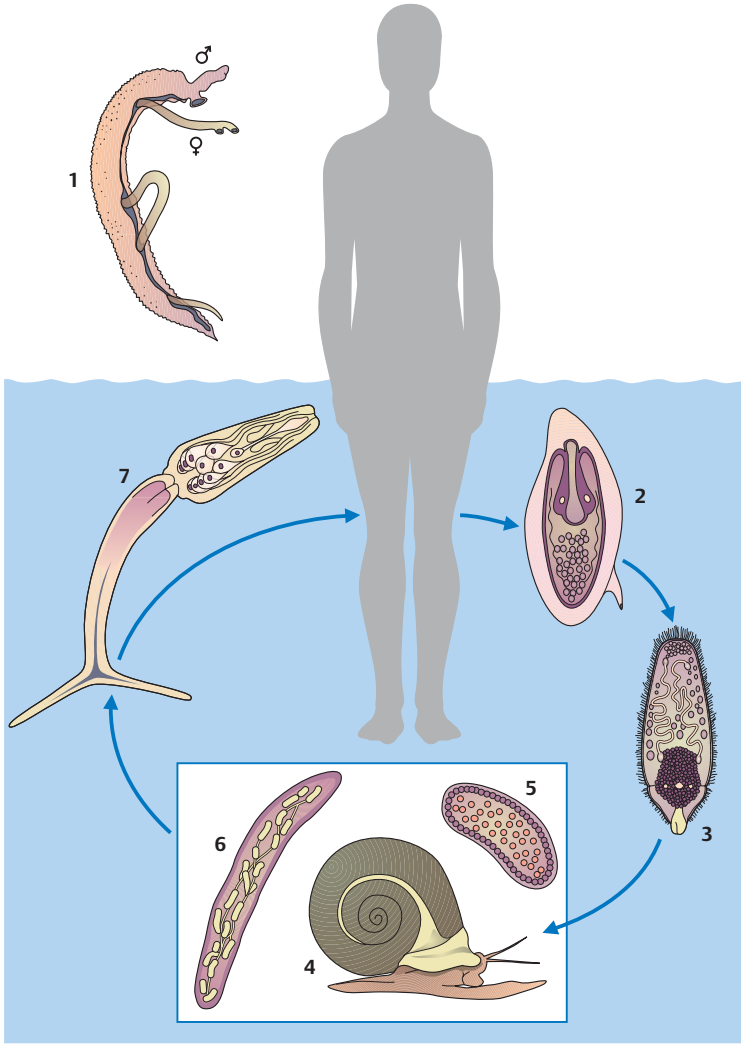


Fig. 10.4 **1** Male and female; **2** egg with miracidium; **3** miracidium; **4** intermediate host (*Biomphalaria glabrata*); **5** sporocyst; **6** daughter sporocyst with cercariae; **7** fork-tailed cercaria (modified after Piekarski G, *Medizinische Parasitologie in Tafeln*. 2nd printing. Berlin: Springer; 1973).

**Migration of Schistosomes in the Human Body**

Infection → schistosomula penetrate subcutaneous tissues → find venous capillaries or lymph vessels → migrate through the venous circulatory system into the right ventricle of the heart and the lungs → travel hematogenously into the intrahepatic portal vein branches where development into adult worms takes place as wells as male-female pairing just prior to sexual maturity → retrograde migration of pairs into mesenteric veins or to the vesical plexus (Table 10.**2**).

Depending on the *Schistosoma* species involved, the prepatent period lasts about four to 10 weeks. Schistosomes remain in the definitive host for an average of two to five years, but in some cases for as long as 20–40 years.

**Epidemiology.** Schistosomosis occurs as an autochthonous infection in tropical and subtropical regions. Aquatic freshwater snails that prefer standing or slow-moving bodies of water are the intermediate hosts for *S. hematobium*, *S. mansoni*, *S. intercalatum*, and *S. mekongi* (Table 10.**2**). The intermediate hosts of *S. japonicum* are amphibious snails also found on moist ground and plants, e.g., in rice paddies.

Although the cycles of all *Schistosoma* species can include animals as hosts, humans are the most important parasite reservoirs (Table 10.**2**). However, animals contribute significantly to the dissemination of the eggs of *S. japonicum* and *S. mekongi*. Travelers to endemic tropical areas can acquire the infection by a single instance of contact with water containing cercariae.

**Pathogenesis and clinical manifestations.** The infection can be divided into the following phases:

- **Penetration phase:** penetration of cercariae into the skin, either without reaction or—especially in cases of repeated exposure—with itching and skin lesions (erythema, papules), which disappear within a few days.

- In the **acute phase**, about two to 10 weeks after a severe initial infection, the symptoms may include fever, headache, limb pains, urticaria, bronchitis, upper abdominal pain, swelling of the liver, spleen and lymph nodes, intestinal disturbances, and eosinophilia (= Katayama syndrome). Due to release of *Schistosoma* antigens, the serum antibody levels (IgM, IgG, IgA) rise rapidly and immune complexes are formed that can cause renal glomerulopathies. These symptoms persist for several days to several weeks. Normally, *Schistosoma* eggs are not yet excreted at the beginning of this phase (see prepatent periods). In low-level infections this phase is usually inapparent or subclinical.

- **Chronic phase:** the most significant phase in pathogenic terms begins after an incubation period of about two months with oviposition by the *Schis-*

***Schistosoma granuloma* in the Liver**

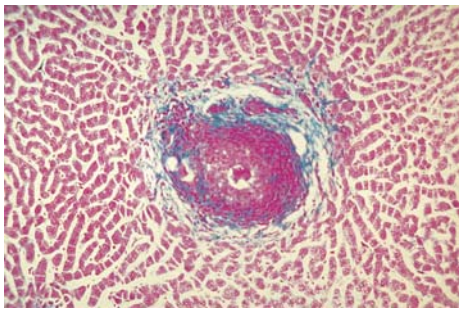

Fig. 10.**5** A section of an egg is visible in the center of the granuloma.

*tosoma* females. A large proportion (up to 50%) of the eggs laid remain in human body tissues, not only near the worms (urinary bladder, intestine), but also in more distant localizations due to hematogenous spreading (mainly to the liver and lungs, more rarely to the CNS, the skin, and other organs), where they lodge in small vessels.

The miracidia, which remain viable for about three weeks, produce antigens (proteins, glycoproteins), which are secreted through the eggshell into the tissue and are still present in the egg after the ciliated larva has died off. After antigenic stimulation of T lymphocytes secreted cytokines contribute to produce granulomatous reaction foci (so-called "pseudotubercles"): above all macrophages, neutrophilic and eosinophilic granulocytes, as well as fibroblasts, aggregate around single eggs or a number of centrally located eggs (Fig. 10.**5**). These foci may merge and form a starting point for larger, granulomatous proliferations that protrude into the lumen of the urinary bladder or intestine. The eggs in the tissues die off within about three weeks and are either broken down or they calcify. The granulomas are replaced by connective tissue, producing more and more fibrous changes and scarring.



The **main forms of schistosomosis** are differentiated according to the localization of the lesions:

- **Urinary schistosomosis (urinary bilharziosis).** Causative agent: *S. hematobium*. Incubation 10–12 weeks or longer, morbidity rate as high as 50–70%. Hematuria (mainly in the final portion of urine), micturition discomfort, hyperemia, increasing fibrosis, 1–2 mm nodules, necroses, ulcers and calcification of the bladder wall, pyelonephrosis and hydronephrosis, urethral strictures, lesions in the sexual organs. In some endemic areas, an increased incidence of urinary bladder cancer has been associated with the *S. hematobium* infection.

**Intestinal schistosomosis (intestinal bilharziosis).** Causative agents: mainly *S. mansoni* and *S. japonicum*, also *S. mekongi* (rare: rectal lesions caused by *S. hematobium*). Incubation four to 13 weeks (acute phase), months to years (chronic phase). The course of an initial infection is only rarely symptomatic (see above: Katayama syndrome), inapparent and subclinical courses being the rule. Manifestations in the chronic phase are restricted almost entirely to large intestine with hyperemia, granulomatous nodules, papillomas ("bilharziomas"), ulcerations, hemorrhages, and increasing fibrosis, abdominal pain and bloody diarrhea.

