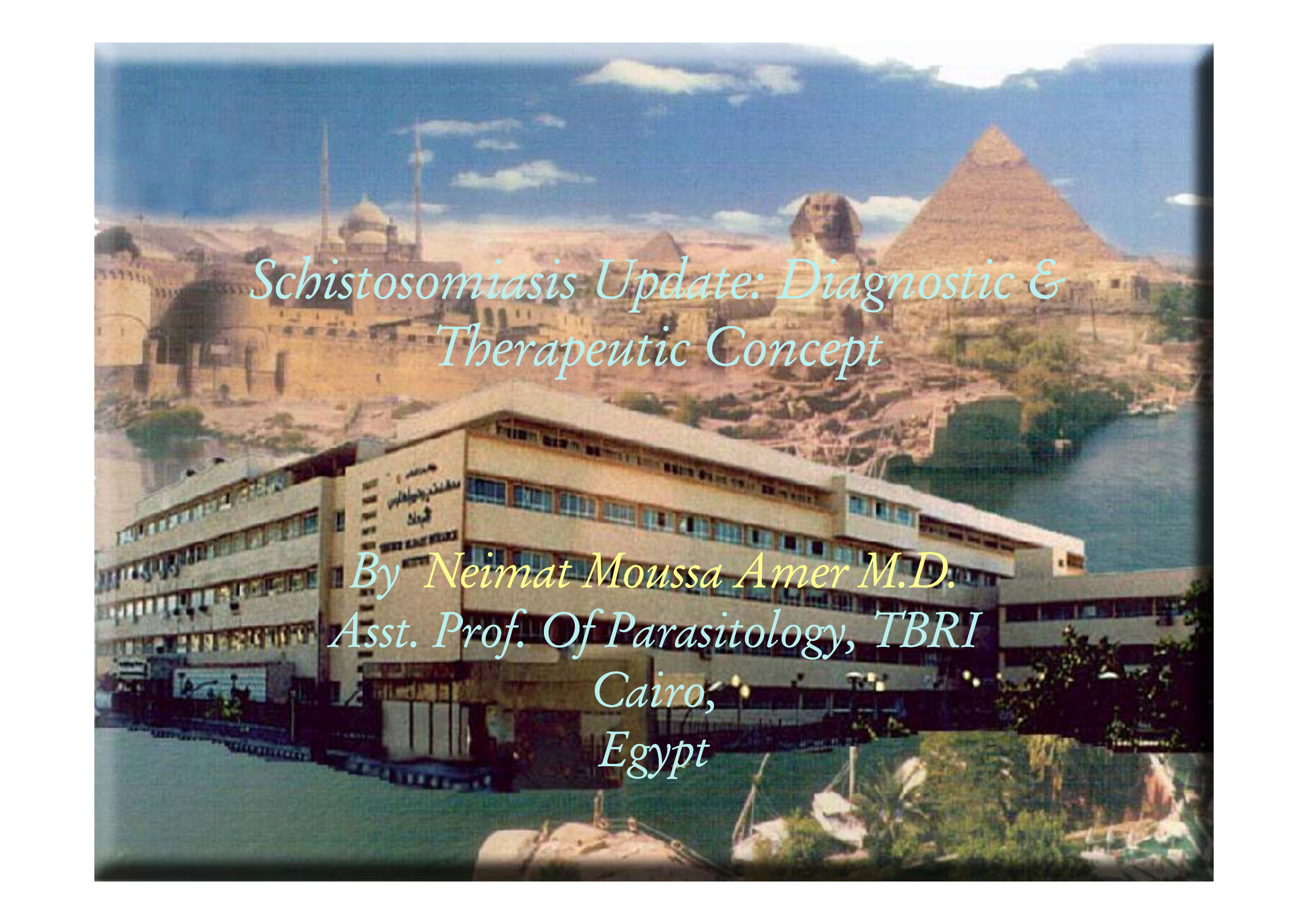


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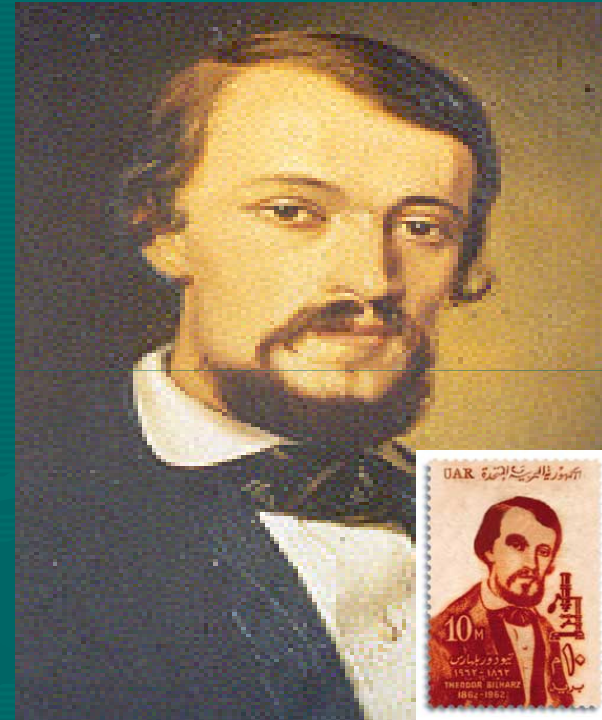


Schistosomiasis Update: Diagnostic & Therapeutic Concept

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Egypt*

Theodore Bilharz

- A German pathologist who discovered in autopsy material, the causative agent of haematuria; schistosome worms, during his work in Egypt in 1851.



www.medizin.uni-tuebingem

What is Schistosomiasis?

