# Helminths (worms)

- **Nematodes**: Round worms, “thread”, bisexual, intestinal, outside

- **Cestodes**: Tape worms, Flat worms, segmented, hermaphrodites, intestinal (larva extraintestinal)

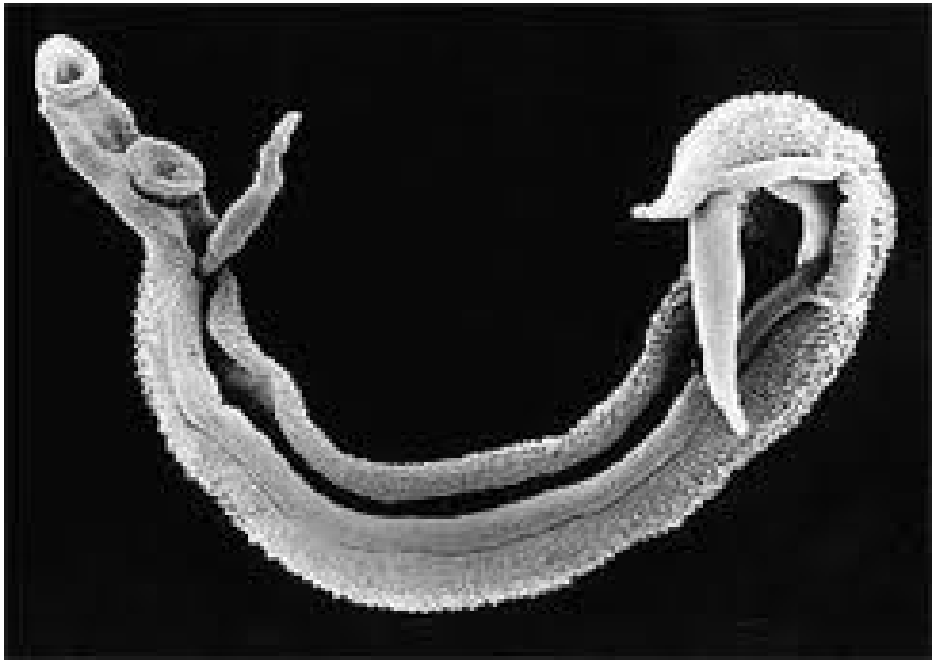
- **Trematodes**: **Flukes, “leaf-shaped”, suckers, hermaphrodites except blood flukes (bisexual). Snail as intermediate host**

# Helminths

# Trematodes

- **Blood flukes**
  - Schistosoma spp
- **Intestinal flukes**
  - Fasciolopsis sp.
  - Heterophyes sp.
  - Metagonimus sp.
  - Echinostoma sp
- **Liver flukes**
  - Clonorchis sp.
  - Opisthorchis sp.
  - Fasciola sp.
- **Lung flukes**
  - Paragonimus spp.

# Schistosoma sp. – Male & female adults



# Biology of the parasite stages (Ctd)

**Eggs:**

- **Non operculated. Contain an embryo (miracidium)**
- **With a lateral or terminal spine**
- **About 50% of the eggs pass through the walls of the organs and are excreted in urine or faeces. The rest are retained in tissues and die within 21 days**
- **Excreted eggs containing miracidium hatch in suitable environment (10-30°c) , in freshwater**
- **Adult ♀ : *S. haematobium* lays 20-200 eggs/day**

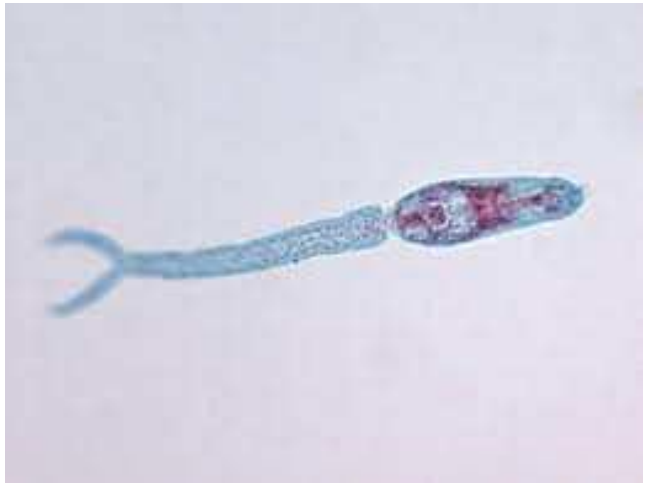
  **_S. mansoni_ lays 100-300 eggs/day**