**Other forms:** the causative agents of the **hepatosplenic form** are mainly *S. japonicum*, less frequently *S. mansoni*. This fibrotic form is caused by eggs deposited around the branches of the portal vein in the liver ("pipestem" fibrosis according to Symmers) and results in circulatory anomalies, portal hypertension, splenomegaly, ascites, hemorrhages in the digestive tract, and other symptoms. **Pulmonary schistosomosis** is observed mainly in severe *S. mansoni* infections, more rarely in infections with other species (including *S. hematobium*). **Cerebral schistosomosis** is relatively frequent in *S. japonicum* infections (2–4%).

**Cercarial dermatitis.** Cutaneous lesions (itching, erythema, urticaria, papules) in humans, caused by (repeated) skin penetration of schistosomatid cercariae parasitizing birds (e.g., *Bilharziella*, *Trichobilharzia*) or mammals (e.g., *Schistosoma spindale*). The infection occurs worldwide in freshwater or brackish water and is known as "swimmer's itch." The symptoms generally abate after a few days. The cercariae of schistosomes from humans can cause similar, although usually milder, symptoms.

**Immunity.** The prevalence and intensity of *Schistosoma* infections rise in endemic regions in children until the age of about 14, followed by a decline usually also accompanied by reduced egg excretion. This acquired immune status, known as "concomitant immunity," is characterized by total or partial protection against cercarial infection. However, the schistosomes already established in the body are not eliminated and may persist for years or even decades.

The immune defense is directed against schistosomula that have penetrated the skin, are a few hours old, and present their own antigens on their surface. Young schistosomula can be killed mainly by eosinophils and macrophages assisted by specific antibodies to these antigens and/or by complement. By the time the schistosomula reach the lungs they are resistant to such cytotoxic attacks. The explanation for this phenomenon is that the older schistosomula are able to acquire host antigens (e.g., blood group or histocompatibility antigens) and to synthesize hostlike macromolecules, thus "masking" their surfaces (= molecular mimicry) to circumvent the immune

response (= immunoevasion). Additional immunoevasive mechanisms have also been described, e.g., shedding part of the tegument and secretion of immunosuppressive substances.

The current immune status of persons infected with *Schistosoma* is apparently also determined by the balance of those antibodies which enhance the above-mentioned immune response (IgE and perhaps IgA) and others that inhibit it (IgM, $IgG_2$, or $IgG_4$).

**Diagnosis.** Following the prepatent period, i.e., four to 10 weeks p.i. at the earliest, the eggs can be detected in stool specimens or in urine sediment (Fig. 10.**1**, p. 545, Table 10.**2**, p. 547). The eggs can also be found in intestinal or urinary bladder wall biopsies. Immunodiagnostic methods (Table 11.**5**, p. 625) are particularly useful for detecting infections before egg excretion begins (important for travelers returning from tropical regions!). Detection of microhematuria with test strips is an important diagnostic tool in bladder schistosomosis. Clinical examination with portable ultrasonic imaging equipment has proved to be a highly sensitive method of detecting lesions in the liver and urogenital tract in epidemiological studies.

**Therapy.** The drug of choice for treatment of schistosomosis is praziquantel, which is highly effective against all *Schistosoma* species and is well tolerated. Oxamniquine is effective against *S. mansoni*.

**Control and prevention.** Current schistosomosis control strategies are based mainly on regular drug therapy of specific population groups. Morbidity, mortality, and egg excretion rates are clearly reduced by such programs. Hygienic and organizational measures (construction of latrines, improvement of water supply quality, etc.) aim to reduce *Schistosoma* egg dissemination and contact with contaminated bodies of water. Individual preventive measures in *Schistosoma*-contaminated areas include avoidance of skin contact with natural or artificial bodies of water (freshwater). Drinking water that could be contaminated with cercariae must be decontaminated before use by boiling, chlorination, or filtration.

## Fasciola species

### Fasciola hepatica (Common Liver Fluke) and F. gigantica (Large or Giant Liver Fluke)

Causative agents of fasciolosis

■ *Fasciola hepatica* and *F. gigantica* are frequent bile duct parasites of domestic ruminants. In their life cycle freshwater snails act as intermediate hosts. Humans become accidentally infected when they eat plants (e.g., watercress) to which infectious parasite stages (metacercariae) adhere. ■

**Occurrence.** *Fasciola hepatica* occurs worldwide as an important parasite in domestic ruminants that can also infect other animal species. Sporadic or endemic *F. hepatica* infections in humans have been reported from about 50 countries or regions on all continents (WHO, 1999). In Asia and Africa, human infections with the 7.5 cm long giant liver fluke (*F. gigantica*) are also reported. The number of persons infected with either *F. hepatica* or *F. gigantica* is estimated at 2.4 million (WHO, 1995).

**Parasites, life cycle, and epidemiology.** *F. hepatica* is a flattened, leaf-shaped parasite about 2–5 cm long and at most 1 cm wide. The cephalic cone with the oral sucker is somewhat demarcated from the rest of the body. A further characteristic feature is the pronounced branching of various inner organs (Fig. 10.**6a**).

Adult liver flukes parasitize in the bile ducts. They produce large (approx. 130 × 85 µm), golden-brown, operculated eggs (Fig. 10.**1**, p. 543) that are shed by the bile duct-intestinal tract route. Under favorable conditions, a ciliate larva, the miracidium, develops in the egg within a few weeks. The miracidia then hatch and penetrate into freshwater snails (*Lymnaea truncatula* in Central Europe), where they transform into sporocysts. After formation of further asexual reproductive stages (rediae), tailed cercariae develop and swarm out of the snails into the open water. They soon attach to plants and encyst, i.e., transform into infective metacercariae, which are then ingested with vegetable food of their definitive hosts. Eating watercress contaminated with metacercariae is one of the sources of infection for humans.

The juvenile liver flukes hatch from the cyst in the small intestine, penetrate the intestinal wall, and migrate through the peritoneal cavity to the liver. After migrating through the hepatic parenchyma for about six to seven weeks, the parasites finally reach the bile ducts, in which they develop to sexual maturity. Egg excretion begins two to three months p.i. at the earliest.

**Liver Flukes**

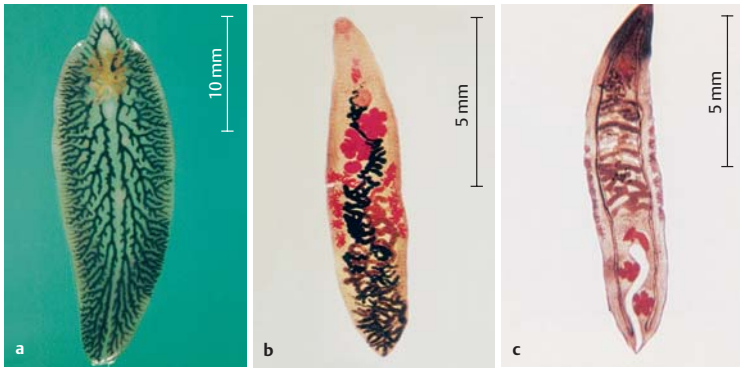


Fig. 10.**6** **a** *Fasciola hepatica,* adult stage with blood-filled intestinal branches; **b** *Dicrocoelium dendriticum*, adult stage; **c** *Opisthorchis felineus*, adult stage (Fig. a: K. Wolff, Zurich; c: V. Kumar, Antwerp).

**Clinical manifestations.** The infection may run an inapparent course or, after an incubation period of four to six weeks, become symptomatic with abdominal pain, hepatomegaly, fever, leukocytosis and eosinophilia (acute phase), or hepatocholangitic symptoms (chronic phase) and anemia. Occasionally, the parasites also migrate into other organs than the liver.

