Schistosoma
(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 diplostomatids are diverse in morphology and biology, some having bizarre divided bodies, some appearing tubular, and one extraordinary group (the schistosomes) being dioecious, forming separate sexes. Male schistosomes have a unique gynaecophoral canal along the length of the body (schisto-soma = split body), in which a female worm resides. The copulatory partners live together inside visceral blood vessels and are commonly known as blood flukes. Eggs are deposited in the circulation and must penetrate the gut or bladder to be excreted with faeces or urine, or become trapped in host tissues causing severe granulomatous reactions. Schistosomes form multiple sporocyst (no redia) stages in snails which produce fork-tailed cercariae that emerge and actively seek hosts (metacercariae are not formed). Infections by *Schistosoma* spp. cause chronic debilitating diseases (schistosomiasis/bilharzia) in humans and some domestic ruminants.

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:	Diplostomatida (‘strigeids’, blood and intestinal flukes mainly of tetrapods, some fish, infection usually by cercarial penetration)
Suborder:	Diplostomata (furcocercous (fork-tailed) cercariae)
Superfamily:	Schistosomatoidea (miracidium penetrates gastropod, bivalve, annelid IH, sporocysts formed, fork-tailed cercariae, penetrates DH)
Family:	Schistosomatidae (blood flukes, cylindrical bodies, in blood vessels of alimentary/urinary tract, separate sexes, male with gynaecophoric canal to hold female)
Genus:	*Schistosoma* (parasitic in blood vessels of mammals/birds)
Species:	various species cause schistosomiasis/bilharzia in humans and ruminants

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.

One diplostomatid suborder has been recognized containing 3 superfamilies. The suborder Diplostomata is characterized by species forming furcocercous (fork-tailed) cercariae which either penetrate invertebrate intermediate hosts (forming metacercariae) or directly penetrate vertebrate definitive hosts (forming adults). Members of the superfamily Schistosomoidea do not form metacercariae in second intermediate hosts and their cercariae have been found to develop not only in gastropods but sometimes in bivalves or annelids. Some 430 species have been described in 5 families (Clinostomatidae, Aporocotylidae, Sanguicolidae, Spirorchiidae, Schistosomatidae), the latter 4 families comprising the blood flukes. The family Schistosomatidae contains the blood flukes living in venous blood vessels of tetrapods, the only trematodes that live in the bloodstream of warm-blooded hosts (rich in glucose and amino acids). Schistosomatids are also unique in that the adults are not hermaphroditic but form separate sexes (males resemble rolled leaves with ventral gynaecophoric canals in which the long slender females reside). At present, 15 genera have been classified into 4 subfamilies distinguished by differences in adult morphology and host specificity: Bilharziellinae (short gynaecophoric canal, female genital pore posterior to ventral sucker; *Bilharziella, Trichobilharzia*); Dendritobilharziinae (short canal, anterior pore, dendritic caeca; *Dendritobilharzia*); Gigantobilharziinae (short canal, anterior pore, no ventral sucker; *Gigantobilharzia*); and Schistosomatinae (well-developed canal; *Austrobilharzia* (incl. *Microbilharzia*)*, Ornithobilharzia, Macrobilharzia, Jilinobilharzia, Allobilharzia, Anserobilharzia, Bivitellobilharzia, Heterobilharzia, Schistomatium, Schistosoma* (incl. *Orientobilharzia*) and *Griphobilharzia*). The first 10 genera infect birds, the next 4 genera infect mammals and the last genus infects reptiles.

Parasite genus	**Definitive hosts**	**Location**	**Intermediate hosts (gastropod family)**	**Distribution**
Bilharziella	Anseriformes, Gruiformes, Ciconiformes, Podicipediformes	visceral	freshwater Planorbidae	Europe
Trichobilharzia	Anseriformes (Anatidae)	visceral, nasal	freshwater Lymnaeidae, Physidae	Global
Dendritobilharzia	Anseriformes, Gruiformes, Pelicaniformes, Gaviiformes	visceral	freshwater Planorbidae	Global
Gigantobilharzia	Passeriformes	visceral	freshwater Physidae	North America
Austrobilharzia (incl. *Microbilharzia*)	Charadriiformes	visceral	marine Nassariidae, Batillaridae, Littoriniidae, Potamididae	Global
Ornithobilharzia	Charadriiformes	visceral	marine Batillaridae	Global
Macrobilharzia	Suliformes	visceral	unknown	North America, Africa
Jilinobilharzia	Anseriformes (Anatidae)	visceral	unknown	China
Allobilharzia	Anseriformes (swans)	visceral	unknown	Northern Hemisphere
Anserobilharzia	Anseriformes (geese)	visceral	freshwater Planorbidae	Northern Hemisphere
Bivitellobilharzia	Elephantidae, Rhinocerotidae	visceral	unknown	Africa, Asia
Heterobilharzia	Carnivora, Artiodactyla, Rodentia	visceral	freshwater Lymnaeidae	North America
Schistosomatium	Rodentia	visceral	freshwater Lymnaeidae	North America
Schistosoma (including *Orientobilharzia*)	Primates, Artiodactyla, Rodentia	visceral, nasal	freshwater Planorbidae, Lymnaeidae, Pomatiopsidae	Eurasia, Africa, South America, China
Griphobilharzia	Crocodilia	visceral	unknown	Australia

