Schistosomiasis: An update

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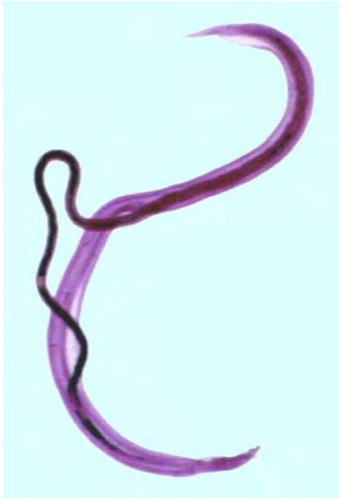
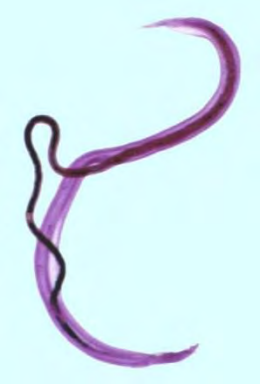
Schistosomiasis



- Historical preview
- What we know about Schistosome infection:
  - Disease Burden & Transmission
  - Epidemiological Transmission control and elimination
- Schistosomiasis
  - Immunomodulation & immunopathogenesis
- Diagnostic & Screening strategies
- Control & Prevention
- Vaccine for Schistosomiasis

Historical timeline:



1950 BC:

Egyptian pharaohs wrote of urinary bladder disturbances, *S. hematobium* denoting the disease was a dripping penis.

1200 BC:

Schistosome ova found in mummies dated from around this time

1851:

Theodor Bilharz, a German pathologist, discovered the parasite while working in Cairo

1915:

Lieper, an English scientist, discovered the intermediate snail host

Schistosomiasis

Species: *S. hematobium, S. mansoni, S. Japonicum, S. mekongi*

Africa **ME** **Indonesia**

85%

All spp cause intestinal infection except *S. hematobium* that causes urinary schistosomiasis

Incidence: 237 million people, Tropical/Sub-tropical regions

At Risk: 732 million in at least 76 countries

Symptomatic: 120 million people

Severe disease: 20 million

Schistosomiasis: 2015

In Middle East-N. Africa

Species: *S. hematobium, S. mansoni,*

Incidence: 12.7 million people

10 millions in Egypt & Yemen

Infection control:

Strategy: *Intersectoral collaboration between health, agriculture, and education*

Eliminated: Iran , Oman , Lebanon , and Tunisia

Reduced: Egypt, KSA, Morocco, Iraq, Syria, Jordon

Geographic distribution

Incubation Periods to Clinical Presentations

~24 hours	Skin Rash with local swelling
~1-2 months	Systemic symptoms, fever, hepatitis etc
~3-6 months to 1+ year	Urinary symptoms, dysuria, hematuria
Years	Bladder Sq cell cancer

Drugs of choice

Praziquantel (20 mg/kg taken orally 3 times over the course of 1 day)

or

Metrifonate (10mg/kg 1x week every other week, with a total of 3 doses) plus ~ steroids

Resistance to praziquantel may be emerging

Clinical Presentation:

24hrs – 4 days:

an itchy papular skin rash ("swimmer's itch") and local swelling

1 – 2 months:

Fever, hepatitis, hepatosplenomegaly, lymphadenitis, eosinophilia which may last for 1-3 weeks, not everyone have these sign/symptoms.

Months – Years:

May have dysuria, hematuria, urethral obstruction, renal damage.

50-70% of people may have some kind of symptomatic urinary tract finding.

Earlier complications (moths-years):

Chronic bacterial UTI, the bladder may develop tubercles, polyps, ulcers, and/or leukoplakia visible upon endoscopic examination.