**Diagnosis.** The manifestations to be expected during the migration phase of the liver fluke include mainly leukocytosis, eosinophilia, and a rise in liver-specific serum enzymes. Detection of eggs (Fig. 10.**1**, p. 543) in stool or duodenal fluid is not possible until at least two to three months p.i. In patients from Asia, differential diagnosis of the eggs of the small intestinal parasites *Echinostoma* and *Fasciolopsis* (Fig. 10.**1**), which are very similar to those of *Fasciola*, must be kept in mind. Other diagnostic tools include detection of serum antibodies (Table 11.**5**, p. 625) and of coproantigen in stool.

**Therapy and prevention.** The drug of choice is triclabendazole, originally developed as a veterinary drug, is now registered ad usum humanum in several countries and is recommended by the WHO. The infection can be avoided by not eating raw watercress and other plants that may be contaminated with metacercariae.

## Dicrocoelium

**Dicrocoelium dendriticum (Lancet Liver Fluke)**
Causative agent of dicrocoeliosis

The lancet liver fluke (0.5–1.0 × 0.2 cm) (Fig. 10.**6b**), a bile duct parasite in sheep, cattle, and other herbivores, occurs frequently in regional foci in the northern hemisphere (for instance southern Germany, Austria, Switzerland, North America). Its life cycle includes two intermediate hosts (terrestrial snails and ants). Humans become infected accidentally when they ingest ants containing infective metacercariae of the lancet liver fluke. Such infections are rare and either run an asymptomatic course or manifest in mild abdominal and hepatic symptoms. Diagnosis is based on detection of eggs in stool (about 40 × 25 µm, oval, dark brown, containing a miracidium with two rounded germinal cells) (Fig. 10.**1**. p. 543). Ingestion of contaminated beef or mutton liver can result in egg excretion in stool without infection (intestinal passage). The eggs of *Opisthorchis* and *Clonorchis* must be taken into consideration for a differential diagnosis (Fig. 10.**1**). Praziquantel has been shown to be effective against *Dicrocoelium* in animals (see also opisthorchiosis).

## Opisthorchis and Clonorchis (Cat Liver Fluke and Chinese Liver Fluke)

Causative agents of opisthorchiosis and clonorchiosis

■ Liver flukes of the genera *Opisthorchis* and *Clonorchis* occur mainly in river and lake regions of Asia and Eastern Europe; *Opisthorchis* is also found further westward as far as northern Germany. The life cycle of these organisms includes two intermediate hosts (aquatic snail, fish). Infections are contracted via raw fish containing infective stages (metacercariae). Diagnosis is based mainly on detection of eggs in stool or duodenal aspirate. ■



**Parasites and occurrence.** The members of these genera resemble the lancet liver fluke (*Dicrocoelium dendriticum*) in size (length 1–2 cm) and form. The position and structure of the testicles (*ophisten*: posterior; *orchis*: testicle; *clon*: branch) allow the discrimination of genera (Fig. 10.**6c**).

*Opisthorchis* and *Clonorchis* occur endemically in river and lake regions: *Opisthorchis felineus* in Eurasia (Russia, Kazakhstan, Ukraine; other endemic foci in the Baltic countries, northern Poland, and northern Germany), *Opisthorchis viverrini* in Thailand and Laos, *Clonorchis sinensis* in far-eastern Russia and other Asian areas (including China, Taiwan, Vietnam and Korea).

The number of persons infected with *Opisthorchis* and *Clonorchis* is estimated at 17 million, with about 350 million persons at risk for infection (WHO, 1995).

**Life cycle and epidemiology.** The definitive hosts of *Opisthorchis* and *Clonorchis* species are fish-eating mammals (cats, dogs, pigs, etc.) and humans, in which these trematodes colonize the bile ducts. The life cycle of these organisms involves various species of aquatic snails (*Bithynia*, etc.) as the first intermediate hosts and freshwater fish species as the second intermediate hosts. The infective metacercariae are localized in the musculature of the fish and, when raw fish is ingested, enter the intestinal tract of the definitive host, from where they migrate through the common bile duct (ductus choledochus) into the intrahepatic bile ducts. The prepatent period is four weeks.

**Pathogenesis and clinical manifestations.** *Opisthorchis* and *Clonorchis* infections cause proliferations of the bile duct epithelium, cystlike dilatation, inflammation, and fibrosis of the bile duct walls as well as connective tissue proliferation in the hepatic parenchyma. A high incidence of bile duct carcinomas has been reported from areas in which *C. sinensis and O. viverrini* are endemic. Clinical symptoms of more severe infections include variable fever, hepatocholangitic symptoms with hepatomegaly, leukocytosis, upper abdominal pains, and diarrhea.

**Diagnosis, therapy, and prevention.** Diagnosis is made by detection of eggs (26–32 µm long) in stool or duodenal fluid (Fig. 10.**1**, p. 543). Differential diagnosis must also consider the eggs of *Heterophyes heterophyes*, *Metagonimus yokogawai*, and other trematode species. Serum antibodies are found in some infected persons. The drug of choice is praziquantel; albendazole can also be used. Reliable preventive measures include boiling or frying fish to kill the metacercariae, which die at temperatures as low as 70 °C, and freezing to – 10 °C for five days (WHO, 1995).



## Paragonimus (Lung Flukes)

Causative agents of paragonimosis

■ Lung flukes of the genus *Paragonimus*, endemic in parts of Asia, Africa, and America, parasitize in pulmonary cysts and cause a tuberculosis-like clinical picture. Following development in two intermediate hosts (freshwater snails and crabs or crayfish), infective stages (metacercariae) can be transmitted to humans by eating the crabs or crayfish uncooked. Parasite eggs are detectable in sputum or stool. ■

**Occurrence.** At least nine *Paragonimus* species are known to be parasites of humans. They are found in East and Southeast Asia (*Paragonimus westermani*, *Paragonimus heterotremus*, and *Paragonimus uterobilateralis*), in North America (*Paragonimus kellicotti*), and in Central and South America (*Paragonimus mexicanus*, etc.). The number of infected persons is estimated at about 21 million (WHO, 1995).

**Parasites, life cycle, and epidemiology.** The plump, approx. 7–15 mm long, coffee bean-like *Paragonimus* species differ in appearance from other trematodes. The sexually mature parasites live in cystlike dilatations in the lungs, usually in connection with the bronchial tree. The yellow-brown, operculated eggs (about 80 × 50 µm) laid by the adult worms are shed either in sputum or stool (Fig. 10.**1**, p. 544). The life cycle then continues in water, where a miracidium develops in each egg, hatches and invades an intermediate host. Egg-shaped cercariae with short tails develop in the first intermediate host, a freshwater snail (*Semisulcospira* and numerous other genera). The cercariae encyst in the second intermediate host (*Crustaceae*: crayfish or crabs) to form the infective metacercariae. When a suitable definitive host ingests the crustaceans uncooked, the young trematodes hatch in the small intestine, migrate through the peritoneal cavity to the diaphragm and finally into the lungs. The prepatent period is two to three months. Parasites that deviate from the normal migration route may enter other organs (e.g., the brain or the skin). Eggs distributed in the blood stream induce inflammatory granulomas in various organs.

Besides humans, crustacean eating mammals (Felidae, Canidae, pigs, etc.) play a significant epidemiological role as reservoir hosts.

Young lung flukes can be localized in the musculature of pigs and other "transport hosts" and be transmitted to humans who ingest the raw meat of these animals.

**Clinical manifestations.** Typical cases are clinically characterized by pulmonary symptoms (chronic cough, bloody expectoration, thoracic pain). Parasites following the normal or deviant migration routes can also cause abdominal, hepatic, pancreatic or CNS symptoms, or skin lesions (swelling, nodules).

**Diagnosis, therapy, and prevention.** An etiological diagnosis is based on detection of eggs in sputum or stool (Fig. 10.**1**, p. 544) and of serum antibodies (Table 11.**5**, p. 625). Regarding the differential diagnosis especially tuberculosis must be kept in mind. The drug of choice is praziquantel, but triclabendazole can also be used (see *Fasciola*, p. 556). Cooking crustaceans before eating them is a reliable preventive measure.

