But, first, what are Trematodes?

→ Common name: Flukes
→ From Phylum: Platyhelminthes
→ Adult trematodes are parasites of vertebrates
  o The trematodes that parasitize humans are called Digenetic Trematodes
    ▪ Digenetic Trematodes—Trematodes whose sexual reproduction in the adult is followed by asexual multiplication in the larval stages in snails
→ Most are hermaphroditic
  o Some are capable of self-fertilization
→ ALL HAVE COMPLEX LIFE CYCLES requiring one or more intermediate hosts
  o Eggs laid by the adult within the vertebrate host pass outside and a larva develops within the eggs
  o The larva is called a miracidium
    ▪ They may hatch and swim away, or in some species, emergence may have to wait upon ingestion of the egg by the next host
    ▪ In either case, development cannot proceed unless the proper first intermediate host—a mollusk (snail or clam)—is available
      1 A complex series of generations follow within the mollusk, resulting finally in the liberation of large numbers of larvae known as cercariae
        a Fates of cercariae:
          i In some species, the cercaria must penetrate directly through the skin of the vertebrate host
            • Mechanism used by schistosomes
          ii In others, the cercariae enter an insect, fish or other second intermediate host
            • Mechanism used by non-schistosome trematodes
          iii In others, it must attach to vegetation and secrete a resistant cyst wall, and wait to be eaten by the final host
  o Hosts involved:
    ▪ Definitive Host—vertebrates (man)
      1 In the DH, there is sexual multiplication that takes place ending in the production of eggs
    ▪ Primary or 1st Intermediate Host—usually a mollusk (snail)
      1 In the 1st IH, there is production of cercariae
    ▪ Secondary or 2nd Intermediate Host—can be a fish, crustacean, or another snail
      1 In the 2nd IH, the cercariae become metacercariae
→ Largest trematode that parasitize humans: Fasciolopsis buski
Smallest trematode that parasitize humans: *Heterophyes heterophyes*

The body of a trematode is covered with a resistant cuticle—which may be smooth or spiny

- The cuticle is also the worm’s integument
  - Trematode integumentary features:
    1. **Non-cellular**
    2. Plays an important role in the absorption of carbohydrates
    3. Serves for secretion of excess metabolites and mucus
    4. Microscopic features:
      - **Anucleated**
      - **Syncytial**
      - With many mitochondria and vacuoles
    5. **NO microtrichia** or pore canals are found in the integument of cestodes

There are two suckers which are important attachment organs:

- **Anterior/Oral sucker**—surrounding the mouth
- **Posterior/Acetabular sucker**—on the ventral surface

The oral cavity leads to a muscular esophagus, from which the intestine branches to form **two intestinal ceca** that both run parallel to each other, ending blindly near the posterior end of the worm

Most of the body, however, is taken up with reproductive organs and associated structures

- There are **two testes** leading to the genital pore, which usually lies in the region of the ventral sucker
- There is a single ovary
- A series of glandular structures called vitellaria, usually in two masses lying lateral to the intestinal ceca
  - Vitellaria produce shell material
- **Vitelline ducts** lead inward to the region of the ovary where the shell is formed over the ovum
- **Uterus** winds forward to the genital pore
  - In some trematodes, it is the largest organ in the body filled with thousands of eggs

Trematode eggs have a smooth, hard shell that is transparent and generally yellow-brown or brown

- Can range from 30 to 175 microns in length
- Most egg have an operculum or lid at one end—an “escape hatch” through which the miracidium emerges
  - The miracidium is ciliated and in some species, it is fully developed when the eggs are passed in the feces
- The shell may be smoothly continuous in outline, or there may be a slight flare, marking the line of cleavage between shell and operculum—the opercular shoulders
Lecture 4: Trematodes 1—Blood Flukes

Parasitology: Schistosoma haematobium, Schistosoma mansoni, Schistosoma japonicum, S. mekongi, S. intercalatum

