Dicrocoelium
(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 plagiorchidans are varied in appearance, most bearing spines and a median ventral sucker and many producing small eggs which hatch after ingestion by snails (first intermediate hosts). Dicrocoeliids multiply in land (not aquatic) snails through multiple sporocyst generations (no redia) and they then form metacercariae in ants (second intermediate hosts). *Dicrocoelium* spp. are small lance-like liver flukes responsible for hepatic cirrhosis and production losses in domestic animals.

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: Xiphidiata (xiphidiocercariae with penetrating stylet in anterior margin of oral sucker)
Superfamily: Gorgoderoidea (miracidia penetrate gastropod, bivalve IH, sporocysts and rediae formed, simple-tailed cercariae with stylet, encysts in open or in second IH, metacercariae eaten by DH)
Family: Dicrocoeliidae (small lancet-like flukes, eggs ingested by snails, no redial stage, two-three IH)
Genus: *Dicrocoelium* (parasitic in liver of ruminants)
Species: various species cause cirrhosis of the liver in domestic animals

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[a]**	**Egg[b]**	**IH1[c]**	**Asexual[d]**	**Cercaria[e]**	**IH2[f]**	**Mode[g]**
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
Haplosplanchnoidea (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

[a] DH = definitive host: F = teleost fish; C = chondrichthyan fish; T = tetrapod; M = mollusc

[b] Fate of egg: A = larva hatches and attaches to IH1, E = eaten by IH1, P = hatches releasing miracidium which penetrates IH1

[c] IH1 = first intermediate host: G = gastropod, B = bivalve, A = annelid, S = scaphopod

[d] Asexual reproduction involves formation of secondary: R = redia, S = sporocyst

[e] F = fork-tailed cercaria, S = simple tailed cercaria, Y = cercaria with stylet

[f] IH2 = second intermediate host: C = chordate, M = mollusc, R = arthropod, A = annelid, E = echinoderm, N = cnidaria, ctenophore

[g] 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. Members of the suborder Xiphidiata are characterized by forming xiphidio-cercariae with a penetrating stylet in the anterior margin of the oral sucker which is used to penetrate second intermediate hosts where metacercariae are formed. Over 1,680 species have been described in 44 families in 4 superfamilies: Allocreadioidea (1,118 spp. in 6 families), Gorgoderoidea (106 spp. in 10 families), Microphalloidea (414 spp. in 12 families) and Plagiorchioidea (47 spp. in 16 families). The superfamily Gorgoderoidea parasitizes fish and tetrapods and the 10 cognate families comprise Atractotrematidae, Cadenatellinae, Haploporidae, Callodistomidae, Dicrocoeliidae, Gorgoderidae, Encyclometridae, Orchipedidae, Paragonimidae, and Troglotrematidae. The family Dicrocoeliidae contains more than 400 species in over 30 genera: including *Allocorrigia, Anchitrema, Athesmia, Brachydistomum, Brachylecithum, Brodenia, Caballerolecythus, Canaania, Concinnum, Conspicuum, Controrchis, Corrigia, Dicrocoelium, Dictyonograptus, Euparadistomum, Eurytrema, Leipertrema, Leptophallus, Lubens, Lutztrema, Lyperosomum, Metadelphis, Paradistomum, Platynosomum, Prosolecithus, Pseudathesmia, Pseudoparadistomum, Robertdigenea, Skrjabinus, Stromitrema, Unilaterilecithum, Yungasicola* and *Zonorchis*. They are small lanceolate flukes infecting the liver, bile ducts, gall bladder, pancreas or intestines of herbivores (ruminants, marsupials, reptiles, amphibians, birds) with indirect life-cycles involving 2 intermediate hosts (firstly molluscs, then insects). The genus *Dicrocoelium* contains some 15 species of liver flukes of domestic and wild herbivores that become infected during grazing when they ingest ants containing metacercariae. Infections have been reported in Europe, Russia, Africa, Asia, North America and South America.