## Cestoda (Tapeworms)

**General.** Various tapeworm species can parasitize in the small intestine of humans, including species from the "lower" (Pseudophyllida) and "higher" (Cyclophyllida) cestodes (from *kestos* = ribbon). These cestode species are hermaphrodites and consist of the head (scolex or "holdfast"), followed by an unsegmented germinative section (neck) and a posterior chain of segments (proglottids). There are no digestive organs, so nutrients are taken up through the absorptive integument. The life cycle of cestodes include one or two intermediate hosts.

Humans can also be infected by larval stages of various tapeworm species (cysticerci, metacestodes). These stages develop in body tissues and generally cause considerably greater pathological damage than the intestinal cestode stages.

### Taenia species

Causative agents of taeniosis and cysticercosis

■ Taeniosis is a small intestine infection of humans caused by *Taenia* species. In the case of *T. saginata*, the intermediate hosts are cattle, in the musculature of which metacestodes (cysticerci) develop and can be ingested by humans who eat raw beef. The infection runs an inapparent course or is associated with mild intestinal symptoms. The metacestodes of *T. solium* develop in the musculature of pigs, or through accidental infection in humans as well (CNS, eyes, musculature, skin), causing cysticercosis. *T. saginata asiatica* is closely related to *T. saginata*, but its metacestodes parasitize mainly in the livers of pigs and ruminants. ■

#### Taenia saginata (Beef Tapeworm)

Causative agent of *T. saginata* taeniosis



**Occurrence.** This species occurs worldwide; the number of infected humans is estimated to be between 40 and 60 million. One indicator of infection frequency is the prevalence of *T. saginata*-cysticercosis in cattle (average prevalence in Europe approx. 0.3–6%, in some non-European regions more than 50%).

**Parasites, life cycle, and epidemiology** (see Fig. 10.**8**, p. 563). *T. saginata* (*taenia*: ribbon; *saginatus*: fattened) grows as long as 10 m and has a scolex with four suckers but a rostellum and hooks are lacking (see *T. solium*). The

proglottids at the posterior end of the chain are longer than wide and each contains a treelike branched uterus containing 80 000–100 000 eggs (= gravid segments) (Fig. 10.**7c, d**). The eggs are released when a proglottid detaches from the tapeworm in the intestinal lumen or when a segment disintegrates outside the host. The eggs are small (diameter approx. 30–40 µm) and round (Fig. 10.**1**, p. 544). The outer shell forms a thick, brownish, radially striped embryophore enclosing an oncosphere with three pairs of hooks. The eggs are highly resistant and can remain infective in a moist environment for weeks or months (however, susceptible to desiccation!). Carried by feces of humans infected with *Taenia*, they contaminate pastures or feed either directly or via sewage. When cattle (or buffalo) ingest the eggs, the oncospheres hatch in the small intestine, migrate into the intestinal wall, and are transported with the bloodstream into the striated musculature, in which they develop into the infective metacestodes or cysticerci (= Cysticercus bovis) within three to four months. Each cysticercus is a pea-sized, fluid-filled cyst containing a single invaginated scolex (Fig. 10.**7e**).

Humans are infected by ingesting raw or undercooked beef containing cysticerci. In the small intestine, the cysticercus evaginates the scolex, at-

**Cestodes**

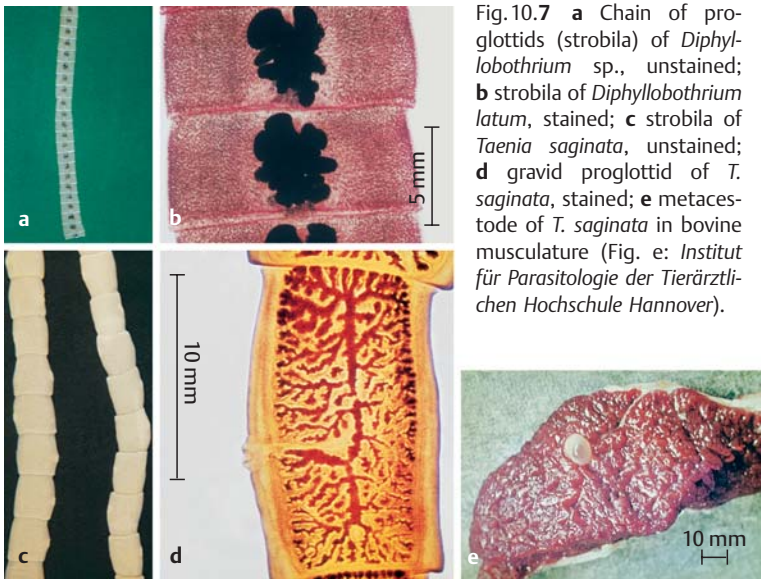


Fig. 10.**7** **a** Chain of proglottids (strobila) of *Diphyllobothrium* sp., unstained; **b** strobila of *Diphyllobothrium latum*, stained; **c** strobila of *Taenia saginata*, unstained; **d** gravid proglottid of *T. saginata*, stained; **e** metacestode of *T. saginata* in bovine musculature (Fig. e: *Institut für Parasitologie der Tierärztlichen Hochschule Hannover*).

taches to the mucosa of the upper small intestine, and develops into an adult tapeworm, which can live for years or even decades. About two to three months after the infection, the first gravid segments detach from the strobila and then appear in feces or they can migrate out of the intestine without defecation. The segments remain motile for some time and frequently leave the stools.

**Pathogenesis and clinical manifestations.** In some infected persons, *T. saginata* causes morphological changes (villus deformation, enterocyte proliferation, cellular mucosal infiltration, etc.) and functional disturbances. Blood eosinophilia may occur sometimes. The infection takes an asymptomatic course in about 25 % of cases. Symptoms of infection include nausea, vomiting, upper abdominal pains, diarrhea or constipation and increased or decreased appetite. Infection does not confer levels of immunity sufficient to prevent reinfection.

**Diagnosis.** A *Taenia* infection is easy to diagnose if the 1.5–2 cm long and 0.7 cm wide segments are eliminated in stool (Fig. 10.**7c, d**). Morphological species differentiation (*T.saginata* vs. *T. solium*) is often not possible based on the gravid proglottids, but can be done by DNA-analysis (PCR). *T. saginata* eggs are shed irregularly in stool and cannot be differentiated morphologically from *T. solium* eggs (Fig. 10.**1**, p. 544). Using an ELISA, coproantigens are detectable in stool fluid even when neither proglottids nor eggs are being excreted.

**Therapy and prevention.** The drug of choice is the highly effective praziquantel. Albendazole, mebendazole, and paromomycin are less reliable. The main prophylactic measures are sewage treatment and the detection of cysticercus carriers at inspection of slaughter animals. Meat containing numerous cysticerci ("measly meat") has to be confiscated, but meat with small numbers of cysticerci can be used for human consumption after deep-freezing that is lethal to the parasites. Individual prophylaxis consists of not eating beef that is raw or has not been deep-frozen.



***Taenia saginata asiatica***

Causative agent of Asian taeniosis

This form of *Taenia* occurs in the small intestine of humans in East and Southeast Asia (Korea, Taiwan, the Philippines, Thailand, Indonesia, Malaysia). Genetic analysis has revealed a close subspecies-relation to *T. saginata* (= *T. saginata asiatica*). The two forms differ in a number of morphological features; in addition, the cysticerci of *T. saginata asiatica* develop mainly in the livers of pigs, but also infect cattle, goats, and monkey species.

