

(SCHISTOSOMIASIS/BILHARZIASIS)

HUMAN BLOOD FLUKES:

- Three major species:
- Schistosoma haematobium
- Schistosoma mansoni
- Schistosoma japonicum

Minor species:

- Mekongi
- Malayensis
- Intercalatum

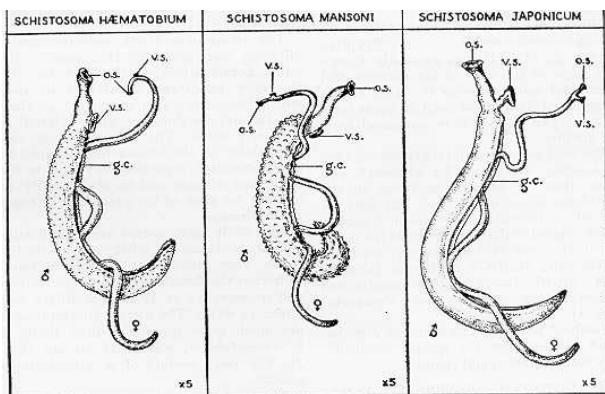


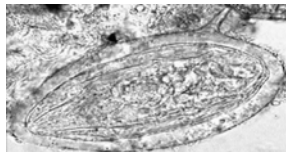
FIG. 2. Schematic representation of the three most important schistosomes of man. *gc*, Gynecophoric canal; *os*, oral sucker; *vs*, ventral sucker. Notice the difference in tuberculations. (From Belding, D. L., *Clinical Parasitology*, Appleton-Century Co., New York, 1942.)

FEATURES OF HUMAN SCHISTOSOMES

- they develop in the portal venous system and adult flukes (depending on species) live in the vein of the intestine or bladder
- Sexes are separate
- Unlike most trematodes, they are not flattened and leaflike.
- They are long and worm-like
- Humans are the only definitive host
- Transmission is by contact with water containing the infective form of parasite (cercariae)

Schistosoma mansoni eggs

These eggs are large (length 114 to 180 µm) and have a characteristic shape, with a prominent lateral spine near the posterior end. The anterior end is tapered and slightly curved. When the eggs are excreted, they contain a mature miracidium

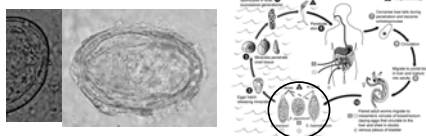


S. haematobium egg: In this species, the eggs are large and have a prominent terminal spine at the posterior end. Length 112 to 170 µm.



S. japonicum egg

the egg is typically oval and has a vestigial spine. Schistosoma japonicum eggs are smaller (68 to 100 µm by 45 to 80 µm) than those of the other species.



Transmission

- Pollution of fresh water with excreta containing Schistosome eggs



- Presence of the snail host



Snail from genus Biomphalaria


- Human contact with water infested with cercaria




<http://www.cdfound.to.it/HTML/sch1.htm>

Main intermediate snail hosts that transmit human schistosomiasis

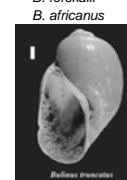
S. Mansoni (<i>Biomphalaria</i>)	S. intercalatum (<i>Bulinus</i>)	S. hematobium (<i>Bulinus</i>)	S. japonicum (<i>Oncamelania</i>)	S. mekongi (<i>Tricula</i>)
Africa B. Pfeifferi B. Alexandrina B. Sudanica	B. globosus B. forskalii	B. truncatus B. globosus B. forskalii B. africanus	O. hupensis	T. aperta




Americas
B. glabrata
B. straminea
B. tenagophila




Biomphalaria glabrata



Bulinus truncatus



Bulinus globosus, the intermediate host snail for *Schistosoma haematobium* (courtesy WHO/TDR)
www.fgp.usd.ac.be/~copper/biostechschisto.html



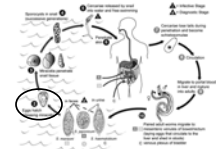
Oncamelania hupensis

Schistosome miracidium

- Eggs hatch releasing **miracidia**
- 200 μ m length and 40 μ m diameter
- Swims at 2 mm/sec by beating of the cilia
- Remain infective for 8-12 h
- Infects the snail
- They accumulate around the snail or in a drop of snail-conditioned water