Late complication (years):

Bladder cancer (squamous cell carcinoma)

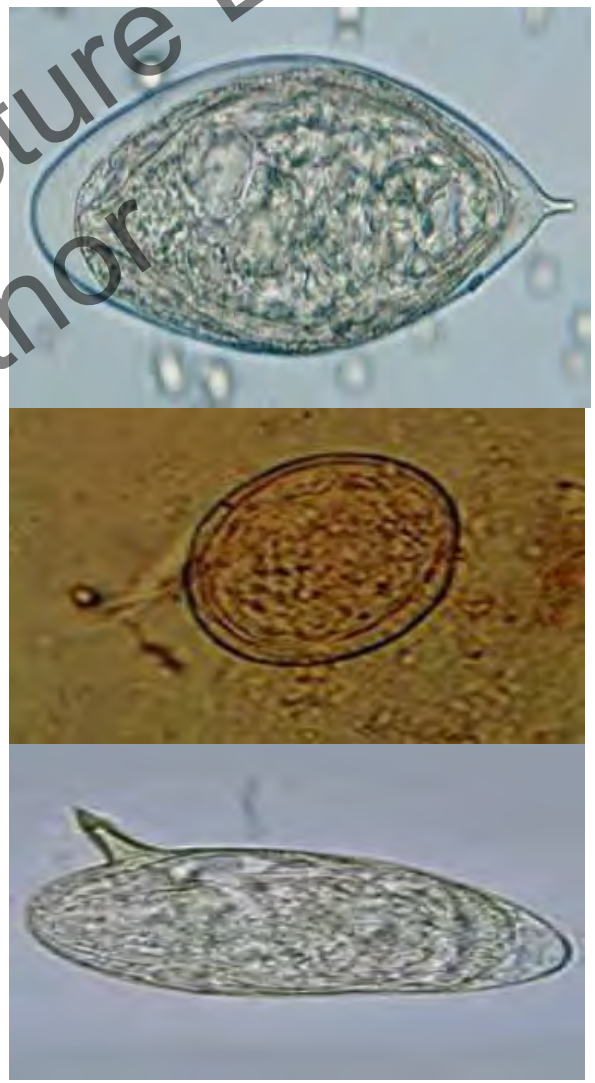
Schistosomiasis

Diagnostics

1. Microscopy:

light-intensity infections (i.e. ≤100 eggs per gram of stool) are often missed

2. Serology



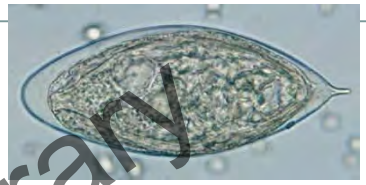
Rapid diagnosis of *Schistosomiasis:*

Point-of-care circulating cathodic antigen (POC-CCA) test

Negative Sample

Patient 1:
Faintly positive test band

Patient 2:
Strongly positive test band



S. hematobium

Clinical-Pathologic Spectrum

Asymptomatic

↓

Cystitis

Obstructive uropathy

Renal failure

Bladder carcinoma

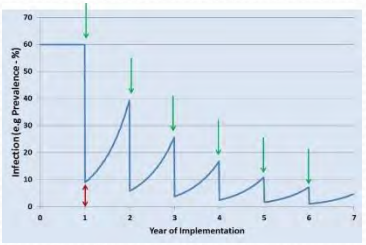
- Urothelial cancer [up to 20%-30% of all cancers in Egypt]

(1960s -1980s, non-sterile injection of tartar emetic lead to HCV infection)

Can schistosomiasis be eliminated?

in our Life time

In 2012, World Health Assembly decided to eliminate it by 2025 ie to reduce the prevalence threshold to <1%



Ongoing Schistosomiasis Control Initiatives:

- PCT dose 40 mg/kg cures only 52% of infection,
- PCT doesn't reduce infection to req level ie <1%
- PCT does not prevent reinfection

- Malnourished Patients highly susceptible to reinfection from contaminated water
- Drugs supply to the most needy is <50%
- Drug compliance is very low, many countries reporting <50%
- Decreased donor funding - fragile global economy

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PLoS One. 2015; 10(4): e0118362

Can schistosomiasis be eliminated?

What to do different?