***Dicrocoelium* species**	**Definitive hosts [adults in liver, bile ducts]**	**First intermediate hosts [sporocysts in tissues]**	**Second intermediate hosts [metacercariae in tissues]**	**Distribution**
D. albicolle (syn. *Distoma*)	Accipitriformes: accipitrid (booted eagle)			Europe
D. antechini	Dasyuromorphia: dasyurid (dusky antechinus, brown antechinus)			Australia
D. chinensis (syn. *D. suppereri, D. orientale*)	Artiodactyla: cervid (sika deer, roe deer), bovid (mouflon)	Stylommatophora (terrestrial snails): bradybaenid (*Bradybaena*), helicid (*Xeropicta*), pleurodontid (*Ganesella*)	Hymenoptera (ants): formicid (*Formica*, *Camponotus*)	China, Japan, Europe
D. colobusicola	Primates: cercopithecid (red colobus, eastern black-and-white colobus)			Africa
D. dendriticum (syn. *D. lanceatum, D. lanceolatum, D. macaci, D. vitrinus*) (little liver fluke, lanceolate fluke, lancet fluke)	Artiodactyla: bovid (sheep, mouflon, goat, chamois, serow, cattle, buffalo, yak), cervid (red deer, fallow deer, roe deer, sika deer, white-tailed deer, mule deer, wapiti, moose, elk), camelid (camel, lama, alpaca), suid (pig); Perissodactyla: equid (horse); Lagomorpha: leporid (rabbit, jackrabbit, hare, mountain hare), ochotonid (pika); Rodentia: murid (mice, rats), sciurid (woodchuck, marmot); Carnivora: canid (North American red fox), mustelid (mink); Primates: hominid (humans)	Stylommatophora (terrestrial snails): enid (*Zebrina* (*Napaeopsis*) *hohenackeri, Z. detrita*), hygromiid (*Helicella corderoi, H. jamuzensis, H. obvia, H. itala, H. candicans, H. madritensis, H. ordenensis, Helicopsis* (*Xeropicta*) *derbentina H.* (*X.*) *krynickii,*), cochliocopid (*Cionella* (*Cochlicopa*) *lubrica*), geomitrid (*Cernuella* (*Cernuella*) *virgata, C.* (*Xeromagna*) *cespitum, C.* (*Microxeromagna*) *vestita, Cochlicella acuta, C. barbara* (= *C. ventricosa*)), bradybaenid (*Bradybaena alma-atini, B. lantzi, B. plectotropis, B. rubens, B. semenovi, Eulota* (*B.*) *maacki*), helicid (*Helicella itala, H. obvia, Helix* (*Monacha*) *carthusiana, Cepaea nemoralis, C. vindobonensis*), clausiliid	Hymenoptera (ants): formicid (*Formica fusca, F. pratensis, F. rufibarbis, F. cinerea, F. mesasiatica, F. gagates, F. sanguinea, F. lugubris, F. cunicularia* (= *F. glebaria*), *F. polyctena, F. nigricans, F. picea, F. subpilosa, Proformica nasuta, Cataglyphus bicolor, Cataglyphis aenescens*)	worldwide, except South Africa and Australia

		(*Clausilia bidentata*, *Laciniaria varnensis*), buliminid (*Chondrula microtraga, C.* (*Jaminia*) *tridens, J. potaniniana*), zonitid (*Aegopis acies*)		
D. eurynorhynchi (syn. *D. kronschnepi*)	Charadriiformes: scolopacid (spoon-billed sandpiper)			Russia
D. hospes	Artiodactyla: bovid (cattle, buffalo, sheep, goat); Lagomorpha: leporid (rabbit); Sauria: varanid (savannah monitor); occasionally Primates: hominid (human)	Stylommatophora (terrestrial snails): achatinid (*Limicolaria flammea, L. felina*)	Hymenoptera (ants): formicid (*Camponotus, Crematogaster, Dorylus* spp.)	Africa
D. infidum (syn. *Eurytrema*)	Serpentes: boid (green anaconda, Brazilian smooth snake)			South America
D. ivoriense	Rodentia: murid (Tullberg's soft-furred mouse)			Africa
D. lasiuri	Chiroptera: vespertilionid (eastern red bat)			Central America
D. lobatum (syn. *Brachylecithum*)	Accipitriformes: accipitrid (Eurasian sparrowhawk)			Europe
D. macaci	Primates: cercopithecid (Japanese macaque)			Japan
D. macrostomum	Galliformes: numidid (helmeted guineafowl)			Africa
D. moschiferi	Artiodactyla: moschid (musk deer)			Asia
D. panduriforme (syn. *Lyperosomum*)	Passeriformes: corvid (Eurasian magpie)			Europe
D. petrowi	Galliformes: phasianid (chukar partridge)			Russia
D. proxillicens (syn. *Platynosomum*)	Psittaciformes: cacatuid (sulphur-crested cockatoo)			North America
D. rileyi	Chiroptera: vespertilionid (big brown bat)			North America
D. sciuri	Rodentia: sciurid (squirrel)			Russia
D. soricis	Eulipotyphla: soricid (common shrew)			Europe