  **_S. japonicum_ lays 500-3500 eggs/day**

  **Others unknown**

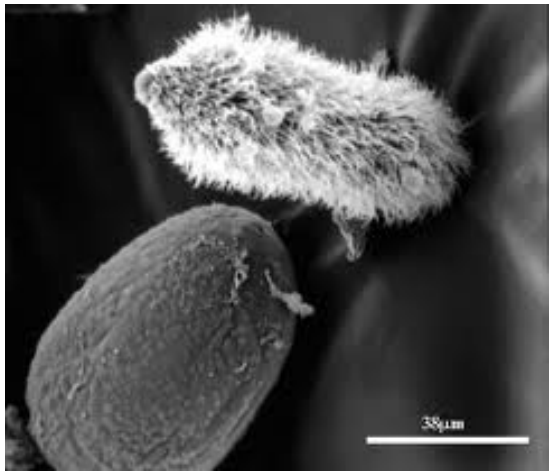
# *S. mansoni* – Eggs with lateral spine

# *Schistosoma* sp. – Larval stages

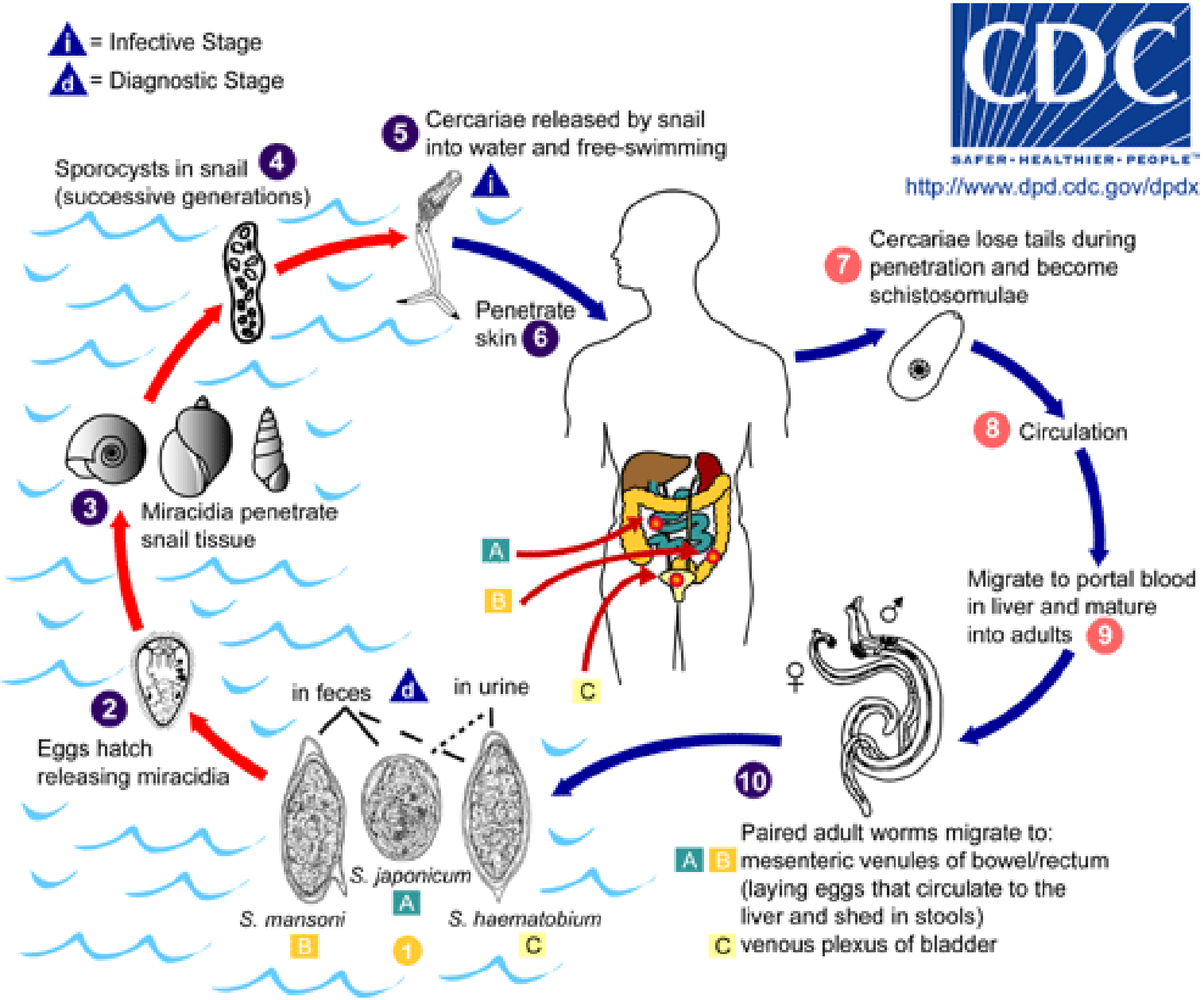


*Cercaria*

*Schistosomula*



*Miracidium*




***Schistosoma spp.***
**Life cycle**

# *Schistosoma spp.* - Life cycle

- **Adult worms, living in pairs, copulate & ♀ produces eggs daily throughout life**
- **Eggs are laid intravascularly towards peripheral branches of the capillary venules**
- **Some eggs cross vessel walls (spine + cytolytic secretions) lumen of urinary (*S.h.)* or bowel (*S.m., S.j., S. me.,S.i*.) and reach outside in excreta (urine/faeces)**
- **Other eggs migrate to liver, lungs, other sites (immune-stimulating & pathogenic agents)**
- **When eggs reach freshwater, they hatch and free a miracidium.**
- **The miracidia behaviour is related to snail hosts, as they must find suitable host (specificity) quickly (8-12h) and develop into other stages**

# *Schistosoma spp.*- Intermediate hosts

| *S.haematobium* | *S. mansoni* | *S. intercalatum* | *S. japonicum* |
|---|---|---|---|
| ***Bulinus africanus***<br>**Sub-Saharan Africa** | ***Biomphalaria pfeifferi***<br>**Sub-Saharan Africa**<br>**Aden, Yemen, Saudi Ar** | ***Bulinus africanus***<br>**(Zaire)** | ***Oncomelania hupensis***<br>**(amphibious)** |
| ***Bulinus forskalli***<br>**Africa, Arabia**<br>**Indian Ocean Islands** | ***Choanomphala group***<br>**Great African lakes (alexandrina)**<br>**Sudan, Egypt (sudanica)** | ***Bulinus forskalli***<br>**(Cameroon, Gabon)** | ***For S. mekongi ,***<br>***Tricula aperta***<br>**(amphibious)** |
| ***Bulinus truncatus, tropicus***<br>**Africa**<br>**Middle East (Iran)** | ***Bi. glabrata***<br>**New World** | | |
| ***Bulinus reticulatus***<br>**Patchy, Africa**<br>**Arabian peninsula** | ***Bi. straminea***<br>***Bi. teganophila***<br>**New World** | | |