***Taenia saginata* and *T. solium*: Life Cycles**

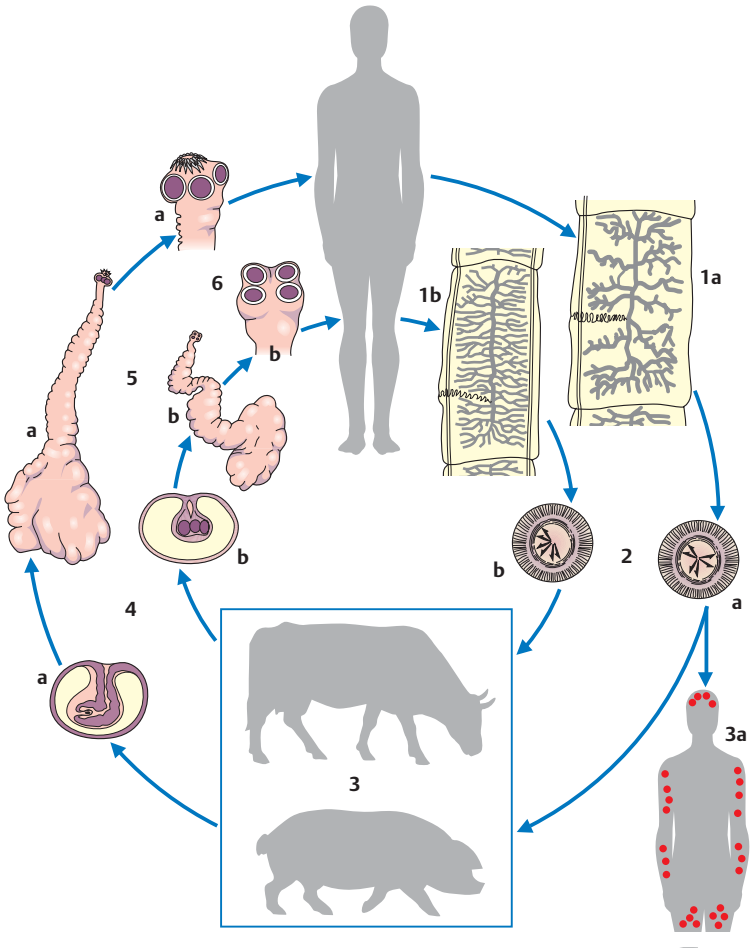


Fig. 10.8 **1a, b** Gravid segment containing eggs of *T. solium* (**a**) and of *T. saginata* (**b**); **2** free *Taenia* eggs; **3** natural intermediate hosts of *T. saginata* (cattle) and *T. solium* (pigs); **3a** human as accidental host of *T. solium*; **4a, b** infective metacestodes of *T. solium* (**a**) and of *T. saginata* (**b**); **5a, b** the same metacestodes with protoscoleces evaginated; **6a, b** "armed" head of *T. solium* (**a**) and "unarmed" head of *T. saginata* (**b**) from human small intestine (modified after Piekarski, G., *Medizinische Parasitologie in Tafeln*. 2nd ed., Berlin: Springer; 1973).
Red dots in human host: possible location of *T. solium* metacestodes.

### Taenia solium (Pork Tapeworm)

Causative agent of *T. solium* taeniosis and cysticercosis

**Occurrence.** *T. solium* is mainly endemic in poorly developed regions of Central and South America, Africa, and Asia, with sporadic occurrence in the USA as well as western, eastern, and southern Europe. In Mexico, 0.1–7% of the rural population are carriers of the adult tapeworm and up to 25% of the pigs carry the cysticerci of *T. solium*. Imported human cases of cysticercosis are being diagnosed in increasing numbers in nonendemic regions (e.g., central Europe, USA).

**Parasite and life cycle.** *T. solium* (*solium*: from the Arabic word *sosl*: chain) is 3–4 m long and is thus smaller than *T. saginata*. The scolex of *T. solium* has a rostellum armed with two rows of hooks in addition to the four suckers (Fig. 10.**8**). Inside the gravid segments, the number of lateral uterus branches is usually 7–13, i.e., less than in *T. saginata* (usually >15).

The life cycle is similar to that of *T. saginata*, except that *T. solium* uses the pig as intermediate host, in which the metacestode (Cysticercus cellulosae) develops to infectivity within two to three months.

**Pathogenesis and clinical manifestations.** *T. solium* in the intestine causes no or only mild symptoms, similar to infections with *T. saginata*.

**Diagnosis, therapy, prevention, and control.** The recommendations made for diagnosis and therapy of *T. saginata* apply here as well. Infections with *T. solium* can be prevented by cooking or deep-freezing the pork (–20 °C for at least 24 hours). Control measures in endemic areas include mass treatment of the population with praziquantel, improvement of hygiene and slaughter animal inspection.

### Cysticercosis

**Causative agent and epidemiology.** The metacestodes of *T. solium*, known as Cysticercus cellulosae, can colonize various human organs (Fig. 10.**8**) and cause the clinical picture of cysticercosis. Infections occur under unhygienic conditions due to peroral ingestion of eggs stemming from the feces of tapeworm carriers (exogenous autoinfection or alloinfection). It is assumed that oncospheres hatching from eggs released from gravid proglottids in the human digestive tract may also cause an infection (endogenous autoinfection). In some countries of Latin America, Asia, and Africa, human cysticercosis is a public health problem. In Latin American countries, seroprevalences up to 10% and above have been found, and cysticerci were detected in 0.1–6% of the autopsy cases.

**Clinical manifestations.** Cysticercosis of the central nervous system (neurocysticercosis) or of the eye (ocular cysticercosis) is among the more severe

forms of the infection. In the CNS, the metacestodes are usually localized in the cerebrum (ventricle, subarachnoidal space), more rarely in the spinal cord; they can cause epileptiform convulsions, raised intracranial pressure, and other neurological symptoms. The cysticerci can also develop in subcutaneous tissues, in the heart, and in the skeletal musculature.

**Diagnosis.** If metacestodes are localized in the subcutis, palpation of subdermal nodules may supply initial evidence of cysticercosis. Tools useful in diagnosing internal organ infections include imaging procedures and immunodiagnostic methods (Table 11.**5**, p. 625). In over 90% of cases of cerebral cysticercosis, the use of purified glycoprotein antigens from *T. solium* metacestodes in a Western blot assay reveals serum antibodies.

**Therapy.** Praziquantel in combination with corticosteroids has proved effective in a large percentage of cases treated (including neurocysticercosis) in which the metacestodes were not yet calcified. Close patient monitoring is required for this therapy. Albendazole is also used in treatment of human cysticercosis.

## Echinococcus

Causative agent of echinococcosis

■ The most important species of the genus *Echinococcus* are *Echinococcus granulosus* (intestinal parasite of Canidae) and *E. multilocularis* (intestinal parasite of fox species, dogs, cats, and other carnivores). Both species occur in Europe. Their metacestodes can cause cystic echinococcosis (CE, hydatid disease) or alveolar echinococcosis (AE) in humans. Humans are infected by peroral ingestion of *Echinococcus* eggs, from which in CE, liquid-filled cystic metacestodes (the hydatids) develop, particularly in the liver and lungs. In AE the metacestodes primarily parasitize the liver, where the metacestodes proliferate like a tumor and form conglomerates of small cysts; secondary metastatic spread to other organs is possible. Clinical imaging and immunodiagnostic methods are used for diagnosis. Treatment involves surgery and/or chemotherapy. ■



**Parasite species.** *Echinococcus* species are small tapeworms that parasitize the small intestine of carnivores and produce eggs that are shed to the environment by the host. Pathogenic larval stages (metacestodes) develop following peroral ingestion of such eggs by the natural intermediate hosts (various mammalian species), as well as in humans and other accidental hosts (which do not play a role in the life cycle). Four *Echinococcus* species are currently known, all of them pathogenic for humans (*Echinococcus granulosus*, *E. multilocularis*, *E. vogeli*, and *E. oligarthrus*).

### Echinococcus granulosus (Dwarf Dog Tapeworm)

Causative agent of cystic echinococcosis (CE)

**Occurrence.** *E. granulosus* occurs worldwide, with relative high prevalences in eastern and southeastern Europe, the Mediterranean countries, the Near East, northern and eastern Africa, South America, and various parts of Asia and Australia. The parasite has become rare in northern and central Europe; most of the human cases of CE diagnosed in these areas are imported, in particular from Mediterranean countries. *E. granulosus* and *E. multilocularis* occur together in some areas.