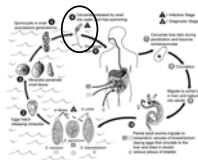
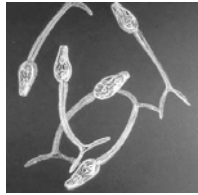


Miracidium Swimming towards Snail Intermediate Host



Cercaria in the water

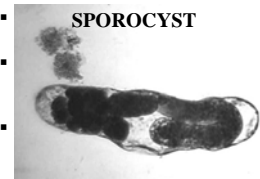
- First escape into the hemolymph and then through the snail's integument
- Swim into the surrounding water to find their definitive host
- Swims by alternating side-to-side rhythmic contractions
- It is composed of a body 125 μ m long by 25 μ m in diameter to which a 200 μ m long tail is attached



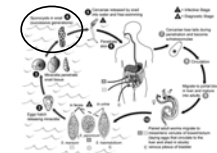
<http://www.personal.leeds.ac.uk/~bgy1mj/cercaria.html>

Intramolluscan stages

- The miracidium penetrates the snail
- It sheds the epithelium and remodel its surface (2 h approx.)
- A new surface layer appears around the newly formed **sporocyst**
- A new syncytial tegument is formed
- Primary sporocyst:** hollow, fluid filled germinal sac
- Daughter sporocysts** in less than a week (35-600)
- Cercaria** by 3-4 weeks after infection (1500/day for 18 days)



SPORO CYST



<http://www.personal.leeds.ac.uk/~bgy1mj/sporocyst.html>

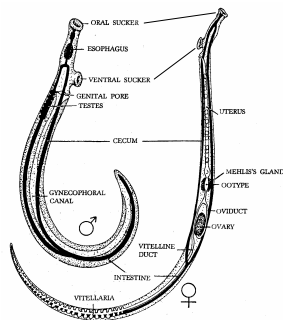
Morphology of Adult Schistosoma

Female worms are thin and long – resides in the gynecophoral canal of male

- reproductive organs are arranged linearly

Both sexes have oral sucker and acetabulum.

Intestine (cecum) divides, then fuses near middle of the body.



Morphology of Adult Schistosoma

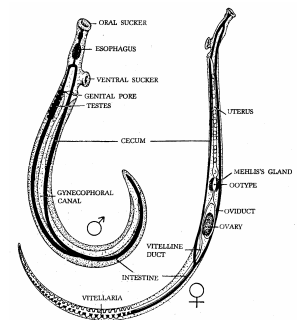
Schistosoma is _____.

Male worms are shorter and stouter than females.

- males have _____

_____ ventral longitudinal groove in which the female resides

- several testes** are located behind the acetabulum



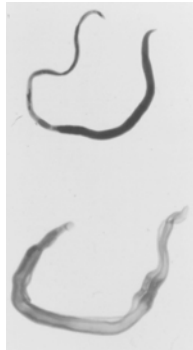
Differences of Adult Schistosoma

Adults of the 3 species differ in:

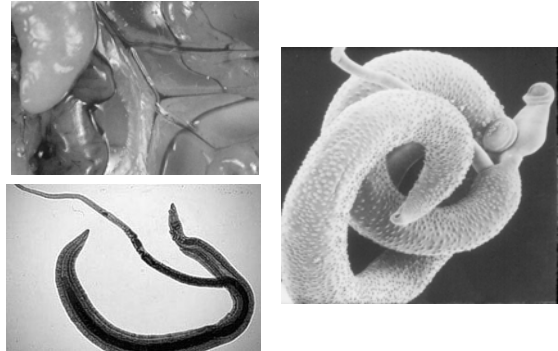
- 1.
- 2.
- 3.
- 4.

However, there is overlap of many characteristics.

We will not be responsible for identification to species.



