

## *Metorchis*

(platyhelminth: trematode)

### Overview

Platyhelminths have triploblastic acoelomate soft bodies which are markedly flattened in profile (hence their common name as flatworms). They undergo protostomial embryonic development but do not moult during growth. On the basis of molecular evidence, they are classified within the Lophotrochozoa despite the absence of lophophore mouthparts and trochophore larvae. Three classes are composed entirely of parasitic flatworms (Cestoda, Trematoda and Monogenea), which have prominent attachment organs (suckers or bothria), syncytial teguments, shell glands and vitellaria involved in ectolecithal egg development, and life-cycles involving a variety of larval stages. Trematodes (flukes) have soft leaf-like bodies with oral and ventral suckers, a blind gut (mouth but no anus) and both male and female reproductive organs (hermaphroditic). Digeneans have indirect life-cycles involving alternation of sexual stages in vertebrates and asexual stages in molluscs. Miracidia released from eggs infect snails (obligate intermediate hosts) where they undergo massive asexual proliferation through sac-like sporocyst and redia stages eventually releasing larval cercariae into the water. Vertebrate (definitive) hosts become infected by penetration of the skin by cercariae or by eating encysted stages (metacercariae) on herbage or in second intermediate hosts. Adult opisthorchiideans are small to medium flukes, often spinose, living in the alimentary tracts of mammals, birds, reptiles and fish. They produce embryonated eggs which only hatch after ingestion by snails (first intermediate hosts) and metacercariae develop in fish (second intermediate hosts). Opisthorchids are parasitic in the bile ducts of fish-eating mammals and infections by *Opisthorchis*, *Clonorchis* and *Metorchis* spp. have been associated with liver disorders in dogs, cats and humans.

### Classification:

Domain: Eukaryota (membrane-bound nucleus)  
Supergroup: Amorphea (unikonts with single flagellum, or nonflagellated amoebae)  
Kingdom: Metazoa (multicellular eukaryotes, heterotrophs, notably animals)  
Group: Protostomia (triploblastic, spiral cleavage)  
Subgroup: Lophotrochozoa (lophophore feeding structure or trochophore larva or neither)  
Phylum: Platyhelminthes (flatworms, acoelomate, most hermaphroditic, prominent attachment organs)  
Clade: Neodermata (syncytial tegument = neodermis)  
Class: Trematoda (flukes, most with dorsoventrally-flattened bodies, sac-like gut)  
Subclass: Digenea (heteroxenous, larval miracidium, sac-like sporocyst/redia stages in mollusc, cercariae/metacercariae)  
Order: Plagiorchiida ('echinostomatids', plagiorchiids', mainly fish hosts, some tetrapods, infection by ingestion of cercariae or metacercariae)  
Suborder: Opisthorchiata (egg eaten by gastropod IH, rediae formed, simple-tailed cercariae, encysts in second IH, metacercariae eaten by DH)  
Superfamily: Opisthorchioidea (small-medium flukes, often spinose, piscivorous DH)  
Family: Opisthorchiidae (medium leaf-shaped flukes, in bile ducts of mammals, rediae without appendages, cercariae with two eyespots, metacercariae in second IH)  
Genus: *Metorchis* (parasitic in bile ducts of piscivorous animals)  
Species: various species cause cholangiohepatitis in mammals

**Parasite biodiversity and host range:** Most Metazoa are multicellular triploblastic animals with differentiated tissues, many being bilaterally symmetrical with a body cavity. Most invertebrate animals are protostomes as their embryonic development involves spiral determinate cleavage. Those that do not moult during their life-cycles are grouped together in the enigmatic clade Lophotrochozoa, including the platyhelminths, rotifers, lophophorates, annelids and molluscs. Platyhelminths (flatworms) have soft acoelomate flat bodies with three-dimensional arrays of muscles that generate a typical writhing motion (cf. longitudinal muscles in nematodes producing a thrashing motion). Flatworms do not have a single unifying characteristic (synapomorphy) but comprise diverse free-living (most Turbellaria) and parasitic (Neodermata) assemblages. Neodermata have non-ciliated syncytial (multinucleate) teguments and 3 classes are recognized, all with prominent attachment organs, namely, Cestoda with anterior bothridia/bothria (true/false suckers), Trematoda with oral and ventral suckers (previously called acetabula), and Monogenea with posterior haptors (opisthaptors). All have shell glands surrounding the ootype, and most exhibit ectolecithal egg development (yolk not present in egg but secreted by accessory glands called vitellaria or yolk glands). Most have indirect life-cycles involving the development of adult worms in vertebrates and larval stages in intermediate hosts (usually invertebrates).

