Trematodes or Flukes

Learning objectives

At the end of the session, the students will know

Classification of Trematodes- Systemic classification

Order	Superfamily	Family	Genus and Species
Strigeida	Schistosomatoidea	Schistosomatidae	*Schistosoma haematobium, S. mansoni, S. japonicum S. mekongi, S. intercalatum*
Echinostomida	Paramphistomatoidea	Zygocotylidae	*Gastrodiscoides hominis, Watsonius watsoni*
	Echinostomatoidea	Fasciolidae	*Fasciola hepatica, F. gigantica, Fasciolopsis buski*
Plagiorchiida	Opisthorchioidea	Opisthorchiidae	*Opisthorchis felineus, O. viverrini, Clonorchis sinensis*
		Heterophyidae	*Heterophyes heterophyes, Metagonimus yokogawai*
	Plagiorchioidea	Troglotrematidae	*Paragonimus westermani, Nanophyetus salmincola*

Classification of Trematodes- Based on the habitat

- Blood trematodes (flukes)
- Hepatic trematodes (flukes)
- Intestinal trematodes (flukes)

General characteristics of trematodes

- Trematodes exist in three morphological forms—adult worm, egg and larva.

Adult Worm

The adult worms are unsegmented and flattened dorsoventrally but some have thick fleshy bodies

Eggs

Oviparous, i.e. they lay eggs; which develop into larvae later in the environment

- Eggs - operculated
- Except Schistosomes are eggs are non-operculated (possess a spine).

Larvae

- Trematodes have five larval forms:
  - Miracidium
  - Sporocyst
  - Redia (first and second generation)
  - Cercaria
  - Metacercaria
- Schistosomes differ from other trematodes as they do not have redia and metacercaria larvae (they possess two generations of sporocyst larvae)

Life cycle

- **Host: Trematodes complete their life cycle in three different** hosts:
  - one definitive host (man)
  - two intermediate hosts.
- **First intermediate host -** fresh water snail or mollusk
- **Second intermediate host -** aquatic plant or fish or crab. How ever, schistosomes do not need a second intermediate host.

Mode of transmission

- **By eating** aquatic plants, fishes or crabs harboring infective form (meta cercariae larva)
- Penetration of free living cercariae larva (infective form, in schistosomiasis).

Treatment

- Praziquantel is the drug of choice for all trematodes infection except
- Fasciola, where triclabendazole is recommended.

Differences between schistosomes and other trematodes

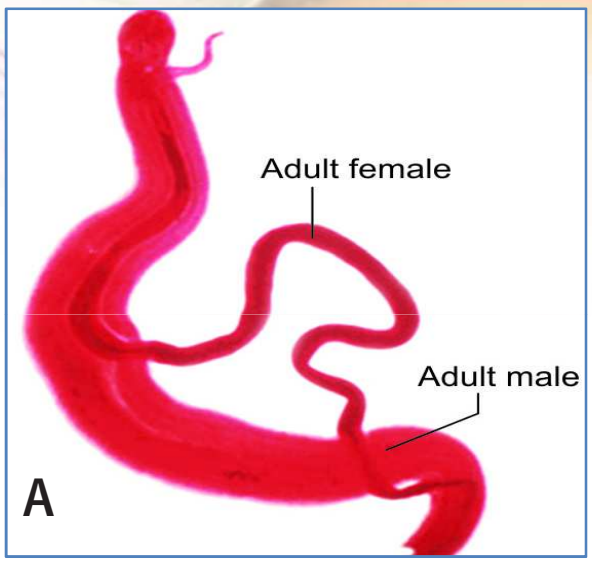
Properties	*Other trematodes*	*Schistosomes*
Host	Definitive: Man Intermediate: • 1st: Snail • 2nd: Plant or fish*	Definitive: Man Intermediate: Snail There is no 2nd intermediate host
Infective form	Metacercaria lava (present inside 2nd intermediate host)	Cercaria lava (present free in water)
Mode of transmission	Ingestion of 2nd intermediate host	Skin penetration
Eggs	Operculated, no spine	Non-operculated, spine present
Larvae	Five stages: Miracidium, sporocyst, redia, cercaria, and metacercaria	Same except: • No metacercaria • No redia • Sporocyst are present in two generations
Adults	Hermaphrodite (male and female organs present in same worm)	Diecious (sexes are separate), female worm lies in the gynecophoric canal of male worm
Fertilization	Self-fertilization	Cross fertilization

Blood flukes

Taxonomy

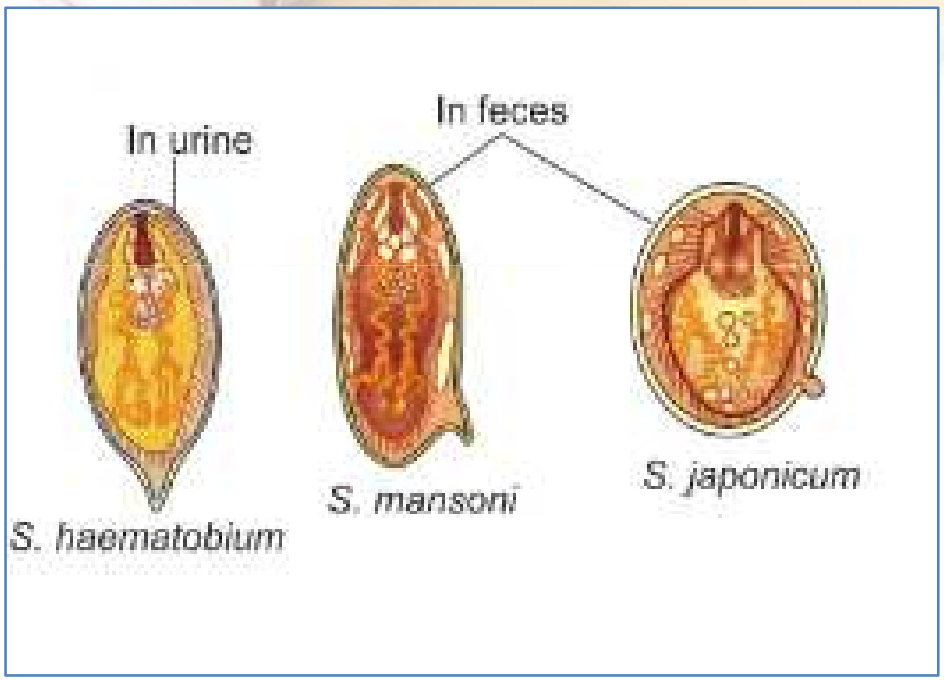
- **Order:** Strigeida
- **Superfamily:** Schistosomatoidea
- **Family:** Schistosomatidae

Morphology-Adult Worm



Adult worms of schistosomes (The thin female worm resides in the gynecophoric canal of the thicker male worm)

Morphology- Eggs



Morphology- Larva

Larval forms are

- Miracidium
- Sporocysts (first and second generations)
- Cercaria.

