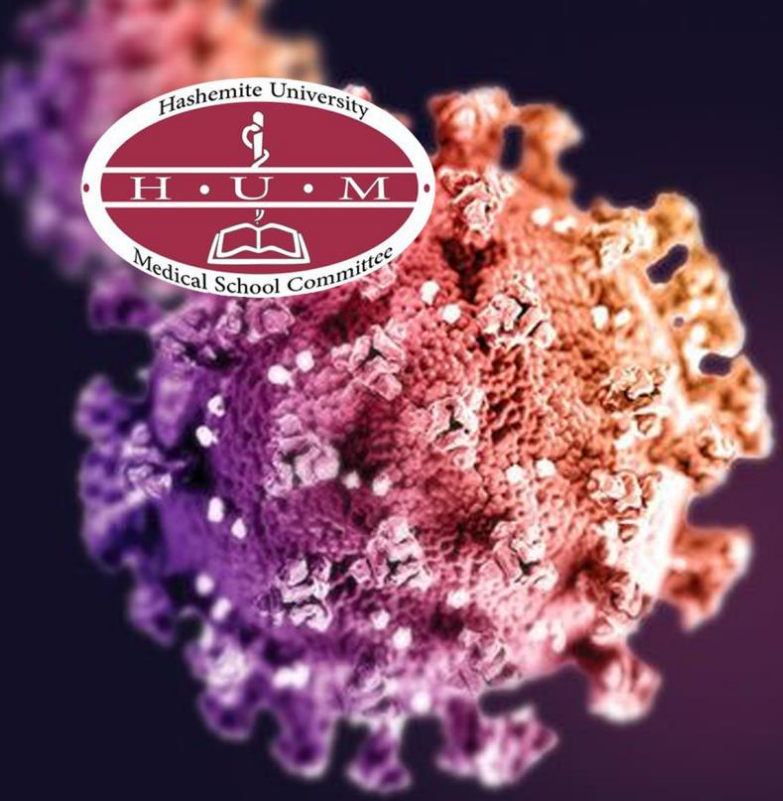


MICROBIOLOGY

DONE BY : Ahmad alzyood

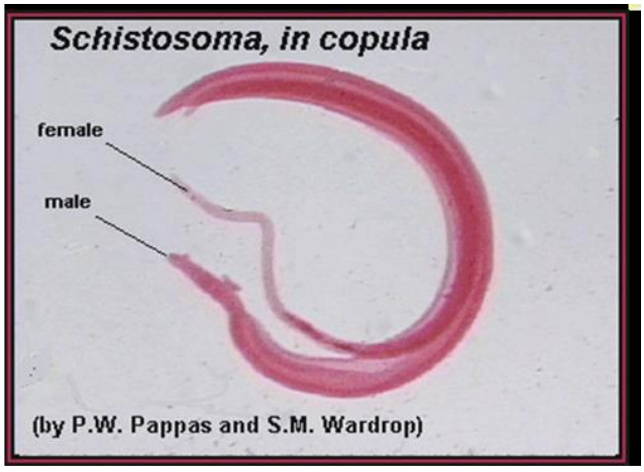
Schistosomiasis

Introduction

- The schistosomes are a group of closely related **flukes** that inhabit the portal vascular system of a number of animals.
- Bilharzia, or bilharziosis, is named after *Theodor Bilharz*, who first described the cause of urinary schistosomiasis in 1851.

- مرض البلهارسيا معروف بمصر بسبب وجود المياه العذبه بكثره – نهر النيل وهو بسببه تُوفي عبدالحليم حافظ.
- المسبّب لهذا المرض هو نوع من الديدان بتكون دائريه

- round shape + the female lives on a groove in male so both are living together
  - The 1 to 2 cm male possesses a deep ventral groove, or "schist." Within this gynecophoral canal it carries the longer, more slender female in lifelong copulatory embrace. من الكتاب



Species

1. Schistosoma mansoni and Schistosoma intercalatum cause **intestinal** schistosomiasis.

2. Schistosoma haematobium causes **urinary** schistosomiasis.

3. Schistosoma japonicum and Schistosoma mekongi cause *Asian* **intestinal** schistosomiasis

طبعا راح نحكي عن اللي بعملو intestinal schistosomiasis

Life Cycle

- After mating تزاوج of the adult worms in **the portal vein**, they ascend to the mesenteric vessels against the flow of blood. S. japonicum enters the superior mesenteric vein, eventually reaching the venous radicals of the small intestine and ascending colon; and end in the descending colon and rectum. S. mansoni and S. haematobium are directed to the inferior mesenteric system. Ultimately coming to rest in the venous plexus of the bladder and other pelvic organs.