Parasite morphology: *Dicrocoelium* spp. form 6 different developmental stages: eggs, miracidia, sporocysts, cercariae, metacercariae and adults. The eggs are relatively small (35-45 x 22-30 µm), asymmetrically oval (slightly flattened on one side), surrounded by a thick dark brown shell with a large indistinct operculum and are embryonated when laid. They contain a pyriform miracidium (25 x 20 µm) which is covered with flattened ciliated epidermal plates with ridged cytoplasmic junctions, an apical papilla with stylet, sensory organs and secretory glands and well-developed circular and longitudinal muscles. Sporocysts have pleomorphic saccular non-ciliated bodies (140-420 µm) with syncytial tegument (derived from the miracidial cytoplasmic ridges) and a thin parenchymal lining forming a brood chamber containing balls of germinal cells. The germ balls in mother sporocysts undergo asexual multiplication to form daughter sporocysts which are released into surrounding tissues. Germ balls within daughter sporocysts multiply asexually producing cercariae directly (rediae stages are not produced). Cercariae are known as xiphidiocercariae as they possess an anterior oral perforator stylet on their elongate ellipsoidal bodies (360-760 x 50-165 µm) and have long simple tails (200-1,000 µm) with a dorsal finfold. They possess an oral sucker, mouth, foregut, bifurcate caeca and numerous glands (notably mucoid glands). Cercariae released from daughter sporocysts come together in groups of 100-600 forming spherules, which then join together to form slimeballs up to 1cm in diameter containing up to 8,000 cercariae. Metacercariae are ellipsoidal encysted stages (480-600 x 260-320 µm) surrounded by cyst walls varying in thickness from 5-96 µm. They contain juvenile flukes that have tissues and organs similar to adults except for primordial developing genitalia. Adult flukes are thin and translucent with dorsoventrally flattened lanceolate bodies (5-15 x 0.9-3.0 mm) strongly tapered at each end. They are covered by an aspinose tegument and have 2 suckers located close to each other - the oral sucker being subterminal and slightly larger than the ventral sucker. They possess a mouth, small pharynx, long oesophagus, 2 blind-ended caeca that do not reach the posterior end (no anus) and an I- or Y-shaped posterior excretory vesicle. Mature adult worms are hermaphroditic and possess both female and male reproductive organs. They contain 2 lobed testes located diagonally next to each other in the anterior third of the body, an elongate cirrus sac and median genital pore. The single globular ovary is located post-testicular and connected to an

extensive uterus filling the posterior body and numerous white vitellaria located in 2 lateral midbody bands. *Dicrocoelium* spp. are commonly differentiated on the basis of differences in testes morphology, uterus orientation and adult fluke size.

Site of infection: Adult flukes infect the bile ducts of their definitive hosts (mammals, birds), sometimes being found in the gall bladder and pancreas in heavy infections. Asexual stages are found predominantly in the digestive glands of their first intermediate hosts (terrestrial snails), while metacercariae are found encysted in the haemocoel, and some in the suboesophageal ganglia, of their second intermediate hosts (ants).

Pathogenesis: Immature flukes migrate up hepatic bile ducts but do not penetrate host tissues. Mature flukes have buccal stylets which irritate the bile duct walls inducing epithelial proliferation and periductal fibrosis resulting in firm, thickened and distended bile ducts (cholangiectasia) with biliary obstruction and dysfunction. The severity of disease depends largely on the intensity of infection, with most light infections being asymptomatic but heavier infections being associated with acute and chronic signs. Most clinical infections in ruminants are chronic in presentation with progressive fibrosis (cirrhosis) initially at hepatic portal triads and then along connecting bile ducts with the accumulation of bright viscid exudates. Symptoms/signs include anaemia, jaundice, eosinophilia, oedema, loss of condition, weight loss, emaciation and reduced meat, milk and/or wool production, while changes in clinical parameters included elevated levels of albumin, total bilirubin, bile acids and others consistent with oxidative liver damage such as increased aspartate aminotransferase (AST), alanine aminotransferase (ALT), glutamate dehydrogenase (GDH) and sometimes gamma-glutamyl transpeptidase (GGT). Acute and severe infections may prove fatal in domestic ruminants and protracted infections have been associated with significant inflammation of the liver (cholangiohepatitis), and sometimes the gall bladder (cholecystitis). Up to 50,000 flukes have been detected in ruminants with severe clinical disease. Several cases of verminous hepatitis have been reported in humans infected with lancet flukes, with abdominal pain, weight loss, recurrent watery diarrhoea, constipation, eosinophilia and anaemia.