Morphology of Adult Schistosoma



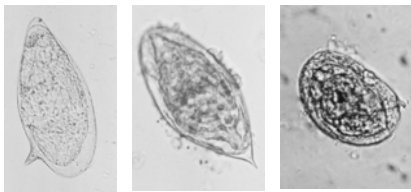
Differences of Schistosoma Eggs

Specific diagnosis is determined by ID of eggs

S. mansoni - elliptical egg with _____

S. haematobium - elliptical egg with _____

S. japonicum - round to oval egg with _____



Differences of Adult Schistosoma

Comparative morphology of the three primary species of human schistosomes

Characteristic	<i>S. haematobium</i>	<i>S. mansoni</i>	<i>S. japonicum</i>
Tegumental papillae	Small tubercles	Large papillae with spines	Smooth
Size			
Male			
Length	10 to 15 mm	10 to 15 mm	12 to 20 mm
Width	0.8 to 1 mm	0.8 to 1 mm	0.5 to 0.55 mm
Female			
Length	ca 20 mm	ca 20 mm	ca 26 mm
Width	ca 0.25 mm	ca 0.25 mm	ca 0.3 mm
Number of testes	4 to 5	6 to 9	7
Position of ovary	Near midbody	In anterior half	Posterior to midbody
Uterus	With 20 to 100 eggs at one time; average 50	Short; few eggs at one time	Long; may contain up to 300 eggs; average 50
Vitellaria	Few follicles, posterior to ovary	Few follicles, posterior to ovary	In lateral fields, posterior quarter of body
Egg	Elliptical, with sharp terminal spine; 112 to 170 μm \times 40 to 70 μm	Elliptical, with sharp lateral spine; 114 to 175 μm \times 45 to 70 μm	Oval to almost spherical; rudimentary lateral spine; 70 to 100 μm \times 50 to 70 μm

Pathogenesis of Schistosomiasis

Eggs that do not leave the body are swept to the pre-sinusoidal capillaries of the liver and are trapped there (or in the bladder wall)

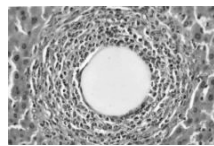
The immune system responds and walls off the eggs with a granuloma, the egg dies

Continuous stimulation of the immune system leads to regulation or fibrosis (less or more morbidity)

Periportal fibrosis leads to portal hypertension

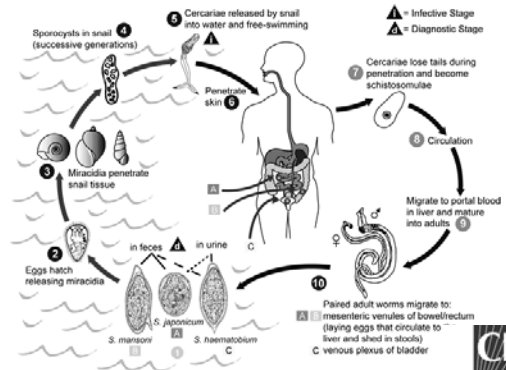
Portal hypertension leads to collateral esophageal varices, blood circulation, loss (Sm; Sj)

Continuous aggravation in the bladder wall leads to carcinoma of the bladder (Sh)



Granuloma in a mouse liver formed around a Schistosoma egg coupled with schistosome egg secreted proteins.
<http://www.york.ac.uk/res/schisto/proteomics.htm>

Schistosome life cycle





Egyptian boy with hepatosplenomegaly, ascites fluid build-up and superficial collateral circulation (NAMRU-3 clinical ward in Cairo)

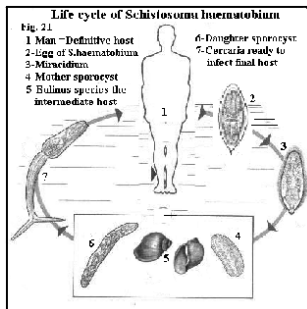
The morbidity spectrum of schistosomiasis mansoni