The trematodes (flukes) and monogeneans have blind sac-like guts (lacking an anus) while the cestodes (tapeworms) lack digestive tracts. Trematodes have leaf-like bodies well adapted to living in confined spaces in tubular organs of vertebrate hosts. Two trematode subclasses are recognized: the Aspidogastrea with relatively few species (obligate external parasites of molluscs,

fish and turtles, adults possessing a large ventral disc divided with numerous alveoli (suckerlets) or rows of suckers and the tegument having short protrusions (microtubercles)); and the speciose Digenea (obligate endoparasites of vertebrates, adults bearing undivided ventral suckers (when present) and life-cycles involving alternation of sexual stages in vertebrates and asexual stages in molluscs). The success of digeneans as widespread parasites has been attributed to their ability to proliferate at 2 separate parts of their life-cycles. Adults worms in vertebrate definitive hosts produce numerous eggs which are excreted and release free-swimming miracidia which seek molluscan intermediate hosts. Massive asexual proliferation occurs in molluscs involving unique sporocysts and rediae. Both stages are sac-like structures with almost no anatomical features (no suckers, no reproductive organs). The difference is that sporocysts lack a gut (they absorb their food), whereas rediae have a mouth, a muscular pharynx and a sac-like gut (they browse on molluscan tissues). Sequential development of these stages varies considerably, with mother sporocysts producing daughter sporocysts or rediae over multiple generations, culminating in the production of cercariae. The infected molluscs are typically rendered sterile ('castrated') with parasites replacing their gonads and producing dozens to thousands of infective cercariae every day. The cercariae are larval forms, almost always with tails, and they actively emerge from molluscs and swim around in water. There is enormous variation in cercarial behaviour, but the 3 most important routes of infection for definitive hosts are by penetration of the skin by cercariae (e.g. blood flukes), by ingestion of encysted stages (metacercariae) on vegetation (e.g. sheep liver flukes), or ingestion of encysted metacercariae in the tissues of a second intermediate host (e.g. human liver flukes). Some 6,700 digenean species belonging to 22 superfamilies have been described in fish and tetrapods. The subclass Digenea is divided into 2 orders: Diplostomida characterized by furcocercous cercariae that penetrate definitive hosts; and Plagiorchiida with variable life-cycles but often involving cercariae being ingested by definitive hosts.

