Fasciolopsis
(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, 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 echinostomatids often have well-developed scales or spines on the anterior tegument and the ventral sucker is near the oral sucker. Fasciolids occur as large flukes in the small intestines and infections by *Fasciolopsis buski* cause enteric diseases in dogs, pigs 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:	Echinostomata (miracidium penetrates gastropod IH, redia formed, simple-tailed cercariae, encysts in open or in second IH, metacercariae eaten by DH)
Superfamily:	Echinostomatoidea (slender worms, adult with scales or spines)
Family:	Fasciolidae (large leaf-shaped flukes, in herbivores, conical anterior end, ventral sucker at level of shoulders)
Genus:	*Fasciolopsis* (parasitic in intestines of man/pigs)
Species:	*F. buski* causes enteritis in dogs, pigs and humans

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. The suborder Echinostomata contains one superfamily Echinostomatoidea whose members form simple-tailed cercariae that encyst in the open or in second intermediate hosts, and the resultant metacercariae are eaten by definitive hosts. Ten families are recognized (Calycodidae, Cyclocoelidae, Echinostomatidae (including Echinochasmidae), Eucotylidae, Fasciolidae, Himasthlidae, Philophthalmidae, Psilostomidae, Rhytidodidae, Typhlocoelidae). The family Fasciolidae contains 6 genera (*Fasciola, Fasciolopsis, Fascioloides, Parafasciolopsis,* *Protofasciola, Tenuifasciola*) which form large leaf-shaped adult flukes in the liver, gall bladder and intestines of herbivorous mammals and undergo asexual development in freshwater snails from the superfamily Lymnaeoidea. The genus *Fasciolopsis* is monotypic with a single species (*F. buski*) described from pigs and humans, with proven zoonotic transmission. More than 10 million people are thought to be infected; mostly in the Indo-Asian subcontinent, particularly in communities consuming freshwater plants as part of their culinary traditions. Several other animal species (dogs, rabbits, rodents) may also act as reservoirs for infection.

***Fasciolopsis* species**	**Definitive hosts [adults in small intestines]**	**Intermediate hosts [sporocysts/rediae in tissues]**	**Infective stages**	**Distribution**
F. buski (giant intestinal fluke)	Artiodactyla: suid (pig); Primates: hominid (human), cebid (squirrel monkey), cercopithecid (rhesus macaque); Carnivora: canid (dog); Lagomorpha: leporid (rabbit); Rodentia: caviid (guinea pig)	freshwater Gastropoda: planorbid (*Segmentina* (*Trochorbis*) *hemisphaerula* (syn. *S. coenosus, S. nitidella, S. calathus, S. largeillierti*), *S. trochoideus, S. hemisphaerula, Hippeutis* (*Helicorbis*) *cantori* (syn. *Hi. smackeri*), *Hi. umbilicalis, He. coenosus, Gyraulus convexiusculus, G. chinensis, Indoplanorbis exustus*, *Polypylis, Planorbis*); and rarely (doubtfully) ampullariid (*Pila,*), lymnaeid (*Lymnaea*)	metacercariae on herbage	cosmopolitan (most prevalent in Asia)

Parasite morphology: *Fasciolopsis buski* forms 7 different stages in its developmental cycle: eggs, miracidia, sporocysts, rediae, cercariae, metacercariae and adult flukes. Eggs are quinone-coloured (yellow-brown, bile-stained), ellipsoidal measuring 130-150 x 65-90 µm, thin-shelled, and have a small operculum at one end (hatching point). They are passed unembryonated and contain yolk cells with uniformly distributed lipid granules. As the eggs mature, they embryonate and eventually hatch releasing ovoid ciliated free-swimming miracidia about 150-200 µm long. The miracidia penetrate snails, lose their cilia and transform into elliptical sac-like mother sporocysts which lack a mouth and a gut. The sporocysts grow in size (ranging from 0.07-1.5 mm) and undergo asexual proliferation whereby germinal cells develop into a second generation (called rediae). In contrast to sporocysts, rediae possess a mouth, pharynx and saccular gut and actively ingest and digest food. Mature rediae are cylindrical in shape measuring 1-1.5 x 0.2-0.3 mm. Rediae escape from the mother sporocyst, invade neighbouring tissue and either produce cercariae or another generation of redia. Cercariae are elongate free-swimming stages with bodies measuring 0.21-0.23 x 0.12-0.15 mm and trailing a long simple club-shaped (leptocercous) tail (2-3 times body length). They possess a mouth, gut, oral sucker, ventral sucker (previously called acetabulum), excretory flame cells and numerous cystogenous glands which impart a dark colouration. Mature cercariae attach themselves to aquatic plants, drop their tails and encyst to become metacercariae. The cysts are ovoid, measure 0.13-0.2 mm in diameter and are surrounded by a conspicuous double-layered wall approximately 7 µm thick. Adult flukes have large dorsoventrally-flattened (0.5-3.5 mm thick) leaf-shaped pink-brown bodies and are distinguished from other fasciolids by their blunt anterior ends lacking cephalic cones and shoulders, possessing unbranched gut caeca and inhabiting the intestines rather than the liver of their definitive hosts. The tegument is covered with transverse rows of small spines facing backwards, occurring mostly around the muscular ventral sucker which is 3-4 times larger than the oral sucker. As worms mature, they grow from 1.0-1.6 x 0.5-0.6 mm to 17-75 x 8-20 mm while developing functional genitalia. Adults are hermaphroditic with two dendritic testes located one behind the other (tandem) in the posterior body, a highly branched ovary located in the midline, a short anterior uterus, and extensive vitellaria (vitelline follicles) located laterally.