Schistosoma spp. are important human and animal parasites throughout Africa, Asia and South America, predominantly in rural areas supporting agriculture and inland fisheries. Parasite distribution is linked to that of their snail intermediate hosts, which differ in their habitat preferences for slow-flowing or still waters. Many human activities also influence parasite distribution, especially the construction of irrigation channels and dams, and flood irrigation of crops. It has been estimated that over 200 million people may be infected worldwide. Infections have been recorded throughout human history, first being mentioned in ancient Egyptian papyri dated from 2000-1000 BC. Haematuria (bloody urine) became the scourge of Napoleon's army in northern Africa at the turn of the 18th century, and the disease later became known as bilharzia in honour of the discoverer of the causative agent. *Schistosoma* spp. vary in their specificity for intermediate hosts, some only developing in humans (and possibly primates) while others may infect domestic and wild animals, acting as reservoirs for human infection. Over twenty species have been described, including four recently transferred from the genus *Orientobilharzia.* Four main groups are recognized on the basis of multiple biological and molecular characteristics: namely, the *japonicum*, *haematobium, mansoni* and *indicum* groups. The epidemiology and host preferences of schistosomes in Africa is complicated by the occurrence of hybrid forms.

***Schistosoma* species**	**Egg size**	**Definitive hosts [location] {clinical disease}**	**Intermediate hosts [sporocysts in tissues]**	**Distribution**
S. haematobium group (African distribution)(terminal-spined eggs) (Pulmonata snails)				
S. haematobium (bladder fluke)	112-170 x 40-70 µm	Primates: hominid (human), cercopithecid (mangabey), plus experimental infections in Primates: cercopithecid (green monkey, baboon, rhesus monkey, macaques); Eulipotyphla: erinaceid (hedgehog); Rodentia: murid (mouse, rat, gerbil), cricetid (hamster); rarely Artiodactyla: bovid (goat) [bladder and mesenteric veins] {haematuria, granulomas}	aquatic Gastropoda: planorbid (*Bulinus africanus* (syn. *Physopsis africana*), *Bu. globosus* (syn. *Ph. globosa*), *Bu. nasutus, Bu. abyssinicus, Bu. umbilicatus, Bu. truncatus, Bu. rohlfsi, Bu. forskalii, Bu. senegalensis, Bu. cernicus, Bu. reticulatus, Bu. ugandae, Bu. beccarii, Bu. nyassanus, Bu. jousseaumei, Bu. guernei, Bu. obtusispira, Bu. wrighti, Ferrissia tenuis*)	Africa, India, Southwest Asia
S. intercalatum	140-240 x 50-85 µm	Primates: hominid (human); Artiodactyla: bovid (cattle, sheep, goat); Rodentia: murid (mice, rats) [mesenteric veins] {diarrhoea}	aquatic Gastropoda: planorbid (*Bulinus forskalii, Bu. africanus* (syn. *Physopsis africana*))	Africa
S. bovis (blood fluke)	182-248 x 45-80 µm	Artiodactyla: bovid (cattle, sheep, goat), suid (pig), camelid (camel); Perissodactyla: equid (horse); Rodentia: murid (mice, rats) [portal, mesenteric & urogenital veins] {diarrhoea, haematuria}	aquatic Gastropoda: planorbid (*Bulinus contortus, Bu. truncatus, Bu. africanus* (syn. *Physopsis africana*), *Bu.* (*Ph.*) *nasutus, Bu. guernei, Bu. forskalii, Bu. abyssinicus, Bu. senegalensis, Bu. globosus, Bu. umbilicatus, Planorbarius metidjensis*)	Africa, Middle East, Southern Europe
S. mattheei	145-250 x 40-70 µm	Artiodactyla: bovid (cattle, sheep, goat, wild ruminants), camelid (camel); Rodentia: murid (mice, rats); Primates: hominid (human) [portal, mesenteric & bladder veins] {diarrhoea, haematuria}	aquatic Gastropoda: planorbid (*Bulinus africanus* (*Physopsis africana*), *Bu. globosus*)	Africa, Middle East
S. curassoni	146 x 63 µm	Artiodactyla: bovid (sheep, goat, cattle) [mesenteric, rectal & bladder veins] {liver, bowel lesions}	aquatic Gastropoda: planorbid (*Bulinus umbilicatus*)	West Africa
S. guineensis	151-189 x 57-64 µm	Primates: hominid (human); Rodentia: murid (mice, rats) [rectal veins]	aquatic Gastropoda: planorbid (*Bulinus forskalii*)	West Africa
S. kisumuensis	123-143 x 49-58 µm	Rodentia: murid (mice, rats) [vascular system]	unknown	Central Africa
S. leiperi	210-305 x 38-65 µm	Artiodactyla: bovid (cattle, antelope, wild ruminants); Rodentia: murid (mice, rats) [mesenteric & portal veins]	aquatic Gastropoda: planorbid (*Bulinus africanus* (syn. *Physopsis africana*))	Africa
S. margrebowiei	70-97 x 50-68 µm	Artiodactyla: bovid (antelope, wild ruminants, cattle, sheep, goat); Primates: hominid (human) [mesenteric & portal veins]	aquatic Gastropoda: planorbid (*Bulinus forskalii, Bu. scalaris, Bu. tropicus, Bu. Bu. natalensis, Bu. bavayi, Bu. beccarii*)	Africa
S. mansoni group (African distribution)(lateral-spined eggs) (Pulmonata snails)				
S. mansoni (Manson's blood fluke)	110-175 x 40-70 µm	Primates: hominid (human), cercopithecid (green monkey, macaque, baboon, rhesus monkey), cebid (capuchin); Eulipotyphla: soricid (shrew), erinaceid (hedgehog); Rodentia: murid (rats, mice, gerbil), cricetid (hamster), caviid (guinea pig); Didelphimorphia: didelphid	aquatic Gastropoda: planorbid (*Biomphalaria pfeifferi, Bi. alexandrina, Bi. glabrata* (*Australorbis glabratus*), *Bi. sudanica, Bi. camerunensis, Bi. angulosa, Bi. tenagophila, Bi. straminea, Bi. amazonica, Bi. arabica, Bi. peregrina, Bi. choanomphala, Bi. stanleyi, Bi. smithi, Au. olivaceus, Tropicorbis centimetralis*); terrestrial	Africa, Southwest Asia, Caribbean, South America