أول اشي
في portal vein بصير نضوج و تزاوج الذكر والانثى
اثناء التزاوج او بعده تنتقل Schistosoma ال حسب نوعها
اذا كانت
S japonicum S mansoni الى small bowel and large bowel التي تبيض هناك ثم يخرج البيض عن طريق البراز stool
اما اذا كانت haematobium --> الى bladder and other pelvic organs وتبيض هناك ويخرج البيض عن طريق البول urine

- On reaching the submucosal venules, the worms initiate oviposition. Each pair deposits 300 (S. mansoni, S. haematobium) to 3000 (S. japonicum) eggs daily for the remainder of its 4- to 35-year life span.

مكان استقرار الدوده هو submucosal venules للمكان اللي بتروحله الدوده زي ما حكينا فوق (حسب النوع)

S. mansoni and S. haematobium --> 300 eggs daily
S. japonicum --> 3000 eggs daily

- Ova lying immediately adjacent to the mucosal surface rupture into the lumen of the bowel (S. mansoni, S. japonicum) or bladder (S. haematobium) and are passed to the outside in the excreta.

البيض بكون قريب من السطح submucosa اللي بخترق وبوصل لل lumen ومنه بطلع اما من البول او البراز

- When the eggs are deposited in fresh water, the miracidia (الكائن اللي جوا البيضه هو miracidia) hatch quickly. On finding a snail host appropriate for their species, they invade and are transformed over 1 to 2 months into thousands of forke-tailed cercariae. When released from the snail, these infectious larvae or cercariae swim about vigorously for a few days. Cercariae coming in contact with human skin during this time attach, discard their tails, and penetrate.

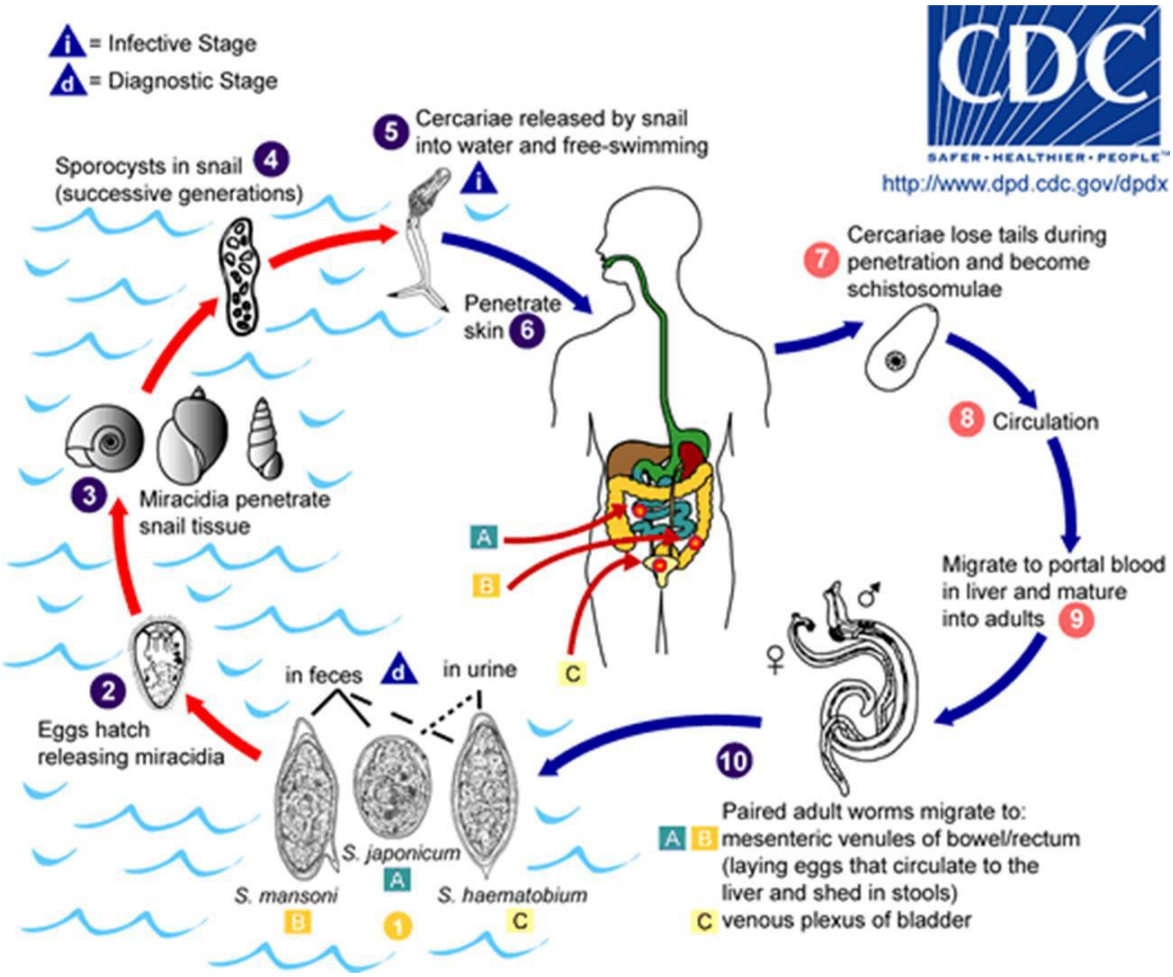
في حالة poor sanitation هاي الفضلات بتوصل لماء نقي
البيض بتفقس و هون الكائن اسمه بكون miracidia
اللي بتدور على snail وبتدخل جواته وبتتحول ل cercariae اللي الها ذيول عشان تسبح فيهم لما تطلع من snail، بمجرد ما تطلع بصير اسمها infectious larvae or cercariae اللي بتسبح وبتدور عالانسان second host .
لما تحتك مع بشرة الانسان بتخترقه وبترمي ذيولها وبتدخل الى ان توصل للدم بتضل يوم ل ثلاث ايام بل skin