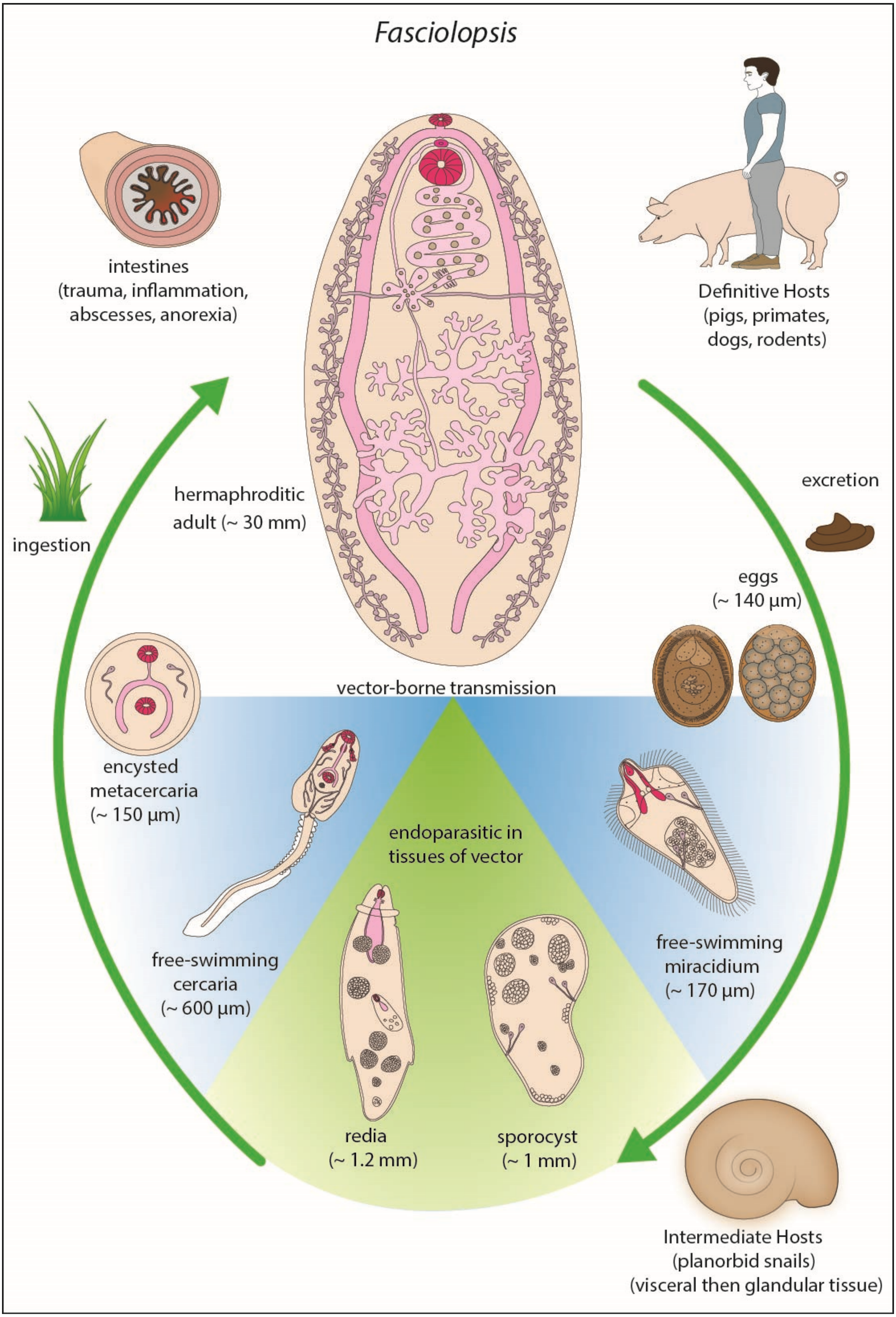
Site of infection: Adult *Fasciolopsis* flukes attach to the intestinal mucosa of their vertebrate definitive hosts, unlike other fasciolids which infect the liver. In light infections, the parasites reside in the duodenum and the jejunum while in moderate to heavy infections the parasites inhabit most of the small intestines and can also be found in the stomach and sometimes the colon. Larval stages in snails vary in their location with most sporocysts forming near the site of miracidial penetration in the foot pad while rediae migrate towards glandular tissue (hepatopancreas and gonads) before finally releasing free-swimming cercariae.