		(opossum); Lagomorpha: leporid (rabbit); Cingulata: chlamyphorid (armadillo); Artiodactyla: suid (pig), bovid (goat); Carnivora: felid (cat), canid (dog) [portal and mesenteric veins] {dermatitis, swamp fever, granulomas, ascites}	Gastropoda: achatinid (*Achatina fulica*)	
S. rodhaini	120-170 x 48-70 µm	Rodentia: murid (rats, mice); Carnivora: canid (dog), felid (serval cat) [mesenteric & portal veins] {diarrhoea}	aquatic Gastropoda: planorbid (*Biomphalaria pfeifferi, Bi. sudanica*)	Africa
S. edwardiense	47-62 x 28-53 µm	Artiodactyla: hippopotamid (hippopotamus) [mesenteric veins]	aquatic Gastropoda: planorbid (*Biomphalaria sudanica,*)	Central Africa
S. hippopotami	93 x 40 µm	Artiodactyla: hippopotamid (hippopotamus) [hepatic veins, pulmonary circulation]	aquatic Gastropoda: planorbid (*Bulinus truncatus*)	Central Africa
S. japonicum group (Asian distribution)(minutely-spined or spineless eggs) (Prosobranchia snails)				
S. japonicum (blood fluke)	70-100 x 50-70 µm	Primates: hominid (human), cercopithecid (macaque); Artiodactyla: bovid (cattle, buffalo, sheep, goat), suid (pig), cervid (water deer, muntjac, sambar); Perissodactyla: equid (horse, donkey); Carnivora: canid (dog, raccoon dog, fox), felid (cat, leopard cat, leopard), mustelid (weasel, ferret-badger, badger), herpestid (mongoose), viverrid (civet); Lagomorpha: leporid (rabbit, hare); Rodentia: murid (mice, rats), cricetid (vole), sciurid (squirrel), hystricid (porcupine); Eulipotyphla: soricid (shrew), erinaceid (hedgehog) [portal & mesenteric veins] {dermatitis, abscesses, anaemia, diarrhoea, granulomas, ascites}	amphibious Gastropoda: pomatiopsid (*Oncomelania hupensis, O. nosophora, O. quadrasi, O. formosana, O. lindoensis, O. chiui, Robertsiella kaporensis, Pomatiopsis lapidaria, Tricula aperta*)	South-East Asia, Philippines, Indonesia
S. mekongi	50-65 x 30-55 µm	Primates: hominid (human); Carnivora: canid (dog), felid (cat) [mesenteric veins] {diarrhoea}	amphibious Gastropoda: pomatiopsid (*Neotricula* (*Tricula*) *aperta, T. bollingi*)	South-East Asia
S. malayensis	50 x 28 µm	Rodentia: murid (rats); rarely Primates: hominid (human) [portal veins]	amphibious Gastropoda: pomatiopsid (*Robertsiella gismanni, R. kaporensis, R. silvicola*)	South-East Asia
sister to *japonicum* clade				
S. sinensium	95-115 x 40-50 µm	Rodentia: murid (rats) [mesenteric veins]	amphibious Gastropoda: pomatiopsid (*Neotricula* (*Tricula*) *aperta, T. bollingi*)	China
S. ovuncatum	65-80 x 40-45 µm	Rodentia: murid (rats, mice) [mesenteric veins]	amphibious Gastropoda: pomatiopsid (*Tricula bollingi*)	Thailand
S. indicum group (Asian distribution)(polymorphic eggs)(Pulmonata snails)				
S. indicum	100-150 x 48-68 µm	Artiodactyla: bovid (cattle, buffalo, sheep, goat), camelid (camel); Perissodactyla: equid (horse, donkey) [portal, mesenteric, pancreatic, hepatic & pulmonary veins] {diarrhoea}	aquatic Gastropoda: planorbid (*Indoplanorbis exustus*)	India, Thailand
S. spindale	284-400 x 80-90 µm	Artiodactyla: bovid (cattle, buffalo, sheep, goat), suid (pig);	aquatic Gastropoda: planorbid (*Indoplanorbis exustus*)	India, South-East Asia