Superfamily (+ no. families)	No. spp.	DH <sup>a</sup>	Egg <sup>b</sup>	IH1 <sup>c</sup>	Asexual <sup>d</sup>	Cercaria <sup>e</sup>	IH2 <sup>f</sup>	Mode <sup>g</sup>
Subclass: Aspidogastrea (large ventral disc with numerous alveoli (suckerlets) or rows of suckers, tegument with short protrusions (microtubercles), obligate ectoparasites on molluscs, turtles, fish)								
Aspidogastroidea (4)	65	M,F,C,T	A	G,B	-	-	-	8
Subclass: Digenea (oral and ventral sucker; syncytial tegument; obligate endoparasites of vertebrates)								
Order: Diplostomida (blood flukes, 'strigeids') ~1,480 species								
Brachylaimoidea (2)	250	T	E	G	S	S,F	M	6,7
Diplostomoidea (5)	800	T	P	G	S	F	C,M,A	6
Schistosomatoidea (5)	430	F,C,T	P	G,B,A	R,S	F	-	1,6
Order: Plagiorchiida ('echinostomatids', 'plagiorchiids') ~5,200 species								
Allocreadioidea (6)	1,118	F,T	P	G,B	R,S	S,Y	C,M,R,A	6
Apocreadioidea (1)	94	F	P	G	R	S	M,A	6
Azygioidea (1)	43	F,C	E	G	R	F	C	3,4
Bivesiculoidea (1)	28	F	P	G	R	F	C	3,4
Bucephaloidea (2)	410	F	P	B	S	F	C	4
Echinostomatoidea (10)	112	F,T	P	G	R	S	C,M,R	5,6,7
Gorgoderoidea (10)	106	F,C,T	P	G,B	R,S	S,Y	C,M,R	5,6,7
Gymnophalloidea (4)	200	F,T	P	B	S	F	C,M,R,A,E,N	3,4,6
Haplospalchnoidea (1)	51	F	P	G	S	S	-	5
Hemiuroidea (15)	1,160	F,C,T	E	G,B,S	R,S	F	C,M,R,N	4
Heronimoidea (1)	1	T	P	G	S	S	-	7
Lepocreadioidea (8)	473	F	P	G	R	S	C,M,R,A,E,N	6
Microphalloidea (12)	414	F,T	P	G,B	S	S,Y	C,M,R,A,E	6,7
Monorchioidea (3)	270	F	E	G,B	R,S	S	C,R,A,E	6
Opisthorchioidea (3)	436	F,T	E	G	R	S	C	6
Paramphistomoidea (5)	74	F,T	P	G	R	S	-	5
Plagiorchioidea (16)	47	F,T	P	G	R,S	S,Y	C,M,R,A	6
Pronocephaloidea (6)	131	F,T	E	G	R	S	-	5
Transversotrematoidea (1)	27	F	P	G	R	F	-	2
LEGEND								
<sup>a</sup> DH = definitive host: F = teleost fish; C = chondrichthyan fish; T = tetrapod; M = mollusc								
<sup>b</sup> Fate of egg: A = larva hatches and attaches to IH1, E = eaten by IH1, P = hatches releasing miracidium which penetrates IH1								
<sup>c</sup> IH1 = first intermediate host: G = gastropod, B = bivalve, A = annelid, S = scaphopod								
<sup>d</sup> Asexual reproduction involves formation of secondary: R = redia, S = sporocyst								
<sup>e</sup> F = fork-tailed cercaria, S = simple tailed cercaria, Y = cercaria with stylet								
<sup>f</sup> IH2 = second intermediate host: C = chordate, M = mollusc, R = arthropod, A = annelid, E = echinoderm, N = cnidaria, ctenophore								
<sup>g</sup> Mode of infection for DH: 1 = cercaria penetrates DH; 2 = cercaria attaches to DH; 3 = cercaria eaten by DH; 4 = cercaria eaten by IH2; 5 = cercaria emerges, encysts in open and eaten by DH; 6 = cercaria emerges, penetrates IH2, encysts and eaten by DH; 7 = cercaria remains in IH1, encysts and eaten by DH; 8 = no cercarial stage, infected IH1 eaten by DH.								

Thirteen plagiorchidan suborders have been recognized containing 19 superfamilies. The suborder Opisthorchiata contains one superfamily Opisthorchioidea comprising tiny to medium-sized flukes which form rediae without appendages, then simple-tailed cercariae that encyst in second intermediate hosts forming metacercariae. Over 400 species have been described in 90 genera in 3 families (Opisthorchiidae, Cryptogonimidae, Heterophyidae). The family Opisthorchiidae is found primarily in the bile ducts of piscivorous mammals and some 30 genera have been recognized in 13 subfamilies: Allogomtiotrematinae (*Allogomtiotrema*, *Satyapalia*); Aphallinae syn. Witenbergiinae (*Witenbergia*); Delphinicolinae (*Delphinicola*); Diasiellinae (*Diasiella*); Metorchiinae (*Holometra*, *Metametorchis*, *Metorchis*, *Parametorchis*); Oesophagicolinae (*Oesophagicola*); Opisthorchiinae (*Agrawalotrema* (syn. *Thaparotrema*), *Amphimerus*, *Cladocystis*, *Clonorchis*, *Cyclorchis*, *Evranchis*, *Nigerina*, *Opisthorchis* (syn. *Hepatiarius*), *Paropisthorchis*, *Pseudogomtiotrema* (syn. *Gomtia*), *Trionychotrema*); Pachytrematinae (*Pachytrema*); Plotnikoviinae (*Plotnikovia*); Pseudamphimerinae (*Erschoviorchis*, *Euamphimerus*, *Pseudamphimerus*); Pseudamphistominae (*Microtrema*, *Pseudamphistomum*); Ratzinae (*Ratzia*); and Tubangorchiinae (*Tubangorchis*). The subfamily Metorchiinae is characterized by small elongate flukes whose uterus and vitellaria extend anteriorly beyond the level of the ventral sucker. The genus *Metorchis* contains over 25 species which have been found in a wide range of fish-eating mammals (8 species) and birds (18 species), mostly from the Northern Hemisphere (Eurasia and North America). *Metorchis* infections in humans are uncommon apart from isolated outbreaks which are often traced to common infected food sources, especially raw sucker fish consumed by indigenous populations. *Metorchis* spp. differ from *Clonorchis* and *Opisthorchis* spp. in that the adult flukes are smaller (shorter and wider), the oesophagus is very short (almost absent), the caeca extend posteriorly to the end of the body, and the 2 testes are usually entire rather than lobed or branched.