❖ There are no rediae and metacercariae stages

SCHISTOSOMA HAEMATOBIUM

- **Habitat -** Adult male worm holds the female worm and resides in the venous plexus of urinary bladder and ureter.

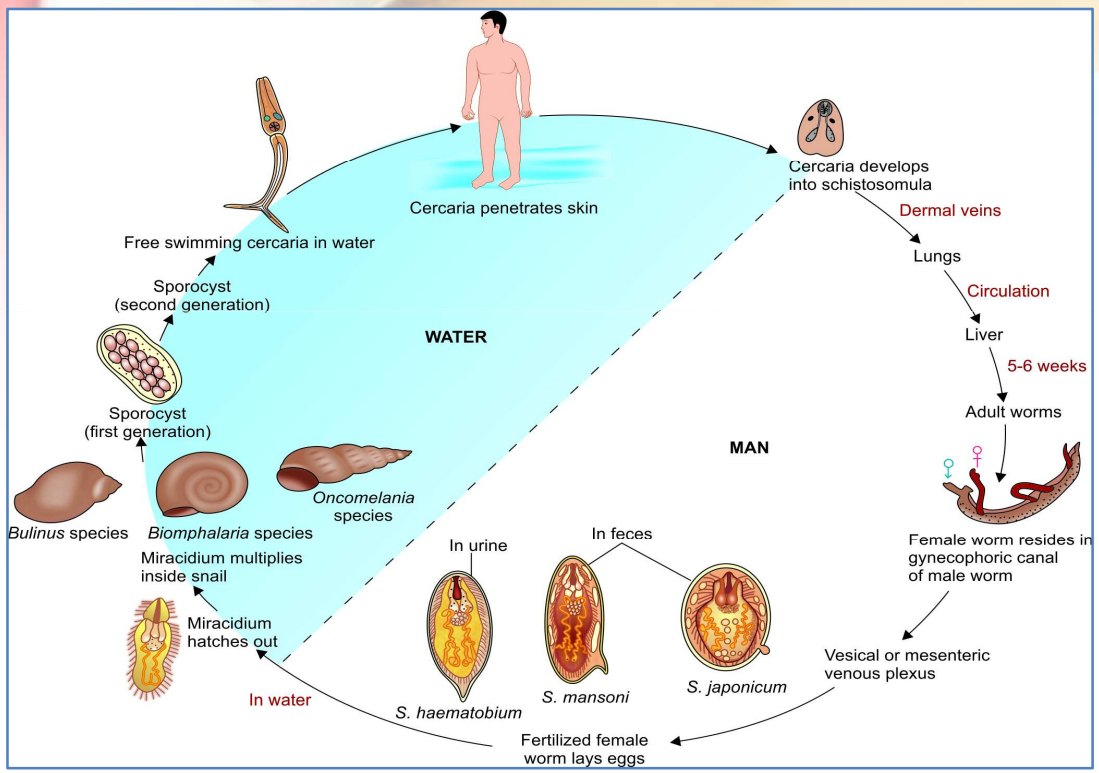
Epidemiology

- *Endemic in 53 countries in the* Middle East, the African continent (across Nile river valley) and the Indian Ocean islands (Madagascar, Zanzibar and Pemba).
- Extremely rare in India.

Life cycle

- **Definitive host:** Man
- **Intermediate host:** Freshwater snails of genus *Bulinus.*
- **Mode of transmission:** Man acquires infection by penetration of skin by the infective form (cercariae) present in contaminated water.

Life cycle of *Schistosoma* species



Pathogenesis and clinical features

Acute Schistosomiasis

- The invasion of cercariae in the skin causes dermatitis at penetration site followed by allergic pruritic papular lesion.
- Migration of schistosomula in lungs causes cough with mild fever.
- **Chronic Schistosomiasis**
- **Urogenital disease**

Pathogenesis and clinical features

Chronic Schistosomiasis

- **Urogenital disease -** cystitis glandularis
- **Obstructive uropathies**
- **Bladder carcinoma -** Squamous cell carcinoma

Laboratory diagnosis

Laboratory Diagnosis	*Schistosoma haematobium*

- **Urine microscopy**—detects terminal spined eggs
- **Histopathology** of bladder mucosal biopsy—detects terminal spined eggs
- **Antibody detection** (serum)—HAMA-FAST-ELISA, HAMA-EITB, IFA, IHA and cercarial Huller reaction
- **Antigen detection** (serum and urine)—CCA and CAA detection by ELISA or dip stick assay.

Cross-over infection

- Though eggs of S. haematobium and S. mansoni are usually found in urine and stool respectively; in heavy infection, S. haematobium eggs can be found in stool and S. mansoni eggs may be passed in urine.
- This is due to adult worms may be found in the vessels that are not their normal habitat.

Schistosoma eggs

Treatment

- Praziquantel is the drug of choice; given 20 mg/kg/dose, two doses in single day.
- **Metrifonate can be give alternatively.**

Prevention

- Proper disposal of human excreta and urine
- Eradication of snails by using molluscicides such as metal salts (iron or aluminum sulfate), metaldehyde, methiocarb and acetylcholine esterase inhibitors
- Treatment of infected persons.

Elimination of schistosomiasis

- The WHO is currently moving towards elimination of schistosomiasis as a public health problem in Africa by 2020 and globally by 2025.
- Achieved through treatment of cases using praziquantel to prevent morbidity in later life and also through mass drug administration in some places (Egypt and China).

SCHISTOSOMA MANSONI

- *S. mansoni* produces intestinal schistosomiasis in humans.
- **Habitat -** Adult male and female worms reside in mesenteric veins draining sigmoidorectal region.
- **Epidemiology**
  - No cases have been reported from India so far.

Morphology

- Adult worms are similar to other schistosomes with
- some minor differences
- Nonoperculated eggs have characteristic lateral spine.
- Fork tailed cercaria is the infective form.

Life cycle

Life cycle of *S. mansoni is similar to S. haematobium except:*

- Humans are the definitive host; sometimes other vertebrate hosts like monkeys, chimpanzees and dogs may act as reservoir and definitive host
- Fresh water snails of *Biomphalaria species are* intermediate hosts
- Pre-patent period is about 4–7 weeks
- Adult worm lives in mesenteric veins draining sigmoidorectal region.