		Perissodactyla: equid (horse, donkey); Carnivora: canid (dog); Rodentia: murid (rats) [portal & mesenteric veins] {diarrhoea, plus cercarial dermatitis}		
S. nasalis (*nasale*)	316-508 x 40-75 µm	Artiodactyla: bovid (cattle, buffalo, sheep, goat); Perissodactyla: equid (horse) [nasal mucosa veins] {coryza, sneezing, dyspnoea, snoring disease}	aquatic Gastropoda: planorbid (*Indoplanorbis exustus*), lymnaeid (*Lymnaea luteola, L. acuminata*)	India, South-East Asia
S. incognitum (syn. *S. suis*)	90-148 x 41-81 µm	Artiodactyla: suid (pig), bovid (cattle); Carnivora: canid (dog); Rodentia: murid (rats) [mesenteric & portal veins] {diarrhoea}	aquatic Gastropoda: lymnaeid (*Radix luteola, R. rubiginosa*)	India, South-East Asia
formerly *Orientobilharzia* (differ from *Schistosoma s.s*. only in number of testes)				
S. turkestanicum	108-135 x 42-48 µm	Artiodactyla: bovid (cattle, buffalo, sheep, goat), camelid (camel); Perissodactyla: equid (horse, donkey); Carnivora: felid (cat) [mesenteric/portal veins] {cirrhosis}	aquatic Gastropoda: lymnaeid (*Radix gedrosiana, R. auricularia, Lymnaea tenera*)	Eurasia
S. harinasutai	111-127 x 27-52 µm	Artiodactyla: bovid (buffalo) [portal & mesenteric veins]	aquatic Gastropoda: lymnaeid (*Radix rubiginosa*)	Thailand
S. bomfordi	125-136 x 53-60 µm	Artiodactyla: bovid (cattle) [mesenteric veins]	aquatic Gastropoda: lymnaeid (*Radix luteola*)	India
S. dattai	120-170 x 43-60 µm	Artiodactyla: bovid (cattle, buffalo, sheep, goat) [portal veins]	aquatic Gastropoda: lymnaeid (*Radix luteola*)	India
Schistosomatium (rodent blood flukes established as laboratory models)				
Schistosomatium douthitti	150 x 60 µm	Rodentia: murid (muskrat, meadow mouse, redback mouse, deer mouse, field mouse, white mouse, rat), echimyid (nutria), cricetid (hamster), caviid (guinea pig); Lagomorpha: leporid (rabbit); Carnivora: canid (dog), felid (cat); Primates: cercopithecid (rhesus monkey), hominid (human) [mesenteric and intra-hepatic veins]	aquatic Gastropoda: lymnaeid (*Stagnicola* spp., *Lymnaea palustris, L. stagnalis, L. emarginata*, *L. natalensis, Pseudosuccinea columella*), planorbid (*Bulinus tropicus, Physa* spp.)	North America, Africa?
Schistosomatium pathlocopticum (possibly syn. of *Sc. douthitti*)	80-126 x 58-87 µm	Rodentia: murid (mice, rats) [mesenteric veins]	aquatic Gastropoda: lymnaeid (*Stagnicola (Lymnaea) palustris*)	North America

Parasite morphology: Blood flukes form five different developmental stages: eggs, miracidia, sporocysts, cercariae and adult worms. Eggs are round to oval in shape, light yellow-brown in colour, most lacking a distinct operculum, but all containing a developing embryonic larva (miracidium). Differences in egg morphology can be used to distinguish between *Schistosoma* species: *S. mansoni* producing oval eggs (114-175 x 45-68 μm) with a sharp lateral spine, *S. japonicum* forming oval eggs (70-100 x 50-70 μm) with a rudimentary lateral spine; and *S. haematobium* producing oval eggs (112-170 x 40-70 μm) with a sharp terminal spine. Miracidia are elliptical free-swimming larval stages (~200 μm long) covered with cilia. Sporocysts appear as pleomorphic sac-like bodies which contain another generation of sporocysts or cercariae. Mature cercariae are elongate free-swimming larval stages (400-600 μm long) consisting of a tapering head (with prominent escape and penetration glands) and a forked tail (furcocercous). Adult flukes are elongate tubular worms (9-28 mm long by 1-2 mm wide), with rudimentary oral and ventral suckers close together near the anterior end. The digestive system comprises the mouth (surrounded by the oral sucker), oesophagus (no pharynx), oesophageal glands and paired caeca which reunite posteriorly forming a single caecum extending the remaining length of the body. Unlike most trematodes, adult schistosomes are not hermaphroditic but are sexually dimorphic. Males are shorter and stouter than females (9-22 mm cf. 12-28 mm long), and they have a longitudinal ventral groove (gynaecophoral canal or schist) in which the longer slender female lies. The suckers on the males are spiny and most of their bodies are finely tuberculated. Males possess 5-9 testes and have a ventral genital pore opening immediately posterior to the ventral sucker. Females possess a single ovary connected to the ventral genital pore by an elongate uterus.