#### Morphology and development

**Adult stage.** *E. granulosus* is a 4–7 mm long tapeworm with a scolex (bearing rostellar hooks) and normally three (two to six) proglottids. A notable characteristic is the uterus with its lateral sacculations, containing up to 1500 eggs (Fig. 10.**10a** p. 569).

**Definitive (final) and intermediate hosts.** The most important definitive host for *E. granulosus* is the dog, whereby other Canidae (jackal, dingo, and other wild canids) are involved in certain regions. Herbivorous and omnivorous vertebrates function as intermediate hosts, in particular domestic animals (ruminants, pigs, horses, camels) and in some areas wild animals as well.

**Life cycle** (Fig. 10.**9**). The adult tapeworms live in the small intestine of the definitive host for about six months, a few for up to two years (Fig. 10.**10c**). Eggs are either released from gravid proglottids in the intestine and shed with feces or pass out of the host still enclosed in the tapeworm segments. The eggs (diameter approx. 30–40 µm) are nearly spherical, contain an oncosphere and feature a radially striped shell. They cannot be morphologically differentiated from the eggs of other *Echinococcus* or *Taenia* species (see Fig. 10.**1**, p. 544). Infection of the intermediate hosts, humans, and other accidental hosts is by peroral ingestion of eggs, from which the oncospheres are released in the small intestine, penetrate into its wall and migrate hematogenously into the liver, as well as sometimes into the lungs and other organs. At first, the oncospheres develop into little vesicles, then gradually into metacestodes.



The metacestode of *E. granulosus* (also known as hydatid cysts, from *hydatis* = water bladder) is normally a fluid-filled cyst with one or multiple chambers, the wall of which is made up of an inner, cellular, germinative layer and an outer, acellular, laminated layer (cuticular layer), enclosed by a layer of host connective tissue (Fig. 10.**10d, f**). Brood capsules develop five to six months or later p.i. on the germinative layer, each containing up to 20 or

***Echinococcus granulosus* and *E. multilocularis*: Life Cycles**

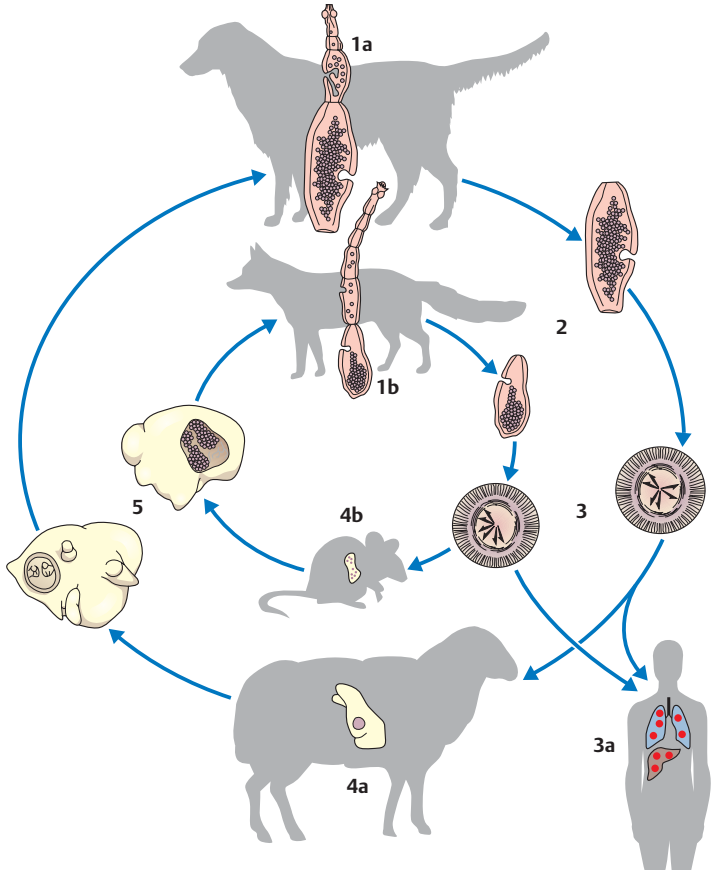


Fig. 10.9 **1a, b** Adult parasites in final hosts: *E. granulosus* in dogs, *E. multilocularis* in red foxes (also: dogs, cats, and other carnivores); **2** gravid proglottids containing eggs; **3** *Echinococcus* eggs, infection of natural intermediate host or humans (accidental host) (**3a**); **4** natural intermediate hosts: of *E. granulosus*: sheep, cattle, horses, and other ungulates (**4a**); of *E. multilocularis*: rodents (**4b**); **5** metacestodes in the livers of intermediate hosts.
Red dots in human host: most frequent location of metacestodes (see text).

more protoscoleces with four suckers and tow rows of rostellar hooks (Fig. 10.**10h**). The thin brood capsules burst to release free protoscoleces into the hydatid fluid, which form, together with the brood capsules, their remains and calcareous corpuscles the so-called "hydatid sand." The size of the cysts depends on their age and other factors. The average cyst diameter in humans is 1–15 cm, although it can vary between a few mm and 20 cm. Cysts in humans often contain smaller daughter cysts.

The life cycle is completed when carnivores ingest *E. granulosus* cysts containing mature protoscoleces with slaughter offal (viscera) or prey. Sexually mature stages then develop in the small intestine of the definitive hosts within five to eight weeks.

**Epidemiology.** There are a number of strains of *E. granulosus* that differ in morphological, biological, and genetic features and partially also in their infectivity to humans. Worldwide, for most of the human cases the sheep strain is responsible which develops in a cycle involving dogs and sheep (and other, less important, intermediate hosts).

Humans are infected by peroral ingestion of *Echinococcus* eggs, either during direct contact with tapeworm carriers or indirectly by uptake of contaminated food or drinking water. *Echinococcus* eggs remain viable for months in a moist environment and can also survive the winter. They are killed rapidly by desiccation. They can also be killed by heat (75–100 °C) within a few minutes and by deep-freezing at –70 or –80 °C for four or two days, respectively. Standard chemical disinfectants have no effect.

The mean annual incidence of CE varies in the countries and areas of the Mediterranean region between about one to 10 new clinical cases per 100 000 inhabitants, although higher incidences (>40 cases/100 000 inhabitants) have been observed in other endemic areas (e.g., South America and China).

**Pathogenesis and clinical manifestations.** Several clinical parameters of human CE and AE are presented and compared in Table 10.**3**.

The CE is always asymptomatic initially and it remains so for longer periods in a proportion of cases (up to 30%), especially when only small, well-



Fig. 10.**10** **a** *Echinococcus granulosus*, adult; **b** *E. multilocularis*, adult; **c** dog intestine with *E. granulosus*; **d** cystic echinococcosis in human liver: mother cyst of *E. granulosus* with daughter cysts; **e** alveolar echinococcosis in liver; **f** cyst of *E. granulosus*: histological section through cyst wall; **g** section through *E. multilocularis* in human liver; **h** isolated protoscoleces of *E. granulosus*; **i** section through metacestodes of *E. multilocularis* with protoscoleces, from rodent. (d: A. Akovbiantz, Waidspital, Zurich.) ▶