Pathogenesis and clinical feature

- **Cercarial Dermatitis**
- **Acute Schistosomiasis (Katayama Syndrome)**
  - Acute phase of disease occurs within 4–8 weeks of infection, especially when the schistosomes start producing eggs.
  - Antigens (released from eggs) and the adult worms stimulate the host humoral response, leading to the formation of immune complexes and serum sickness like illness called **Katayama fever**

Chronic Schistosomiasis

- Intestinal disease - granuloma formation around the eggs in the intestine.
- Hepatosplenic disease - Granuloma formation and fibrosis in liver
- Pulmonary involvement
- Neuroschistosomiasis involving brain and spinal Cord
- Kidney: Nephrosclerosis and kidney failure
- Liver abscess: *S. aureus colonizes the granuloma leading to liver abscess.*

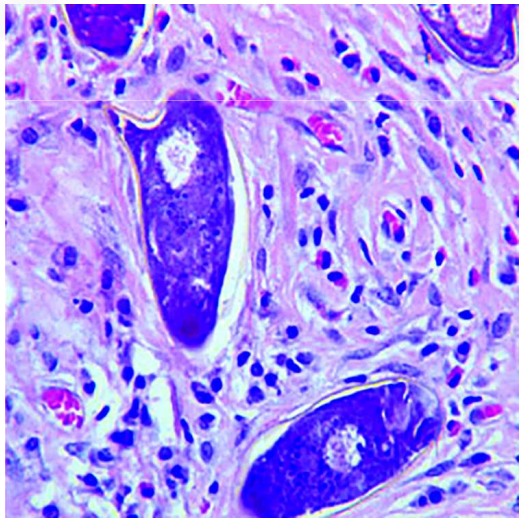
Laboratory diagnosis

Stool Microscopy:

- Acute cases, eggs with lateral spine can be demonstrated in stool or rarely in urine
- In chronic cases or in patients with low worm burden, the number of eggs excreted in stool is less and intermittent.

Laboratory diagnosis (cont..)

- **Rectal Biopsy Specimen -**Histopathological demonstration of lateral spined eggs in biopsy material from rectal mucosa



Laboratory diagnosis (cont..)

- **Antibody Detection -** Less useful as they cross-react with other helminth infections
- **Antigen Detection -** Useful for assessing the severity of disease and to monitor the efficacy of treatment.
  - ELISA is available to detect circulating schistosome antigens (CCA and CAA) in the serum and urine
  - Dipstick test is available for detecting CCA in urine

Treatment

- Praziquantel is the drug of choice; given 20 mg/kg/dose, two doses in single day.
- Oxamniquine is also very effective.

SCHISTOSOMA JAPONICUM

- Most pathogenic species among the schistosomes.
- Only schistosome species that shows zoonotic transmission.

Habitat and epidemiology

- **Habitat -** Adult worms reside in the mesenteric veins draining the ileocecal region.
- **Epidemiology -** *Most commonly in China,* Indonesia and Philippines. It is eradicated from Japan since 1960.
- No cases have been reported from India so far.

Morphology

- Adult worms are similar to other schistosomes with the following differences:
- **Tegument: The body surface is smooth**
- Eggs are relatively smaller and more spherical than those of other schistosomes and have rudimentary lateral spine

Life cycle

- Life cycle of **S. japonicum is similar to that of *S. mansoni*** with few exceptions:
- Definitive host is mainly man and some times domestic animals like cat, dog and cattle
- Intermediate host—snails of *Oncomelania species*
- Prepatent period is around 5 weeks
- **Higher egg output: The female worm lays more than** 3,000 eggs/day.

Pathogenesis and clinical features

- Cercarial dermatitis
- Katayama fever
- Intestinal disease: Deposition of egg granulomas in the intestinal wall (large intestine) leads to mucosal hyperplasia, ulcers, micro abscess formation and sometimes, pseudopolyposis with blood loss
- Hepatosplenic disease
- Cerebral schistosomiasis
- Carcinoma: Both colorectal carcinoma and liver carcinoma

Laboratory diagnosis

- The diagnostic methods of *S. japonicum is similar to that of S. mansoni.*
- *The additional information tests:*
  - Pyrosequencing
  - Magnetic fractionation method

Treatment

- Praziquantel is given 20 mg/kg/dose, three doses in single day.

Vaccine

- No vaccine is licensed

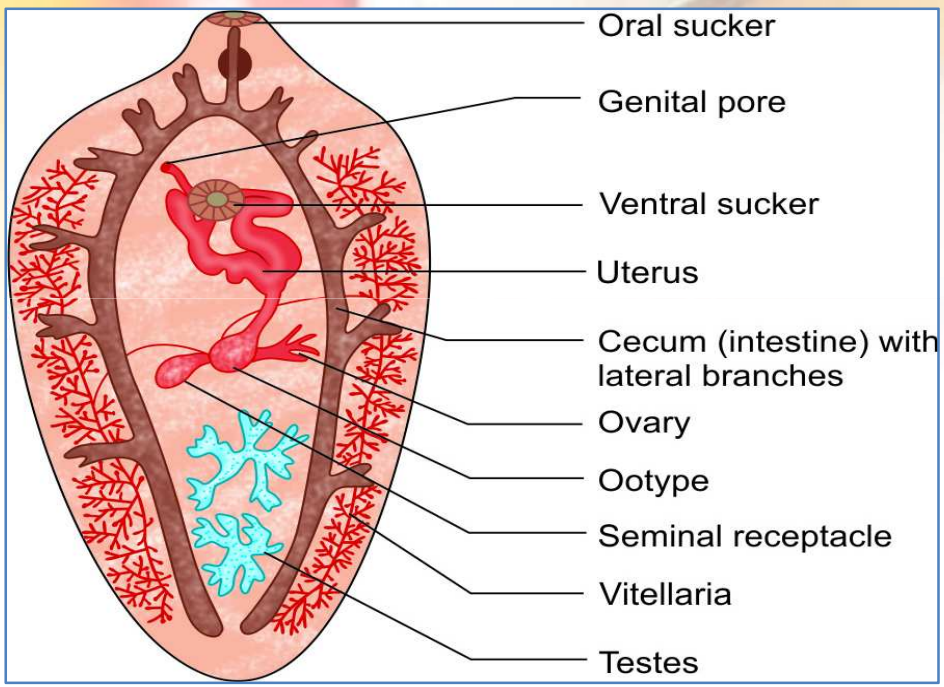
Comparison of species of *Schistosoma*.

