**Parasitology Trematoda Lecture 5 د. حذام**

**Blood flukes 10 - 2 -2020**

**Blood flukes or Schistosom****es: Intestinal schistosomiasis Geographic Distribution:**

* *Schistosoma mansoni* : this parasite is hyperendemic in the Nile Delta and Middle East. It also found in parts of South America the Caribbean, and Africa.
* *S. japonicum* is confined to the Far East and occurs mainly in China, Japan, Taiwan & Philippines.

***Schistosema mansoni* (intestinal schistosomiasis, intestinal bilharziasis, katayama syndrome or schistosomal dysentery).**

***Schistosoma japonicum* :The oriental blood fluke (schistosomiasis japonicum, intestinal bilharziasis or katayama syndrome).**

**Morphology:**

***Schistosema mansoni***

1. The male measure 6.4-9.9 mm holding the female 7.2-14 mm in its Gynecophoric canal.
2. The male tegument is provided with warty spines.
3. Number of testes are 6-9 forming grape –like cluster.
4. The most important structure in female is a short uterus containing very few eggs (1 to 3only).
5. Natural habitat is the branches of the inferior mesenteric vein, adjacent to the lower colon, intrahepatic portal vein, vesicle venules and pulmonary arterioles.
6. The eggs are large rounded at both ends with conspicuous lateral spine. Egg size 120 X 45 µm to 75 X 65 µm.
7. Biomphalaria snail is the intermediate host.
8. Infection may persist for up to 32 years.

***Schistosoma japonicum***

1. Adult male measures 12-20 mm X 0.6 mm holding the female in its Gynecophoric canal in a continuous copulation. Female are much more delicate 15-30 mm X 0.1 mm.
2. The tegument is smooth.
3. The oral and ventral suckers are sub equal.
4. Long ventral sex canal with large testes usually (7).
5. Eggs are rounded 70-100 µm contain ciliated miracidium with minute blunt projection (knob like) on the outer surface. The gravid female may discharged 3500 eggs daily.
6. The earliest habitat of the young adults is the **tributaries of the superior mesenteric vein** of the small intestine. Later some worms migrate into the **inferior mesenteric vein or hepatic portal vein**.
7. Life spans in human: 4~5 years, longest: 35 years.
8. Can produce zoonotic infection.

**Life cycle:**



Eggs are eliminated with feces . Under optimal conditions the eggs hatch and release miracidia , which swim and penetrate specific snail intermediate hosts . The stages in the snail include 2 generations of sporocysts and the production of cercariae . Upon release from the snail, the infective cercariae swim, penetrate the skin of the human host, and shed their forked tail, becoming schistosomulae . The schistosomulae migrate through several tissues and stages to their residence in the veins (, ). Adult worms in humans reside in the mesenteric venules in various locations, which at times seem to be specific for each species. For instance, **S. japonicum** is more frequently found in the superior mesenteric veins draining the small intestine, and **S. mansoni** occurs more often in the inferior mesenteric veins draining the large intestine. However, both species can occupy either location, and they are capable of moving between sites, the females deposit eggs in the small venules. The eggs are moved progressively toward the lumen of the intestine, and are eliminated with feces. Various animals, such as dogs, cats, rodents, pigs, hourse and goats, serve as reservoirs for S. japonicum.

**Pathogenesis:**

* The incubation period in *S. mansoni* is about 2 weeks longer than that of *S. japonicum.*
* Infection with *S. mansoni* may persist for up to 32 years and infection with *S. japonicum* may persist up to 5 years.
* The intestinal lesions caused by *S. mansoni* typically in the colon rather than small intestine (natural habitat is the **branches of the inferior mesenteric vein**).
* The number of eggs produced by *S. mansoni* are few (5-6 eggs daily), thus the intestinal and hepatic fibrosis develop more slowly.
* The number of eggs produces by *S. japonicum* is greater than that produced by other spp. (3500 eggs daily).
* In heavy infection with *S. japonicum* the picture end with fibrosis, papillomas, stenosis of the small intestine, hepatic fibrosis, ascites, splenomegaly and pulmonary fibrosis.
* The earliest habitat of the young adults of *S. japonicum* is the tributaries of the superior mesenteric vein of the small intestine. Later some worms migrate into the inferior mesenteric vein or hepatic portal vein.
* 1- **Prepatent period: (*S. japonicum* & *S. mansoni*)** like in vesicle schistosomiasis.
* **2. Early acute stage: (Katayama fever).**  Like in vesicle schistosomiasis.