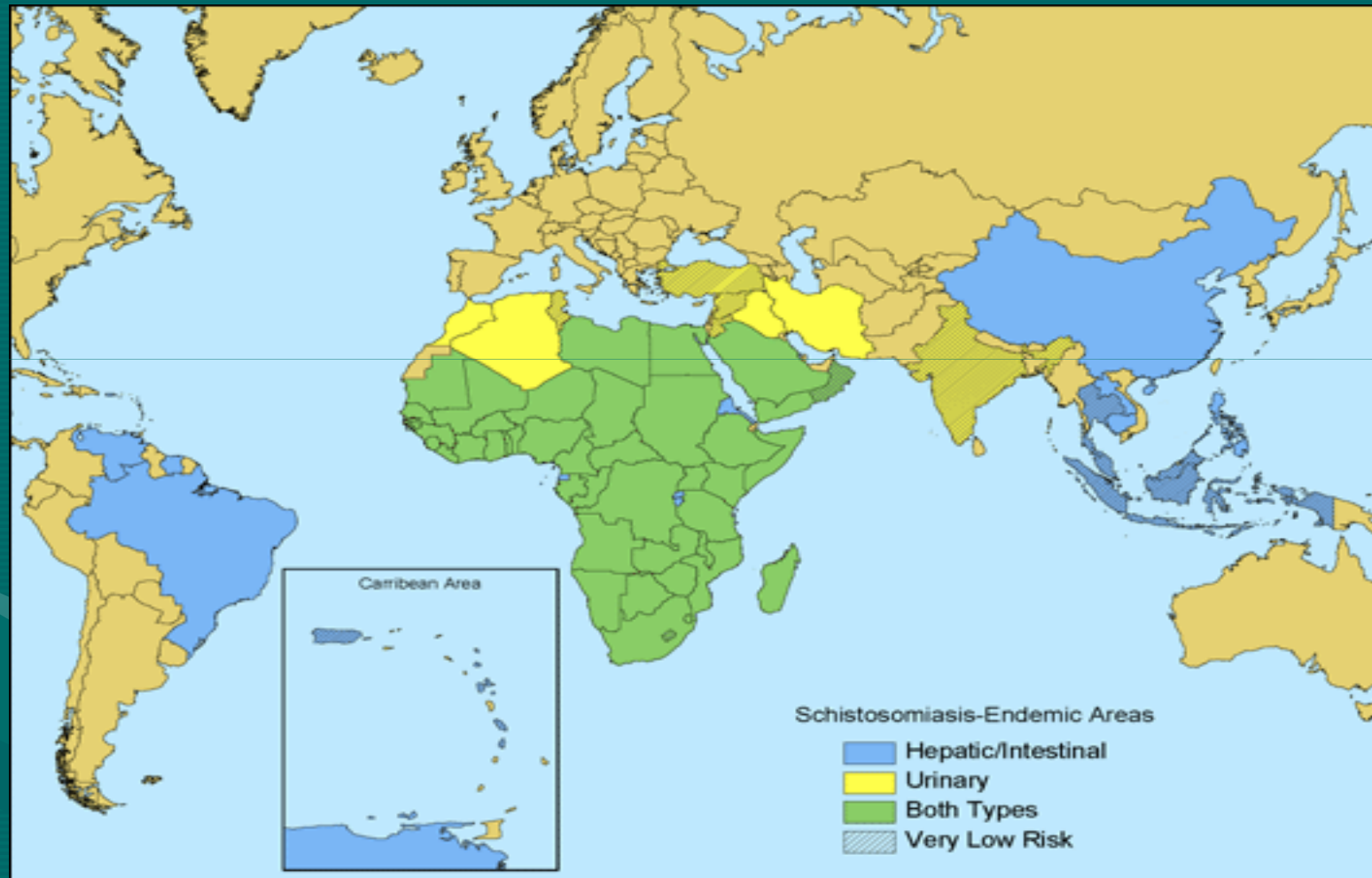


- It is a chronic debilitating disease that is caused by a parasitic trematode worm (Schistosome).

Image from Wellcome Trust

- It continues to threaten millions of people particularly the rural poor in the developing countries.
- Of the estimated 200 million infected people, more than half have symptoms and 20 million exhibit severe disease manifestations.