Features	*Schistosoma haematobium*	*Schistosoma mansoni*	*Schistosoma japonicum*
Habitat of adult worm	Vesical and pelvic venous plexuses	Mesenteric veins draining sigmoidorectal region	Mesenteric veins draining ileocecal region
Tegument	Small tubercles	Large papillae with spines	Smooth
Size (male)	15 × 0.9 mm	12 × 0.8–1 mm	15 × 0.5 mm
Size (female)	20 × 0.25 mm	16 × 0.25 mm	22 × 0.3 mm
Number of testes	4–5 in cluster	6–9 in cluster	7 in linear
Uterus	With 20–100 eggs at one time	Short; one egg at one time	Long; contain 50 eggs at one time
Egg	Elliptical with sharp terminal spine; 112–170 × 40–70 μm in size Egg shell is not acid-fast, miracidium larva inside egg is acid-fast	Elliptical with sharp lateral spine; 114–180 μm × 45–73 μm in size Eggs shell is acid-fast	Oval to almost spherical; rudimentary lateral knob; 70–100 μm × 50–65 μm in size Egg shell is acid-fast
Egg discharged in	Urine	Feces	Feces

LIVER FLUKES – FASCIOLA HEPATICA

- Fasciola hepatica, also known as the common liver fluke or sheep liver fluke.
- The disease is called fascioliasis.

Morphology- Adult



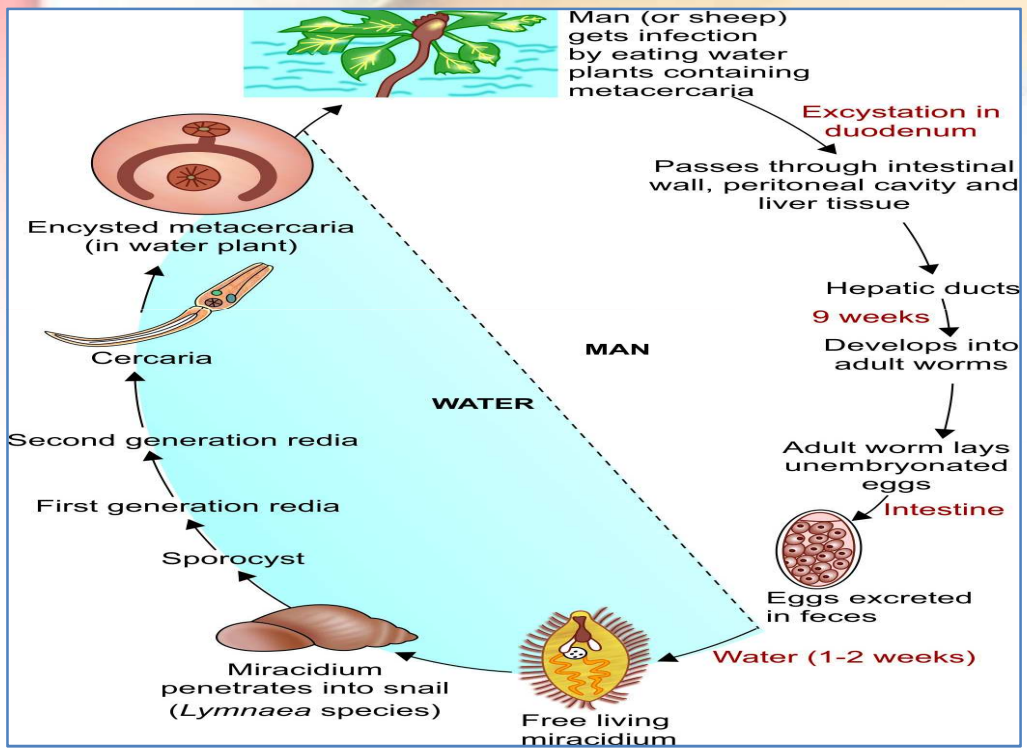
Egg

Eggs are oval, bile stained, unembryonated and operculated

Life cycle

- **Host: Sheep is the principal definitive host. Goats cattle** and humans are other definitive hosts.
- The amphibian snails (Genus: *Lymnaea) are the first intermediate* hosts
- Water plants serve as the second intermediate hosts.
- **Mode of transmission: The sheep and other definitive** hosts including man get infection by eating water plants and water cress containing metacercariae.

Life cycle


Man (or sheep) gets infection by eating water plants containing metacercaria
Excystation in duodenum
Passes through intestinal wall, peritoneal cavity and liver tissue
Hepatic ducts
9 weeks
Develops into adult worms
MAN
Adult worm lays unembryonated eggs
Intestine
Eggs excreted in feces
Water (1-2 weeks)
Free living miracidium
Miracidium penetrates into snail (Lymnaea species)
Sporocyst
First generation redia
Second generation redia
Cercaria
Encysted metacercaria (in water plant)
WATER

Pathogenesis

- Incubation period varies from days to few months.
- **Acute disease -** develops during metacercarial migration (1–2 weeks after infection) and includes fever, Right upper-quadrant pain, hepatomegaly and eosinophilia.
- **Chronic phase -** Liver parenchyma is inflamed with formation of multiple subcapsular abscesses (called as liver rot). Bile duct obstruction by adult worm and biliary cirrhosis are also reported but less commonly.
- Halzoun or Marrara syndrome

Laboratory diagnosis

- **Stool Microscopy -**Typical operculated eggs can be demonstrated in the stool specimen
- Operculated eggs of *F. hepatica* are morphologically similar to that of *F. gigantica, F. buski, Echinostoma and Gastrodiscoides*
- **Spurious infection (pseudofascioliasis):** eggs may be detected in the stool of people who have eaten *F. hepatica infected liver. This can be* differentiated from true infection by stool examination of the patient, 3 days after a liver free diet.

Laboratory diagnosis (cont..)

- **Antibody Detection -** helps in early diagnosis before the eggs are detected in stool.
  - ELISA, counterimmune electrophoresis and Western blot techniques
- **Molecular Methods -** PCR-based methods are available to detect *F. hepatica specific genes in stool specimens. PCR is highly sensitive*
- **Other Methods -** Imaging methods