'Intestinal' asymptomatic schistosomiasis at the Egyptian village level



Clinical symptoms

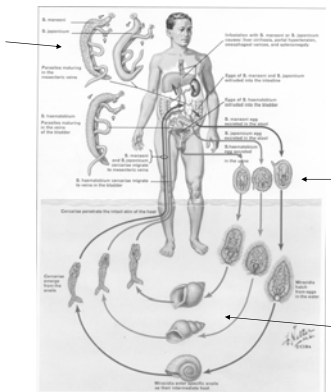
- Schistosomiasis is an immunologic disease.
- Symptoms are rarely seen except in heavily infected individuals.
 - Skin penetration-local dermatitis: within 24 h
 - Migration of the schistosomula: chills, fever, sweating, cough, diarrhea, leukocytosis
- Acute phase (Katayama diseases by *S. japonicum*)
 - fever, chills, headache, anorexia, urticaria, and diffuse megaly, lymphadenopathy and diffuse vasculitis lesions
 - 2-3 weeks after the infection and usually lasts 1-2 months (typhoid fever)
- Chronic disease-most important
 - Fatigue, bowel and bladder symptoms, hepatic dysfunction
 - Hepatosplenomegaly because of portal obstruction
 - *S. haematobium*: urinary tract infection, inflammation, squamous cell epithelioma, hydronephrosis and fibrosis of ureters



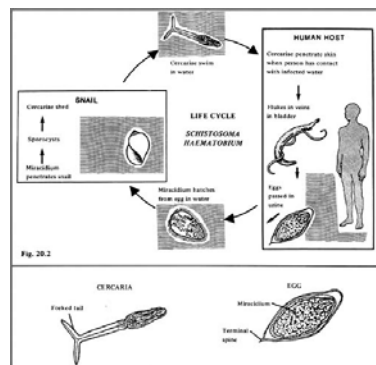
SCHISTOSOMA HAEMATOBIMUM

causes urinary schistosomiasis, schistosomal hematuria, vesical schistosomiasis, or urinary bilharziasis

Differences in Life Cycles of 3 species

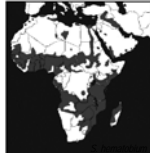
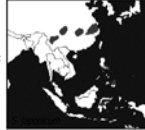
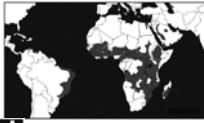


LIFE CYCLE



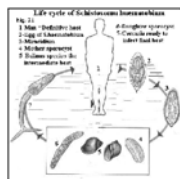
Geographic distribution

- *Schistosoma mansoni*
 - Africa (52 countries) , Caribbean, Eastern Mediterranean, South America
- *Schistosoma japonicum*
 - Asian countries and the Pacific region
- *Schistosoma haematobium*
 - Africa (54 countries), Eastern Mediterranean
- *Schistosoma intercalatum*
 - African Countries (10)



GEOGRAPHICAL DISTRIBUTION
Tropical and subtropical. Africa, Iran, Iraq, Saudi Arabia, Yemen, Syria, India, Mauritius, Malagasy Republic, Zanzibar

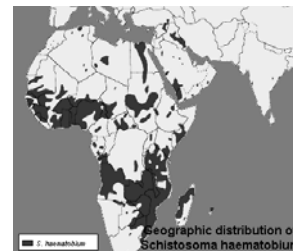
Snail: *Bulinus truncatus*



Schistosoma haematobium

Distribution - through Africa and in parts of the Middle East

Co-exists with _____ in much of Africa especially along the Nile River Valley.



PATHOGENESIS

Eggs trapped in the bladder wall and surrounding tissues cause inflammatory formation of granulomata reactions with the (contains egg, toxic products, eosinophils, epitheloid cells, and lymphocytes). Many of the eggs die and become calcified known as "sandy producing what are patches" in the bladder. In heavy infection, eggs can be carried to other parts of the body

PATHOGENESIS

skin rash at site of cercarial penetration (swimmer's itch)
within a few days after penetration, the young flukes become coated with host red cell antigens and histocompatibility antigens, so they are not recognized as foreign and live free from host attack to develop and produce eggs for long periods
it is the eggs not the adult flukes which are responsible for the clinical features and damage to the bladder or ureters

SYMPTOMATOLOGY

in some areas, *S. haematobium* infection has been linked to an increase in *Salmonella typhi* and *S. paratyphi* carriers following acute infection patients are more likely to become urinary rather than fecal carriers

patients may also exhibit a syndrome of chronic, intermittent, enteric bacteremia that clinically resembles Kala-azar

Both of these chronic bacterial infections have been attributed to a mechanism of adhesion of the bacteria to the integument of the intravascular schistosomes.