***Echinococcus granulosus* and *E. multilocularis***

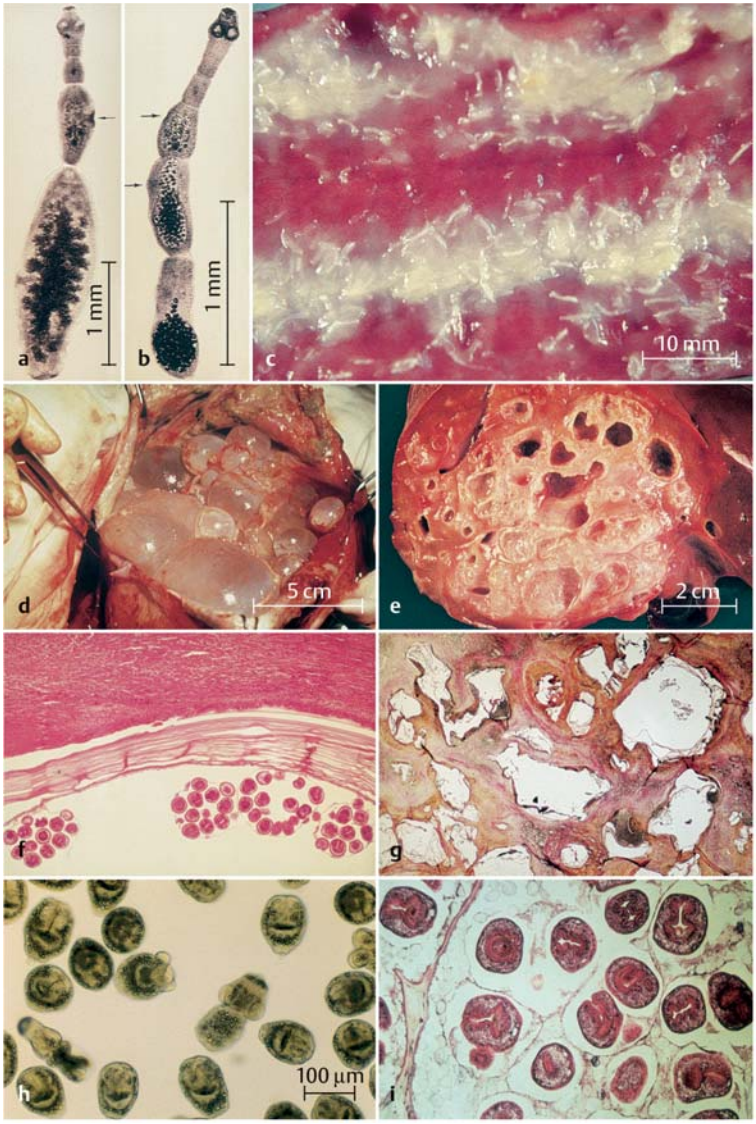

Table 10.**3** Clinical Parameters of Human Cystic and Alveolar Echinococcosis[1]

| **Clinical parameters** | **Cystic echinococcosis**<br>Causative agent:<br>*E. granulosus* | **Alveolar echinococcosis**<br>Causative agent:<br>*E. multilocularis* |
|---|---|---|
| Incubation period: | Months to several years | >5–15 years |
| Metacestode: | | |
| ■ Typical form: | Cysts (see text) | Alveolar conglomerates (see text) |
| ■ Growth: | Expansive | Infiltrative, like malignant tumor |
| Primary target organs: | Liver (60–70%), lungs (15–25%), less frequently spleen, kidneys, musculature, CNS, etc.<br>Approx. 70% of patients have solitary cysts | Liver (98–100%) |
| Complications: | Secondary echinococcosis[2], mainly in peritoneal and pleural cavities | Metastasis to abdominal organs, lungs, brain, bones, etc. |
| Manifestations of disease in age groups: mean and (extremes[3]) | 38 years<br>(3–86) | >54 years<br>(20–84) |
| Symptoms: | Depends on localization, size, and number of cysts | Depends on extent of changes in liver and other organs |
| ■ Liver: | Upper abdominal pains, hepatomegaly, cholestasis, jaundice, etc. | Upper abdominal pains, jaundice, weight loss, also fever and anemia |
| ■ Lungs: | Thoracic pains, cough, expectoration, dyspnea, etc. | Thoracic pains, etc. |
| ■ CNS: | Neurological symptoms | Neurological symptoms |
| Lethality in untreated patients: | Exact data unavailable | Very high: >94–100% |

[1] For further information see Amman and Eckert: *Gastroenterological Clinic N. Amer.* 1996: 25: 655–689.
[2] See text for explanation.
[3] According to a study conducted in Switzerland.

encapsulated or calcified cysts are present. Symptoms may appear after months or years when one or more cysts begin to disrupt organ functions due to their size, expansive growth, or localization (Table 10.**3**). Acute symptoms may appear following spontaneous, traumatic, or intraoperative cyst ruptures, whereby the release of antigen containing hydatid fluid can cause symptoms of anaphylactic shock. There is also a risk that protoscoleces will be released and develop into new cysts in the human host (secondary CE). On the other hand, cyst rupture can also result in spontaneous cure.

**Diagnosis** is based on detection of cysts using imaging techniques (ultrasonography, computer tomography, thoracic radiography, etc.) in connection with serological antibody detection (Table 11.**5**, p. 625). Specific antibodies occur in about 90–100% of patients with cystic hepatic echinococcosis, but in only about 60–80% of cases with pulmonary echinococcosis. Diagnostic cyst puncture is generally not advisable due to the risks described above (secondary echinococcosis, anaphylactic reactions).

**Therapy.** The disease can be cured by removing the *Echinococcus* cysts surgically. Inoperable patients (e.g., with multiple cysts in lungs and liver) can be treated during several months with albendazole or mebendazole. Chemotherapy results in cure in about 30% of cases and in improvement in a further 30–50% (WHO, 1996). PAIR (**p**uncture **a**spiration **i**njection **r**easpiration) therapy is a new technique still under evaluation: after puncturing the cysts (not all cysts are suitable, e.g., pulmonary cysts!) under ultrasonic guidance, most of the hydatid fluid is aspirated, after which an adequate amount of 95% ethanol is injected into the cyst, left in it for 15 minutes and removed (reaspirated). If effective, the PAIR procedure often succeeds in killing the germinative layer and protoscoleces by ethanol. Since long-term experience with this method is lacking, it is recommended that the procedure be accompanied by a short-term drug regimen (WHO, 1996).

**Control and prevention.** Control of CE in humans includes regular mass treatment of dogs to eliminate *E. granulosus*, preventing access of dogs to viscera of domestic or wild animals, and dog population control. Special hygienic principles must be observed when handling dogs in endemic areas.



### Echinococcus multilocularis (Dwarf Fox Tapeworm)

Causative agent of alveolar echinococcosis (AE)

*E. multilocularis* is widespread in the northern hemisphere with endemic regions in Europe, Asia (Turkey, Iran, Russia, and bordering countries all the way to Japan), and North America (Alaska, Canada, northern and central US states) (Fig. 10.**11**). In Central Europe, the parasite is widely distributed with prevalence levels in foxes exceeding 50% in some areas.

**Distribution of *Echinococcus multilocularis***

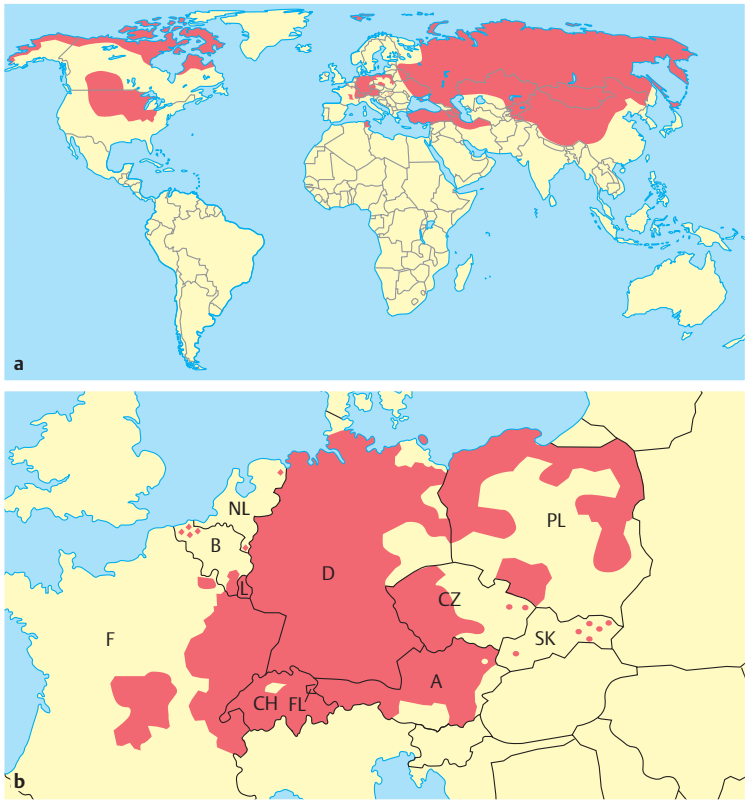


Fig. 10.**11** **a** Approximate global distribution (status: 1999); **b** approximate distribution in Central Europe (status: 1999) (© Institut für Parasitologie, Universität Zürich, J. Eckert, F. Grimm, and H. Bucklar). A: Austria, B: Belgium, CH: Switzerland, CZ: Czech Republic, D: Germany, F: France, FL: Liechtenstein, L: Luxembourg, NL: the Netherlands, PL: Poland, SK: Slovak Republic. Foci have been located in Denmark and on the Norwegian Svalbard Islands in the Arctic Ocean.