<i>Metorchis</i> species	Definitive hosts [adults in bile ducts]	First intermediate hosts [sporocysts/rediae in tissues]	Second intermediate hosts [metacercariae in tissues]	Distribution
<i>M. bilis</i> (syn. <i>M. albidus</i> , <i>M. crassiusculus</i> )	Carnivora: canid (dog, fox), felid (cat), mustelid (Eurasian otter, mink), ursid (bear); Rodentia: cricetid (hamster, muskrat); Pinnipedia: phocid (seal); Primates: hominid (human), Suliformes: phalacrocoracid (great cormorant); Accipitriformes: accipitrid (white-tailed sea-eagle, eastern imperial eagle, golden eagle, long-legged buzzard, rough-legged buzzard, marsh harrier); Anseriformes: anatid (red-breasted merganser, garganey, mallard, duck)	freshwater Gastropoda: bithyniid ( <i>Bythinia tentaculata</i> , <i>B. inflata</i> , <i>B. troscheli</i> )	freshwater Cypriniformes: cyprinid (ide, roach, dace, tench, minnow, gudgeon, verkhovka, crucian carp, silver carp)	Eurasia, North America
<i>M. butoridi</i>	Pelecaniformes: ardeid (striated heron)			Russia
<i>M. conjunctus</i> (syn. <i>Distoma conjunctum</i> , <i>Parametorchis noveboracensis</i> , <i>P. canadensis</i> , <i>P. manitobensis</i> ) (Canadian liver fluke)	Carnivora: canid (dog, red fox, gray fox, silver fox, red wolf, gray wolf, coyote), procyonid (raccoon), mustelid (American mink, fisher, ferret), ursid (bear), felid (cat); Rodentia: cricetid (muskrat, cotton rat); Primates: hominid (human)	freshwater Gastropoda: amnicolid ( <i>Amnicola limosa</i> )	freshwater Cypriniformes: catostomid (white sucker, longnose sucker), cyprinid (creek chub, fallfish); Perciformes: percid (yellow perch); Salmoniformes: salmonid (brook trout, char); Esociformes: esocid (northern pike)	North America
<i>M. hovorkai</i>	Anseriformes: anatid (ferruginous duck)			Europe
<i>M. kimbangensis</i>	Siluriformes: silurid (Amur catfish)			Vietnam
<i>M. orientalis</i> (syn. <i>M. felis</i> )	Carnivora: canid (dog), felid (cat); Primates: hominid (human); Anseriformes: anatid (duck, goose); Galliformes: phasianid (chicken)	freshwater Gastropoda: bithyniid ( <i>Parafossarulus striatulus</i> )	Cypriniformes: cyprinid (stone moroko, Chinese false gudgeon, pseudogoby)	Asia
<i>M. taiwanensis</i>	Anseriformes: anatid (duck)	freshwater Gastropoda: bithyniid ( <i>Bythinia fuchsianus</i> ,	Cypriniformes: cyprinid (stone moroko); Gobiiformes:	Asia

		<i>Parafossarulus striatulus</i> )	odontobutid (sleeper)	
<i>M. tener</i>	Anseriformes: anatid (common merganser)			Europe
<i>M. ussuriensis</i>	Anseriformes: anatid (duck)	freshwater Gastropoda: bithyniid ( <i>Parafossarulus spiridonovi</i> , <i>Boreoelona ussuriensis</i> )	freshwater fish: Gobiformes: odontobutid (Chinese sleeper); Cypriniformes: cyprinid (lake minnow); tadpoles: Anura: ranid (Dybowski's frog); snails: Gastropoda: bithyniid ( <i>Parafossarulus spiridonovi</i> , <i>Boreoelona ussuriensis</i> )	Russia
<i>M. xanthosomus</i> (syn <i>M. coeruleus</i> , <i>M. intermedius</i> , <i>M. pinguinicola</i> , <i>M. nettioni</i> )	Anseriformes: anatid (duck, garganey, red-throated diver, common scoter, red-breasted merganser, teal); Gruiformes: rallid (coot, western swamphen); Podicipediformes: podicipedid (little grebe); Charadriiformes: alcid (razorbill), Accipitriformes: accipitrid (marsh harrier, long-legged buzzard); Passeriformes: corvid (carrion crow); Sphenisciformes: spheniscid (African penguin); Galliformes: phasianid (chicken)	freshwater Gastropoda: bithyniid ( <i>Bythinia tentaculata</i> )		Europe, Africa, Indochina, Asia, South America
<i>M. zacharovi</i>	Anseriformes: anatid (duck)			Russia