- There are five species of schistosomes that can infect humans, of which *S. mansoni*, *S. japonicum* and *S. haematobium* are the most important ones.

Global Distribution of Schistosomiasis



Cited from CDC

Pathogenesis & Clinical Picture

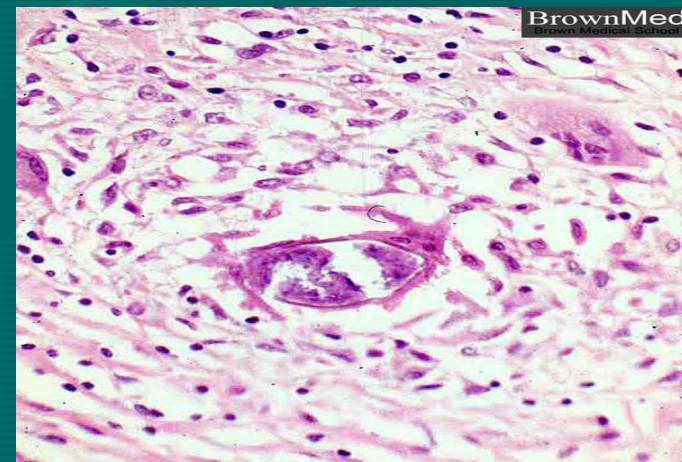
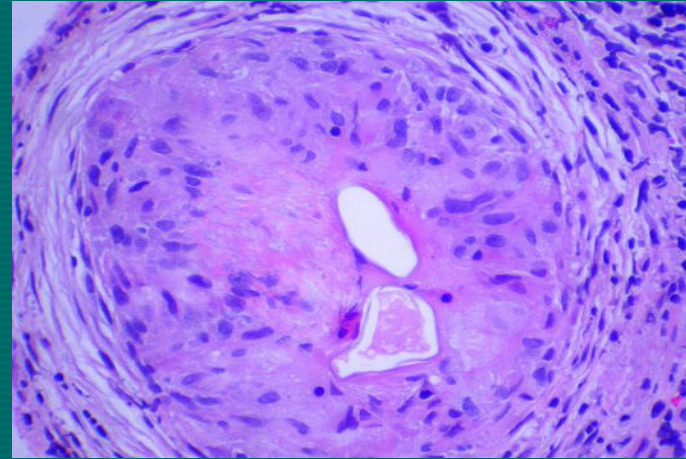
- Schistosomiasis is characterized by three distinct syndromes:
- Cercarial Dermatitis
- Acute Schistosomiasis
- Chronic Schistosomiasis



