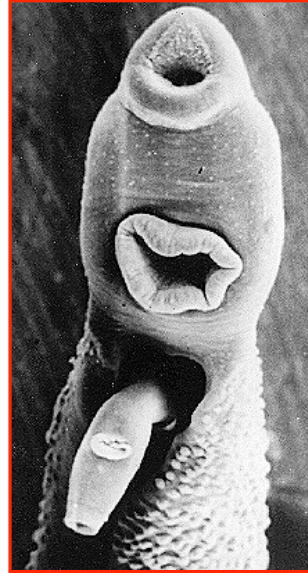


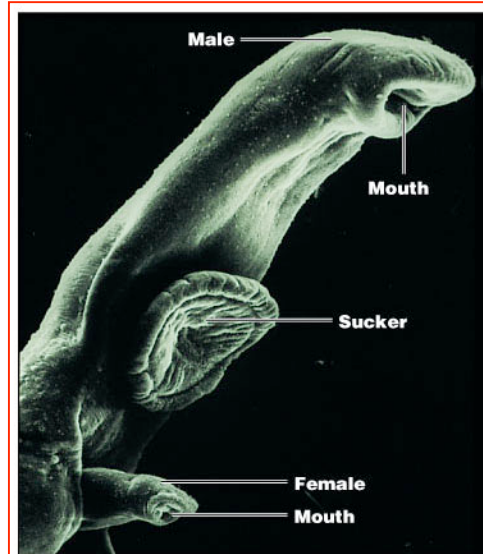
Schistosomes

- Different type of trematode
 - Sexes are separate
 - Adults are round, not flattened
 - Eggs have no operculum
 - Cercaria have a forked tail
- What properties are similar?
 - Two suckers
 - Similar tegument
 - Incomplete digestive tract
 - Intermediate host is a snail
 - Similar life cycle stages



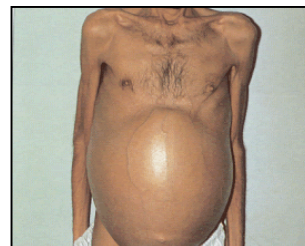
Schistosoma sp. - blood flukes

- **Definitive Hosts:** Humans, wild mammals including dogs, cats, deer, primates, horses, swine, cattle. Least host specific.
- **First Intermediate Host:** aquatic snails.
- **Second Intermediate Host:** None
- **Geographic Distribution:** Depends on the species. See distribution slides



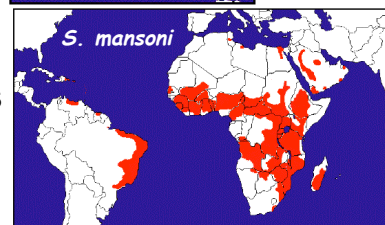
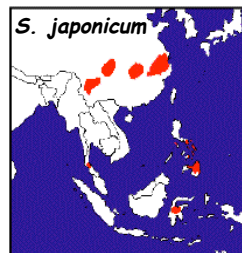
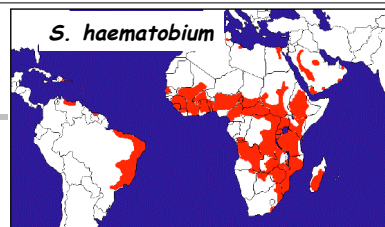
Schistosomiasis - "Bilharzia"

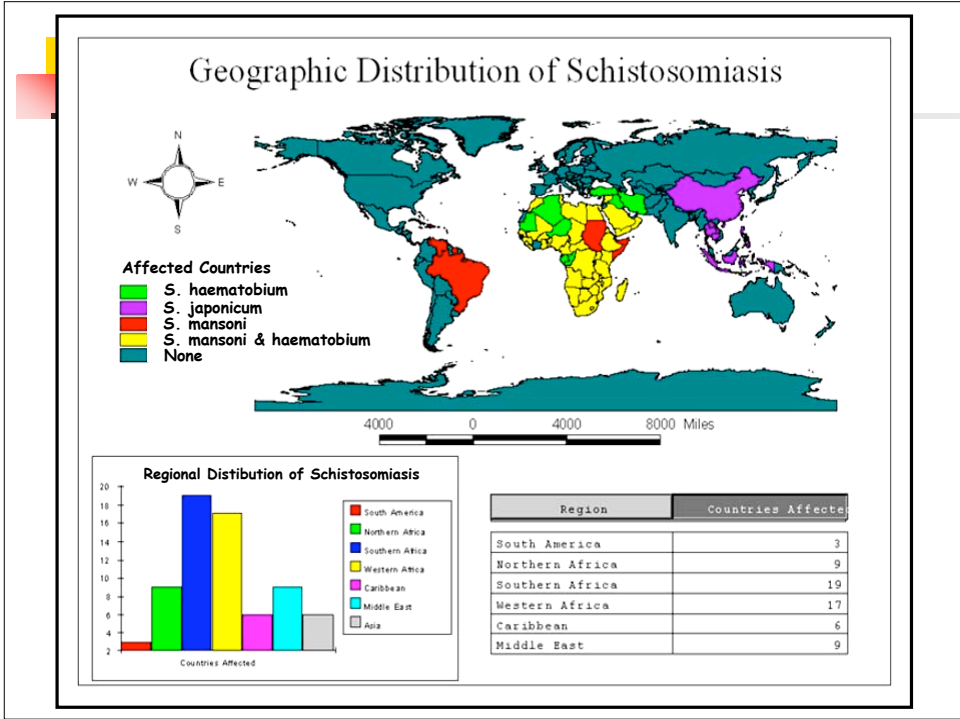
- Originally called Bilharzia in honor of Theodor Bilharz
- 200 million people in 76 countries
- Can have infections for decades
- Phases of infection
 - Migratory Phase
 - Time from penetration to maturity and egg production - often asymptomatic
 - Acute Phase - Katayama fever
 - When schistosomes begin producing eggs (4-10 weeks)
 - Fever, fatigue, headache, malaise
 - Chronic Phase
 - GI bleeding and diarrhea
 - Portal hypertension, blockages
 - Ascites