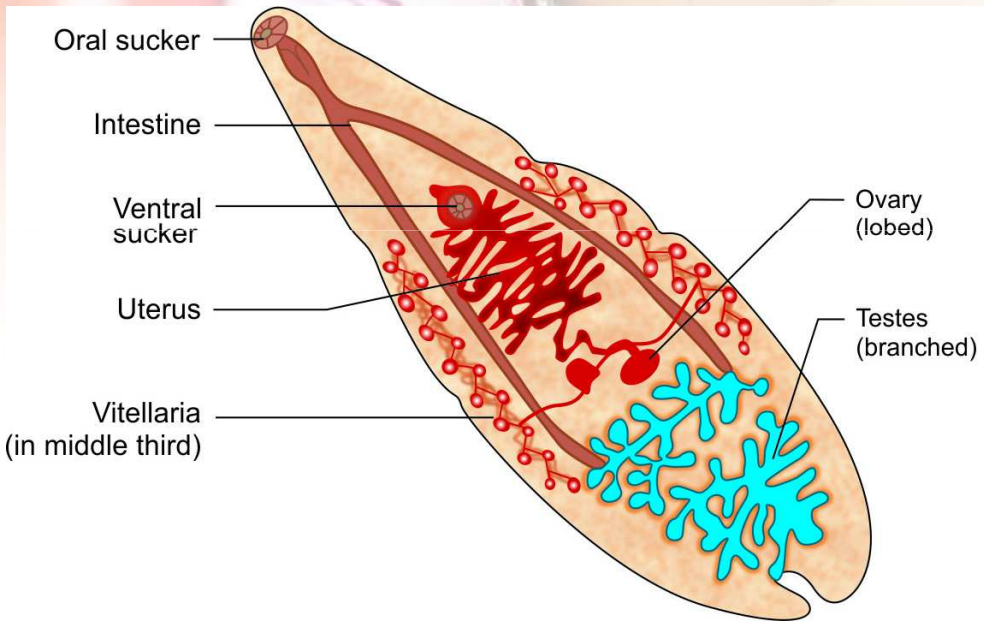
FASCIOLA GIGANTICA

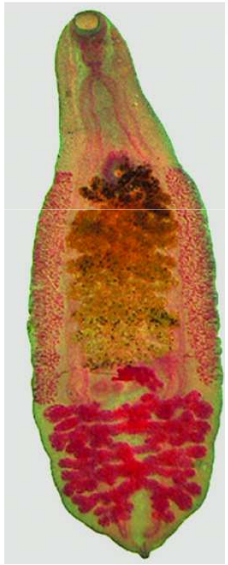
- Life cycle: Similar to that of *F. hepatica. Only difference* is first intermediate host is aquatic snail
- Clinical features and laboratory diagnosis and treatment: Same as that of *F. hepatica.*

CLONORCHIS SINENSIS

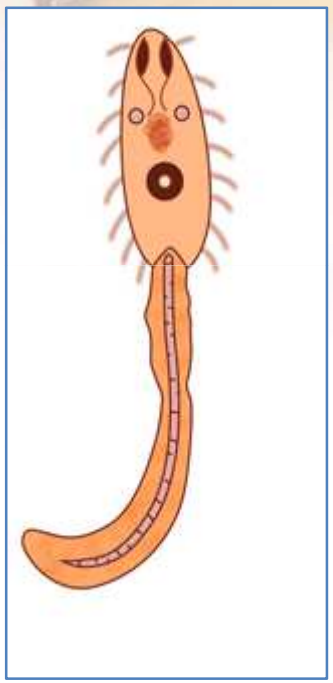
- **Habitat -** Adult worm lives in the bile duct, pancreatic duct and common bile duct of man and other domestic animals.
- **Epidemiology -** found primarily in Eastern Asia like China, Korea, Japan and Malaysia; infects over 35 million peopleglobally.
- However, infections from India are not reported so far though the first case was detected from Kolkata.

MORPHOLOGY
ADULT WORM



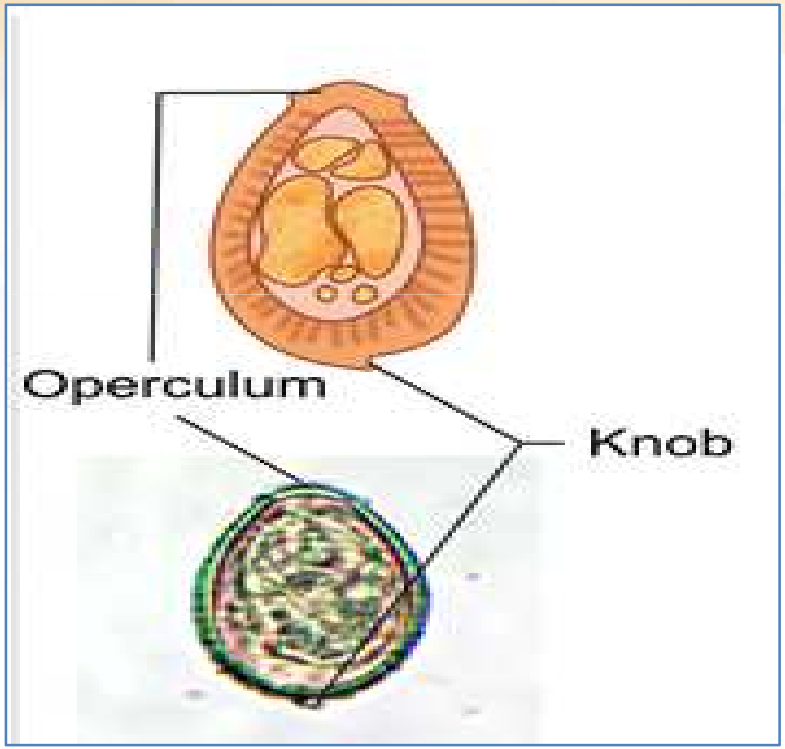


MORPHOLOGY
CERCARIA LARVA

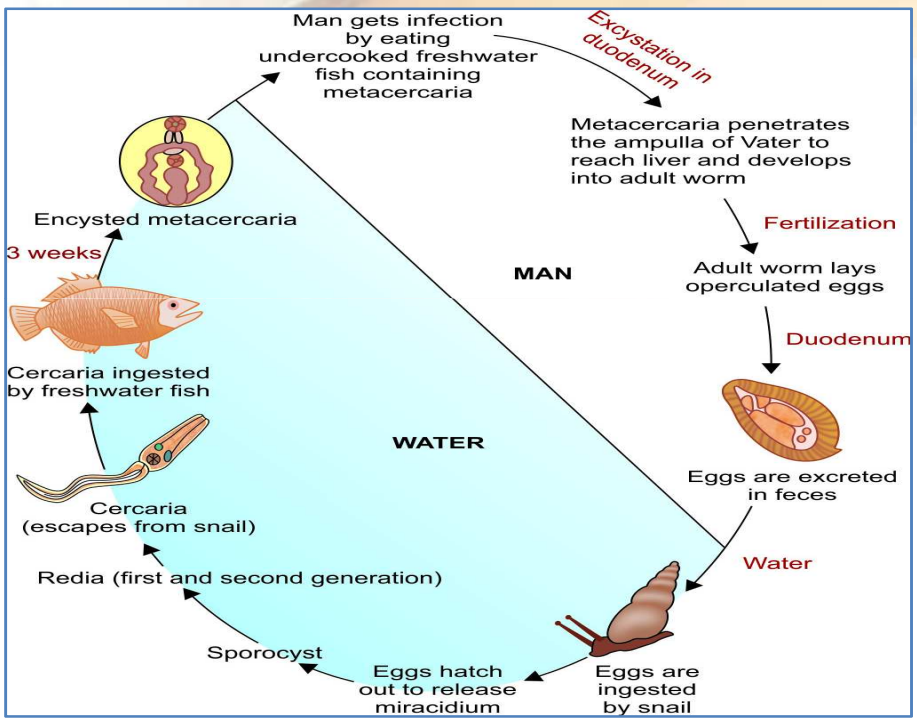


MORPHOLOGY
EGG

(saline mount) showing the small knob at the abopercular end (flask-shaped appearance)



Life cycle of Clonorchis sinensis



Pathogenesis

- **In light worm burden: People are usually asymptomatic**
- **In chronic infection with heavy worm burden:**
  - Mechanical obstruction of the bile duct and irritation due to toxin released by the flukes leads to cholangitis, dilatation of the bile duct and bile retention
  - **Bile duct carcinoma: Chronic irritation of the bile** duct for long periods can lead to **cholangiocarcinoma.**

Laboratory diagnosis

- **Stool Microscopy -** Demonstration of the characteristic flask-shaped eggs in the stool establishes the diagnosis.
- **Antibody detection: ELISA using recombinant** propeptide of cathepsin L proteinase (rCsCatLpropeptide) is available for detection of specific IgG4 antibodies.
- **Antigen detection: ELISA is also available for detection** of circulating antigen in the serum

Laboratory diagnosis (cont..)