Pt. Wikipedia.org

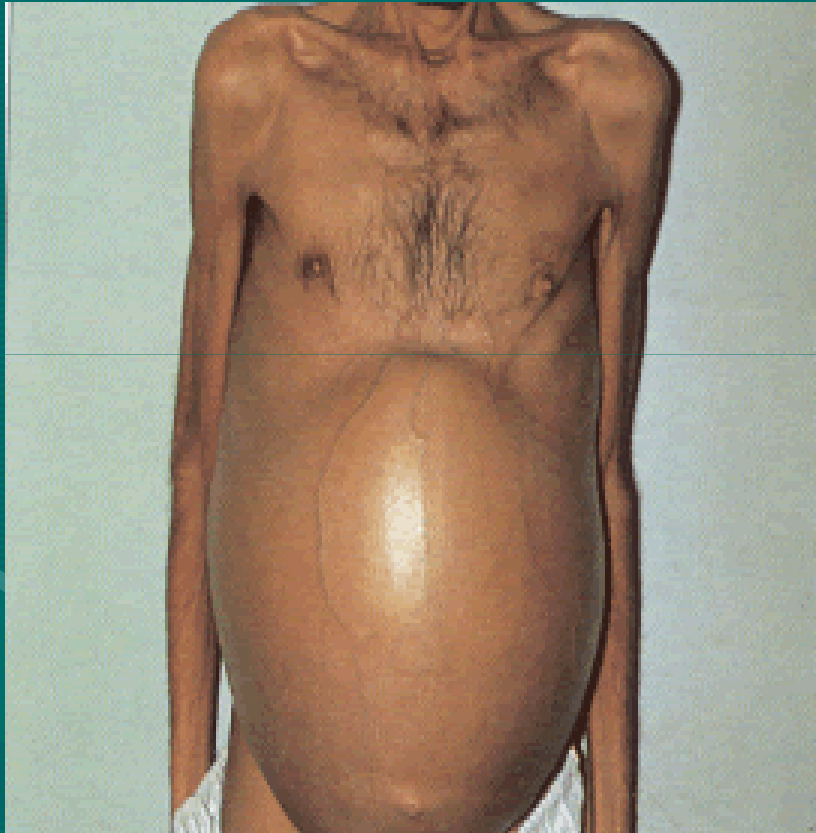
Pathogenesis (cont.)

- Rather than being excreted, however, some of the eggs may lodge in tissues of the host and it is the presence of these retained eggs with granuloma formation, that cause the pathology of schistosomiasis.