**Parasite morphology:** *Metorchis* spp. form 7 different developmental stages: eggs, miracidia, sporocysts, rediae, cercariae, metacercariae, and adult flukes. Eggs are ovoid in shape measuring from 22-32 µm in length by 11-20 µm in width. They are yellow-brown and slightly constricted anteriorly with a distinct subterminal operculum. The eggs are embryonated and contain a well-developed lanceolate miracidium with a covering of cilia, small primitive gut cells at the pointed anterior end and larger central granular cells. Sporocysts are pleomorphic sac-like structures with thin walls and no organs other than balls of germinal cells. Sporocysts undergo asexual reproduction producing rediae which then produce cercariae. Rediae are also sac-like structures, measuring 1.6-1.9 x 0.2-0.3 mm, but they have digestive tracts comprising a prominent oral sucker with a mouth, pharynx, oesophagus and bifurcate caecum. Cercariae are pleurolophocercous with oval-trapezoidal bodies (up to 0.3 mm long by 0.05-0.11 mm wide) and elongate tubular tails (up to 0.9 mm long) with dorsoventral fin folds. Their bodies are covered by spinose tegument and contain 2 eyespots, a sucker-like mouth and prominent anterior penetration glands. Metacercariae are essentially tail-less cercariae that have become encapsulated by a thin cyst wall (0.02-0.07 mm) forming transparent ovoid cysts (0.21-0.42 mm in diameter). Adult flukes are worms that are distinctively pyriform, measuring from 1.8-6.8 mm long by 0.3-1.6 mm wide. They have a translucent spiny cuticle, 2 weakly developed suckers (oral and ventral) almost equal in size, an oval pharynx, short oesophagus (almost absent), and bifurcate intestinal caeca extending to the posterior end of the body but still blind-ended (no anus). Adult worms are hermaphroditic and possess both male and female reproductive organs. They have 2 spherical testes diagonally apposed to each other in the posterior body, the testes being entire (not branched or lobed). A single round ovary is located immediately anterior to the testes (pre-testicular) and is connected to a highly folded uterus opening into a genital pore located just in front of the ventral sucker. A large seminal receptacle is present near the ovary and numerous vitelline follicles are located in lateral fields extending anteriorly past the ventral sucker. The uterus in gravid worms is filled with numerous small embryonated eggs.

**Site of infection:** Adult *Metorchis* flukes infect bile ducts in the livers of their definitive hosts (piscivorous mammals), but in heavy infections they may also occur in extrahepatic ducts, the gall bladder and sometimes pancreatic ducts. Asexual developmental stages (sporocysts and rediae) form in the digestive glands and gonads of their first intermediate hosts (snails), while encysted metacercariae develop in the tissues of their second intermediate hosts (fish).

**Pathogenesis:** Light infections by *Metorchis* are often asymptomatic while heavier infections (> 200 worms) may cause clinical disease characterized by inflammation (cholangiohepatitis) and sometimes obstructive jaundice. Mature flukes cause mechanical and chemical irritation to the bile ducts by moving, attaching and feeding on epithelial tissues, releasing excretory-secretory (ES) products with toxic/allergenic properties, and stimulating molecular and cellular host immune responses which may contribute to tissue damage. Infections have been associated with epithelial hyperplasia, inflammation, ductal thickenings, nodular or cord-like swellings in the hepatic parenchyma, the accumulation of viscid yellow-green fluid, and verminous granulomas. Common symptoms of acute infections include abdominal pain, urine discolouration, headache, fever, and eosinophilia. Heavy and/or chronic infections may cause cholangiohepatitis with periductular fibrosis, liver cirrhosis, hepatic and biliary lesions, ulceration and necrosis of hepatic and biliary tissue, haemorrhage, anaemia, jaundice, anorexia, emaciation, and rarely death. Chronic infections in pancreatic ducts may result in pancreatic inflammation and fibrosis leading to impairment of both endocrine and exocrine functions. While disease is rare in humans (mostly occurring in indigenous communities in North America), infections have been associated with emaciation and mortality in companion animals, esp. sled dogs and cats. Infected dogs experience severe weight loss with marked bile duct and periductal inflammation, cirrhosis and verminous granulomas. Chronic infections in cats caused biliary epithelial hyperplasia resulting in icterus, bloody urine, and severe intermittent diarrhoea that recurred over months.