Site of infection: Paired adult worms live inside venous blood vessels in specific sites within the bodies of their mammalian definitive hosts. In humans, *S. mansoni* lives principally in the portal veins draining the large intestine, *S. japonicum* in the mesenteric veins of the small intestines, and *S. haematobium* infects veins of the urinary bladder plexus. Fluke eggs penetrate into the lumen of the intestines or bladder to be voided with host faeces or urine. Many eggs, however, may be swept away in the host circulation and become trapped in various host tissues and organs. Asexual developmental stages (sporocysts) develop throughout the tissues and organs of freshwater snail intermediate hosts.

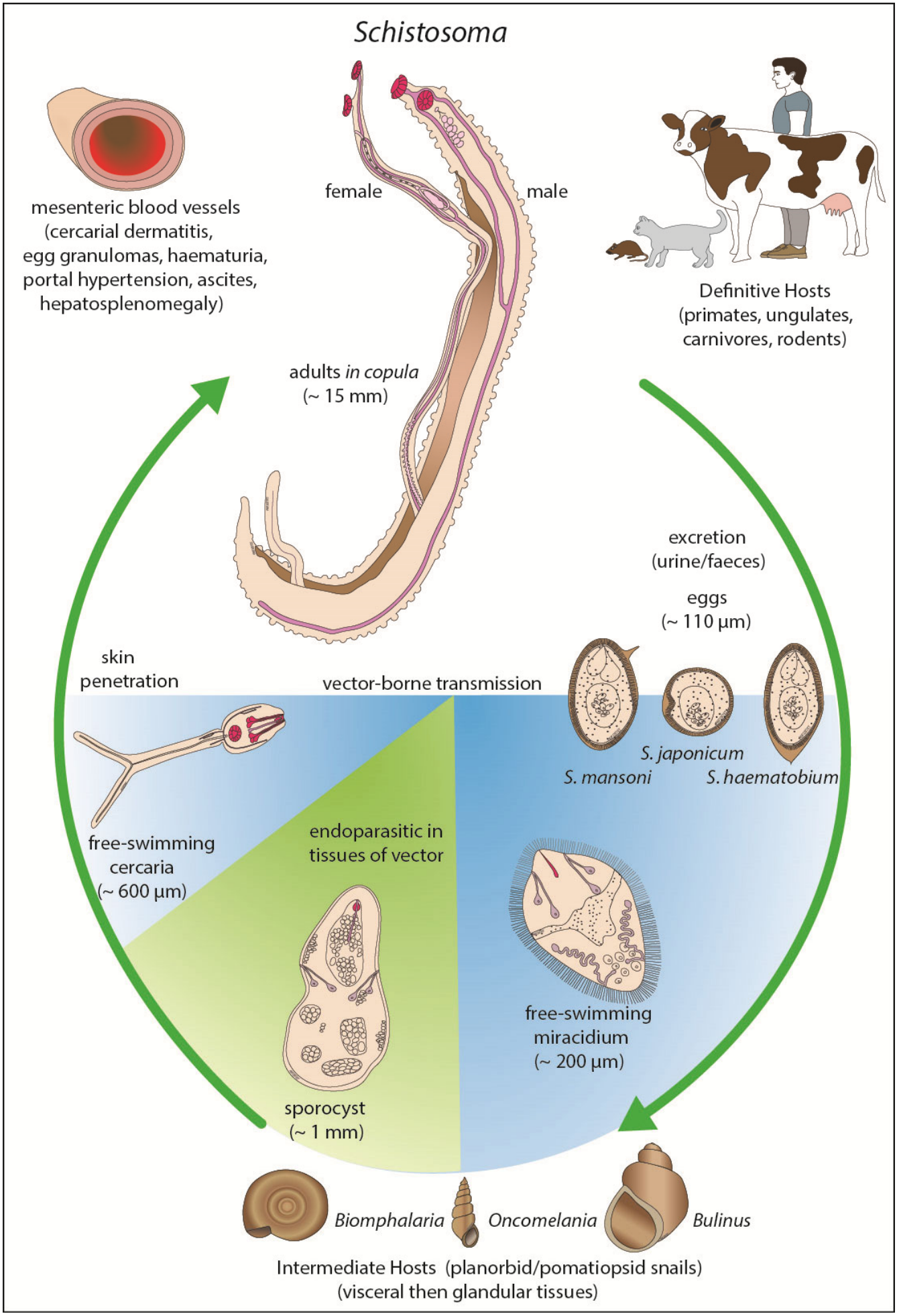
Pathogenesis: Schistosomiasis (or bilharziasis) is unusual amongst helminth diseases for two reasons: much of the pathogenesis is due to the eggs (rather than larvae or adults); and most of the pathology is caused by host immune responses (delayed-type hypersensitivity and granulomatous reactions). However, the severity of disease is dependent not only on the strength of the inflammatory and immune responses but also on the intensity of infection, previous exposure, extent of hepatic fibrosis, age, nutritional status and genetic background affecting host susceptibility/resistance. The course of infection is often divided into three phases: migratory, acute and chronic. The migratory phase begins when cercariae penetrate and migrate through the skin. This is often asymptomatic, but in sensitized patients, it may cause transient hypersensitivity, pruritus and dermatitis ('swimmers' itch') within the first few days after infection. Cercarial excretory/secretory (ES) products have been shown to induce oedema and neutrophil infiltration in the skin. Schistosomula then migrate from the lungs to the liver over several weeks, occasionally causing pulmonary lesions, congestion, pneumonitis and toxic reactions. The acute phase (sometimes called Katayama fever) occurs 2-8 weeks after infection and is coincident with schistosomula migration and the onset of egg laying by adult worms. It is characterized by allergic responses (serum sickness due to overwhelming immune complex formation), pyrexia, rash, urticaria, fatigue, aches, cough, dyspnoea, lymphadenopathy, gastrointestinal discomfort and eosinophilia. Hosts exhibit strong proinflammatory cell-mediated immune responses during the acute phase, where non-egg antigens (cercariae, schistosomula, schistosomes) elicit type 1 $CD4^+$ helper T-lymphocyte (T_h1) responses via effector cytokines (interleukin-1 (IL-1), IL-6 and tumour necrosis factor-alpha (TNF-α). The chronic phase occurs months to years after infection in response to the cumulative deposition of fluke eggs in tissues and the host reactions that develop against them. In order to complete the life-cycle, eggs deposited in small venules must exit the host by traversing vascular endothelia, interstitial tissues and mucosal linings to reach the lumen of the bladder or gut. Miracidia developing within the eggs secrete hydrolytic enzymes among other molecules, which are released through the porous eggshell. In addition to their lytic activity, these secretions elicit granulomatous responses involving motile immune cells (macrophages, neutrophils, eosinophils) which assist in the movement of the granuloma through the tissues. Not all the eggs laid by female worms successfully penetrate the gut or bladder walls, however, and many are swept away in the circulation and become trapped in various organs. The strong granulomatous responses result in extensive fibrosis with the deposition of collagen leading to fibro-obstructive disease. Eggs surrounded by inflammatory cells form characteristic pseudotubercles (abscesses), sometimes coalescing to form larger granulomatous reactions (polyps), which become encapsulated and eventually calcified. The resultant effects on host tissues are manifold and clinical symptoms vary depending on organ involvement, the most frequent being urinary, intestinal and hepatosplenic symptoms. Urinary infections by *S. haematobium* may cause irritative micturition syndrome with dysuria, proteinuria and haematuria (blood in urine), progressing to thickening of the bladder wall, chronic cystitis, polyps, vesical masses, fibrosis and calcification resulting in hydroureter and hydronephrosis. Constant disruption of the bladder wall may also be precancerous leading to bladder carcinoma (other *Schistosoma* spp. have not been associated with colon or liver cancer). Infections in the gut may cause intestinal hyperplasia, micro-abscesses, polyposis, ulceration, abdominal pain, diarrhoea and sometimes complicated enteropathies (erosive lesions, occlusions, prolapses, fistulas). Hepatosplenic symptoms arise from egg congestion of the portal venous circulation with occlusion of intrahepatic veins and periportal (Symmer's clay pipe-stem) fibrosis. The resultant portal hypertension often leads to hepatomegaly, splenomegaly, ascites, and sometimes gross enlargement of oesophageal and gastric veins (varices) which may burst. Other organ systems may be impacted, with cardiopulmonary, renal, genital and neurological symptoms arising infrequently (loosely designated as ectopic). Eggs may reach the lungs from vesical veins or through the porto-cava shunt leading to pulmonary