Pathogenesis & Clinical Picture

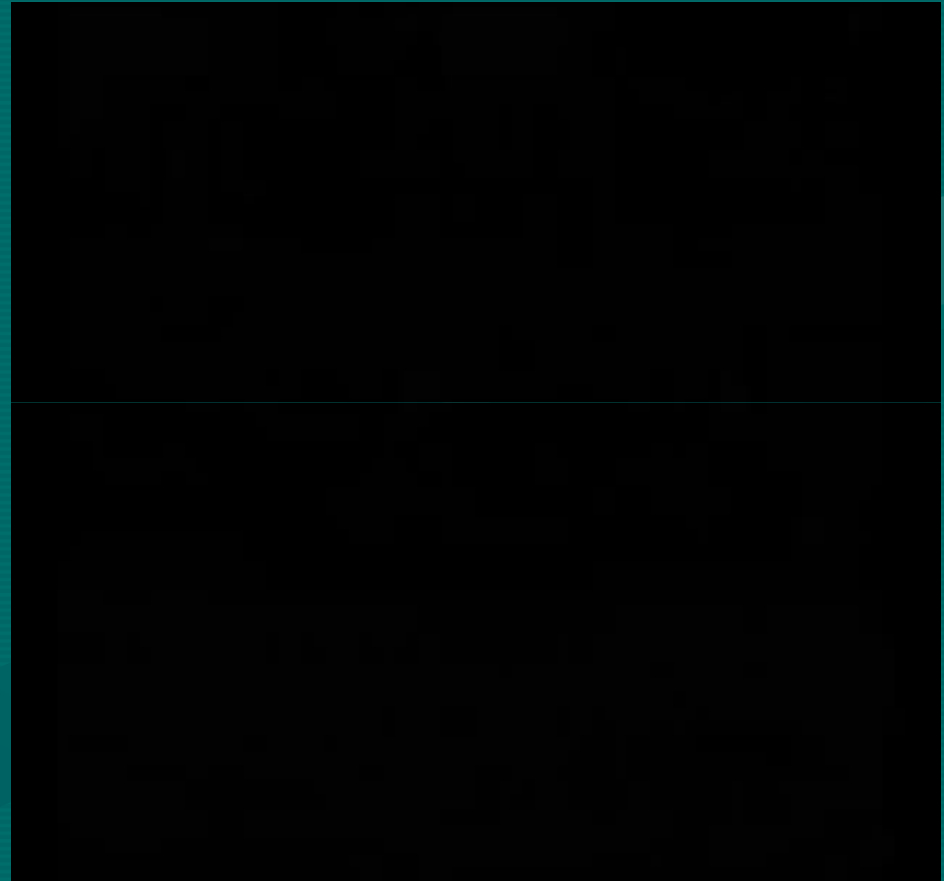
(cont.)



- Eggs lodged in the liver result in portal fibrosis, portal hypertension, splenomegaly, ascites, oesophageal and gastric varices. Exsanguination from bleeding esophageal varices is the major cause of death

Control

- 1- Safe water supply.
- 2- Sanitation.
- 3- Snail control:
 - Chemical Molluscicides
 - Biological Control
 - Certain plants with molluscicidal effect



Control *(cont.)*

4- Health education:

- Knowledge of the complex life cycle of the parasite.
- Advertising campaigns through mass media.
- Explaining the danger of infection & the availability of free diagnosis & treatment.

Control (cont.)



The Carter Center/Emily Staub



Diagnosis

- Physical & Clinical Examination
- Parasitological Methods
- Immunological Methods



Diagnosis

Physical & clinical examination:

- The clinical diagnosis is difficult as most symptoms are non-specific
- In chronic urinary schistosomiasis, haematuria is a useful indicator



Diagnosis *(cont.)*

Parasitological Methods:

- In principle, parasitological methods have 100 % specificity
- The sensitivity can be low
- They are divided in to qualitative techniques & quantitative techniques

Parasitological Diagnosis

Qualitative

Quantitative

Direct

Concentrated

Sedimentation (Urine)

MIFC (Stools)

Filtration Nucleopore (Urine)

Kato (Stool)