**The pathogenesis divided into three consecutive periods:**

1. **Prepatent period**: from skin penetration until the mature worm reaches the pelvic venules, in this period petechial haemorrhage, papular pruritic rash and small foci of oesnophilic and inflammatory changes in lung & liver.
2. **Acute stage** of active egg deposition, extrusion and trapping of eggs in perivascular tissue.
3. **Chronic stage** of stable egg output, tissue proliferation and repair by fibrosis and granuloma formation.

**Prepatent period:**

**Schistosome dermatitis (*swimmer’s itch)*:** resulting from contact with cercaria of Schistosome. The lesion consist of an initial pickling sensation accompanied by erythema and local or general urticaria, petechial haemorrhage, papular pruritic rash, soon the irritation subsides leaving a macula at the site of penetration but in few hours the reaction reach its maximum between second and third day, then gradually decreased.

**Acute stage:** Toward the end of prepatent period the patient may be symptomless or having increasing malaise and afternoon fever, moderate hepatic pain or epigastric distress and oesinophilia **(Katayama syndrome).** Katayama syndrome run more sever in patient with S. japonicum than in other type of schistosomiasis.

* **Late acute stage in *S. mansoni***:
* peptic ulcer, malabsorption syndrome,
* gastrointestinal bleeding (bloody diarrhea= dysentery)
* rectal polyp, thrombophlebitis, hepatic fibrosis and portal hypertension,
* Frank ascites is has less frequent.
* Very heavy infection produce sever toxic symptoms.
* **3. Chronic stage of stable egg output, tissue proliferation and repair by fibrosis and granuloma formation in *S. mansoni*.**
* The intestinal lesions typically in the colon (large intestine) rather than small intestine.
* The number of eggs produced are few, thus the intestinal and hepatic fibrosis develop more slowly.
* **The acute stage of *S. japonicum* is characterized by :**
* diarrhea with pus and blood (dysentery),
* loss of appetite and weight,
* egg in feces,
* daily fever,
* epigastric pain,
* ascites,
* Liver enlargement and granuloma around eggs.
* The colon (mucosa congestion, edema and egg granuloma) and spleen (splenomegaly) may involve in some cases.
* Ectopic lesion (lung & brain) may also develop.
* Then after few weeks the patient feels better & returns to work, but the symptoms may return on physical exertion.
* The blood picture is that of anemia, increase in Abs level & eosinophilia.
* As the **chronic stage** develops:
* The liver becomes increasingly fibrosed with multiple granulomas in the parenchyma.
* **Liver cirrhosis** is the prominent syndrome of this stage.
* Chronic colonic schistosomiasis characterized by **fibro obstructive lesion.**
* The mesentery and the omentum may be thickened so as to bind down the colon and separate the abdomen into upper and lower portion.
* Later there are:
* Increasing ascites and emaciation,
* Dyspnea on slight exertion,
* Dilatation of the superficial abdominal veins,
* Myocarditis due to egg infiltration to the cardiac wall.
* Cerebral schistosomiasis.

**Diagnosis**

1. **Eggs detection**
2. Microscopic identification of eggs in stool.
3. Tissue biopsy (the bladder) may demonstrate eggs when a urine examination is negative.
4. Miracidial hatching test.
5. Rectal biopsy **– *S. mansoni, S. Japonicum*.**
6. **Serological & immunological tests:**
7. Total L IgE examination.
8. Specific IgE (Rast test) P3 antigen.