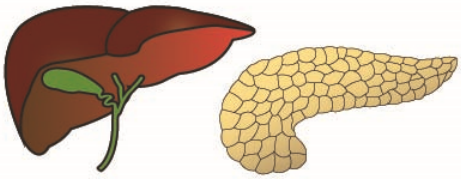
Developmental cycle and mode of transmission: *Dicrocoelium* spp. have indirect heteroxenous life-cycles involving 3 different types of hosts: adult flukes undergo sexual reproduction in mammals and birds (definitive hosts); asexual stages reproduce in land snails (first intermediate hosts); and metacercariae form in ants (second intermediate hosts). Gravid flukes produce embryonated eggs which are released into the gut lumen and excreted with host faeces onto pastures where they remain viable for extended periods. The eggs are ingested by snails, but in this case by terrestrial snails rather than aquatic snails like most other Digenea. A wide range of pulmonate land snails (Stylommatophora) may act as first intermediate hosts in which parasites reproduce asexually; with reports including members of the superfamilies Helicoidea (bradybaenids, geomitrids, helicids, hygromiids, pleurodontids), Cochliocopoidea (cochliocopids), Zonitoidea (zonitids), Enoidea (enids (buliminids)), Clausilioidea (clausiliids), and Achatinoidea (achatinids). Ingested eggs hatch releasing their enclosed ciliated miracidia in the snail gut which then penetrate the gut wall shedding their cilia and forming sporocysts in snail tissues, predominantly the digestive gland (hepatopancreas). Two generations of sporocysts are formed over a period of 3-5 months, with germ balls in mother sporocysts giving rise daughter sporocysts whose germ balls then produce cercariae (redial stages are not formed). Cercariae migrate to the pulmonary chamber of the snail where they secrete a thin cyst wall and become coated with snail mucus forming small spherules that join together to make up slime balls. These mucilaginous balls are coughed up and expelled through the respiratory orifice (pneumostome) onto plants or other substrates when snails move. The slime balls are then eaten by field ants which act as second intermediate hosts. In the ant, the cercariae penetrate the gut, shedding their tails, and form encysted metacercariae in the body cavity (haemocoel) over 1-2 months. Within each ant, 1-2 cercariae also migrate to the suboesophageal ganglia where they encyst becoming 'brain-worms' which alter the ant's behaviour and cause tetany. When the environmental temperature drops each evening (< 15-20°C), infected ants move up vegetation and clamp onto grass tips when their mandibles undergo tetanic seizures (muscle spasms or cramps). The torpid ants are more susceptible to ingestion by grazing animals during peak foraging times at dusk and dawn (as temperatures warm again in the morning, the ants return to normal). When infected ants are ingested by suitable definitive hosts, the metacercariae excyst in the duodenum releasing juvenile worms which migrate up into the bile ducts within hours of infection and then mature to adult flukes over several weeks. The prepatent period (time from infection to first egg release) ranges from 48-96 days and the whole parasite life-cycle may be completed within 6 months. Transient infections may occur in humans following the accidental ingestion of infected ants on fruit, vegetables, salads, herbs or in drinking water.

Differential diagnosis: Infections in animals are conventionally diagnosed by the microscopic detection of characteristic fluke eggs in faecal samples, usually following concentration by sedimentation and/or floatation. Alternatively, infections may be diagnosed at necropsy by the detection of adult flukes in dissected bile ducts. Coprological examination may be used to diagnose infections in humans, but care should be taken to rule out pseudo-parasitism in people who have eaten uncooked infected liver (they do not become infected but simply pass intact eggs in their faeces). Blood biochemical profiles may reveal increased levels of albumin, total bilirubin, bile acids, alkaline phosphate, aspartate aminotransferase (AST), alanine aminotransferase (ALT), glutamate dehydrogenase (GDH), sometimes gamma-glutamyl transpeptidae (GGT) and immunoglobulin E, although such changes are relatively nonspecific. Immunoserological tests (complement fixation, haemagglutination, immunofluorescence, enzyme immunoassays) have been used to detect host antibodies against somatic and excretory-secretory antigens, but they have demonstrated poor specificity. Molecular characterization techniques have revealed genetic variation between a limited range of