SYMPTOMATOLOGY

in light infections, symptoms may not develop for years

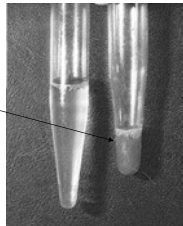
in heavy infections, symptoms may be just noticed as early as 1 month after infection following prolonged untreated infection and marked cellular response, the ureters may become obstructed and the bladder wall thickened, leading to abnormal bladder function with painful and frequent urination, urinary infection, and eventually kidney damage.

terminal hematuria is the most characteristic symptom.

Pathology of *Schistosoma haematobium*

1. _____
- eggs in the tissues of the urinary bladder cause inflammation. Intense pain occurs at end of urination.

2. _____
- blood in the urine is common



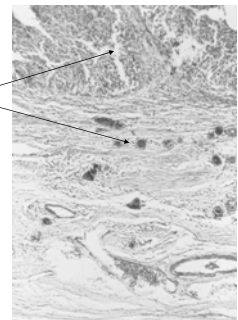
Schistosoma haematobium

Adults live in the _____

Most eggs pass through the wall of the urinary bladder and are voided in the urine.

Invasion of other organs by eggs?

Thus, this species is considered to be the **least pathogenic** of the 3 species.



LABORATORY DIAGNOSIS:

specific

Finding the eggs or occasionally the hatched miracidia in the urine

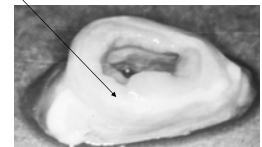
occasionally, eggs can be found in faeces detecting eggs in rectal biopsy or bladder mucosal biopsy

Eggs of *S. haematobium*. White Ciliated, and rapidly motile arrows show the position of the miracidium

Pathology of *Schistosoma haematobium*

3. _____
deposition around eggs in the urinary bladder wall is common and tissues lose their elasticity.

4. Infection also increases the likelihood of



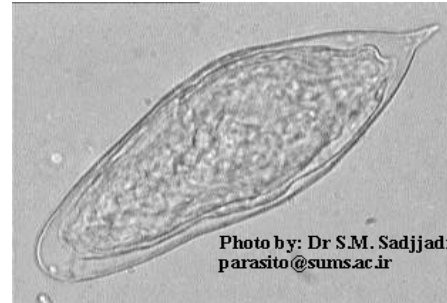
Again, all pathology is caused by the eggs.

Adults cause no pathology.

NON-SPECIFIC FINDINGS

hematuria
proteinuria
cells, especially eosinophils can
often be found in the urine
bacteriuria may accompany urinary
schistosomiasis

Schistosoma haematobium egg



Schistosoma mansoni

Diagnosis

- Travel history (in non-endemic areas).
- A history of dermatitis or Katayama fever.
- Urine dipstick for blood +/- protein (terminal haematuria)
- Blood eosinophilia
- Urine microscopy (for the ova)
- Stool microscopy
- Rectal biopsy
- Serological markers