**Treatment:**Praziquantel **[Biltricide (bil= bilharzia, tri= three sp, cide= kill)]**.

* ***S. mansoni, S. japonicum*: 2-3 doses of 30mg/kg**

**Control:**

* Educate people to not urinate or defecate in fresh water supplies
* Eliminate snail vectors by making the water habitat unsuitable (increase water flow, remove vegetation)
* Provide piped water to avoid direct contact with cercariae
* Mass drug treatment of communities to reduce reservoir of infection.

**Cercarial dermatitis: (swimmer’s itch)**

* Cercarial dermatitis is caused by the cercariae of certain species of schistosomes whose normal hosts are birds and mammals other than humans.
* These cercariae seem to have a chemotrophic reaction to secretions from the skin and are not as host-specific as other types of schistosomes.
* They attempt to, and, sometimes may actually, enter human skin.
* The penetration causes a dermatitis which is usually accompanied with intense itching, but the cercariae do not mature into adults in the human body.
* Cases of cercarial dermatitis can occur in both fresh and brackish water environments.
* Cercarial dermatitis occurs on the exposed skin outside of close-fitting garments.
* Characterized by an early **type I hypersensitivity** reaction and a late phase of cutaneous inflammation both associated with a polarized **Th2-type acquired immune** **response.**

**Host immune responses to Schistosomiasis**

The process involved in immune responses against *Schistosoma* is complex, due to:

* The antigenic variation during the life cycle (cercaria, schistosomula, adult and egg).
* The intensity of expression of antigenic component in the parasitic organism,
* The mechanism by which *Schistosoma* evades host immune system.
1. **During the first 4-5 weeks** following exposure to *Schistosoma* (early acute stage) when host immune system is directed against **adult worm antigens**, the immune response is primarily **Th1** in nature, with production of **interferon-γ (IFN-γ)** and **tumor necrosis factor-α (TNF-α)**.
2. During the normal infection when *Schistosoma* **eggs** are produced (late acute stage),
* The **soluble egg antigen (SEA)** stimulates immune response to become highly **Th2-polarized** which end by formation of granuloma**.**
* After development of the **Th2** response, there are notable increases in **plasma IgE** levels and the number of **circulating eosinophils**, which reflects the production of **IL-4** and **IL-5**, the signature cytokines of **Th2** cells helping class switching of **B cells** to **IgE** isotype.
1. In the chronic phase the immune response is the **Th2 type**, with elevated levels of **IL-4**, **IL-5**, and **IL-10** and decreased levels of **IFN- γ. IL-13** stimulates myofibroblasts to make collagen, which can lead to excessive fibrosis associated with granuloma formation and resolution

**Evasion of host immunity by Schistosomes**

Adult and larval worms must migrate through the host's blood circulation and avoid the host's immune system. The worms have many tools that help in this evasion, which including:

 **1. Tegument :**

**A. Protect the worm from the host immune elements:** tegument coats the worm and acts as a physical barrier to host antibodies and complement.

**B. Shedding or replacement of surface**: The outer layer of the tegument is rapidly replaced.

**C. Weak immunogenic:** Outer lipid bilayer posses of few antigens (the membrane proteins found in inner bilayer).

**D. Coating with host proteins**: Schistosomes take up host blood proteins, ex. blood group antigens & MHC class I & II molecules, therefore, the worms are seen as “self”.

**2. Molecular mimicry:** The parasite is able to mimic a host structure or function. Ex. schistosomes have E-selectin that may help in adhesion or invasion.

**3. Exploitation host signals:** Schistosomes actively use host immune molecules to grow & reproduce. Parasites might express receptors for these molecules which lead to enhance the growth of the parasite.

**4. Immunosuppresion / immunomodulation:** (very complex and not well understood).

1. **Production of Antioxidant proteins:** Schistosomes are able to produce a number of antioxidant proteins that block the effect of superoxide produce by host immune system.
2. **Defense against host MAC (membrane attack complex):** decay accelerating factor (DAF) and CD59 are found on host cells and protects host cells by blocking formation of MAC. (DAF) and CD59 also found on **the tegument of schistosomes blocking formation of MAC.**

 **End of lecture 5: Trematodes**