Diagnosis *(cont.)*



Different types of ova as seen under the microscope

Diagnosis *(cont.)*

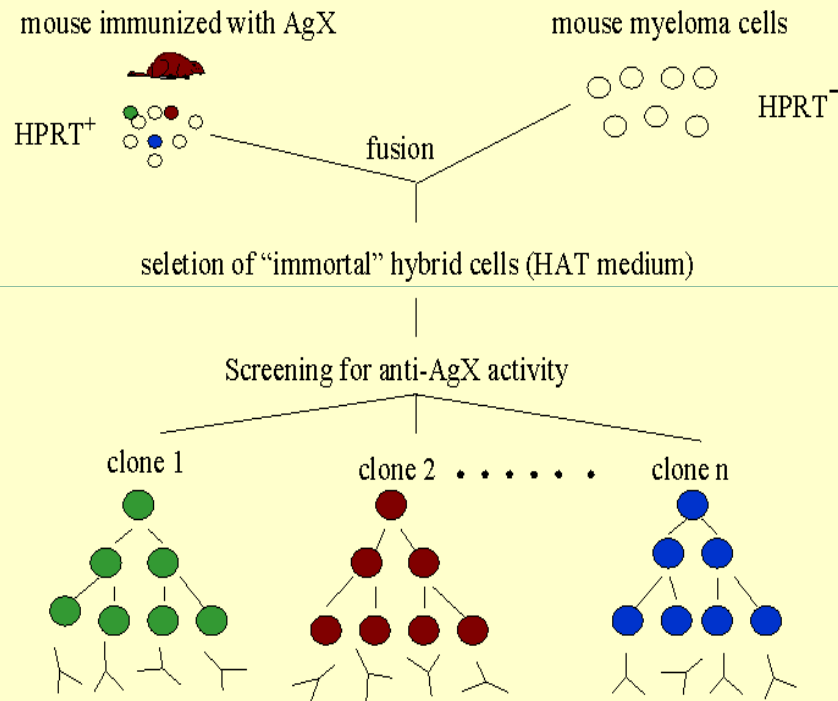
Immunological Methods:

Antibody detection assays:

- The most frequently used technique nowadays is ELISA, but antibody levels generally do not differentiate between past and present infection and do not give any information about intensity of infection.
- Therefore, can not be used as a cure monitor.

Diagnosis (cont.)

Production of monoclonal antibodies



Circulating Antigen Assays:

- Circulating antigens are defined as soluble substances released by the parasite into the blood stream of the host, and are claimed to be the main antigenic stimuli of the immune response.
- Sandwich ELISA is used to detect circulating schistosoma antigens (CSA) in serum as well as in urine.
- The use of monoclonal antibodies (Mabs) greatly improved the sensitivity and specificity of circulating schistosome antigens detection assay and proved to be an efficient immunodiagnostic tool for schistosomiasis.
- It acts as a reliable cure monitor.

Courtesy to El-Demerdash Z- TBRJ

Treatment

- While the distribution of schistosomiasis has changed over the last 50 years and there has been successful control programmes, the number of people estimated to be infected or at risk of infection has not been reduced.

Treatment (cont.)



Praziquantel

- Chemotherapy with praziquantel is the mainstay for morbidity control.
- Praziquantel will certainly remain to be the drug of choice over the next several years, since the 54th World Health Assembly recently put forth a target to treat at least 75% of school age children in areas with high burdens of schistosomiasis with praziquantel by 2010.

Treatment *(cont.)*

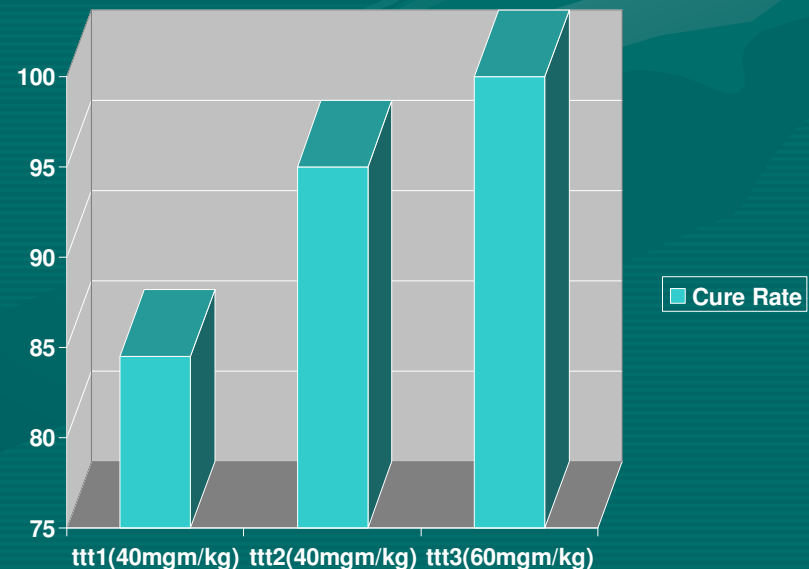
- PZQ is administered in a single oral dose and is nowadays less costly than its predecessors, ensuring compliance and generalized access to the drug.
- Reports of possible resistance to PZQ have come from Egypt and Senegal.
- In Senegal, a number of factors have been proposed to account for the low cure rates.
- In Egypt, PZQ has been copiously used and the impact of the drug on schistosomiasis has been significant. Unfortunately, reports of resistance to PZQ have recently appeared. However, the reality of these reports is difficult to establish, because it is often difficult to distinguish between host factors and parasite factors. The host immune system plays an active role in the process of killing PZQ-damaged worms, normal parasites might survive ttt in immuno-compromised hosts.