- During a 1- to 3-day in the skin, the resulting schistosomula enter small venules and find their way through the right side of the heart to the lung.

خلال يوم ل 3 ايام بتضل بالبشره للما توصل الدم
بتروح عن طريق venules ثم vein ثم RA ثم RV وبتعبر الرئه وبتوصل لل LA and LV ثم aorta ثم تنطلق نحو gut الى ان توصل لل portal vein
المحطه الاولى اللي بصير فيها التزواج زي ما حكينا ثم الانتقال لل bowel or bladder حسب النوع ثم عن طريق البول او البراز

- After a delay of several days, the parasites enter the systemic circulation and are distributed to the gut.
  Those surviving passage through the pulmonary and intestinal capillary beds return to the portal vein(مكان النضوج جنسيا والتزاوج), **where** they mature to sexually active adults over 1 to 3 months.

ثلاث شروط عشان تكتمل ال cycle
1-انه البيض الموجود بالفضلات يوصل لماء عذب او نقي وهذا اما غالبا بل bad sanitation او طفل بعملها وببلينا
2-انه تلاقي ال miracidia مضيف وهو snail
3-انه بيجي انسان بسبح بالماء ويصير احتكاك



Epidemiology

- The widespread distribution and extensive morbidity of schistosomiasis makes it the single most important helminthic infection in the world today which kill 1 million annually. المرض فتاك حاصد للأرواح ، ايضا مزمن
وما اله علاج بالكامل
- The continued presence of the parasite depends on the disposal of infected human excrement into fresh water, the availability of appropriate snail hosts, and the exposure of humans to water infected with cercariae.
هذول نفسهم الثلاث عوامل اللي لازم تصير عشان تكمل life cycle
وبتتوفر في الدول اللي فيها تجمعات مائيه وانهار مثل العراق السودان ومصر
- The most common way of getting schistosomiasis in developing countries is by wading or swimming in lakes, ponds and other bodies of water which are infested with the snails

- The disease is found in Africa, the Caribbean Eastern South America, East Asia and in the Middle East.
- Schistosoma mansoni is found in parts of South America and the Caribbean, **Africa, and the Middle East.**
- S. haematobium **in Africa and the Middle East.**
- S. japonicum in the Far East.
- S. mekongi and S. intercalatum are found focally in Southeast Asia and central West Africa, respectively.

Pathogenesis

- There are three major clinicopathologic stages in schistosomiasis.
1. The first stage is initiated by the penetration and migration of the schistosomula.
اللي بتعمل رياكشن واضح وبنشوفه وهو skin dermatitis
2. The second or intermediate stage begins with oviposition and is associated with a complex of clinical manifestations.
وهون الأعراض بمكان وجود الباراسايت
اذا bladder or bowel
3. The third or chronic stage is characterized by granuloma formation and scarring around retained eggs. This is the **most morbid** phase.