# Schistosomiasis – Intermediate hosts

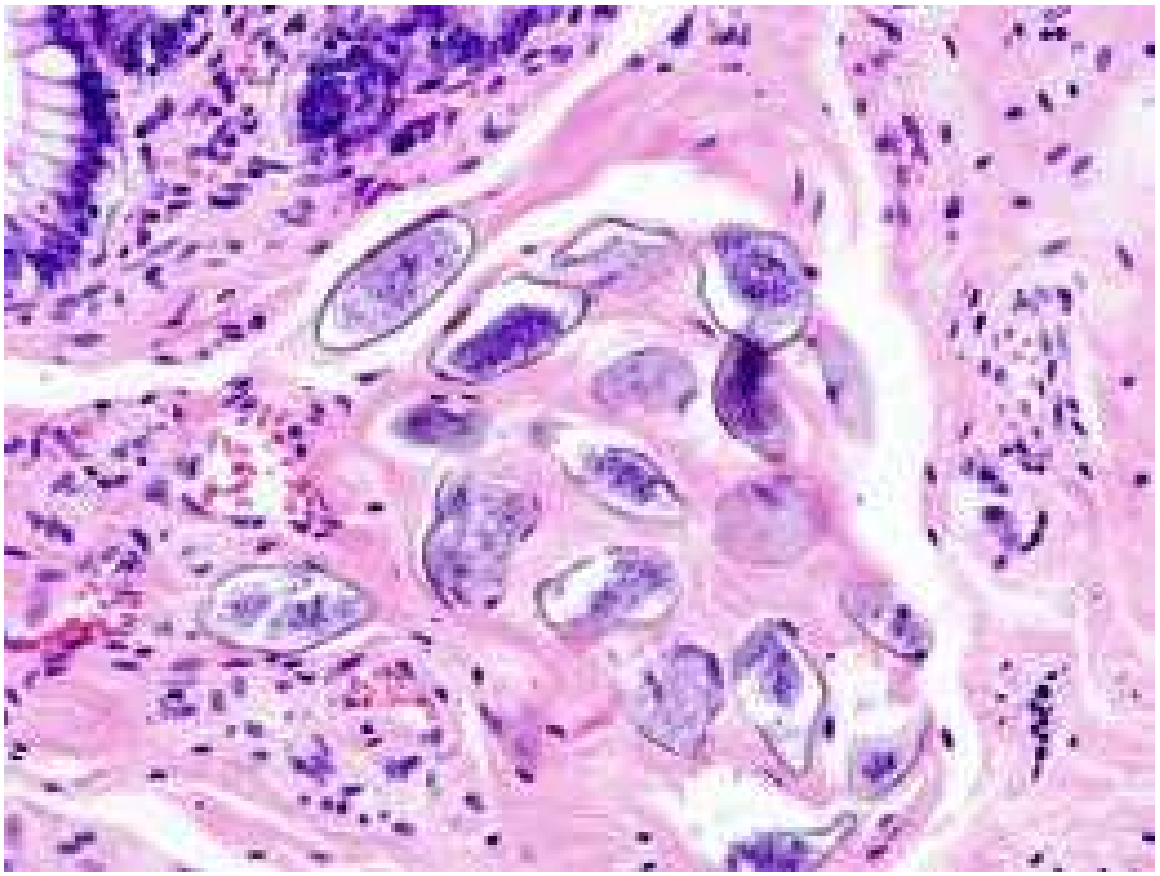
*Bulinus globosus*

*Biomphalaria glabrata*

*Oncomelania hupensis*

# Schistosomiasis - Transmission


# Schistosoma sp. – Eggs



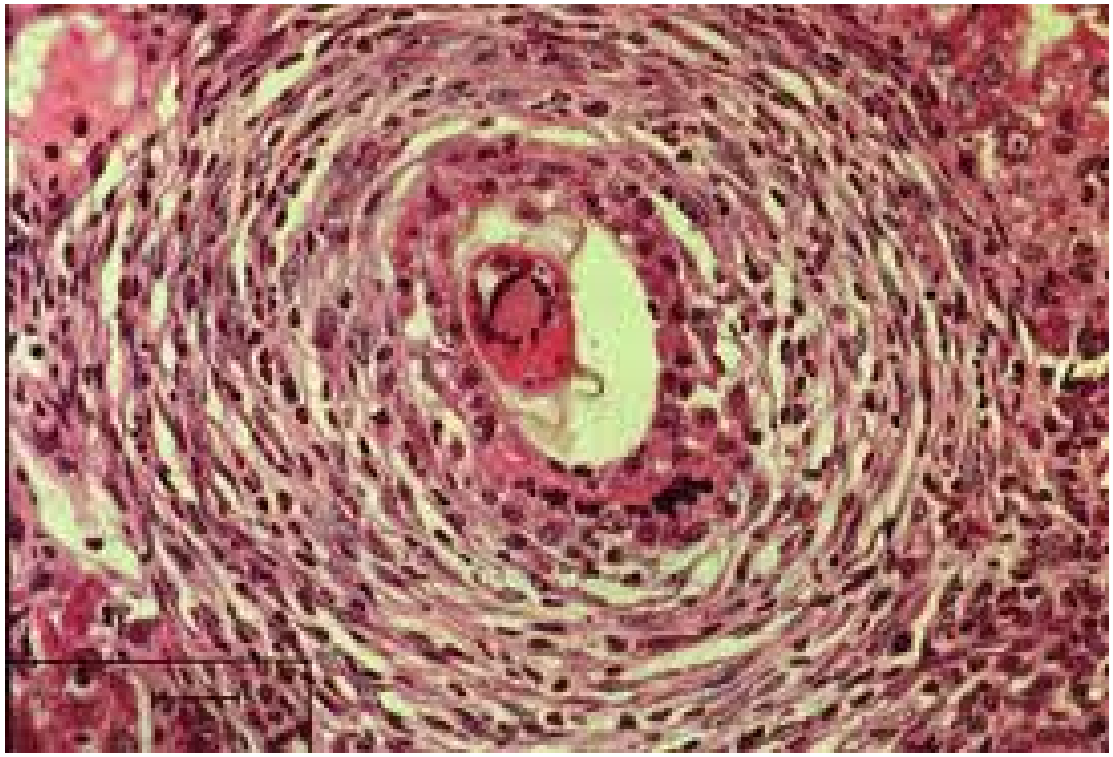
# Schistosomiasis – Pathology

- **Linked with the stages of the cycle:**

1. **Cercarial invasion & schistosomula migration**
2. **Maturation of schistosomula, pairing & start eggs laying**
3. **Established infection with continuous eggs laying**
4. **Late stages & complications**

**NB: It is difficult to link the pathology to each stage, as epidemiological, immunological & physiological interactions!**

# Schistosomiasis - Liver granuloma



# Schistosomiasis – Pathology (Ctd)

## *S. mekongi*

- **Clinical manifestations similar to *S. japonicum* but few research data**
- **Morbidity &n pathology is mixed with presence of *Opistorchis viverrini***

## *S. intercalatum*

- **Few data**
- **Mild disease with non specific lesions: muscular congestion, oedema, bleeding & ulceration reported**
- **Similar lesions to S.mansoni in portal tracts but no hypertension**

# Schistosomiasis – Clinical features

# Schistosomiasis – Immunity

- **All races are susceptible**
- **Schistosomiasis is a chronic disease with granulo matous reactions to eggs causing morbidity**
- **Only few people develop acute toxemic schisto or Katayama syndrome when cercariae invade**
- **Development of acquired immunity is slow & inefficient**
- **IgG/IgM antibodies seem to antagonize protective effects of immune system in young children (unknown mechanisms)**
- **Re-infection is unopposed**
- **BUT prevalence and intensity of infection decrease in teenage & later ⟶ theory is :**

# Schistosomiasis – Immunity (Ctd)

  - Decrease might be due to changing social habits (less water contacts)
  - + tissue fibrosis (eggs do not reach exterior)
  - + death of some worms (no eggs laid)
- Many people in endemic areas seem to have immunity to super-infection & few clinical signs
- Protective immunity is directed against cercariae and schistosomula. This reduces the no. of adults. Two mechanisms: Antibody-dependant cell-mediated cytotoxicity (eosino+ IgG) and process involving IgE + macrophages
