NEGLECTED TROPICAL DISEASES: Soil transmitted infections

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Neglected Tropical Diseases

- Neglected tropical diseases (NTDs) are most common conditions affecting the poor in Sub-Saharan Africa.
- Mainly chronic illnesses identified as causing morbidity & mortality amongst the world's poorest populations.
- Together, burden of disease is 50% the malaria disease burden.
- 85% of NTD disease burden is helminth infections.
- NTDs are disabling, disfiguring and chronic conditions.
- In extreme poverty setting, 51% live on less than $1.25 per day, 73% on less than $2.
- NTDs effect grouped with TB, HIV/AIDS, and malaria. (geographical overlap)

Geographical overlap of NTDs

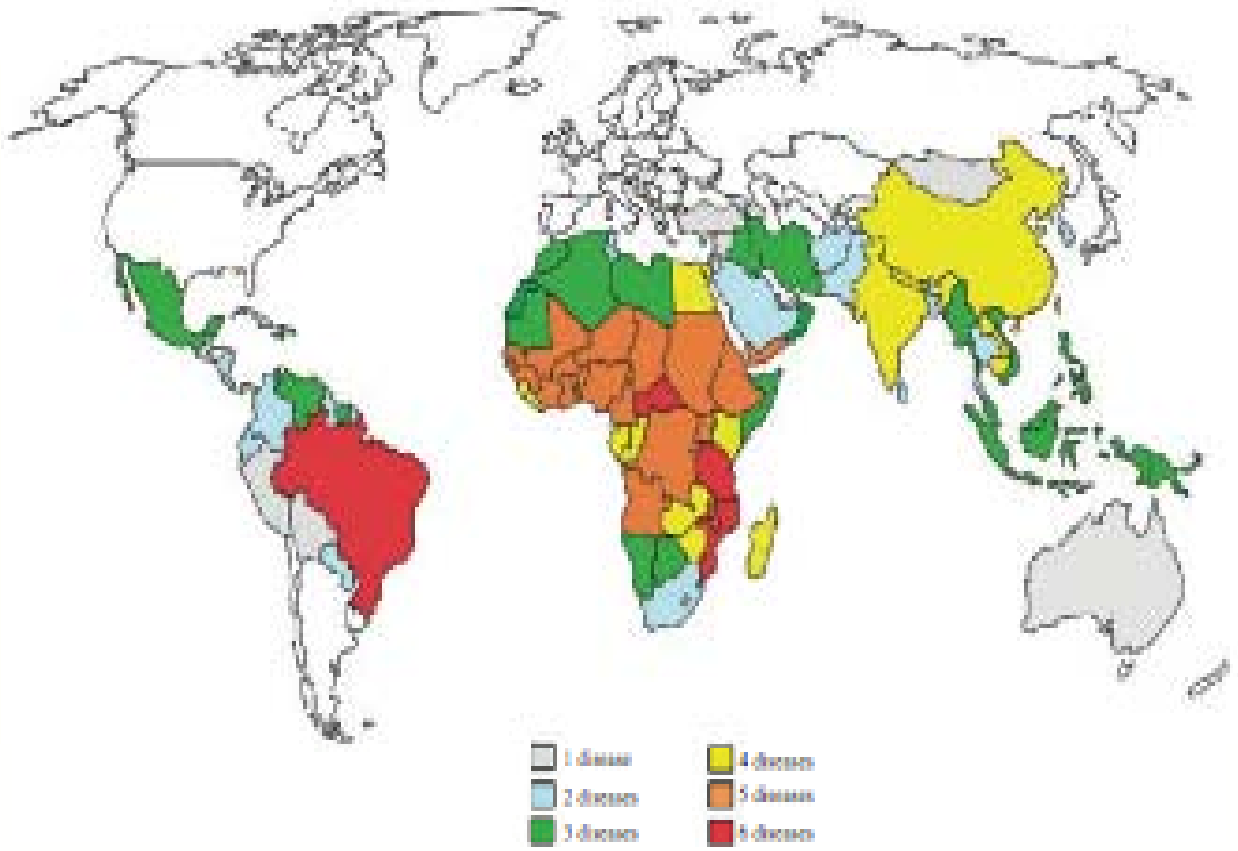


Fig. 1. The geographic overlap of the Neglected Tropical Diseases (NTDs). Of the 56 nations with five or more co-endemic NTDs, 40 are found in Africa, nine in Asia, five in the Americas, and two in the Middle East. Map prepared Molly Brady, Emory University and reproduced in Molyneux et al. (287).