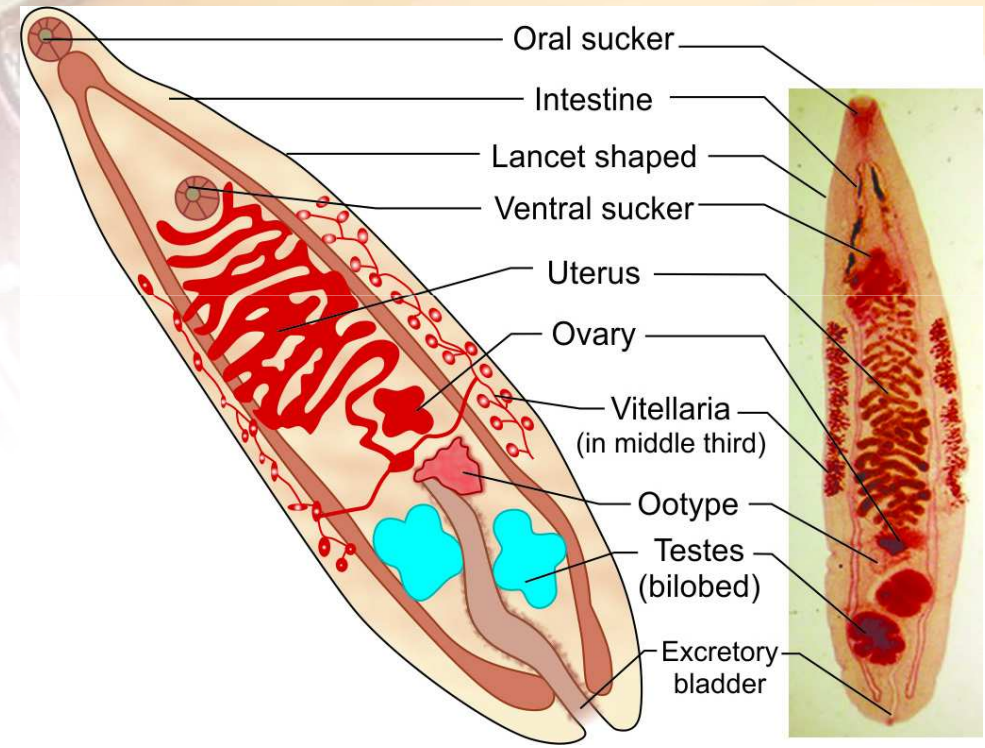
- Molecular Methods - multiplex PCR; Real-time PCR is developed targeting mitochondrial NADH dehydrogenase subunit 2 (nad2) DNA elements.

Treatment

- Praziquantel (25 mg/kg, three doses in 1 day) is the drug of choice

OPISTHORCHIS VIVERRINI - MORPHOLOGY

- ADULT WORM



MORPHOLOGY- Eggs

- Eggs measure 27 µm × 15 µm in size, flask shaped with an operculum and a knob, similar to that of *C. sinensis*.

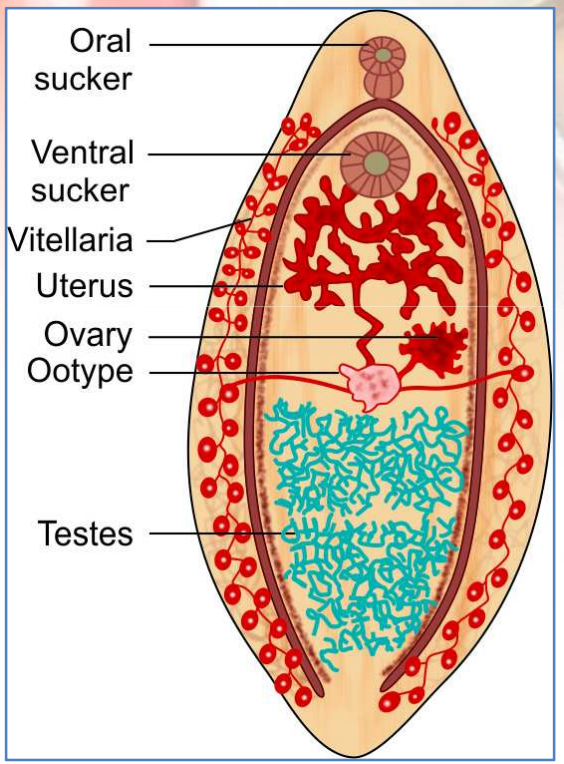
MORPHOLOGY-LARVAE

- Metacercaria is the infective form of the parasite.
- Found in the flesh of the fresh water fish. Other larval stages are cercaria, redia, sporocyst and miracidium.

INTESTINAL FLUKES- FASCIOLOPSIS BUSKI

- **Habitat -** found in the mucosa of duodenum and jejunum of man and pig.
- **Epidemiology -** *mainly endemic in Southeast Asian countries* such as India, China, Pakistan, Bangladesh, Thailand and Malaysia.
- Risk factors include poverty, unhygienic sociocultural practices, food habits and availability of open type of pig farms