Schistosoma mansoni adult male and female

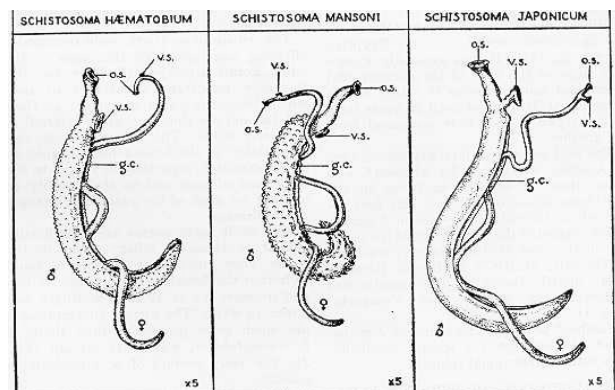
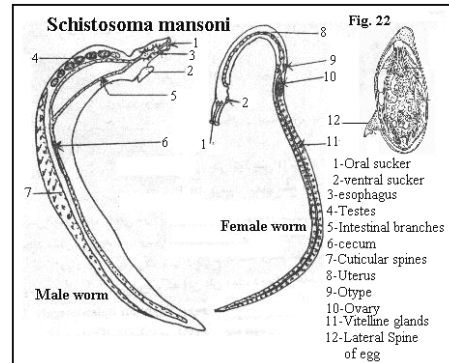
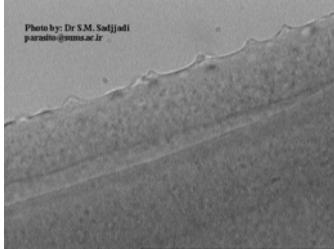


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GEOGRAPHICAL DISTRIBUTION

Parts of Africa, Middle East, South America (Brazil), West India

Biomphalaria snail



PATHOGENESIS/SYMPTOMATOLOGY

splenomegaly
portal hypertension
ascites
ova can be deposited in the spinal cord, lungs, and the body other organs of
Salmonella infections can become chronic and prolonged

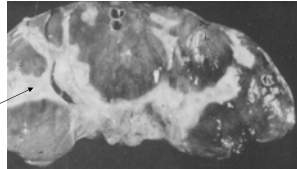
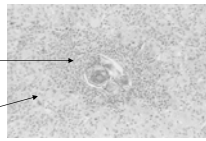
PATHOGENESIS/SYMPTOMATOLOGY

skin rash after cercarial penetration
flukes acquire host antigen protecting them from host immune response
eggs penetrate through the intestinal wall and are excreted in the faeces often with blood and mucus
host reaction to eggs leads to the formation of granulomata, ulceration, and thickening of the bowel through wall a proportion of the eggs reach the liver the portal vein
reaction to the eggs causes thickening of the portal vessels known as claypipe-stem fibrosis
hepatomegaly with fibrosis

Pathology of *Schistosoma mansoni*

2. Eggs are swept up the hepatic portal vein into the liver

- _____ is followed by scar tissue formation of _____
- **cirrhosis** and **hepatosplenomegaly** occur

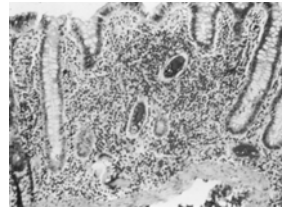


Cirrhosis – areas of scar tissue in liver

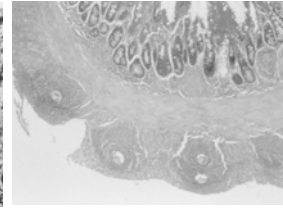
Pathology of *Schistosoma mansoni*

1. Eggs in the _____ stimulate host inflammatory reaction followed by fibrous scar tissue deposition.

- Fibrous scar tissue forms nodules along the large intestine.
- Some eggs make their way through the intestine to enter the feces



Inflammatory reaction to eggs



Fibrous scar tissue nodules

Schistosoma mansoni egg in section of liver

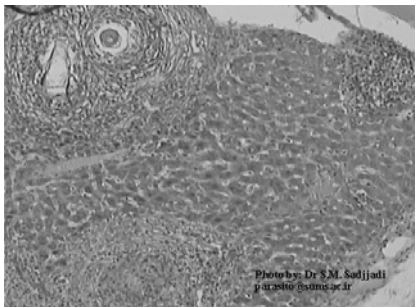


Photo by: Dr S.M. Sadjjadi
parasito@sumed.ac.ir

Pathology of *Schistosoma mansoni*

- _____ (accumulation of fluid in abdominal cavity) is common
- This produces the typical "**swollen belly**" associated with chronic schistosomiasis



LABORATORY DIAGNOSIS

finding *S. mansoni* ova in faeces
occasionally may also be found in the urine following fecal contamination