Immunity

- The major clinicopathologic manifestations of schistosomiasis result from the host's cell mediated immune response to the presence of retained eggs.
  ➔ Not all eggs are excreted into the environment, and those left behind in tissue serve as antigenic stimuli for our immune system, which walls them off in eosinophilic granulomas ("Splendore-Hoeppli reactions").
- Present evidence suggests that both suppressor T lymphocyte activity and antibody blockade are involved.
- The correlation in humans between HLA types A1 and B5 and the development of hepatosplenomegaly suggests that the extent of the immunoregulation is influenced, at least in part, by the genetic background of the host.
- As evidenced by their prolonged survival, the adult worms are remarkably well tolerated by their hosts. In part, this tolerance may be attributable to the formation of IgG4 blocking antibodies early in the course of infection.

-1بقاء بعض البيض في داخل mucosa or submucosa راح يحفز جهاز المناعه انه يعمل رياكشن ضدها وبكون على شكل.granuloma
-2مع الوقت بخف هذا الرياكشن وال granuloma اللي بتتكون بتكون اقل حجما من الفترة الاولى لبيه ؟؟
بعض المقترحات كالتالي:
انه الخلايا الليمفاويه المثبطه بتشتغل وبتثبط ردة فعل المناعه
كمان فيه اجسام مضاده بتكون مضاده للاجسام المضاده اللي ولدها جهاز المناعه ضد البيض
--اللي بستفيد هو adult worm
لهيك اغلب المصابين بعد الانفكشن بتلاقي عنده دود لكن اذا احتك معinfectious cercariae
المناعه بتتصدالها وبتقتلها قبل ما توصل portal vein

Clinical Manifestations

➢ Early Stage

- Within 24 hours of penetrating the skin, a large proportion of the schistosomula die. In S. mansoni and S. haematobium infections, immediate and delayed hypersensitivity to parasitic antigens results in an intensely **pruritic papular skin rash** that increases in severity with repeated exposures to cercariae.
- As the viable schistosomula begin their migration to the liver, the rash disappears and the patient experiences **fever, headache, and abdominal pain** for 1 to 2 weeks.

-1خلال يوم من لما تدخل cercariae وتخترق الجلد
اغلبها بموت ف وجود بقايا الكائن antigens بحفز جهاز المناعه ومدام موجوده بالجلد فبكون dermatitis or skin rash
-2 لانه فيه لسا جزء عايش منها والي هو ببلش يروح لل portal vein عن طريق الدم
فببلش تطلع حراره عالمصاب مع صداع ووجع ببطنه وهالحكي من اسبوع بعد التعرض للطفيليات

➢ Intermediate Stage

هاي المرحله بتصير بسبب ردة فعل المناعه على البيض اللي بتحطه الدود لهيك بزيد من ال antigens الغريبيه فبصير فيه رياكشن

- One to two months after primary exposure, patients with severe S. mansoni or S. Japonicum infections may experience the onset of **an acute febrile illness** that bears a striking resemblance to serum sickness.
- The onset of oviposition leads to a state of relative antigen excess, the formation of soluble immune complexes, and the deposition of these in the tissues of the host.
- In addition to **the fever and chills**, patients **experience cough, urticaria, arthralgia, lymphadenopathy, splenomegaly, abdominal pain, and diarrhea**.

  1- cough and urticaria due to passing of s. into pulmonary vessles to go to gut.

  2- Lymphadenopathy + splenomegaly --> involvement of RES.

➢ Chronic Stage

هاي المرحله هي الاكثر انها تكون متعبه للمريض

واللي بيعملها هو البيض اللي ضل في submucosa وما راح على lumen وطلع برا الجسم

--لانه البيض بيحمل antigens غريبه ، المناعه رح تتحفز وبكون نوع الالتهاب بيعمل Granuloma

هاي ال granuloma بتكون من عمل T cell + eosinophiles

- Approximately one half of all deposited eggs reach the lumen of the bowel or bladder and are shed from the body. Those retained induce inflammation and scarring, initiating the final and most morbid phase of schistosomiasis.
- **Soluble antigens excreted by the eggs** stimulate the formation of T lymphocyte–mediated eosinophilic granulomas.

- Inflammatory and fibrotic reactions to retained **eggs** cause chronic disease, the severity of tissue damage is directly related to the **total number of eggs retained**.

- In S. haematobium infection, the **bladder** mucosa becomes thickened, papillated, and ulcerated. Hematuria and dysuria result; repeated hemorrhages produce anemia.