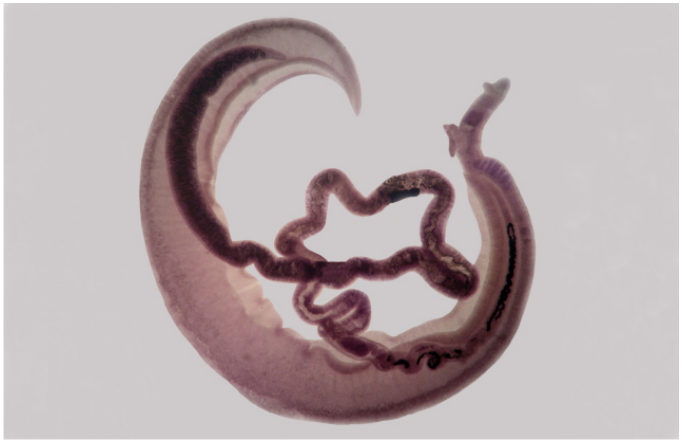
fibrosis and arteritis, with the resultant pulmonary hypertension contributing to right cardiac insufficiency. Lesions may develop in the kidney parenchyma causing glumerulonephritis leading to renal failure. Genital lesions may be inflammatory, hypertrophic or fibrotic: involving the prostate and seminal vesicles in men and the vulva, vagina and uterus in women. Neurological symptoms include cerebral and medullar syndromes, cerebral granulomas being associated with focal encephalitis and epileptic convulsions, and medullar lesions causing transverse, ischaemic or vascular myelitis or myeloradiculitis. Host cell-mediated immune responses during the chronic phase switch to prohumoral and delayed-type hypersensitivity responses, where egg-antigens elicit T_h2 cellular responses via effector cytokines (particularly IL-10); such responses being more conducive to fibrogenesis and healing (also possibly providing protection against severe disease). Schistosomiasis in domestic animals is more severe in small rather than large ruminants: sheep often developing anaemia and hypoalbuminaemia due to mucosal haemorrhages and dyshaemopoesis, while cattle only occasionally display haematuria due to bladder damage. At necropsy, haemorrhagic lesions may be present in the intestinal mucosa during the acute phase of infection, but as disease progresses there may be marked thickening, oedema, fibrosis, and organ enlargement due to egg granulomata and associated inflammation. An unusual species (*S. nasalis*) found in the nasal mucosa mainly of cattle has been associated with copious mucopurulent discharge, snoring, dyspnoea, abscess formation and occlusion of nasal passages. Other schistosomes, such as those that normally infect birds (e.g. *Trichobilharzia* and *Austrobilharzia*) may also cause 'swimmers' itch' in humans when the cercariae penetrate the skin but are unable to complete their development.