Rectal biopsy especially after a patient has been partially treated

Schistosoma mansoni egg in section of intestine

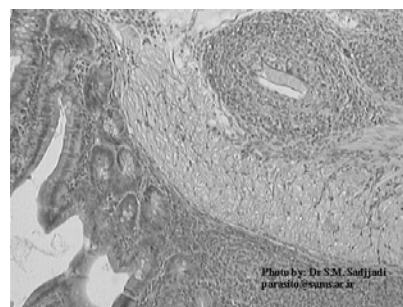


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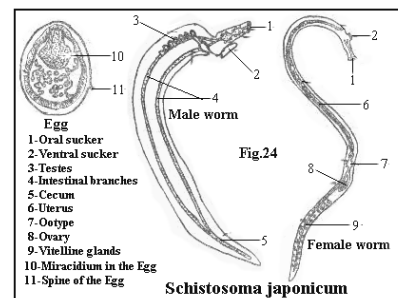
SCHISTOSOMA JAPONICUM

OTHER FINDINGS
mucus and blood are often present in fecal specimens
blood eosinophilia
for patients with hepatic involvement, increased liver enzymes,
low serum albumin,
increased serum protein due to increased globulin

GEOGRAPHICAL DISTRIBUTION

China, Philippines, Western Indonesia
Eastern Visayas and Mindanao

Oncomelania snail



LABORATORY DIAGNOSIS

Finding of the ova in faeces
Typical ova on rectal biopsy
Serologic tests
Circumoval Precipitin Test (COPT)
ELISA

PATHOGENESIS/SYMPTOMATOLOGY

skin rash at the site of cercarial penetration
20-60 days after infection, patient develop fever, muscular and abdominal pain, spleen enlargement, urticaria, and eosinophilia (Katayama reaction or Katayama fever)
Reactions to eggs in the tissue can cause intestinal or hepatosplenic disease with dysentery, liver fibrosis, marked hepatosplenomegaly egg deposition in the lungs, CNS, and other parts of the body
Portal hypertension with prominent ascites

**OTHER SCHISTOSOMA
SCHISTOSOMA INTERCALATUM**

similar to Schistosoma mansoni In terms of life cycle, pathology and clinical feature
intermediate host is the Bulinus snail

SCHISTOSOMA MEKONGI

similar to Schistosoma japonicum in terms of life cycle, pathology, and clinical features

intermediate host is the snail
Lithoglyphopsis aperta

OTHER FINDINGS

Mucus and blood in fecal specimen
blood eosinophilia
in patients with hepatic involvement
raised hepatic enzymes,
low serum albumin,
increased total protein due to increased globulin

Treatment of schistosomiasis

Type of Compound	<u>Praziquantel</u>	<u>Oxamniquine</u>
	Isoquinilone	Tetrahydroquinilone
Active against	All Species	<i>S. mansoni</i>
Dosage	40-60mg/kg Single dose	15-40mg/kg 1-2 doses
Cure Rate	70%-100%	80%-100%
Main Side Effects	Diarrhea, Nausea Abdominal pain	Dizziness Drowsiness
Price/adult dose	\$0.25 - \$3	\$2 - \$5
Mode of Action	Calcium Channel blocker ?	Delayed action Alkylation ?

As with egg excretion
Effective treatment also requires host responsiveness

TREATMENT

Praziquantrel
40-50 mg/kg Single dose
25 mg/kg Two doses
20 mg/kg Three doses

**Control measures/
Possible Points of Attack**

- Sanitation, Water Supply & Community** •
 - Health education; Hygiene •
 - Socioeconomic development ==> toilets & water systems •
- Snail Control** •
 - Molluscicides; Competitors/Predators; Habitat •
 - reduction/closed irrigation; Environmental modification
- Chemotherapy** •
 - Target, Coverage -- Process & Outcome Indicators •
 - Delivery options/Integration with other control programs •
 - Prevalence/**Intensity/Morbidity** •
 - Vaccine (not for a long time)** •
 - Discovery, Process development, Testing •
 - Re-infection studies & immune correlates •