Bethony et al, 2011 Immunological Reviews 239:237-270

What are the NTDs?

- NTDs are a group of chronic parasitic & other infectious diseases that:
  - The most common infections in the developing countries of Africa, Asia and the Americas
  - Ancient conditions having affected humankind for thousands of years
  - Affect the poorest people living in rural areas, and among the urban poor
  - Have high morbidity but low mortality, producing disabling effects thru child development & education, pregnancy outcomes and worker productivity
  - Promote poverty and interfere with economic development.

Common NTDs

- 13 core NTDs targeted due to prevalence & burden of disease.
- Vector-borne protozoan infections
  - Human African Trypanosomiasis
  - Leishmaniasis
  - Chagas disease
- Bacterial infections
  - Trachoma
  - Leprosy
  - Buruli ulcer
- Helminth infections
  - Schistosomiasis
  - Hookworm
  - Ascariasis
  - Lymphatic filariasis
  - Onchocerciasis
  - Trichuriasis
  - Dracunculiasis

Major helminthiases

The major human helminthiases and their global prevalence and distribution

Disease	Major etiologic agent	Global prevalence	Regions of highest prevalence
Soil-transmitted nematodes			
Ascariasis	*Ascariasis lumbricoides* (roundworm)	807 million	Developing regions of Asia, Africa, and Latin America
Trichuriasis	*Trichuris trichiura* (whipworm)	604 million	Developing regions of Asia, Africa, and Latin America
Hookworm	*Necator americanus*; *Ancylostoma duodenale*	576 million	Developing regions of Asia, Africa, and Latin America (especially areas of rural poverty)
Strongyloidiasis	*Strongyloides stercoralis* (thread worm)	30–100 million	Developing regions of Asia, Africa, and Latin America (especially areas of rural poverty)
Filarial nematodes			
LF	*Wuchereria bancrofti*; *Brugia malayi*	120 million	Developing regions of India, Southeast Asia, and sub-Saharan Africa
Onchocerciasis (river blindness)	*Onchocerca volvulus*	37 million	Sub-Saharan Africa
Loiasis	*Loa loa*	13 million	Sub-Saharan Africa
Dracunculiasis (guinea worm)	*Dracunculus medinensis*	0.01 million	Sub-Saharan Africa
Platyhelminth flukes			
Schistosomiasis	*Schistosoma haematobium*; *Schistosoma mansoni*; *Schistosoma japonicum* (blood flukes)	207 million	Sub-Saharan Africa Sub-Saharan Africa and Eastern Brazil China and Southeast Asia
Food-borne trematodiases	*Clonorchis sinensis* (liver fluke); *Opisthorchis viverrini* (liver fluke); *Paragonimus spp.* (lung flukes); *Fasciolopsis buski* (intestinal fluke); *Fasciola hepatica* (intestinal fluke)	>40 million	Developing regions of East Asia
Platyhelminth tapeworms			
Cysticercosis	*Taenia solium* (pork tapeworm)	0.4 million (Latin America only)	Developing regions of Asia, Latin America, and sub-Saharan Africa

Hotez, et al, JCI 2008;

Why neglected?