- Partial concomitant immunity (resistance of an infected person to re-infection by a same organism)

# Schistosomiasis – Immunity (Ctd)

- **Adult worms evade response by adding a layer of host specific antigens to their tegument so they will be unharmed if re-infection but cercariae may be destroyed**
- **Production of blocking antibodies (IgM, IgG) in early infancy**
- **Known factors in acquired immunity are : IgE response, high levels of interferon & tumour necrosis factor α and peripheral blood mononuclear cells (further research)**
- **Antibodies specific to each stage are long lived & persist even after therapy. The most useful schisto antigen is the cathode-associated antigen (diagnosis)**

# Schistosomiasis – Differential Diagnosis

- Can be confused with many other diseases
- Acute schisto must be differentiated from typhoid, brucellosis, malaria, leptospirosis & other causes of pyrexia
- Pyrexia/eosino occus in trichinosis, visceral larva migrans, and in other Trematodes infections
- In established schisto, S.h. must be differentiated form haemoglobinuria, cancer of urogenital tract, acute nephritis, renal TB
- S.m. may suggest peptic ulcer, biliary disease, pancreatitis
- Distinguish from various dysentery (amoebic, ulcerative colitis, polyposis)
- In hepatosplenic schisto, differentiate from kala-azar (visceral leishm), chronic leukaemias, myeloproliferative syndromes, thalassaemias & tropical spenomegaly syndr
- Consider schisto if: cor pulmonale, epilepsy, myelopathy and spinal cord compression

# Schistosomiasis – Diagnosis

- **Direct visual demonstration of eggs in stool/urine or from biopsy material (rectal, liver, other)**
- **Hatching tests to see if eggs are viable**
- **Detection of schisto antigens in serum/urine**
  - **Circulating anodic antigen (CAA)**
  - **Circulating cathodic antigen**

**Glycoprotein Antigen associated with gut of the adult worm. It is genus specific & indicate active infection**

- **Detected by enzyme immunoassay. High sensitivity & specificity but expensive and high tech**
- **All other techniques are indirect: clinical, immunological, radiological, ultrasounds, endoscopy**