- Presence of these shoulders is characteristic of the eggs of certain species
  - Trematode eggs cannot be successfully concentrated by the zinc-sulfate technique
    - Use the formalin-ether technique instead

- Spines may be present:
  - Very small and inconspicuous spines in Clonorchis and Opisthorchis
  - Striking spines in certain species of Schistosoma
    - Eggs of schistosomes are non-operculate, and the egg is irregularly ruptured in hatching

BLOOD FLUKES

Major parasitic species:
- S. haematobium
- S. mansoni
- S. japonicum

Minor parasitic species:
- S. mekongi—from the Mekong Basin
- S. malayensis
- S. intercalatum—from Africa

Major Features of Blood Flukes
- Eggs of S. mansoni, S. japonicum, S. intercalatum, and S. mekongi are found in the feces
  - Eggs of S. haematobium are occasionally seen in the stool but usually occur in the urine
- They develop in the portal venous system and adult flukes live in the vein of the intestines or urinary bladder
- Sexes are separate (diecious)
  - Males and females are dissimilar in appearance
  - Females:
    - Longer and slender
  - Males:
    - Characteristically incurved ventrally to form a gynecophoral canal in which the female reposes
- Unlike most trematodes, they are NOT flattened or leaf-like—they are long and worm-like (vermiform)
- Humans are the ONLY definitive host
- Transmission is via contact with water containing the infective form of the parasite which are the cercariae
Infectious process: Takes place via the direct penetration of the cercariae through the skin and invade the circulatory system
  - The females leave the male worms to deposit their eggs in small venules near the lumen of the intestine or urinary bladder and withdraw as the eggs are laid so that the eggs are firmly wedged into the small venules
    - Spiny eggs of *S. mansoni* and *S. haematobium* assist in their retention in the blood vessels
  - An enzyme elaborated by the miracidium diffuses through the egg shell and helps to digest the overlying tissue
    - The action of this enzyme, together with necrosis of the tissue caused by pressure and the effect of the spine, are factors that will liberate the egg from the tissues into intestinal lumen or urinary bladder lumen

Again, the schistosome eggs are non-operculated—therefore, they hatch by rupture if they come in contact into fresh water
  - The miracidium that escapes will swim to search an appropriate snail host
    - If successful, it penetrates the snail, and within the snail, it undergoes a cycle of development, eventually giving rise to a large number of cercariae infective to humans
      1. Cercariae of schistosomes have a forked tail and glands at the anterior end that assist in penetration of the skin
        - During this process, the tail is lost and profound metabolic changes take place
          - Ex: From aerobic to anaerobic respiration of the cercariae

The immature fluke is referred to as the schistosomulum
  - Remains in the subcutaneous tissues for about 2 days
  - After invasion of the blood vessel, the young flukes are carried to the lungs and then to the liver sinusoids—and commence growth
    - After two weeks or so, the maturing worms again migrate against blood flow in the portal system to their final location in mesenteric or vesicular veins

A. *Schistosoma mansoni*
  - Causative agent for intestinal schistosomiasis
  - Adults live in the smaller branches of the inferior mesenteric vein in the region of the lower colon
  - They subsist on ingested blood
  - Smallest of all schistosomes
    - Females up to 1.6 cm
    - Males up to 1 cm
Lecture 4: Trematodes 1—Blood Flukes

Parasitology: Schistosoma haematobium, Schistosoma mansoni, Schistosoma japonicum, S. mekongi, S. intercalatum

Life Cycle
1—Miracidia hatch from eggs in water
2—Miracidia infect an intermediate host, the snail called Biomphalaria
3—Cercariae emerge from the snail and swim freely in the water
4—Cercariae enter unbroken skin—schistosomules develop to adults in veins of liver
5—Worms migrate from liver to mesenteric veins
6—Eggs are passed out in feces
7—Ulit na sa #1

Diagnosis
Find S. mansoni eggs in the feces
- Occasionally, they can be found in the urine after fecal contamination
- Rectal biopsy during chronic stages of infection by this parasite
  - Adequate sampling via rectal biopsy involves taking 4 snips
    - Anterior
    - Posterior
    - And both lateral rectal walls