Treatment (cont.)

Our work in 2005 showed that there has not been an increase of drug failure, despite 10 years of therapeutic pressure in villages where there had been resistant infections and worms with decreased response to PZQ.

Data showed that these villages have experienced a significant decrease in the prevalence & intensity of *S.mansoni* infection with present infection rate of 10.9% in 2005 compared with 25.9% in 1994.

Results of PZQ treatment of schistosomiasis in 5 Egyptian villages

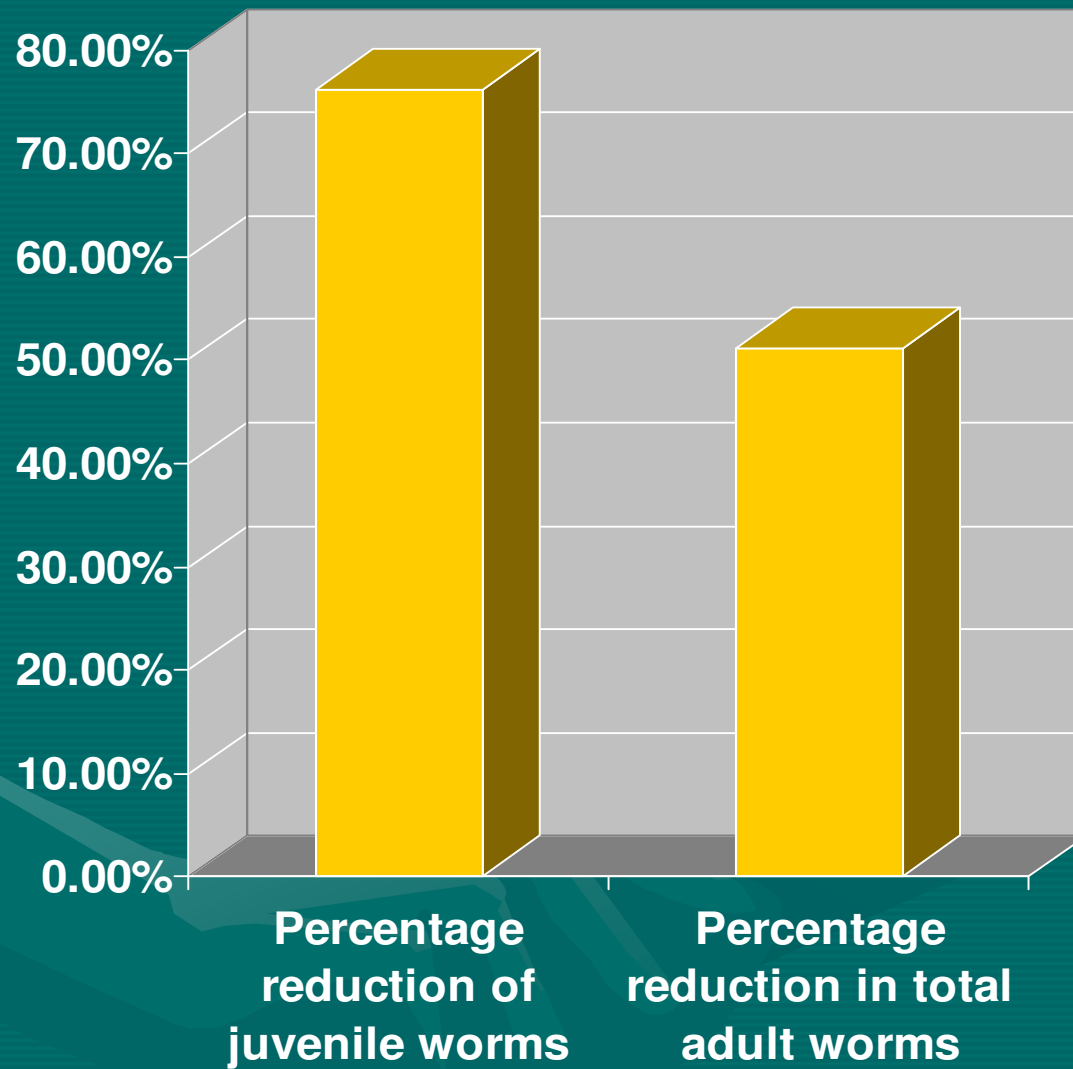


- However, the prospect of having a single drug available for a disease affecting 200 millions of people is...quite alarming.

Treatment (cont.)

Artemether

- Two decades ago, a group of Chinese scientists discovered the antischistosomal properties of artemether, a derivative of the antimalarial drug artemisinin.
- In contrast to praziquantel, artemether exhibits the highest level of activity against 1-to-3-weeks-old liver stages, while the invasive stages and the adult worms are less susceptible. Adult female worms are somewhat more susceptible to artemether than male worms.
- We evaluated the effect of an Egyptian strain of artemesia namely *A.inculta* as a schistosomicidal agent on juvenile worms & adult worms in infected mice, receiving ethanol extract of the plant in a dose of 800 mgm/kg intragastrically 7, 14 & 21 days PI.



■ Effect of artemesia extract on juvenile & adult worms in mice infected with 100 cercariae

Treatment (cont.)

Drug Combination:

- Drug combinations may help to improve treatment success rates and prevent the development of resistance. The combination of artemether and praziquantel is being tested in clinical trials in China and Egypt.