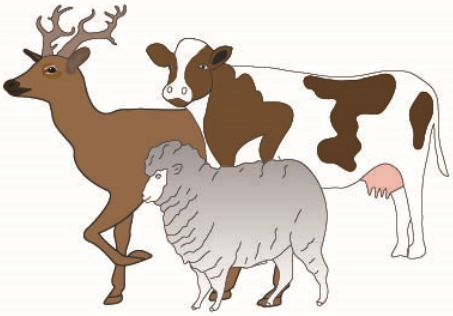
species from humans and domestic animals following polymerase chain reaction (PCR) amplification of nuclear genes (18S, 5.8S and 28S ribosomal RNA, internal transcribed spacer region 2).

Treatment and control: Infections by adult flukes have been successfully treated with several anthelmintic drugs, notably praziquantel (isoquinoline), triclabendozole (halogenated benzimidazole-thiol) and mirazid (oleoresin extract of myrrh), but they were less effective against juvenile or immature stages. Other broad-spectrum anthelmintic drugs, including benzimidazole-methylcarbamates (albendazole, fenbendazole, luxabendazole, mebendazole), benzimidazole-thiazolyls (cambendazole, thiabendazole) and probenzimidazole (thiophanate), have been used to treat infections, but at higher doses than recommended for other helminth infections. Treatment with the deacetylated (amine) metabolite of diamphenethide also appeared effective, but high doses were found to have serious side-effects. It is also recommended that repeat treatments be used to prevent re-infection as ants hibernate and may carry infections over seasons. The prevention of infections in free-range and natural ecosystems is particularly difficult due to the faecal contamination of pastures by livestock and the wide distribution and abundance of both land snails and formicid ants. Management of intermediate host populations using molluscicides and insecticides is contraindicated in most ecosystems due to concerns over toxicity and unintended ecological consequences. Several attempts have been made to reduce intermediate host populations in domestic and peridomestic situations by introducing poultry to eat snails and ants. Other farm management practices have included rotating livestock between pastures, restricting their grazing in evenings and mornings using barriers, and optimizing regular anthelmintic drenching regimes (for therapy and prophylaxis).

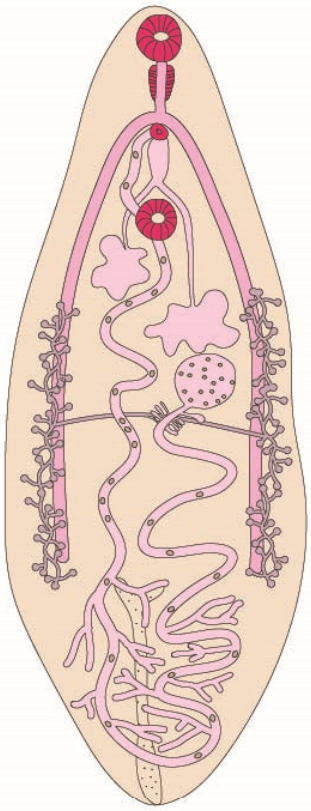
Dicrocoelium



liver, bile ducts, pancreas
(irritation, inflammation,
fibrosis, biliary obstruction)



Definitive Hosts
(herbivores,
esp. ungulates)



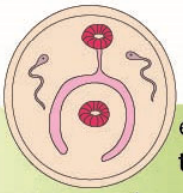
hermaphroditic
adult
(~ 10 mm)

ingestion

excretion

egg
(~ 40 µm)

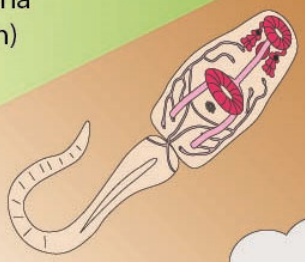
vector-borne transmission



encysted within
tissues of IH-2

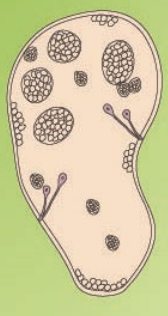
metacercaria
(~ 500 µm)

endoparasitic
in tissues of
vector (IH-1)



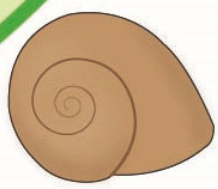
cercaria
(~ 1 mm)

miracidium
(~ 25 µm)