Pathogenesis: The clinical consequences of infections by *Fasciolopsis buski* can be negligible, mild or severe, depending largely on the intensity of infection (number of worms per individual host). Most infections are clinically asymptomatic and significant worm burdens (in the order of hundreds) are usually required to cause clinical disease (called fasciolopsiasis). Worms feed actively on the intestinal mucosa, causing inflammation, ulceration and abscesses. Infections are typically over-dispersed in endemic regions, with many individuals having light infections (involving < 100 worms) that remain asymptomatic or produce mild nonspecific symptoms such as fever, headaches, dizziness, abdominal pain and discomfort, loose stools with alternating constipation, anaemia with eosinophilia, asthenia (weakness) and pallor. Clinical disease worsens in moderate to heavy infections (involving hundreds to thousands of worms), with most symptomatology attributed to traumatic, obstructive and/or toxic effects, often cumulatively. The presence of > 400 worms may prove fatal in children. Adult worms attach to the intestines causing mechanical damage, irritation, erosion, ulceration, abscesses, sometimes perforation, haemorrhage, anaemia, catarrhal inflammation, excessive mucus production, hyperaemia, maldigestion, malnutrition, anorexia and weight loss. Heavy infections by these large worms may also cause partial or complete intestinal obstruction with abdominal colic, epigastric pain, fever, acute ileus and nausea. The absorption of worm metabolites may provoke allergic and toxigenic responses, involving the development of ascites (fluid accumulation in peritoneal cavity), facial or orbital edema, anasarca (generalized oedema) and toxaemia. Both mechanical and metabolite effects lead to inflammatory responses, often involving tissue invasion by leucocytes and eosinophils. Clinical disease may progress through 3 different stages: latency (often asymptomatic for months then developing mild anaemia); diarrhoeic (intestinal inflammation, erosion and ulceration with excessive mucus secretion producing epigastric pain, diarrhoea (yellowish stools without blood), nausea, vomiting and anorexia, sometimes accompanied by allergy and toxaemia); and oedematous (progressive anaemia with fluid accumulation in abdomen (ascites), then genitals, lower limbs, upper limbs, face and lungs culminating in dyspnoea, cardiac insufficiency, hypothermia, dry skin, weakness and possibly death from exhaustion). The intensity of infection and severity of disease is strongly linked to impoverished economic status, rural communities with limited health infrastructures, poor sanitation and unhygienic dietary practices. It is estimated that 10 million human *Fasciolopsis* infections occur annually, infections being more prevalent in children 2-10 years of age who become infected when playing in lakes and ponds.