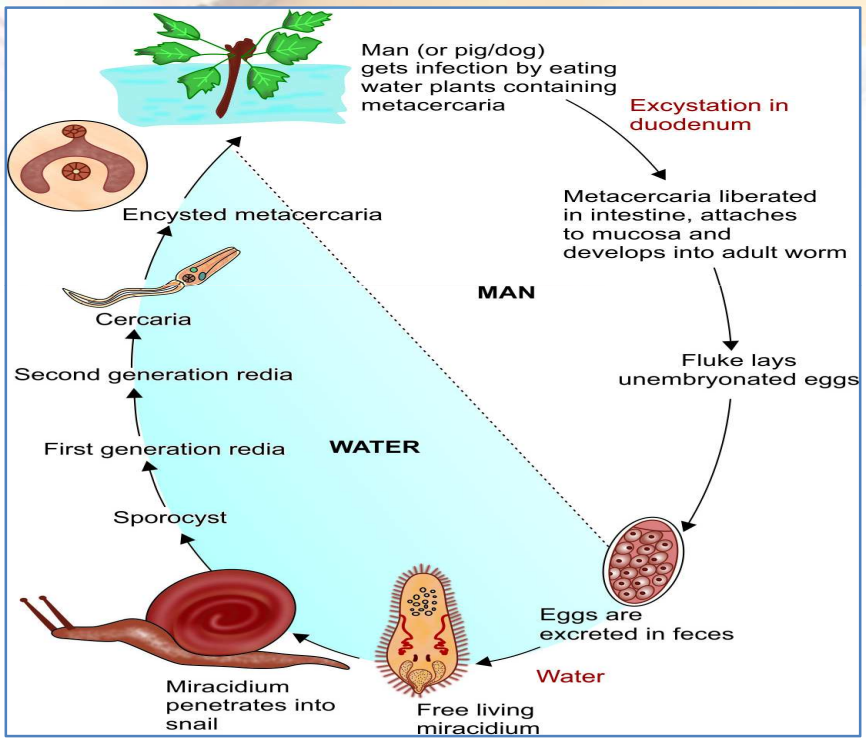
Morphology- Adult Worm



MORPHOLOGY (cont..)

- Eggs are large (130–140 µm × 80–85 µm size), operulated and bile stained eggs, similar to that of *F. hepatica.*
- **Larvae -** Metacercaria is the infective form to man and pig.

Life cycle


Man (or pig/dog) gets infection by eating water plants containing metacercaria
Excystation in duodenum
Metacercaria liberated in intestine, attaches to mucosa and develops into adult worm
MAN
Fluke lays unembryonated eggs
Eggs are excreted in feces
Water
Free living miracidium
Miracidium penetrates into snail
Sporocyst
First generation redia
Second generation redia
Cercaria
Encysted metacercaria
WATER

Pathogenesis

- **Light infection: It may be asymptomatic or its** attachment to intestinal mucosa leads to local inflammation, ulcerations with mucus and blood in stool
- **In severe infection: Partial obstruction** of intestinal tract, malabsorption and protein losing enteropathy, marked eosinophilia and leukocytosis

Laboratory diagnosis

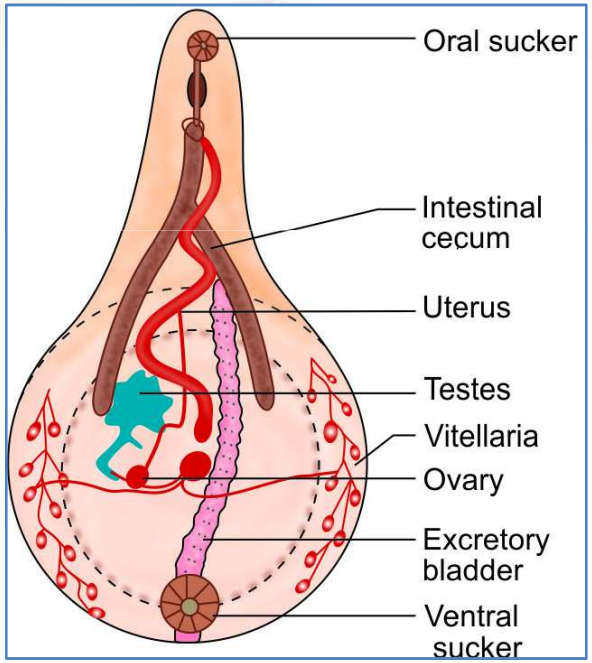
- Detection of large number of operculated eggs in the stool sample gives probable diagnosis of *F. buski.*

Treatment

- Praziquantel is the drug of choice. It is given as 25 mg/kg, three doses in 1 day
- Niclosamide is given alternatively.

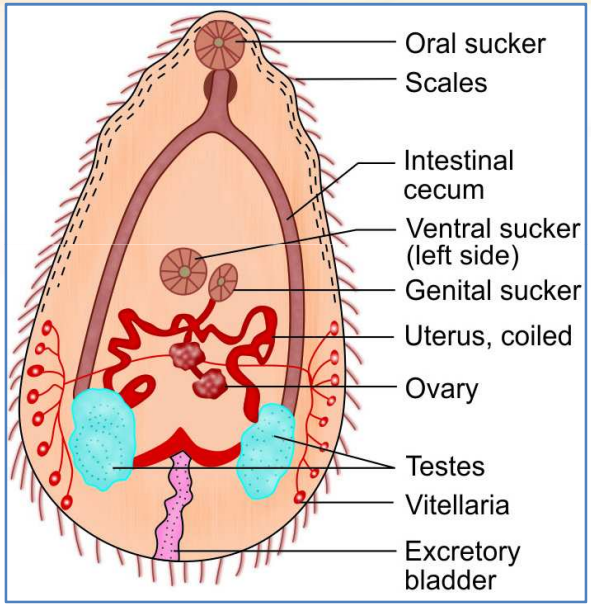
OTHER LESS COMMON INTESTINAL TREMATODES

- **Gastrodiscoides hominis**



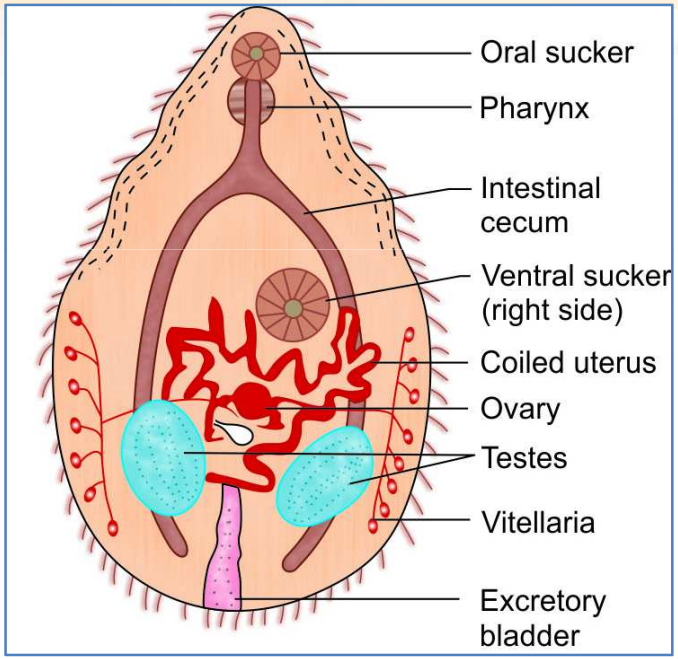
OTHER LESS COMMON INTESTINAL TREMATODES

- Heterophyes heterophyes



OTHER LESS COMMON INTESTINAL TREMATODES

- Metagonimus yokogawai



LUNG FLUKE – PARAGONIMUS WESTERMANI

- *Paragonimus westermani* is also known as oriental lung fluke.
- Causes endemic hemoptysis in man.