Distribution

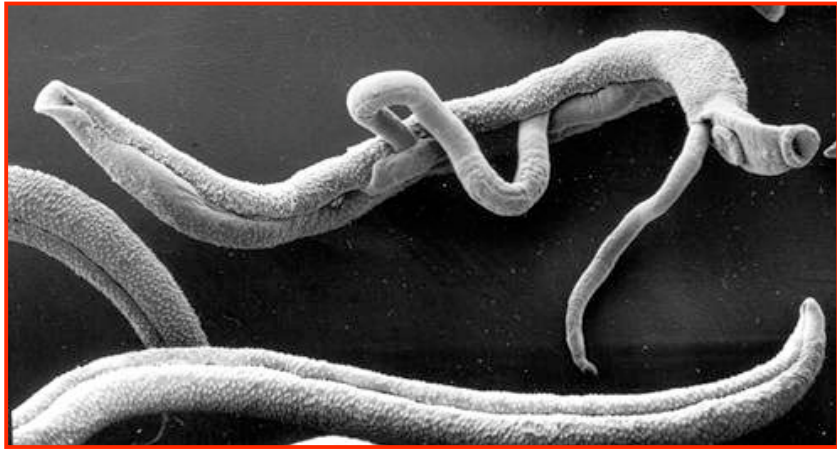
- *S. haematobium*
 - Africa, Middle East
- *S. japonicum*
 - Japan, China, Taiwan, Philippines, Indonesia
- *S. mansoni*
 - Africa, Middle East, S. America, Caribbean Islands





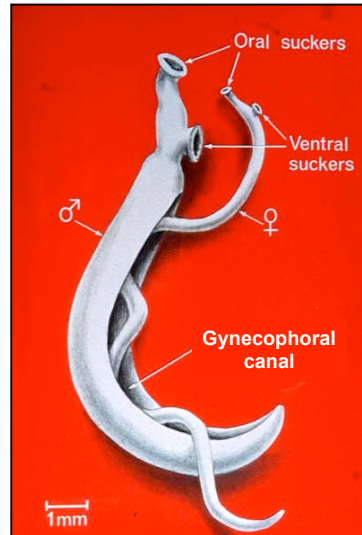
Locked in Life's Embrace

- Worm pairs can live for more than 5 years in a host



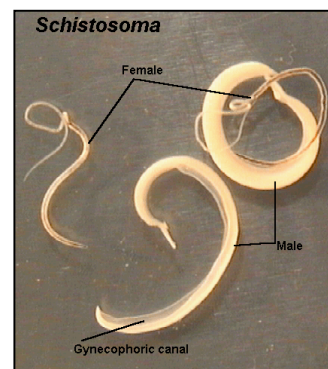
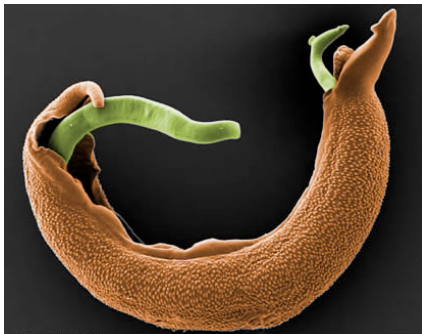
Adult Schistosome Biology

- “Schisto” - split body
- Male and female worms
- Both sexes have oral and ventral suckers - male suckers are larger and stronger
- Male - gynecophoral canal
- Female - resides in canal
 - Final reproductive maturation occurs associated with the male
 - Unique phenomenon in nature