PREVENTION AND CONTROL

- Health Education
- Control snail vector
- Environmental method
- Removing the environmental requirement of the snails
- drainage of breeding sites and proper management of irrigation system
- removal of shade or shelter from the sun by clearing vegetation
- armed bodies of water
- prevention of breeding on the banks of streams or irrigation canals by living these concretes or making these more perpendicular
- acceleration of flow of water by proper grading and clearing of the stream bed and removal of debris
- construction of ponds if the area cannot be drained
- covering snail habitats with land fills
- Chemical method
- Environmental sanitation

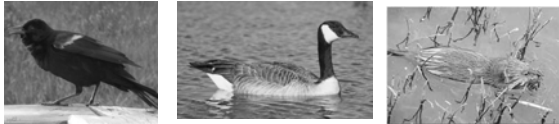
Swimmer's Itch

3 genera of schistosomes cause swimmer's itch in the Midwest:

Gigantobilharzia - adult blood flukes occur in mesenteric veins of _____

Trichobilharzia - adults in mesenteric veins of _____

Schistosomatium - adults in mesenteric veins of _____



Swimmer's Itch

Swimmer's itch is caused by _____

Swimmer's itch is common in Midwest and along coastal areas of the U.S.

- itch was first described at U. Michigan Biological Station in 1936

- extensively studied in Wisconsin in the 1930's & 40's

- problem is common in Wisconsin lakes and occasional outbreaks occur (recent outbreak in Half Moon Lake in Eau Claire)

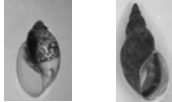


Life Cycle of Swimmer's Itch

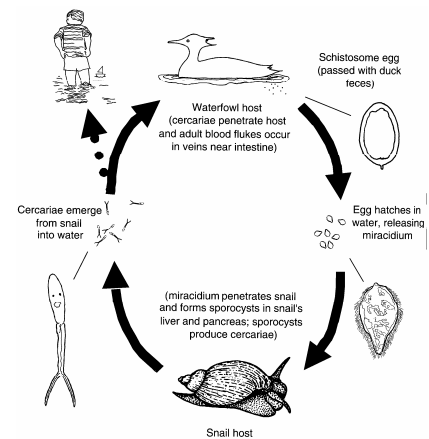
Humans become infected when snail intermediate hosts of these parasites release _____ which mistake humans for the definitive host.

Infection results when _____

Snail hosts are common pond snails in the genera *Physa* and *Lymnaea*.



Life Cycle

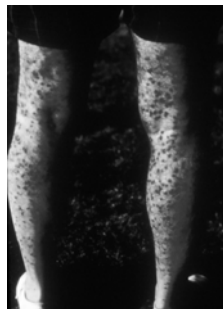


Pathology of Swimmer's Itch

Dermatitis is mild in initial exposures but may become severe in persons exposed to previous outbreaks – called _____

Itching and breaking of skin may lead to secondary infections.

Rash has been misdiagnosed as the _____



Pathology of Swimmer's Itch

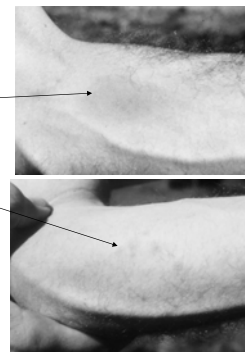
Cercariae penetrate epidermis but are unable to enter the dermis.

Cercariae die in the epidermis and an _____ is produced against the dead cercariae

Formation of a _____

(dermatitis) occurs at the sites of cercarial penetration.

Intense itching also occurs.



Swimmer's Itch

Swimmer's itch is a problem to _____

- Swimming beaches are common sources of infection.
- First outbreaks occur in late June and early July when vacationers are numerous.

But problem is often kept hushed, as resort owners don't want you to know that swimmer's itch is a problem in their lake, as they don't want to lose business.



Treatment and Prevention of Swimmer's Itch

TREATMENT - topical creams such as _____ reduce the itching and _____ reduce the inflammatory response



PREVENTION – best way to reduce swimmer's itch is to _____

- Snail control efforts (using copper sulfate as molluscicide) have been attempted but generally have been unsuccessful.
- Removal of bird or mammal definitive hosts is not possible.