Symptoms and Pathogenesis
- Skin rash after cercarial penetration (Swimmer’s Itch)
- S. mansoni acquires host antigen thereby protecting them from the host’s immune response
- Eggs penetrate through the intestinal wall and are excreted in the feces often with blood + mucus
- Host reaction to eggs leads to the formation of:
  - Granulomata
  - Ulceration
  - Thickening of intestinal wall
- Eggs can reach the liver via the portal vein
  - Reaction the eggs causes thickening of the portal vein known as Claypipe-Stem Fibrosis
- Other reactions:
  - Liver
    - Hepatomegaly
    - Ascites—abnormal accumulation of serous fluid in the spaces between tissues and organs in the cavity of the abdominal cavity
    - Increased liver enzymes
    - There is hypoalbuminemia + increased globulin levels
  - Spleen
    - Splenomegaly
Concomitant infections:
- *Salmonella*

Ova can be deposited in the:
- Spinal Cord
- Lungs

Eosinophilia

B. *Schistosoma japonicum*
- Common name: Oriental blood fluke
- Causative agent for: Intestinal schistosomiasis
- Lives in: Superior Mesenteric Vein (SMV)
- Occurs in: China, Taiwan, Japan, Philippines, and Indonesia
- Primary intermediate host: *Oncomelania quadrasi* (a snail)
- Unlike *S. mansoni*, *S. japonicum* can be found in all *mammals* exposed to infected water

**Morphology**
- The sexes are separate:
  - **Females:**
    - Up to 2.6 cm in length
  - **Males:**
    - Up to 2.2 cm in length
- *S. japonicum* produces more eggs than *S. mansoni* and *S. haematobium*
  - The eggs are smaller and almost spherical

**Life Cycle**
1. Miracidia hatch from eggs in water
2. Larval multiplication in *Oncomelania quadrasi*
3. Cercaria enters intact skin
4. Schistosomules develop to adults in veins of liver
5. Worms migrate from liver to mesenteric veins (SMV)
6. Eggs are passed out in the feces
7. Making ulit #1

**Diagnosis**
- Identification of eggs in stool
  - Eggs are oval/spherical and have spines
    - The spines are absent in some strains
  - Size: 55-85 microns by 40-60 microns
- Rectal biopsy in chronic cases
- Serology
  - Circumoval Precipitin Test (COPT)
  - ELISA
Symptoms and Pathogenesis

- Skin rash at the site of cercarial penetration
- 20-60 days after infection, patient may develop:
  - Fever
  - Myalgia
  - Abdominal pain
  - Splenomegaly
  - Urticaria—hives (pantal); well-circumscribed areas of erythema and edema involving the epidermis and dermis that are very pruritic
  - Eosinophilia
    - All these constituting Katayama Reaction/Katayama Fever

- Adult *S. japonicum* inhabit the branches of the SMV adjacent to the small intestine
  - However, the inferior mesenteries and caval system may also be invaded as the worms tend to migrate away from the liver

- Because of the egg morphology of *S. japonicum*, more egg can be lodged in the general circulation, to be filtered out in the liver, lungs, and in other organs
  - Therefore, infection with even a few worms of this species can be very serious
  - Reaction to eggs:
    - Intestinal disease
    - Hepatosplenic disease
    - Dysentery
    - Liver fibrosis
    - Marked hepatosplenomegaly

- Hepatic and Pulmonary Cirrhosis are commonly seen in chronic stage of this infection

- CNS Symptoms may be present if the eggs are lodged in or near nerve tissue

- Mucus and blood in fecal specimen

- Blood eosinophilia

- In patients with hepatic involvement:
  - Elevated liver enzymes
  - Hypoalbuminemia
  - Increased total protein due to increased globulin