Adult Schistosome Biology

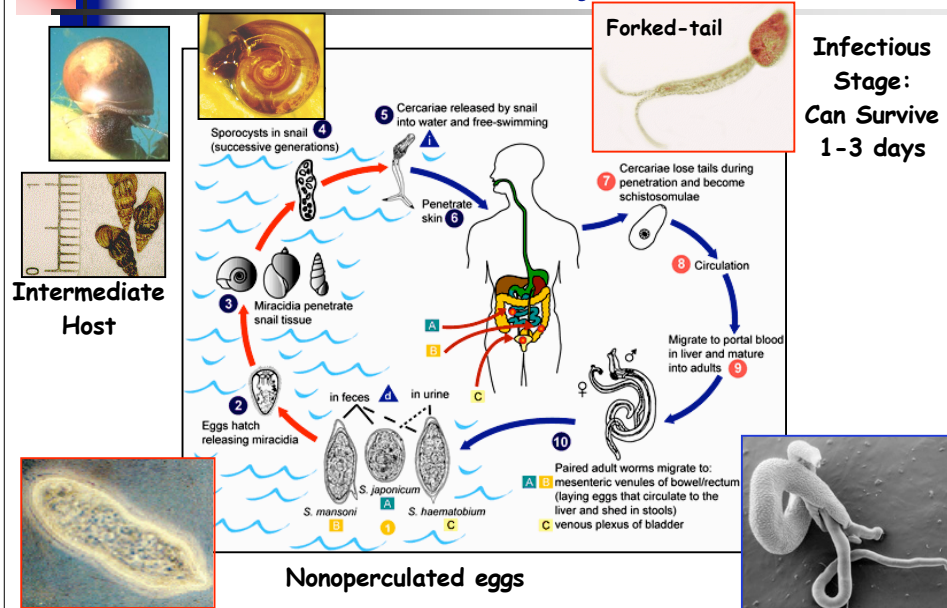
- Male/female pair copulate throughout life - produce eggs
- Some differences among the species - ie. males will contain 5-9 testes depending on species.
- Males are generally shorter and stouter



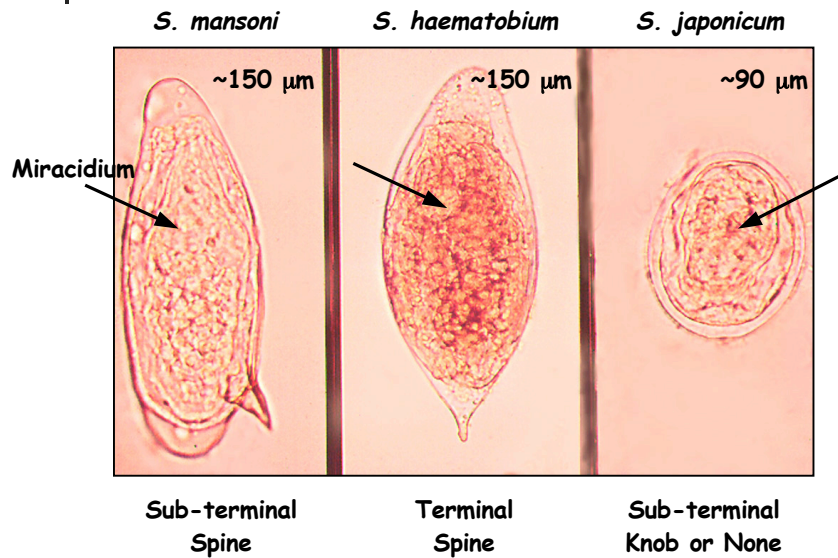
Schistosome Comparison

	<i>haematobium</i>	<i>japonicum</i>	<i>mansoni</i>
Adults			
<i>Male</i>			
Length (mm)	10–14	12–20	6–12
Number of testes	4	7	6–9
Posterior union of intestinal ceca	Midbody	Posterior to midbody	Anterior to midbody
Tegument	Scattered tubercles and blunt, short spines	Minute spines	Numerous tubercles and large, sharp spines
<i>Female</i>			
Length (mm)	16–20	16–28	7–17
Ovary	Posterior to midbody	Midbody	Anterior to midbody
Number of eggs in uterus	20–100	50 or more	1 usually
Eggs produced/female/day	?	1400–3500	100–500
Location in host			
Primary	Bladder and pelvic plexuses	Both superior and inferior mesenteric veins	Veins of small and large intestine near ileocecal junction
Secondary	Portal and mesenteric veins	Portal vein	Hemorrhoidal and hepatic veins
Prepatent period in weeks			
Eggs	10–12	5–7	7–8
Length (µm)	112–170	70–100	114–175
Width	40–70	50–65	45–68
Color	Golden brown	Golden brown	Golden brown
Spine	Terminal	Subterminal knob or none	Subterminal
Passed in	Urine	Feces	Feces