**Developmental cycle and mode of transmission:** These liver flukes have indirect 3-host life-cycles involving transmission between hermaphroditic adult parasites in fish-eating mammals, asexual multiplicative larval stages in freshwater snails, free-swimming aquatic stages and then encysted infective stages in freshwater fish. Adult liver flukes lay embryonated eggs which pass through the bile ducts to the intestines and are excreted with host faeces into the external environment. Eggs ending up in freshwater are ingested by aquatic snails, mostly bithyniid and amnicolid species, which act as first intermediate hosts. The eggs hatch in the snail intestines releasing the ciliated miracidia which penetrate through the gut wall into the hepatopancreas where they shed their cilia and form sac-like sporocysts. These stages undergo asexual reproduction forming rediae which escape and invade the digestive gland and gonads where they feed on snail tissues and produce more rediae or cercariae. Mature cercariae emerge from snails into the surrounding aquatic environment. They have powerful tails and actively swim about for up to 3 days exhibiting positive phototaxis (towards light), negative geotaxis (against gravity) and chemotaxis (swim towards chemicals released by fish). When they encounter freshwater fish, the cercariae penetrate the skin or gills shedding their tails and encysting as metacercariae in subcutaneous or muscular tissues. Various species of freshwater fish may act as second intermediate hosts, particularly catostomids and cyprinids, but also including some percids, salmonids and esocids. Metacercariae of several *Metorchis* spp. have also been found in tadpoles of several ranid frog species as well as some bithyniid snails infected by cercariae. Infections may accumulate over time in freshwater fish and the encysted metacercariae may survive in host tissues for over 1 year. Definitive hosts become infected when they consume raw or undercooked freshwater fish containing viable metacercariae which excyst in the intestines releasing juvenile stages that migrate through the common bile duct to the intrahepatic bile ducts. Here they attach, feed and develop into adults worms which cross-fertilize and produce embryonated eggs. Final hosts are generally piscivorous vertebrates, mostly wild carnivores or birds that live near water to hunt fish, but companion animals (esp. sled dogs) and humans may also be infected in domestic situations. The prepatent period (time from infection to first release of eggs) is around 1 month and it is thought the adult worms may live for up to 7 years.

**Differential diagnosis:** Patent infections are conventionally diagnosed by the microscopic detection of fluke eggs in faecal samples, either in smears or following concentration. However, the eggs of many liver fluke species (and genera) appear similar in morphology so differential diagnosis is difficult. Adult worms may be recovered from faecal samples following chemotherapy or from duodenal or bile samples obtained by endoscopy or exploratory surgery. Indeed, medical imaging techniques such as X-rays (cholecystochoangiography), ultrasound, computed tomography (CT) and magnetic resonance imaging (MRI) may be used to aid diagnoses by demonstrating structural anomalies due to inflammation, fibrosis, blockage or filling defects. Infections by metacercariae in fish may be detected by microscopic examination of dissected muscles, usually in squash preparations or following pepsin-acid digestion. An enzyme immunoassay has been developed to detect specific antibodies in host serum samples against crude worm antigens, but varying levels of cross-reactivity were observed. Molecular characterization techniques have been used to explore parasite genetic variation by polymerase chain reaction (PCR, including realtime PCR) amplification of nuclear (18S ribosomal RNA, internal transcribed spacer regions 1 and 2) and mitochondrial (cytochrome c oxidase subunit 1, NADH dehydrogenase subunit 1) gene sequences.