C. *Schistosoma haematobium*

- The most common causative agent for: Urinary schistosomiasis
  - The other schistosomes can cause urinary schistosomiasis, too.
Lecture 4: Trematodes 1—Blood Flukes  #AsturiaNOTES

**Parasitology: Schistosoma haematobium, Schistosoma mansoni, Schistosoma japonicum, S. mekongi, S. intercalatum**

- Causes: *Schistosomal hematuria, Vesical schistosomiasis,* or *urinary bilharziasis*
- Occurs in: The **tropics** and **subtropics**
- Intermediate Hosts: Snail of the genera *Bulinus, Physopsis,* and *Biomphalaria*

**Morphology**
- Sexes are separate:
  - Females:
    - Up to **2 cm**
  - Males:
    - Up to **1.5 cm**
- Eggs
  - Can **112-170 microns** in length and **40-70 microns** in breadth
  - Possess a **conspicuous terminal spine**
  - Color: **Light yellowish brown**

**Life Cycle**
- 1—Miracidia hatch from eggs in water
- 2—Larval multiplication takes place in the **intermediate host,** usually a *Bulinus* snail
- 3—Cercaria penetrate intact skin
- 4—Schistosomules develop adults in the veins of the liver
- 5—Worms migrate from liver to veins surrounding urinary bladder and adjacent organs
- 6—Eggs are then passed in the **urine**

**Diagnosis**
- Finding the eggs or occasionally, the hatched miracidia by the **centrifugation** and **sedimentation** of urine
  - The containers of the urine should **NOT** contain **preservatives** if the eggs are to be hatched
- Occasionally, eggs can be found in the feces
- **Rectal biopsy**

**Pathogenesis**
- After the worms mature in the **liver sinusoids,** they migrate from that organ, and the majority of them reach the **vesical, prostatic,** and **uterine plexuses** by way of the **hemorrhoidal veins**
- The eggs are deposited in the walls of the urinary bladder, and sometimes, in the **uterine, vaginal,** and **prostatic walls**
  - Those deposited in the wall of the bladder may break through into the **lumen** and escape in the **urine**
Swimmer’s Itch
Within a few days after penetration, the young flukes become coated with the host rbc antigens and histocompatibility antigens—making them ‘unrecognizable’ by the immune system and live free from host attack.

Eggs are the ones responsible for symptoms, not adult worms
- Eggs trapped in the bladder wall and surrounding tissues cause inflammatory reactions with the formation of granulomata
  - The granuloma contains:
    1. Egg
    2. Toxic products
    3. Eosinophils
    4. Epitheloid cells
    5. Lymphocytes
- Many of the eggs die and become calcified—producing sandy patches in the urinary bladder
- In heavy infections, the eggs can be carried to other parts of the body

Symptoms
- In light infections, symptoms may not develop for years
  - However, in heavy infections, symptoms can develop as early as 1 month after the infection
- If untreated, the ureters may become obstructed and the urinary bladder wall can become thickened
  - Leading to:
    - Abnormal bladder function
    - Painful and frequent micturition
    - UTI
    - And eventually, kidney damage

Terminal hematuria
- In some areas, there is concomitant infection with S. typhi or S. paratyphi
- Patients may exhibit a syndrome of chronic, intermittent, enteric bacteremia that clinically resembles Kala-azar
  - Both of these bacterial infections have been attributed to a mechanism of adhesion of the bacteria to the tegument of the intravascular schistosomes (blood flukes)
- Some other findings:
  - Hematuria
  - Bacteriuria
  - Proteinuria
  - Eosinophiluria

D. Schistosoma mekongi
- A schistosome from the Mekong River basin in Southern Laos and Cambodia
Resembles *S. japonicum* in adult structure and life cycle and its ability to infect non-human vertebrates
- However, its eggs are smaller than eggs of *S. japonicum*
  - 30-55 microns by 50-65 microns
- The disease in humans caused by *S. mekongi* is similar with the clinical features of *S. japonicum* but are milder