Generalized Life Cycle

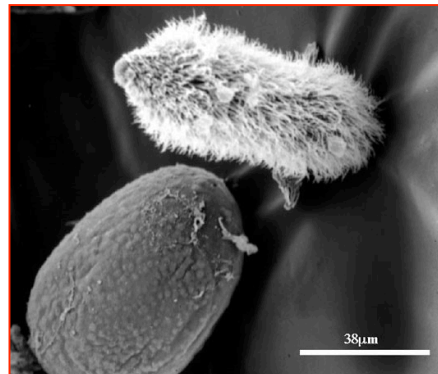


Classical Diagnosis



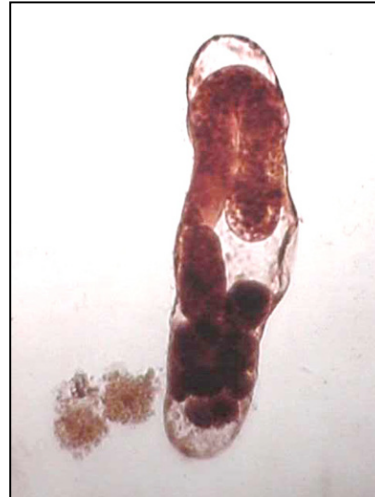
Schistosome Miracidium

- 200 μm length and 40 μm diameter
- Passed in the feces within an ovoid egg
- 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



Intramolluscan Sporocyst

- The miracidium penetrates the snail
- It sheds the epithelium and remodel its surface (~2 h)
- 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)

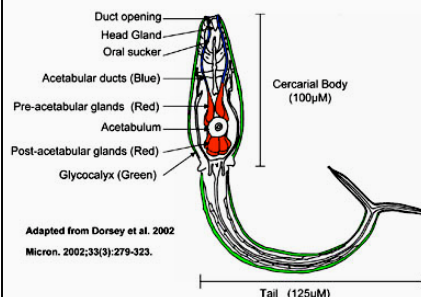


Cercaria

- Composed of a body 125 μm long by 25 μm in diameter to which a 200 μm long tail is attached
- Swims by alternating side-to-side rhythmic contractions to find their definitive host
- Covered by a single continuous syncytial **tegument** 0.5 μm thick on the body and 0.2 μm thick on the tail
- **Glycocalyx** (highly antigenic) 1-2 μm thick cover the surface of the tegument
- **Unicellular (penetration) glands** that secrete proteinases that digest extracellular proteins

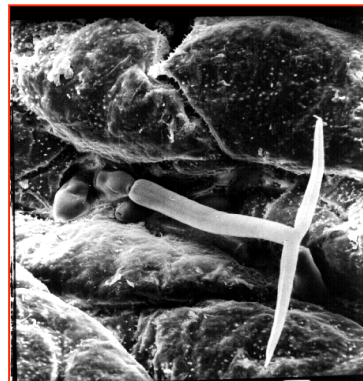


Diagram of *Schistosoma mansoni* cercaria



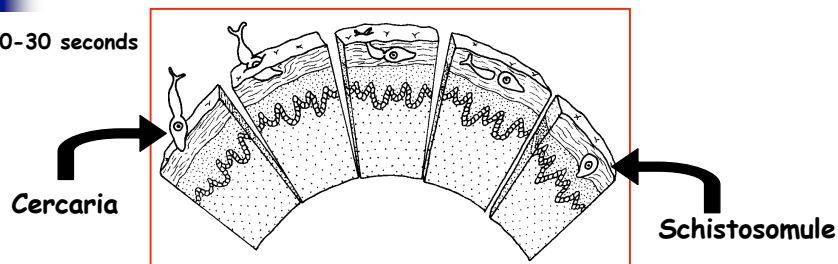
Cercaria to schistosomula

- Tail is lost
- Shedding of most of the glycocalyx
- Penetration glands empty
- Formation of a new membrane on the syncytial surface.
- Several new glycoproteins not found in the cercaria
- Loss of resistance to the hypo-osmolar stress of fresh water
- Change from aerobic to anaerobic metabolism



Cercaria penetration

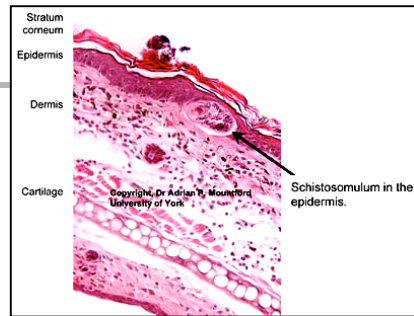
10-30 seconds



- As little as a 3 minute exposure to water containing cercaria will permit infection.
- Requires ~30 minutes to reach subepithelial layers
- Carried by circulatory system - finish development in the liver