## Morphology and development

**Adult stage.** *E. multilocularis* is only 2–4 mm long. Typically, the adult cestode has five (two to six) proglottids and is characterized by a sac-shaped uterus containing up to 200 eggs (Fig. 10.**10b**).

**Definitive hosts, intermediate hosts, and accidental hosts.** The most important definitive hosts for *E. multilocularis* are red and polar foxes, although other wild carnivores (e.g., coyotes, raccoons, wolves) as well as dogs and cats can also carry this tapeworm species. The intermediate hosts are usually rodents (field mice, voles, muskrats, etc.). Accidental hosts include humans and various mammalian animals such as monkey species, domestic and wild pigs, horses, and even dogs.

**Life cycle.** The *E. multilocularis* cycle is similar to that of *E. granulosus* (Fig. 10.**9**). In natural intermediate hosts, protoscoleces develop in the metacestode (see description below) within 40–60 days. Ingestion of metacestodes containing protoscoleces by a definitive host results in development of a new generation of tapeworms in its small intestine with infective eggs produced as early as 26–28 days p.i.

The **metacestode** of *E. multilocularis* is a conglomerate with an alveolar structure comprised of small cysts (microscopical to 3 cm in diameter) surrounded by granulomatous or connective tissue. Each cyst is structured as in *E. granulosus*, but contains a gelatinous mass. *E. multilocularis* rarely produce (small numbers of) protoscoleces in humans (max. 10% of cases) (Fig. 10.**10e, g, i**).

A pathologically significant aspect is that the individual cysts proliferate by exogenous budding and that thin cellular, rootlike extensions of the germinative layer can infiltrate into surrounding tissues. Presumably, cell groups released by these structures or very small vesicles spread hematogenously to cause distant metastases, e.g., in the brain or bones. Therefore the metacestode behaves like a malignant tumor. Metacestode conglomerates can grow to 20 cm in diameter in humans and may develop central necrosis and cavitation.

**Epidemiology.** In Europe, *E. multilocularis* develops mainly in a sylvatic cycle with the red fox as the definitive host and main source of human infections. Dogs and cats can become carriers of *E. multilocularis* by eating small mammals containing metacestodes. In the environment, the eggs of *E. multilocularis* show resistance similar to that of *E. granulosus*. The eggs are transmitted to humans by various routes, but it is not yet clear which are the most important:



Contamination of hands with eggs of *E. multilocularis* by touching definitive hosts (fox, dog, cat) having such eggs adhering to their fur or from working with soil or plants contaminated by the feces of definitive hosts.

Ingestion of contaminated food (wild berries, vegetables, windfall fruit, etc.) or drinking water.

Despite the frequent and widespread occurrence of *E. multilocularis* in foxes, the incidence of AE in humans is currently low. Statistics on national or regional incidences recorded in recent years in France, Germany, Austria, and Switzerland varied between 0.02 and 1.4 new cases per 100 000 inhabitants per year. It is possible that the growing fox population and increasing invasion of cities by foxes, combined with other factors, may raise levels of incidence in the future. In a highly endemic focus in China 4% of several thousand persons had documented AE.

**Pathogenesis and clinical manifestations.** The initial phase of an infection is always asymptomatic. Following a long incubation period, usually 10–15 years, the infection of the liver may present with symptoms resembling those of a malignant tumor (Table 10.**3**). The infection runs a slowly progressing, chronic course, lasting several weeks to several years. The lethality rate can exceed 94% in untreated patients. Spontaneous cure is possible, although no reliable statistics are available.

**Diagnosis.** The diagnostic procedure for AE is the same as for CE. Sensitive and specific methods are available for serological antibody detection (ELISA, Western blot) (Table 11.**5**, p. 625).

**Therapy.** Radical surgical removal of the parasites is potentially curative, but not always a feasible option (in only 20–40% of clinically manifest cases). During to the infiltrative mode of growth of *E. multilocularis* metacestodes it is impossible to be certain that all parts of the parasite have been removed, so that chemotherapy with mebendazole or albendazole must be carried out following such surgery for at least two years with patient monitoring continued for up to 10 years. Chemotherapy lasting years, or even for the life of the patient, is required in inoperable cases (WHO, 1996). Long-term studies have revealed that chemotherapy combined with other medical measures significantly increases life expectancy and quality of life in the majority of patients.

**Control and prevention.** Trials are currently in progress to evaluate drug-based control of *E. multilocularis* in fox populations, but an established and effective control program is not yet available. Personal prophylaxis in endemic areas should include special precautions when handling potentially infected foxes and other definitive hosts. Thorough washing, and better yet cooking, of low-growing cultivated and wild plants and windfall fruit before eating them and washing the hands after working with soil are further basic preventive measures. Persons known to have had contact with definitive hosts that are confirmed or potentially infected carriers, or who are in frequent contact with foxes or are exposed to other concrete infection risks can have their blood tested for antibodies to *E. multilocularis*, the objective being exclusion or early recognition of an infection.

***Echinococcus vogeli* and *E. oligarthrus***

Causative agents of polycystic echinococcosis

These two species, endemic in Central and South America, develop in wild animal cycles (bush dog/*paca* and wild felids/agoutis, paca etc., respectively). In humans, these organisms cause the rare polycystic echinococcosis, which affects the liver, lungs, and other organs.

## Hymenolepis

### Hymenolepis nana (Dwarf Tapeworm)

Causative agent of hymenolepiosis

**Occurrence, morphology, and life cycle.** *Hymenolepis nana*, 1–4 cm long (rarely 9 cm) and 1 mm wide, is a small intestinal parasite that occurs worldwide, the highest prevalences being found in warm countries and in children. The final hosts are rodents and humans. Infection results from peroral ingestion of eggs, from which oncospheres hatch in the small intestine, penetrate into the villi, and develop there into larvae (cysticercoids). The larvae then return to the intestinal lumen, where they develop into adult tapeworms within two to three weeks. Alternatively, *H. nana* develops in a cycle with an intermediate host (insects: fleas, grain beetles, etc.). The closely related species *Hymenolepis diminuta* (10–60 mm) is not as frequent in humans. The developmental cycle of this species always involves intermediate hosts (fleas, beetles, cockroaches, etc.).

**Clinical manifestations and diagnosis.** Infections are often latent, but sometimes cause indeterminate gastrointestinal distress. The eggs (elliptical, about 60 × 50 µm, Fig. 10.**1**, p. 544) are released from the cestode in the intestine and are found by normal stool examination procedures.

**Therapy and prevention.** Praziquantel or albendazole are the drugs of choice. Preventive measures include general hygiene and treatment of infected persons.



## Diphyllobothrium

### Diphyllobothrium latum (Broad Tapeworm, Fish Tapeworm)

Causative agent of diphyllobothriosis

**Occurrence, morphology, and life cycle.** This tapeworm is endemic in lake regions in Europe (above all in Russia, less frequently in Scandinavia, Germany, Switzerland, Italy, etc.), Asia, and America and parasitizes in the small