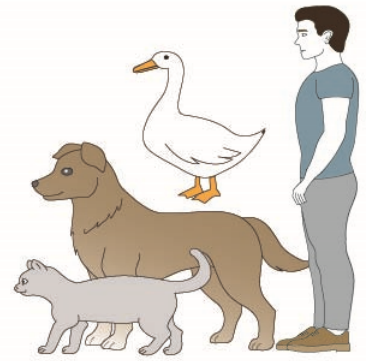
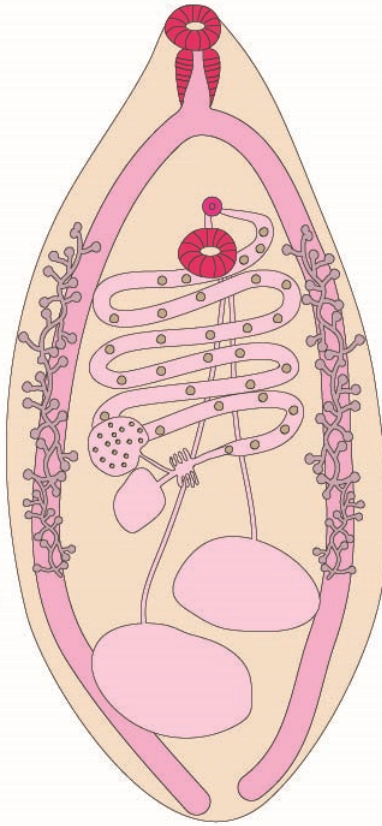
**Treatment and control:** Clinical *Metorchis* infections have been successfully treated with broad spectrum anthelmintics: notably the isoquinoline (praziquantel) and the benzimidazole (mebendazole), with low toxicity and minor side effects such as abdominal pain, nausea and diarrhoea. Various preventive strategies targeting transmission cycles have been implemented in endemic regions even though their effectiveness is often diminished due to the abundance of aquatic environments in Holarctic (Nearctic and Palaearctic) zoogeographic zones with suitable snail vectors, freshwater fish and wild animals supporting sylvatic cycles, and indigenous populations, companion animals, nomadic life-styles and dietary customs supporting peridomestic cycles and rapid re-

infection. Where possible, every effort should be undertaken to prevent faecal contamination of water by providing facilities for better sanitation, including sewage and water treatment. While it may be desirable to reduce freshwater snail populations (first intermediate hosts) to minimize parasite asexual amplification, the indiscriminate use of toxic molluscicides in natural waterways is not advised due to unforeseen ecological consequences. Similarly, attempts to reduce freshwater fish populations (second intermediate hosts) in natural lakes, ponds and streams are at best impractical and at worst harmful to aquatic ecosystems and associated biota. The best way to reduce infections in humans and domestic animals has proven to be reducing or eliminating their consumption of raw, undercooked or lightly salted fish as part of their traditional dietary practices. Metacercariae are killed when fish are cooked at temperatures above 63°C, or freezing them at -20°C for at least 7 days. Public health education campaigns have targeted indigenous communities in endemic regions to convince them to change their culinary customs and to stop feeding untreated trash fish to working dogs.

# Metorchis



liver, bile ducts  
(trauma, irritation,  
inflammation, granulomas,  
obstructive jaundice)



Definitive Hosts  
(carnivores, piscivores)

excretion



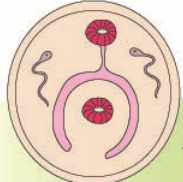
egg  
(~ 30 μm)



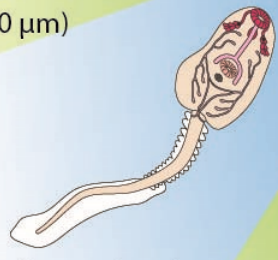
vector-borne transmission

encysted within  
tissues of IH-2

metacercaria  
(~ 300 μm)



endoparasitic in  
tissues of vector (IH-1)



free-swimming  
cercaria  
(~ 1 mm)



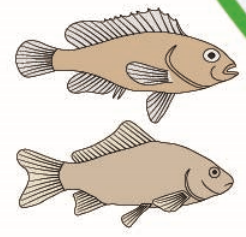
free-swimming  
miracidium  
(~ 30 μm)



redia  
(~ 1.8 mm)