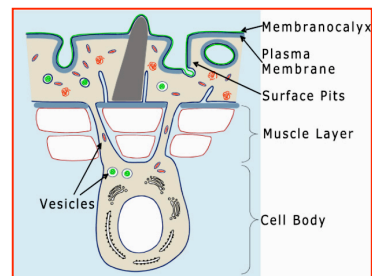
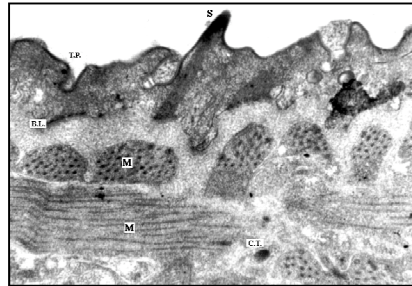
Schistosomula

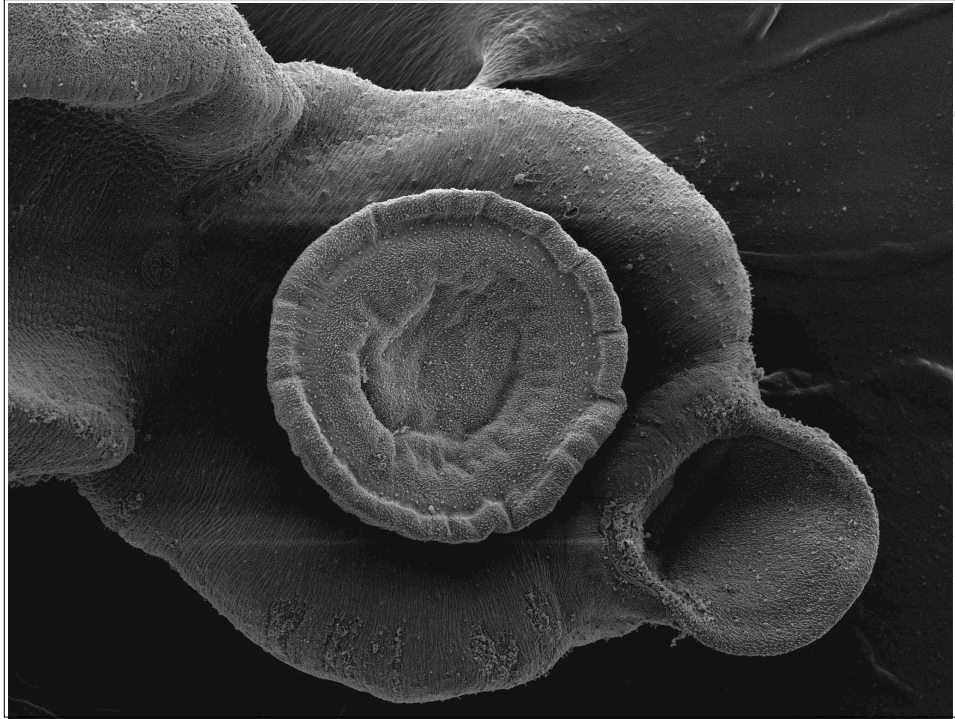
- 3-4 days in the subdermal layers
- Bloodstream briefly passing through the right side of the heart into the pulmonary artery
- Pulmonary capillaries around the 4th day and remain for 2-3 days
- After passing through the lungs schistosomula come to rest in the hepatic portal vein



The Tegument

- The outer surface has folds and is pitted with numerous opening of tubular canals
 - Males:
 - Warty tubercles with many spines which help to maintain the position of the pair against the blood flow
 - Female:
 - Wrinkled annularly and is smooth except for dense spination around the excretory pore.
- Underlying the tegument is a basal lamina from which microtubules extend into the tegumentary matrix





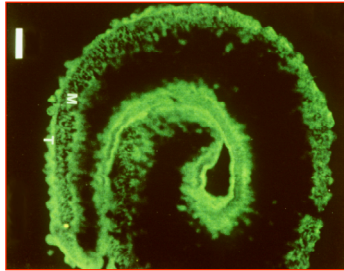
Schistosomes and sugar

- Adult schistosomes consume their dry weight in glucose every 5 hours
- Glucose is transported across the host-interactive tegument
- This implies the presence of host-interactive glucose transporter proteins
- 3 schistosome glucose transporter homologs have been clones and studied.