- The activity of artemether (ART) against different developmental stages of schistosomes alone and in addition to praziquantel (PZQ) was investigated by Botros et al at TBRI (2005).
- Combined treatment of ART (4 and 6wk PI) and PZQ resulted in >90% worm eradication and amelioration of *Schistosoma mansoni* eggs from the tissues, with minor histological changes in the liver.
- This combination is not planned in malaria-endemic areas because of the risk that it might induce resistance to artemisinin in malaria parasites.

Treatment *(cont.)*

Mirazid

- Mirazid contains an extract (an oleo gum resin) from the stem of *Commiphora molmol* (syn. *Commiphora myrrha*), the myrrh tree.
- The effectiveness of Mirazid is controversial, as data from different laboratories is equivocal.

Schistosomiasis & Hepatitis C

- The prevalence of antibodies to Hepatitis C Virus (HCV) in Egypt is among the highest in the world. From the 1950s until 1982 hundreds of thousands were infected during mass campaigns to control schistosomiasis using mass therapy with intravenous antimony compounds, but little is known about current risk factors and rates of transmission. Early treatment of schistosomiasis in patients with virus C is recommended.

Schistosomiasis Vaccine

- Effective vaccines are a long way from being developed, even when good candidates have been identified, they may take many years to pass through pre-clinical trials. Although a vaccine against schistosomiasis, does not yet exist, recent studies have shown the efficacy of chemoprophylaxis of artemether.



Conclusion

- *Control of Schistosomiasis is not an easy task.*
- *Even after successful treatment, re-infection easily takes place in most endemic areas, unless transmission is cut off somewhere between the intermediate host & the final host.*



Thank You

ONE WORLD