Developmental cycle and mode of transmission: Schistosomes have indirect digenetic life-cycles, involving sexual reproduction in vertebrate definitive hosts and asexual reproduction in snail intermediate hosts. The transmission and epidemiology of infections is dependent on water as a medium for motile parasite stages to actively seek hosts (miracidia seeking snails and cercariae seeking vertebrates). Infections are more prevalent in children who are in contact with infected water and in adults labouring in or near water (washing clothes and utensils, farmers, fishermen). Female worms in host veins produce numerous eggs (200-3,000 per day) which use proteolytic enzymes (and sometimes spines) to penetrate the gut or bladder wall and exit the host in faeces or urine. When deposited in water, the embryonated eggs hatch releasing free-swimming miracidia which only live for several hours. In that time, they actively seek suitable intermediate hosts (aquatic or amphibious snails) using chemotaxis and phototaxis (despite absence of eyespots). All *Schistosoma* spp. demonstrate quite narrow host specificity for particular snails: *S. mansoni* infects aquatic *Biomphalaria* spp. (large flat spiral snails ~14 mm in diameter with ~3 whorls and apical aperture), *S. japonicum* infects amphibious *Oncomelania* spp. (small elongate snails ~8 mm long with 4-5 whorls and dextral (right-sided) aperture), and *S. haematobium* infects aquatic *Bulinus* spp. (medium ovoid snails ~12 mm long with 2-3 whorls and sinistral (left-sided) aperture). The snails live in aquatic habitats, including standing waters, flowing streams, irrigated areas, marshy grounds and wet savannah, and they are quite resistant to drought, climate change and pollution. The miracidia invade the soft tissues of the snail and form a mother sporocyst near the site of penetration. Daughter sporocysts are produced 2-6 weeks after infection and they migrate to other organs in the snail (especially the digestive gland or gonads). Schistosomes do not produce redia stages; instead the daughter sporocysts produce cercariae which emerge into the water in their thousands beginning 4 weeks after infection. The fork-tailed cercariae are rapid swimmers and they periodically swim to the surface of the water and then sink in the water column, repeating this fixed behaviour for up to 2-3 days. Hosts entering water bodies in close proximity induce changes in this cyclic swimming behaviour, with cercariae swimming laterally beneath the water surface. The cercariae are attracted to skin secretions and when they come into contact with a prospective definitive host, they attach and actively penetrate the skin within minutes, losing their tails in the process. After 2-3 days, the schistosomula ('little schistosomes') enter the blood and/or lymphatic system and are carried to the right side of the heart and then the pulmonary circulation where they undergo rapid growth for 7-10 days. Schistosomules then move through the left side of the heart and are carried via the systemic circulation to hepatic portal veins where they develop for 3 weeks. Young adult worms then pair, mate and migrate to their predilection sites in the veins of the gut or bladder. Egg production begins from 4-8 weeks after infection, and adult worms normally live for 2-5 years, although some may survive much longer.

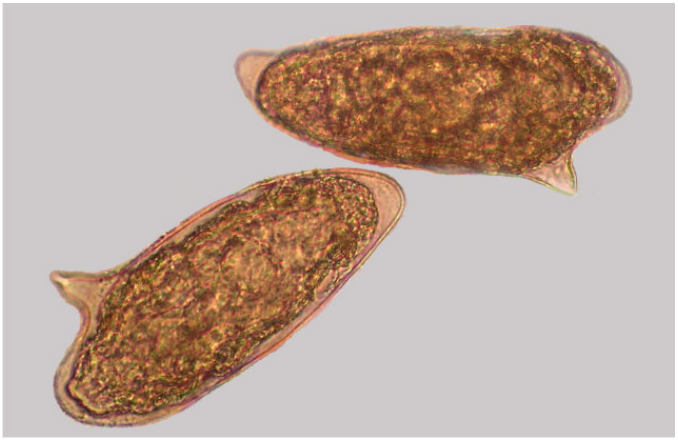
Differential diagnosis: Infections are conventionally diagnosed by the microscopic detection of fluke eggs in faecal or urine samples, often after concentration by sedimentation/floatation or filtration techniques. The eggs are sufficiently characteristic to facilitate specific diagnosis. The eggshell is acid-fast when stained with modified Ziehl-Neelsen stains. Various refinements of coprological tests have been developed to improve sensitivity, including incubating faeces to hatch miracidia which migrate towards a light source. On occasion, microscopy of rectal biopsies (snips) has been used to diagnose *S. haematobium* infections. Various medical imaging techniques may be used to locate worms *in situ*, including radiology, ultrasonography, computerized tomography (CT) and magnetic resonance imaging (MRI). Many immunoserological tests (agglutination, fluorescence, enzyme immunoassays) have been developed to detect host antibodies against infection, but most have experienced cross-reactivity problems and cannot discriminate between active and previous infections. Several techniques (electrophoresis, immunoblotting, chromatography) have also been developed to detect parasite antigens in blood, urine and even milk samples, but most are not species-specific. More recently, molecular techniques have been used to detect, quantify and characterize parasite DNA in host samples by polymerase chain reaction (PCR) amplification of specific gene sequences (nuclear 18S and 28S ribosomal DNA, repetitive sequences, mitochondrial DNA). Excellent results have been obtained in species discrimination, molecular epidemiology and quantifying parasite burdens, but most assays are not yet available outside of specialist laboratories.