Reservoir host: Pigs
Intermediate Host: *Lithoglyphopsis aperta*

*E. Schistosoma intercalatum*
- Similar to *Schistosoma mansoni* in terms of life cycle, pathology, and clinical feature
- Occurs in: Western and Central Africa
- Adult worms are found in the mesenteric vessels and eggs are voided in feces
  - Eggs resemble those of *S. haematobium* but can be differentiated by a slight bend in the terminal spine
    - The egg shell is Ziehl-Neelsen positive
  - Other schistosomes are NOT

Intermediate Host: *Bulimus* snail

**PATHOGENESIS AND SYMPTOMATOLOGIES BY SCHISTOSOMAL INFECTIONS IN GENERAL**
- Following penetration of the skin by cercariae of a schistosome, a transient reaction may be seen
  - Petechial hemorrhages occur at the site of penetration together with some localized edema and pruritus
    - Petechia—A minute reddish or purplish spot containing blood that appears in skin or mucous membrane as a result of localized hemorrhage
    - The edema and pruritus stay to a maximum of 24-36 hrs and disappear in 4 days or less
- During the succeeding 3 weeks, there may be transient toxic and allergic reactions that may be accompanied by the following generalized symptoms depending on the intensity of infection:
  - Fever
  - Malaise
  - Giant urticarial
  - Vague GIT problems
- Migration of the worms throughout the lungs may cause:
  - Cough
  - Hemoptysis—Coughing with blood
- During their establishment in the liver sinusoids, there may be acute hepatitis
- When the flukes reach the mesenteric or vesical venules and egg laying occurs, this is the ACUTE STAGE OF THE DISEASE
Symptoms of the acute stage may range from mild to severe and the degree of the severity is NOT proportional to the number of parasites involved.

- With the extrusion of eggs through the intestinal wall or urinary bladder wall, the patient becomes symptomatic again with:
  - Generalized malaise
  - Fever
  - Urticaria
  - Abdominal pain
  - Liver Tenderness (at RUQ)
  - In *S. mansoni* or *S. japonicum*, there may be diarrhea or dysentery at this stage
  - In *S. haematobium*, there is hematuria at the end of micturition, and sometimes, dysuria

  1. **Dysuria**—difficult or painful discharge of urine

> In **schistosomiasis japonicum**, the early symptoms tend to be quite severe in heavily infected persons, with abrupt onset of fever, chills, and the other signs and symptoms mentioned previously coming from 4-6 weeks after infection.

- There is often a significant mortality rate at this stage of the disease—which is called Katayama fever
  - Katayama-like syndrome can be seen in patients with other forms of schistosomiasis but NOT as common

> The chronic stage of the disease comes on gradually.

- Egg deposition takes place in the smaller vessel located near the intestinal lumen or urinary bladder lumen
  - Many eggs remain where deposited
  - Secretions of the contained miracidia evoke abscess formation around them and they are liberated into the lumen of the affected organ
  - Other eggs are dislodged and swept into the circulation—it is these embolic eggs that produce most of the pathologic changes seen in chronic schistosomiasis

> **Hepatosplenic schistosomiasis**

- The most common form of chronic schistosomiasis with *S. japonicum* or *S. mansoni*
  - Though symptoms in *S. japonicum* are milder
  - Can also occur in *S. haematobium*

- Hepatic parenchymal damage, unresolved after successful treatment with praziquantel, is found in approximately 50% of patients with infection by *S. japonicum*

- Eggs, carried back through the mesenteric vessels, lodge in the liver, where granulomas form around them
Over a period of time, shorter time for heavy infections and longer time (many years) in light infections, the liver becomes grossly enlarged and the left lobe becomes disproportioned.