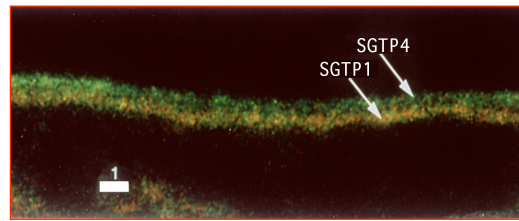
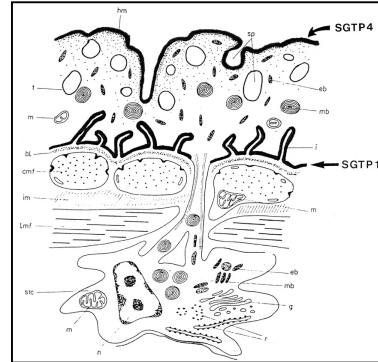
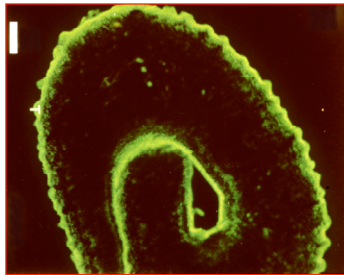


Asymmetric distribution of the Glucose Transporters within the tegument

SGTP1

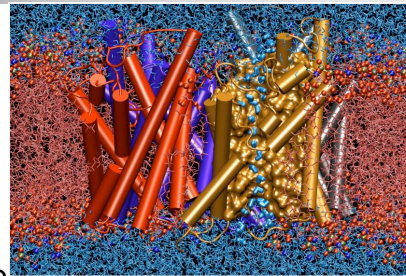


SGTP4



Schistosomes and water

- Aquaporins
integral membrane proteins
(nobel prize in Chem 2003)
- Water channels
rapid movement of water
(now other specific solute channels)
- Schistosome aquaporin is important for osmotic regulation and volume regulation
- Aquaporins of other species can act as conduits for other metabolites (glycerol, ammonia, urea)
- Possible other roles in Schistosomes
(e.g. drugs, antimonials in schistosomes!)



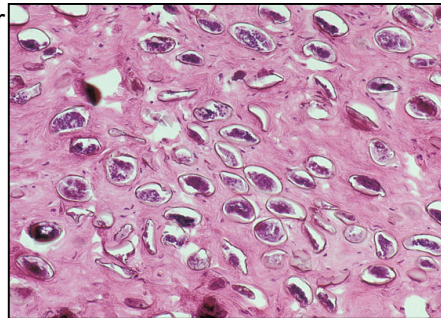
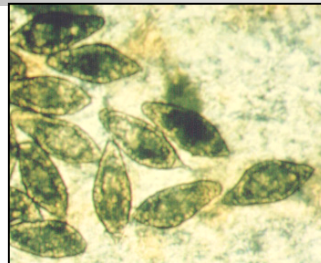
S. haematobium

- **1st Schistosome worm to be discovered - 1850**
- **Definitive Hosts:** Humans. Very host specific with no known reservoir hosts.
- **First Intermediate Host:**
 - Aquatic snails - mainly *Bulinus sp.*
- **Second Intermediate Host:** None
- **Transmission to D.H.:** Cercaria burrow into the skin.
- **Location in D.H.:** Worms live principally in veins of urinary bladder



S. haematobium Pathology

- Eggs lodge in bladder wall - inflammation
 - Migratory and acute phases are similar to other two species.
 - Chronic infections occur
 - rarely cause ascites or enlargement of spleen and liver - less serious than other infections
 - Frequently causes painful urination and blood in the urine.
 - Fibrotic calcification
 - May cause bladder cancer.
 - Many Cases are asymptomatic.



The 2 faces of schistosomiasis

The morbidity spectrum of schistosomiasis mansoni

'Intestinal' asymptomatic schistosomiasis at the Egyptian village level

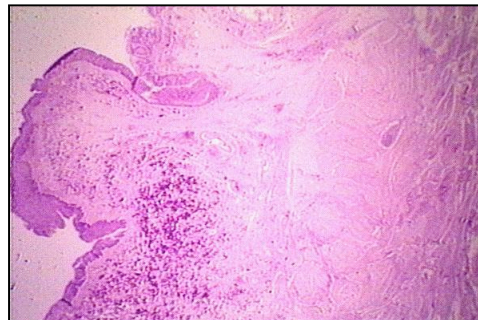
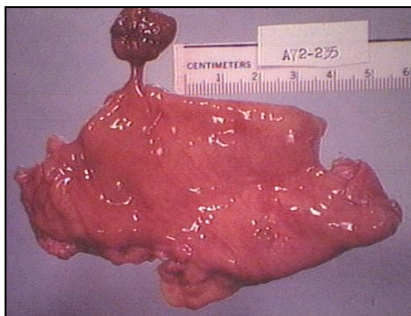


Egyptian boy with hepatosplenomegaly, ascites fluid build-up and superficial collateral circulation (NAMRU-3 clinical ward in Cairo)