# Schistosomiasis – Diagnosis – Direct

**DIRECT DIAGNOSIS:**

- **Usually 3 specimen are needed**
- **Egg counting: indirect estimate of worm load BUT variation of daily output is high and submitted to peaks**

**Urinary schistosomiasis:**

- **Microscopic exam of sedimented/centrifuged urine (Beware of mansonuria!)**
- **Filtration techniques (urine passed through filter by syringes/pumps). The eggs are retained/ counted and can be stained by different stains**

# Schistosomiasis – Diagnosis – Direct

**Intestinal schistosomiasis:**

- **Eggs in faeces under microscopes or sedimented**
- **Direct method has low sensitivity**
- **Many concentration techniques are described (rmoval of fat & debris, mucus)**
- **Standard tool : Cellophane thick faecal smear**

  **Kato Katz technique (20-50mg stool)**
- **Watery stools cannot be processed by KK**
- **Sensitivity : lower limit is 50-100 eggs/g of stool**
- **Glass sandwich technique: no reagent, cheap and similar results to KK but for endemic areas**

# Schistosomiasis – Diagnosis – Direct

**Miracidial hatching :**

- **To demonstrate viability of eggs. Very sensitive**

**Rectal biopsy:**

- **Small biopsy specimen of mucosa (also from other organs) is soaked in water and examined under microscope**
- **Eggs of S.h. in rectal snips are non-viable and appear dark**

# Schistosomiasis – Diagnosis – Indirect

## Chemical reagent strips (CRS):

- Detects red blood cells. High specificity/sensitivity
- Most frequently used in S.h. infections
- Strips change color in presence of blood (orthotolidine)
- Can be used in areas of low or high transmission, good for surveys & chemotherapy
- False + in myoglobinuria & bacterial peroxidases (high bacterial infections)
- CRS also for proteinuria but less easy to read

# Schistosomiasis – Diagnosis – Indirect

## Immunodiagnosis:

- Detects specific Ab or genus-specific antigens
- Ab to adult worms, schistosomula, cercariae or eggs are detected by ELISA, RIA (radioimmunoassay), GPT (gel precipitation tech, IHA (indirect haemagglutination), LAT (latex agglutination), etc.
- Cannot indicate duration, activity or quantum of infection
- Costly, skilled personnel & slow
- Lack of standardization in procedures & reagents
- Improved area with production of monoclonal Ab and detection of CAA & CCA in serum or urine
- Choice of method depends on cost, need for rapidity, skilled personnel & facilities, etc.

# Schistosomiasis – Diagnosis – Indirect

## Radiology:

- Plain abdominal radio to detect calcification
- Intravenous pyelography to detect bladder & ureteral changes or obstructive uropathy
- Isotope renography or computed tomography for cerebral schistosomiasis
- Myelography for suspected cord damage
- Portal venography for hepatosplenic schistosomiasis

# Schistosomiasis – Diagnosis – Indirect

## Ultrasonography:

- Expanded use, non invasive, simple, portable, no health hazards
- High specificity/sensitivity (except for hydroureter & ureteral calculi)
- Is better for measuring size of liver & spleen
- Best for grading schisto periportal fibrosis, portal hypertension, hydronephrosis, bladder wall lesions & renal, bladder stones
- With US, schisto hepatic fibrosis can be differentiated from cirrhosis
- In use to determine the decrease in morbidity after population-based chemotherapy

# Schistosomiasis – Management

- **Huge advances since the 60' ies!**
- **In population, the aim is to reduce the egg excretion and reduce contamination of water supplies**
- **PRAZIQUANTEL is the drug of choice**
  - **Highly effective against all species, in other trematodes & cestodes infection too.**
  - **Single dose 40mg/kg and 60 for *S.jap* and *S.mek***
  - **Well tolerated**
  - **Resistance has been documented for *S. mansoni*, surveillance is needed!**
- **OXAMNIQUINE is effective only against *S. mansoni* (resistance also known)**
- **Artemisin derivates kill immature worms *(S. jap)***

**NB. As artemisin derivates are used for malaria, wider use for schisto would not be advisable**

# Schistosomiasis – Control in Tanzania


**Funded by the Bill & Melinda Gates Foundation**

**+ WHO**
**"Great Neglected Diseases Programme"**