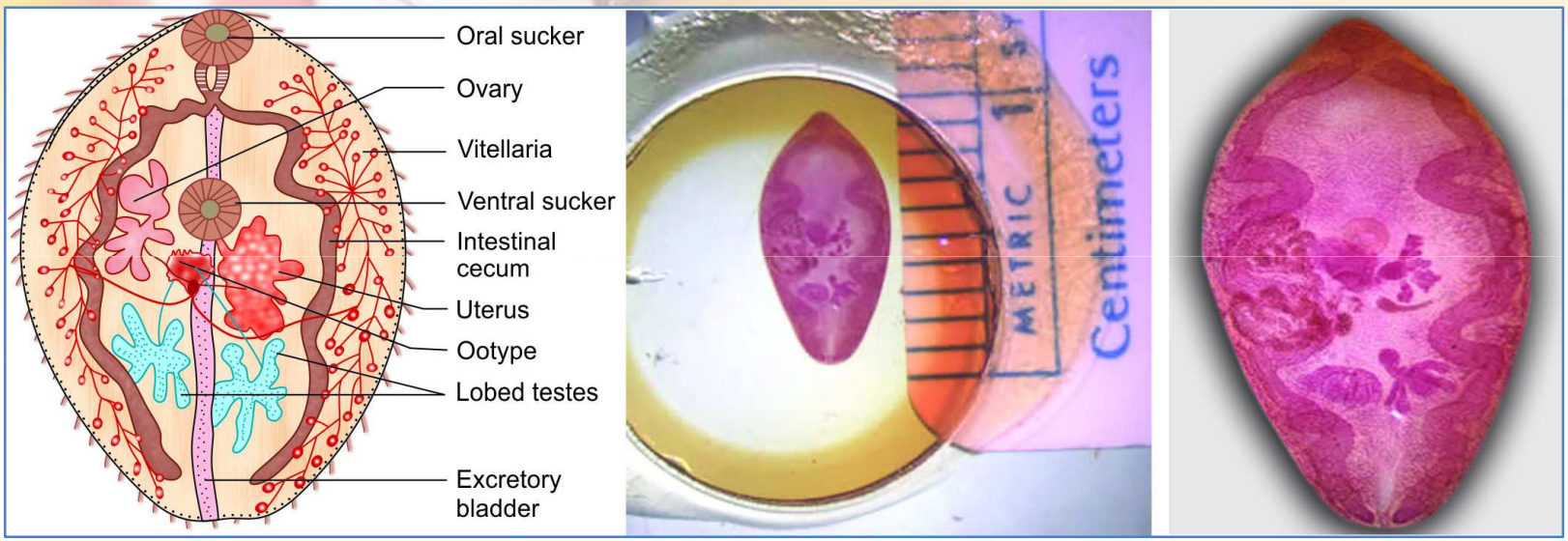
Epidemiology

- Paragonimiasis is endemic in Northeast states of India.
- Many cases are reported from **Manipur** with a prevalence of 6.7%.

Habitat

- Adult worm lives in the parenchyma of lung.

MORPHOLOGY – ADULT WORM



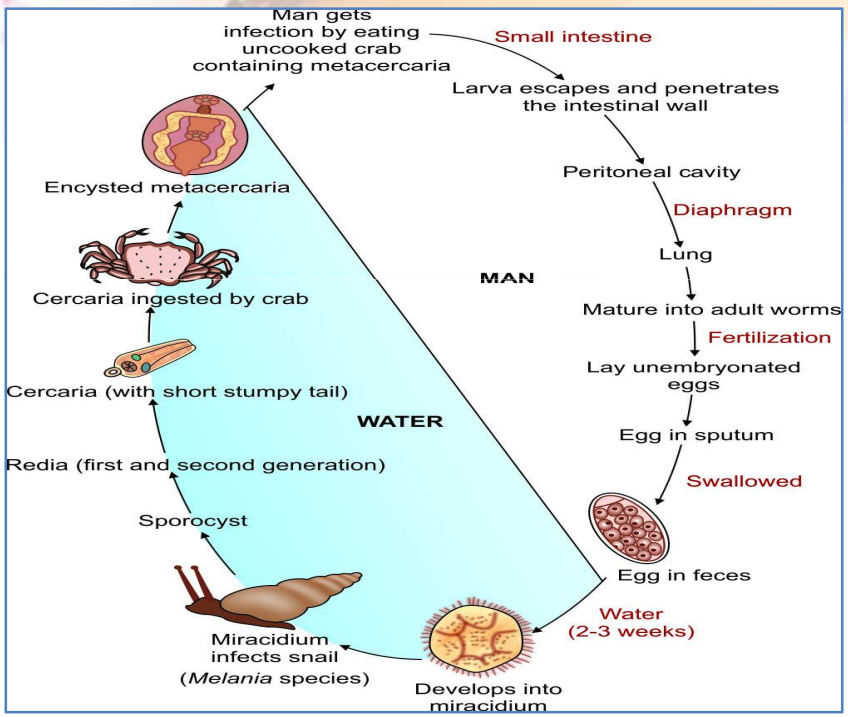
LIFE CYCLE

- **Host: *P. westermani completes its life cycle in one definitive*** host (man, or dogs and cats)

Two intermediate hosts:

- first—snail (Genus: *Melania* or *Semisulcospira* and *Brotia* species),
- second—crabs or crayfishes.
- **Mode of transmission: Man acquires infection by** eating uncooked, partially cooked, salted, or pickled crab or crayfish

Life cycle (cont..)



Pathogenesis

- Pulmonary Paragonimiasis
- Extrapulmonary Paragonimiasis –
  - Cerebral paragonimiasis
  - Cutaneous paragonimiasis: Migratory subcutaneous nodules
  - Larva migrans

LABORATORY DIAGNOSIS

Laboratory Diagnosis	*Paragonimus westermani*

- **Sputum microscopy**—detects operculated eggs
- **Serological tests**—antibody detection (DIGFA, ELISA, western blot), antigen detection (Dot ELISA)
- **Imaging methods**—MRI, CT scan, X-ray can detect lesions in lungs and other organs
- Peripheral blood eosinophilia.

TREATMENT

Treatment	*Paragonimus westermani*
❑ Praziquantel (25 mg/kg/dose, three doses per day for 2 days) is the drug of choice for treatment of paragonimiasis ❑ Bithionol and niclofolan can also be used with 100% cure rate without any side effect ❑ Triclabendazole is also recommended ❑ Surgical management may be needed for pulmonary or cerebral lesions.	