So need to use combine approach:

- PCT, clean water, sanitation/hygiene, snail control,
- Development of vaccines or new drugs.
- **Plus include pre-school children for PCT**

Accurate infection monitoring by Geographic Information System (GIS)

* Immune modulators with PZQ to develop resistance to re-infection
IL10 blocks resistance to re-infection

Reliable constant drug supply:

Project Last Mile 2009: Coca-Cola, the Gates Foundation and the Global Fund
Using Coca-Cola supply chain to deliver drugs AIDS, tuberculosis and malaria to ten African countries.

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2015dx.doi.org/10.1016/S61536-7
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Immunopathogenesis of human schistosomiasis

M. L. BURKE, M. K. JONES, G. N. GOBERT, et al
Parasite Immunology 2009, **31:**163–176

Parasite & Host factors:

Schistosome virulence factors [Tegument proteins & phosphotidylcholine] facilitate immune evasion

Immune response: CD4 Th2 cell-mediated immune response against parasite egg antigens

Pathology: perioval granuloma formation in target organs, liver fibrosis, visceral fibrosis, renal

Later stages:

- Th1 response - protect against granuloma formation by down-regulation of the response to newly deposited eggs

Schistosomiasis might induce autoimmune activity

[IL-10 inhibiting the production of pro-inflammatory mediators such as IFN-γ), TNF-α and nitric oxide]

Diagnostic Clues

- ✓Urine Exam: May reveal RBCs and mild albuminuria
- ✓Detection of eggs in urine during the active infection
  [**Nuleopore filtration**: Typical terminal-spined eggs]
- ✓Serology: Ab/Ag. Assays; ELISA
- ✓PCR

Diagnosis & Essays

Clinical approach:

For returned travelers: serology ++ is the most useful test. As the parasite burden is low.

In endemic areas: Microscopy ++ (spp. & infection burden)

Serology +/-

Diagnostic screening in endemic areas:

screen all individuals/travelers with freshwater exposure, even in the absence of symptoms

Neuroschistosomiasis: PCR on CSF

Infection intensity: important in endemic areas, as parasite burden may correlates with complications.

For intestinal schistosomiasis;

Light infection (up to 100 eggs/gram), moderate 100-400; severe >400 eggs/gram).

For urinary schistosomiasis:

Light to moderate (up to 50 eggs/10 mL) or severe (>50 eggs/10 mL).

Diagnosis & Essays

Screening tools:

Serology, urinalysis, urine dipstick & microscopy positive 4-6 weeks following exposure

Essay sensitivities:

Serology Ab titer does not correlate with parasite burden. Negative means no infection

** A large retrospective study of 1107 Pts in London; all cases were diagnosed by serology or microscopy:*

Urine dipstick for Ag detection & eosinophilia: 50% sensitive
ELISA: 72 percent of ova-positive cases
Microscopy, stool and urine: 45 percent of cases

** A systematic review of 90 studies, mostly in Africa with microscopy as standard:*

Urine microhematuria test strips have high sensitivity/specificity
Point-of-care circulating cathodic Ag test had 89% sensitivity but modest 55% specificity

Schistosomiasis

Principle of Management:

1. Reversing acute disease
2. Preventing complications
3. Preventing neuroschistosomiasis

- Praziquantel
  - Wait & treat ------- 40 mg/kg
  - Resistance: artemisinin/mefloquin esp. early stage of infection !!!

- Chemoprophylaxis
  - ✓Prevention
    - ✓***Mass chemoprophylaxis***
    - ✓***Population deworming:*** ivermectin 200mcg/kg & albendazole 400 mg

- **No vaccines available yet**

Development Status of Current Vaccine Candidates

Candidate Name/Identifier	Preclinical	Phase I	Phase II	POC	Phase III
SmTSP-2*c* (tetraspanin D)		X			
SmTSP-1	X				
Sm29	X				
Sm23	X				
Sm-p80	X				
Sh-GST28			X		
Sm14*e*		X			
Sm28-GST*e*		X			
Sm28-TPI*e*		X			
Sm97 paramyosin*e*		X			
CT-SOD	X				