Treatment and control: The drug of choice for the treatment of *Schistosoma* infections is praziquantel, a single oral dose being very effective, with low toxicity and good tolerance, even in severe clinical cases. Nitridazole and metrifonate are effective against *S. haematobium*, and oxamniquine against *S. mansoni*, but they have mild side-effects. In some areas, domestic livestock are still treated with older drugs such as antimonial, stibophen, niridazole and trichlorphon, although dosages are protracted. Caution is advised in treating clinical cases as the dislodgement of damaged flukes may result in emboli and occlusion of major veins. While timely treatment is effective, cured individuals rapidly become re-infected in endemic areas. Various control programmes have therefore been developed based on mass chemotherapy in conjunction with preventive measures, including improved sanitation, snail vector control, modifying habitats and farming practices, and public education campaigns. Water contamination can be reduced by preventing the ingress of parasite eggs as well as curtailing the asexual amplification cycle in snail hosts. The provision and use of latrines contains sources of infection, and modern biocomposting toilets appear to be effective in killing parasite eggs when used properly. Snail populations may be reduced by the strategic use of molluscicides (niclosamide or copper sulphate), draining marshes and swamps, and clearing channels of vegetation. Irrigation practices can be modified to avoid long-standing still waters, and different or improved crops can be used which are less dependent on lengthy immersion in water. In endemic areas, farmers (and visitors) need to be aware of the dangers of immersion in potentially contaminated waters. Considerable resources have been devoted to the development of cellular, subcellular and recombinant vaccines, and promising results have been obtained with parasite membrane proteins in animal models of disease.


Schistosoma
mesenteric blood vessels
(cercarial dermatitis,
egg granulomas, haematuria,
portal hypertension, ascites,
hepatosplenomegaly)
female
male
adults *in copula*
(~ 15 mm)
Definitive Hosts
(primates, ungulates,
carnivores, rodents)
excretion
(urine/faeces)
eggs
(~ 110 µm)
skin
penetration
vector-borne transmission
S. japonicum
S. mansoni
S. haematobium
free-swimming
cercaria
(~ 600 µm)
endoparasitic in
tissues of vector
free-swimming
miracidium
(~ 200 µm)
sporocyst
(~ 1 mm)
Biomphalaria
Oncomelania
Bulinus
Intermediate Hosts (planorbid/pomatiopsid snails)
(visceral then glandular tissues)

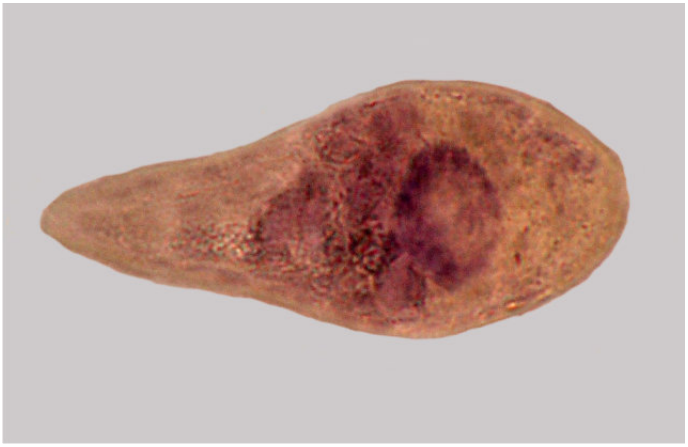


Schistosoma adult worms *in copula*



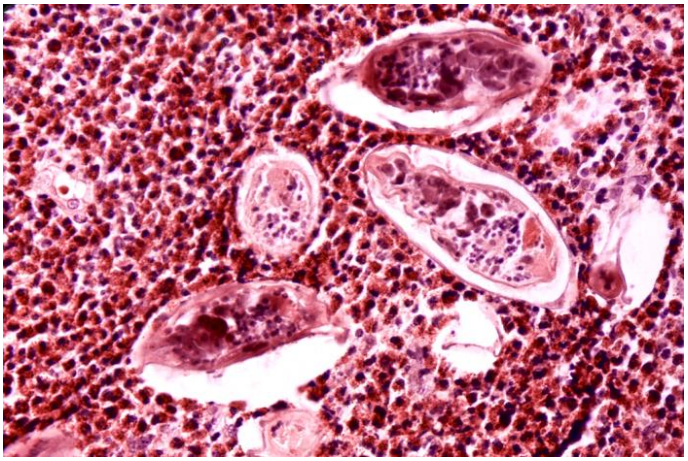
Schistosoma mansoni eggs

Schistosoma japonicum egg



Schistosoma miracidium

Schistosoma cercaria



Schistosoma haematobium egg granulomas