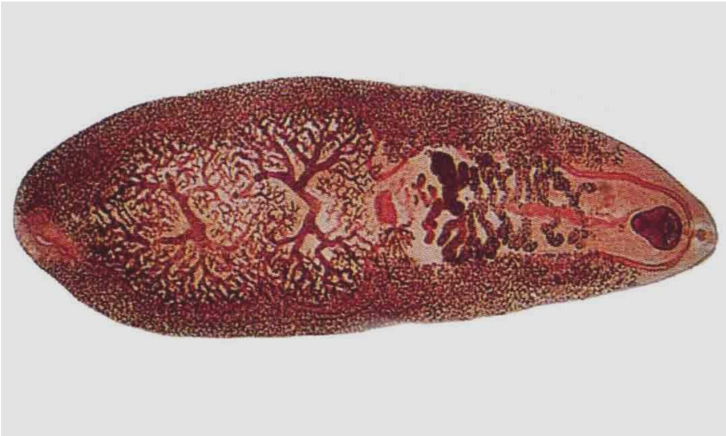
Developmental cycle and mode of transmission: This trematode species has an indirect heteroxenous life-cycle involving sexual developmental stages (adults) in mammalian definitive hosts, free-swimming aquatic stages, asexual developmental stages (larvae) in molluscan intermediate hosts, free-swimming and then encysted stages on aquatic vegetation. Unembryonated eggs released by adult worms are shed in host faeces into the external environment. The eggs embryonate in water over 2-12 weeks depending on temperature (slower in cold water) and then hatch releasing their enclosed miracidia. These stages are ciliated and actively swim about using chemotactic cues to find aquatic pulmonate snails which they must invade within 6-52 hours or die. They can only undergo further development in specific snail species (planorbids) which act as intermediate hosts suitable for parasite asexual development. Miracidia invade the snails by penetrating through the head, foot, tentacles or mantle shedding their ciliated plates in the process. They develop into larger mother sporocysts within snail tissues (often in haemolymph sinuses) which undergo asexual reproduction producing and releasing first-generation rediae that penetrate the snail digestive gland and respiratory cavity where they settle and undergo further asexual reproduction to produce second-generation (daughter) rediae or cercariae. Sporocysts do not have digestive organs but absorb nutrients from their snail hosts, while rediae have mouths and guts to actively feed on snail tissues. Cercariae are transmissive stages which use their mouthparts and glandular secretions to penetrate host tissues and escape from snails into the surrounding environment. The time from infection of the snail to the first release of cercariae ranges from 4-7 weeks, but parasites can survive for months in aestivating snails which bury themselves in soil during dry periods. Cercariae often emerge from snails during the day, although some variation has been observed in their daily pattern. The cercariae are free-swimming stages and can survive in water for up to 64-72 days. Eventually, the cercariae drop their tails and form encysted metacercariae sometimes at the surface of the water but mostly on floating or submerged aquatic vegetation, including edible varieties of water chestnuts, water caltrop, watercress, water spinach, water lotus, water lily, water hyacinth, water bamboo, gankola or water morning glory. Definitive hosts become infected when they ingest raw aquatic plants or drink water containing metacercariae, although some infections may be contracted during food preparation when cooks peel pods or stalks using their teeth. Ingested metacercariae excyst in the gut releasing immature worms which attach and develop into adults over 1-3 months. Mature worms may produce up to 25,000 eggs daily and adults generally live for 6-12 months.

Differential diagnosis: Infections by adult *F. buski* are conventionally diagnosed by the microscopic detection of eggs in faecal preparations, including smears (e.g. Kato-Katz) and sediments (e.g. formalin-ethyl-acetate, merthiolate-iodine-formalin), but their specific identification is difficult due to the similar egg morphologies of many fasciolid species. Eggs, and sometimes adult worms, may also be recovered occasionally from other biological samples, such as vomitus, gastric washes and duodenal aspirates. The relatively large adult worms may also be detected *in situ* by gastrointestinal endoscopy. Infections are often associated with a systemic inflammatory eosinophilia and sometimes by a developing anaemia, as revealed by haematological assessments. Immunoserological tests (enzyme immunoassays) have been developed to detect host antibodies against parasite excretory/secretory antigens, but they have demonstrated problems with sensitivity and specificity. Molecular techniques have recently been applied to the characterization of fasciolid species and strain variations following the polymerase chain reaction (PCR) amplification of nuclear (18S and 28S ribosomal RNA, internal transcribed spacer regions 1 and 2 (ITS1, ITS2)) and mitochondrial (NADH dehydrogenase subunit 1 (Nad1), cytochrome c oxidase subunit 1 (cox1) gene sequences.

Treatment and control: Various anthelmintics have been used to treat fasciolopsiasis in humans and animals; including isoquinolines (praziquantel) interfering with parasite muscles, benzimidazoles (thiabendazole, mebendazole, triclabendazole) inhibiting microtubules, tetrahydropyrimidines (pyrantel) and imidazothiazole (levamisole (causing neurointerference, salicylanilides (niclosamide, oxyclozanide, rafoxanide), halogenated phenols (bithionol) and substituted dihydroxybenzene (hexylresorcinol) inhibiting energy provision, and even the halogenated hydrocarbon (tetrachloroethylene) acting as a purgative. These drugs exhibited variable efficacy and produced few side-effects, with praziquantel being very effective even in severe cases with mild transient side-effects, including dizziness, drowsiness and epigastric pain. Attention should be paid to contra-indications for agricultural use as many have mandatory meat with-holding periods after application to livestock. Various preventive strategies have been developed to break the parasite life-cycle between snail vectors and definitive hosts. It must be remembered that digenean trematodes are unique in that they may undergo massive proliferation in both definitive and intermediate hosts (sexual in the former, asexual in the latter) leading potentially to widespread and heavy contamination of freshwater sources. Every effort should be made to eliminate faecal contamination of water by improving sanitation to limit promiscuous defaecation, introducing sewage and water treatment and prohibiting the use of human 'night soil' and pig excrement as fertilizers in agriculture. Reducing snail populations by the application of molluscicides may be feasible in some peri-domestic situations, but the potential always exists for considerable ecological harm (to crops, fish and the environment). Definitive hosts must avoid eating uncooked aquatic vegetation and cooks should not use their teeth to peel aquatic plants. Drying vegetables or steeping (immersing) them in boiling water for at least 30 seconds has been shown to be effective in killing attached metacercariae. Aquatic green fodder should not be used to feed pigs and farm animals should have access to clean treated water supplies. Regrettably, changes in dietary and agricultural practices are difficult to institute in many circumstances due to entrenched local customs, poverty, unhygienic conditions and the abundance of stagnant waters in wet tropical regions. Nonetheless, education programmes should target not only mothers within families (most often involved in food preparation) but also school children (before cultural norms develop).