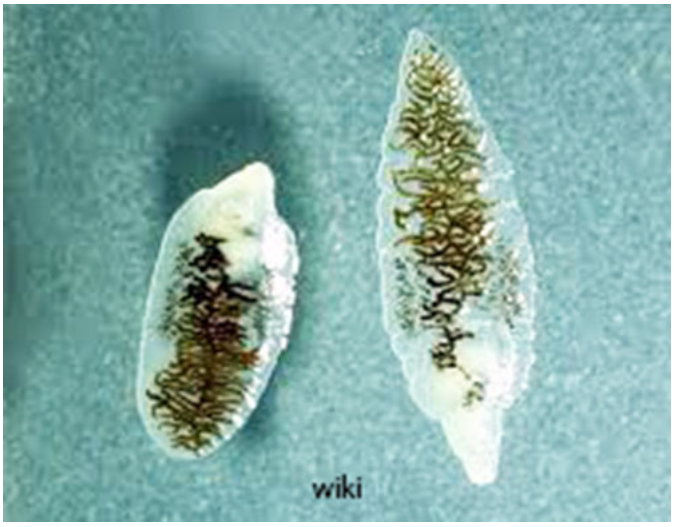
slime ball
containing
cercariae

sporocyst
(~ 300 µm)



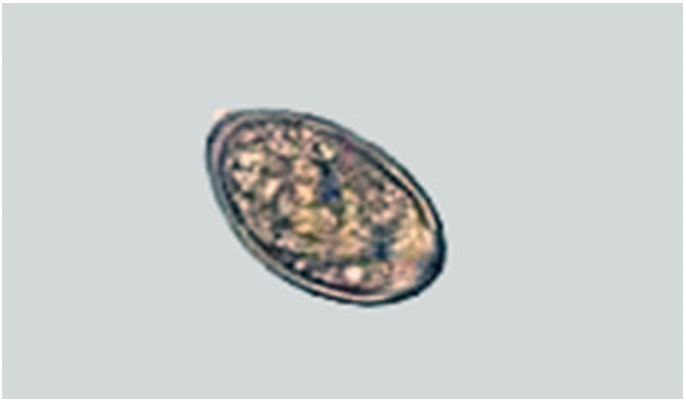
Second Intermediate Hosts
(IH-2) (formicid ants)
(haemocoel, ganglia)

First Intermediate Hosts
(IH-1) (bradybaenid snails)
(intestines then glandular tissues)



Dicrocoelium adult worms

Dicrocoelium adult worm



Dicrocoelium egg

Dicrocoelium cercaria

Other pancreatic flukes

***Eurytrema* species**	**Definitive hosts [adults in pancreatic ducts, sometimes bile ducts]**	**First intermediate hosts [sporocysts in tissues]**	**Second intermediate hosts [metacercariae in tissues]**	**Distribution**
E. brumpti	Primates: hominid (chimpanzee, gorilla)			Africa
E. cladorchis	Artiodactyla: cervid (deer), bovid (cattle, goat)			China, India
E. coelomaticum	Artiodactyla: bovid (sheep, cattle, goat, buffalo), camelid (camel); Lagomorpha: leporid (hare)	terrestrial Gastropoda: bradybaenid (*Bradybaena similaris*)	Orthoptera: tettogoniid (*Conocephalus maculatus*)	Brazil, Asia
E. escuderoi	Artiodactyla: bovid (cattle, carabao)			Philippines
E. fukienensis	Artiodactyla			Asia
E. hydropotes	Artiodactyla: cervid (water deer)			Asia
E. pancreaticum (syn. *E. media, E. dajii, E. ovis, E. parvum*)	Artiodactyla: bovid (cattle, water buffalo, sheep, goat), camelid (camel), cervid (deer), suid (pig); Lagomorpha: leporid (hare); Primates: tarsiid (Philippine tarsier), hominid (human)	terrestrial Gastropoda: bradybaenid (*Bradybaena similaris, B.* (*Cathaica*) *ravida*), eulotid (*Eulota lantzi*)	Orthoptera: tettogoniid (*Conocephalus maculatus*), gryllid (*Oecanthus*)	Southeast Asia, India, South America
E. procyonis	Carnivora: procyonid (raccoon), felid (cat), canid (fox)	terrestrial Gastropoda: polygyrid (*Mesodon thyroidus*)	arthropod?	North America
E. satoi	Primates: cercopithecid (macaques), hominid (gorilla)			Africa
E. sphaeriorchis	Artiodactyla			Asia
E. tonkinense	Artiodactyla: bovid (cattle)			Vietnam