- The enlarged liver is NOT tender
  - The spleen may be barely palpable or enlarged

**Portal hypertension**

- Results from obstructive liver disease
- Will lead to esophageal varices
  - Can possibly bleed
- Can finally form massive ascites

**Intestinal Schistosomiasis**

- More common: *S. japonicum* and *mansonii*
- Less common: *S. haematobium*
- This disease may involve the entire intestinal tract but is more confined in the large intestine
- May present a picture suggestive of granulomatous colitis with abdominal cramping and tenderness and intermittent bloody mucoid stool
- Intestinal polyposis—small clump of cells (neoplasm) that forms on the lining of the intestinal tract
  - Common in: *S. mansonii*
    - In such patients, the diarrhea is more pronounced and the protein-losing enteropathy results in weight loss and anemia
  - Diagnosed by colonoscopy

**Hepatoplastic and intestinal involvement** are ALWAYS PRESENT in *S. mansoni/japonicum*

**Urinary schistosomiasis** by *S. haematobium*

- First sign of infection: Terminal hematuria
- Other signs:
  - Dysuria
  - Polyuria
  - Eosinophiluria
  - Bactiuria
  - Obstructive uropathy—occurs in persons with high total egg burden
  - Urinary bladder cancer
    - A form of squamous cell carcinoma
    - Site of origin: Where there has been heavy egg deposition
      - Heavy egg deposition promotes urothelial carcinogenesis
- Nephrotic syndrome—kidney disease with proteinuria, hypoalbuminemia, and edema
  1 Can also be seen in infections with \textit{S. mansoni}
- Immune complex nephropathy

\textbf{Pulmonary Involvement}
- Most commonly seen in: \textit{S. haematobium}
  - But can be seen in all forms of schistosomiasis
- Egg deposition in the lungs leads to fibrosis of the pulmonary bed and resultant cor pulmonale characterized by:
  - Exertional dyspnea
  - Cough
  - Occasional hemoptysis
- There is dilatation of pulmonary artery (PA) and right ventricular hypertrophy
  - Can be seen in CXR

\textbf{Cerebral Involvement}
- Most commonly seen in: \textit{S. japonicum}
  - Can also be seen in \textit{S. mansoni/haematobium} but BOTH usually affect the spinal cord
- Neurologic symptoms include:
  - Lethargy/Confusion
  - Seizures
  - Expressive Aphasia
  - Optical field defects

\textbf{Transverse Myelitis}
- Usually in the lumbar area
- Seen in spinal cord involvement
- Usually in \textit{S. mansoni} infection

\textbf{Schistosomal Dermatitis}
- Many schistosomal cercariae that ordinarily infect birds and semi-aquatic mammals are capable of penetration into human skin \textbf{BUT NOT} able to produce permanent infection
  - A dermatitis may be produced from the penetration by the cercariae of human schistosomes \textbf{BUT} the dermatitis produced by non-human schistosomes are more \textbf{severe}
- There is evidence that exposure to the cercariae of non-human schistosome \textbf{enhances resistance against infection of human schistosomes} (tara, pa-infect na tayo charot)

\textbf{TREATMENT}
- Praziquantel
  - 40-50mg/kg body weight—single dose
  - 25 mg/kg body weight—two doses
Lecture 4: Trematodes 1—Blood Flukes
Parasitology: Schistosoma haematobium, Schistosoma mansoni, Schistosoma japonicum, S. mekongi, S. intercalatum

- 20 mg/kg body weight—three doses

**EPIDEMIOLOGY, PREVENTION, AND CONTROL OF SCHISTOSOMIASIS**

- **80M** are infected with *S. japonicum*
- Health Education
- Control of Snail vector
  - Environmental method
    - Drainage of breeding sites and proper management of irrigation systems
    - Removal of shade or shelter from the sun by clearing vegetation around bodies of water
    - Prevention of breeding on the banks of streams or irrigation canals by leaving 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
    - Use of molluscsicides

-end-

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2. Lecture notes by RAsturiano from the lecturer

Downloadable for free at: [www.theelusivedoktora.wordpress.com](http://www.theelusivedoktora.wordpress.com)

For any corrections you may find, content or otherwise, email me at: ram.ustmedicine@gmail.com

-THANKS-

*AsturiaNOTES*

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#TheElusiveDoktora