S. haematobium

- Chief symptoms linked to urinary system
- Hematuria - bloody urine
- Not all eggs get lodged - remainder are passed in urine

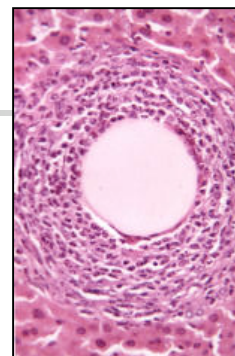
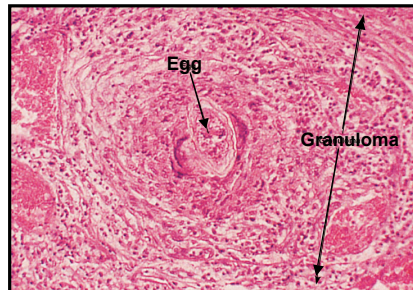


S. mansoni

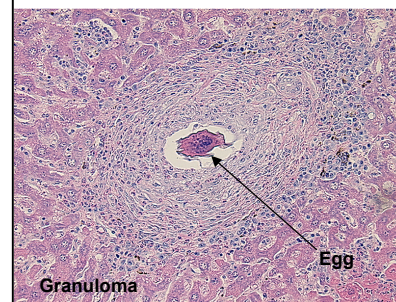
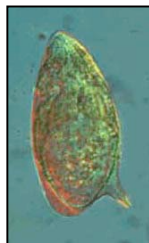
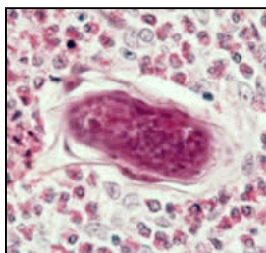
- **Definitive Hosts:** Humans, and many wild mammals including monkeys and rodents.
- **First Intermediate Host:** Aquatic snails - *Biomphalaria sp.*
- **Second Intermediate Host:** None
- **Transmission to D.H.:** Cercaria burrow into the skin.
- **Location in D.H.:** Portal veins of the large intestine.



S. mansoni Pathology



S. mansoni egg granuloma



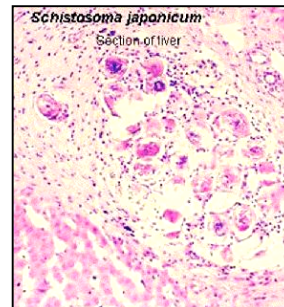
S. japonicum

- **Definitive Hosts:** Humans, wild mammals including dogs, cats, deer, primates, horses, swine, cattle. Least host specific.
- **First Intermediate Host:** aquatic snails - *Oncomelania sp.*
- **Second Intermediate Host:** None
- **Transmission to D.H.:** Cercaria burrow into the skin.
- **Location in D.H.:** Veins of the small intestine.

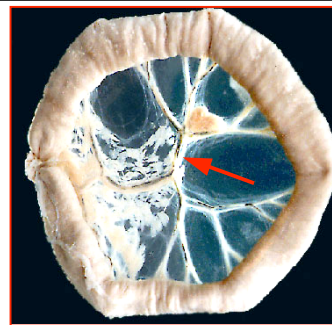
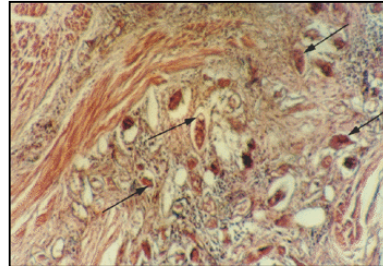
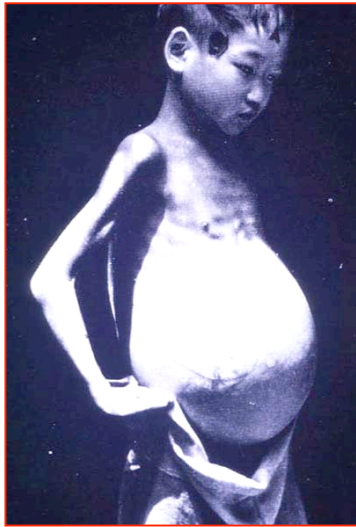


S. japonicum Pathology

- **Pathology:** Most pathology is due to the body's inflammatory response to the eggs. Eggs lack spine so they are transported by blood easier than the other species
- Produces the most eggs of the 3 species
- Large number of eggs can be deposited in ectopic sites - brain
- Almost all brain lesions found in schistosomiasis patients are due to *S. japonicum* infections.



S. japonicum Pathology



Non-human Schistosomes

- Schistosome dermatitis
 - AKA - Swimmer's itch
- Treatment is hydrocortisone or antihistamine creams.
- Prevention
 - Avoid lakes in late summer with high snail population
 - Rinse with fresh water after swim
 - Rub body with a towel as soon as you leave the water.