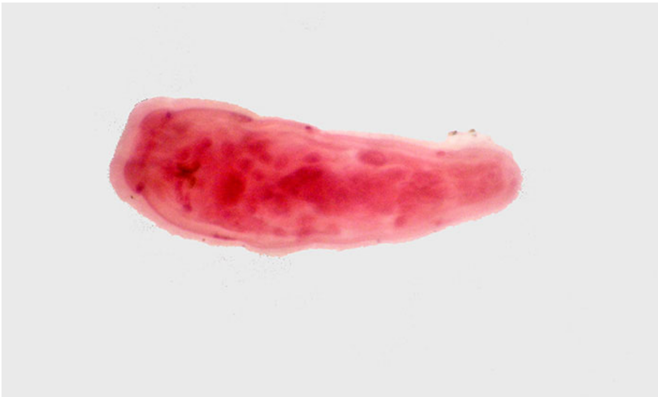


Fasciolopsis
intestines
(trauma, inflammation,
abscesses, anorexia)
Definitive Hosts
(pigs, primates,
dogs, rodents)
ingestion
hermaphroditic
adult (~ 30 mm)
excretion
eggs
(~ 140 µm)
vector-borne transmission
encysted
metacercaria
(~ 150 µm)
endoparasitic in
tissues of vector
free-swimming
miracidium
(~ 170 µm)
free-swimming
cercaria
(~ 600 µm)
redia
(~ 1.2 mm)
sporocyst
(~ 1 mm)
Intermediate Hosts
(planorbid snails)
(visceral then glandular tissue)

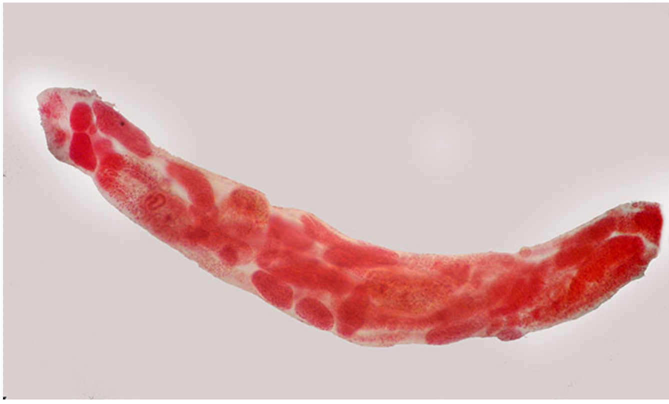


Fasciolopsis adult worm

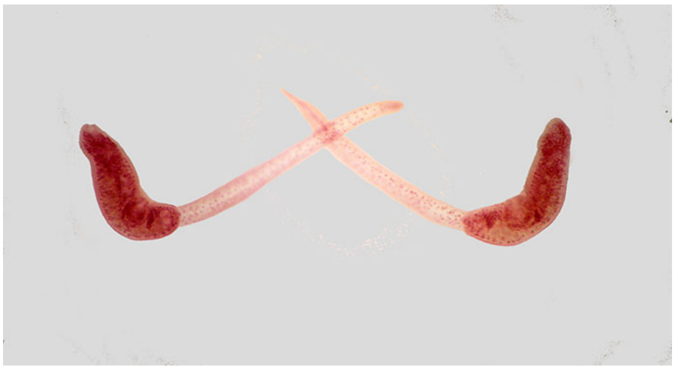
Fasciolopsis egg



Fasciolopsis miracidium



Fasciolopsis redia



Fasciolopsis cercariae