هون المكان اللي بتواجد فيه هذا النوع هو bladder

لهيك الاعراض هتشمل

1- bladder mucosa is inflamed+thickened+ulcerated

2- in severe infection, muscular layer is involved +loss of bladder capacity + congested

3- hematuria and dysuria that may lead to anemia

4- obstruction leads to renal failure + uremia

5- bladder carcinoma as a complication

- In severe infections the muscular layers (not only mucosa and submucosa) of the bladder are involved, with loss of bladder capacity and contractibility. Progressive obstruction leads to renal failure and uremia.
  Bladder carcinoma is frequently seen.

- In S. mansoni and S. japonicum infections, the bowel mucosa is congested, thickened, and ulcerated. Polyposis has been reported.

هون لما يكون المكان هو bowel
وجود البيض راح يحفز رياكشن فبتضرر ال mucosa وبنتج عنها تقرحات ودم وايضا اسهال ووجع بالبطن
احيانا البيض لموجود بروح وبعمل اعراض بل portal vein هسا رح نحكي عنها

- Patients experience abdominal pain, diarrhea, and blood in the stool. Eggs deposited in the larger intestinal veins may be carried by the portal blood f low back to the liver, where they lodge in the presinusoidal capillaries, leading to the development of periportal fibrosis and hepatic enlargement. Severity of the liver involvement is linked to the HLA type.

البيض بروح من intestinal veins الى منطقه قبل الدخول بالكبد وبنسميها presinusoidal capillaries
وممكن تؤدي ل portal hypertension
وهيك هتعمل
1- hepatosplenomegaly
2- ascites

- Immune complexes shunted to the systemic circulation may induce **glomerulonephritis**. Occasionally, eggs may be deposited in the central nervous system, where they may cause **epilepsy or paraplegia**.

- portal hypertension may lead to

1- Ascites

2- rupture of veins in lower esophagus (weak area) that lead to vomiting of blood (hematemesis)

3- hepatosplenomegaly

Diagnosis

- CBC: <u>eosinophilia</u> is characteristic
- LFT: <u>serum globulin</u> rise, <u>ALT</u> slightly rise
- **Definitive diagnosis** requires the recovery of the characteristic eggs in urine, stool, or biopsy specimens.
- The eggs of S. mansoni are oval, possess a sharp lateral spine, and measure 60 by 140 µm. Those of S. haematobium differ primarily in the terminal location of their spine. The eggs of S. japonicum, in contrast, are more nearly circular, measuring 70 by 90 µm. A minute lateral spine can be visualized only with care.
- In S. haematobium infections, eggs are most numerous in urine samples obtained at midday. Eggs of S. mansoni and S. japonicum are passed in the stool.

S. mansoni	S. haematobium	S. japonicum
oval, possess a sharp **<u>lateral</u>** spine, and measure 60 by 140 µm. 	oval, possess a sharp **<u>terminal</u>** spine, and measure 60 by 140 µm. 	nearly circular, measuring 70 by 90 µm. A minute lateral spine 

- Cystoscopy with biopsy of the bladder mucosa may be required for the diagnosis of mild infection.
- Results of rectal biopsy may be positive when those of repeated stool examinations are negative. Because dead eggs may persist in tissue for a long time after the death of the adult worms, active infection is confirmed only if the eggs are shown to be viable.

لانه البيض بتعشش بال rectum لهيك لما نوخذ منه biopsy ببين انه فيه بيض وبوزتف لكن لما نوخذ ال stoolبتطلع negative لهيك انه نعتمد انه اكتف لازم البيض يكون عايش

- Conventional serologic tests detect circulating antibodies with sensitivities exceeding 90% but cannot distinguish active from inactive infection.

بدنا نميز اذا المرض اكتف او لا
بنشوف اذا فيه antibodies
لكن بضل فيه نسبة خطأ 10 %
ثانيا بنوخذ نزعة من bladder or bowel

Treatment

- No specific therapy is available for treatment of **schistosomal dermatitis**. Antihistamines and corticosteroids may be helpful in ameliorating their more severe manifestations.
- Several anthelmintic agents may be used. Praziquantel, which is active against all three species of schistosomes, is the agent of choice.

Prevention

- It has proved both difficult and expensive to control this deadly disease.
- Programs aimed at interrupting transmission of the parasite by the provision of pure water supplies and the sanitary disposal of human feces are often beyond the economic reach of the nations most seriously affected.
- Similarly, measures to deny snails access to newly irrigated lands are expensive.
- Chemical molluscicides have been shown effective in limited trials.
- Mass therapy of the infected human population has, until recently, been severely limited by the toxicity of effective agents.
- Currently, there is intense interest in developing a vaccine suitable for human use.