Schistosomiasis

- Tissue damage (granulomas) in response to eggs lodging in tissues

• <i>S. haematobium</i>	Granulomas in urinary bladder wall	Africa, Middle East
• <i>S. japonicum</i>	Granulomas in intestinal wall	East Asia
• <i>S. mansoni</i>	Granulomas in intestinal wall	African, Middle East, South American, Caribbean
• Swimmer's itch	Cutaneous allergic reaction to cercariae	U.S. parasite of wildfowl

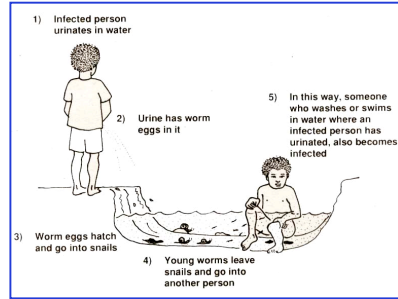
Daily activities

- Washing clothes
- Wading in streams
- Residents often defecate, urinate, work and play in the same water
- People who work catching fish, planting rice, washing clothes and vegetables get infected easily.

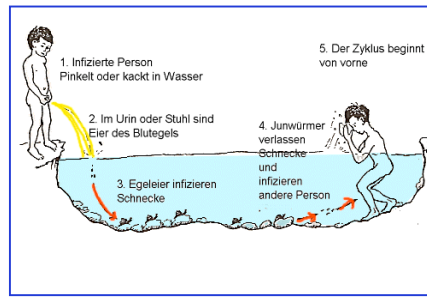


Public Health Education

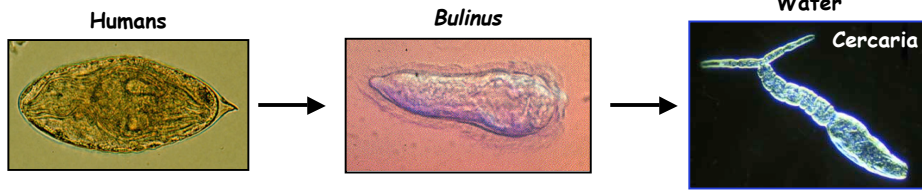
South African



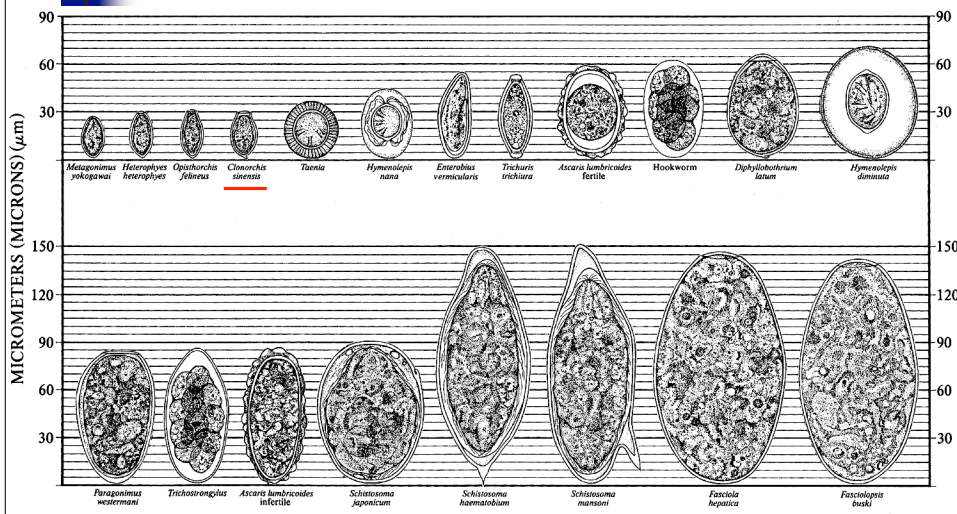
German



S. haematobium



Comparative Egg Size





Schistosomiasis Treatments

Praziquantel Oxamniquine Metrifonate

Type of Compound	Isoquinilone	Tetrahydroquinilone	Organophosphorous
Active against	All Species	<i>S. mansoni</i>	<i>S. haematobium</i>
Dosage	40-60mg/kg Single dose	15-40mg/kg 1-2 doses	7-10mg/kg 3 doses/2 weeks
Cure Rate	70%-100%	80%-100%	50%-90%
Main Side Effects	Diarrhea, Nausea Abdominal pain	Dizziness Drowsiness	Nausea
Price/adult dose	\$0.25 - \$3	\$2 - \$5	\$0.30
Mode of Action	Calcium Channel blocker ?	Delayed action Alkylation ?	Energy Inhibition???