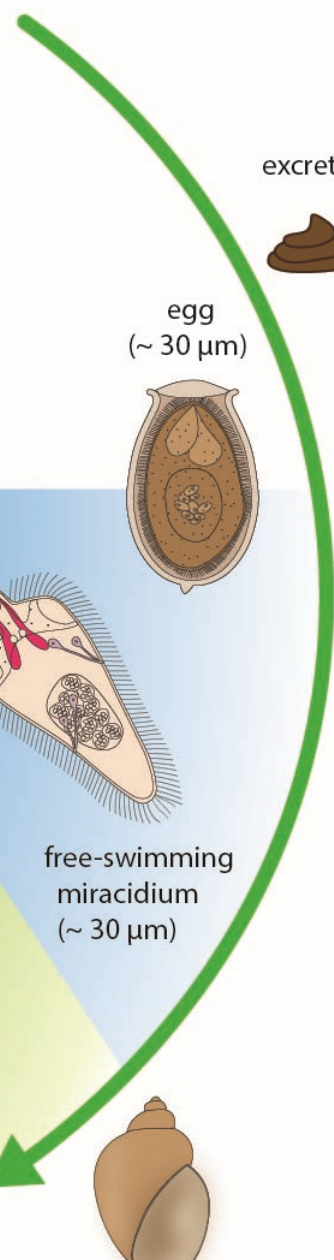
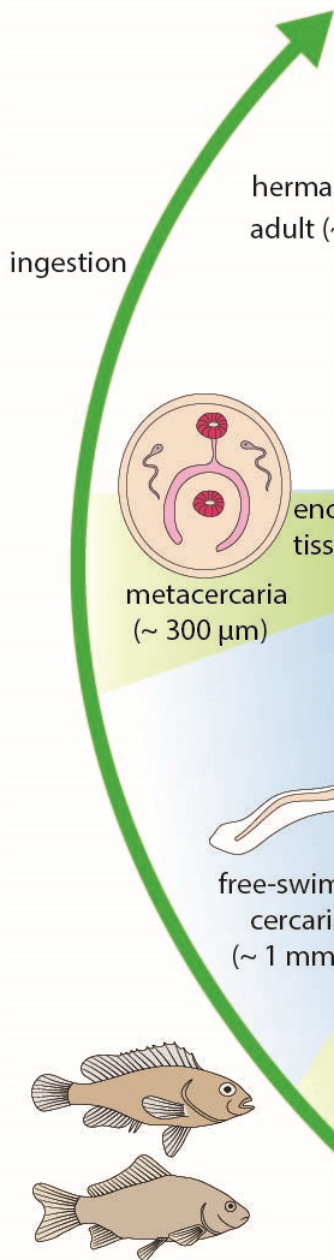
sporocyst  
(~ 1 mm)

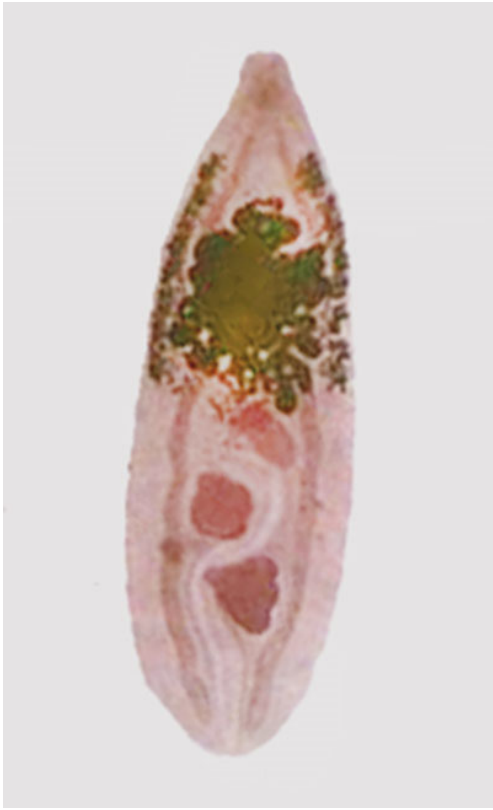


Second Intermediate Hosts  
(IH-2) (freshwater fish)  
(tissue cysts)

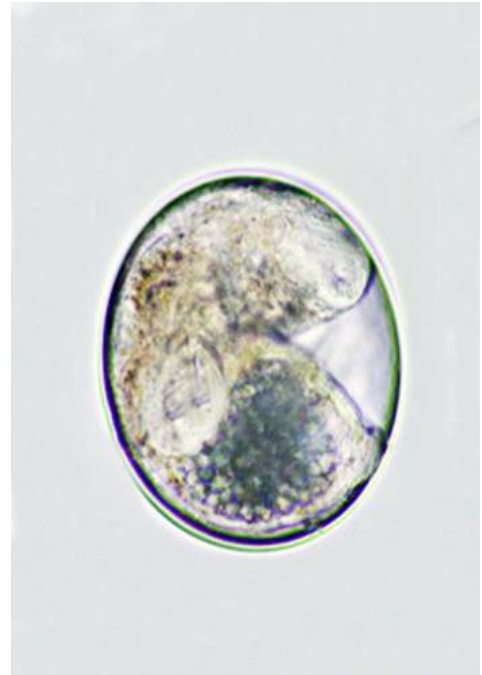


First Intermediate Hosts  
(IH-1) (bithyniid snails)  
(visceral then glandular tissue)





*Metorchis* adult worm



*Metorchis* metacercaria