- NTDs remain relatively unknown to the general public.
- Partly due to decreased media coverage of these infections.
- Decreased investment by pharmaceutical companies in new treatments.
- NTDs no longer restricted geographically- immigrants & travelers. (Imported NTDs)

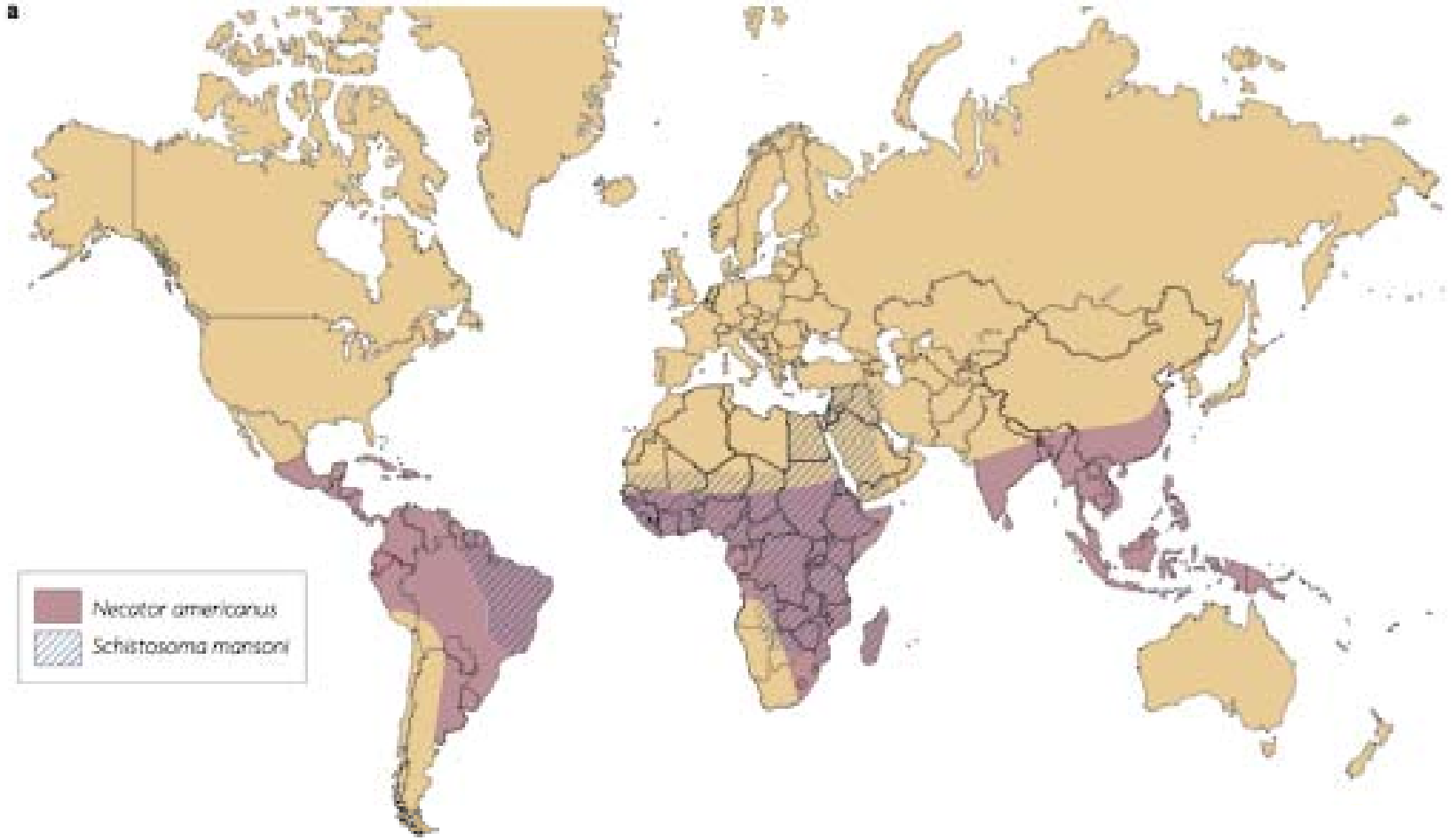
Global burden of NTDs

- Common features:
  - High endemicity in rural & impoverished urban areas of low income countries
  - Impair childhood growth, intellectual development, education & worker productivity
  - Many NTDs are disfiguring & stigmatizing
  - Few or no commercial markets for drugs & vaccines
  - Pharmacopoeia has remained unchanged for years
  - Cause ~534,000 deaths annually
  - 4^{th} most important group of communicable diseases worldwide.

Distribution

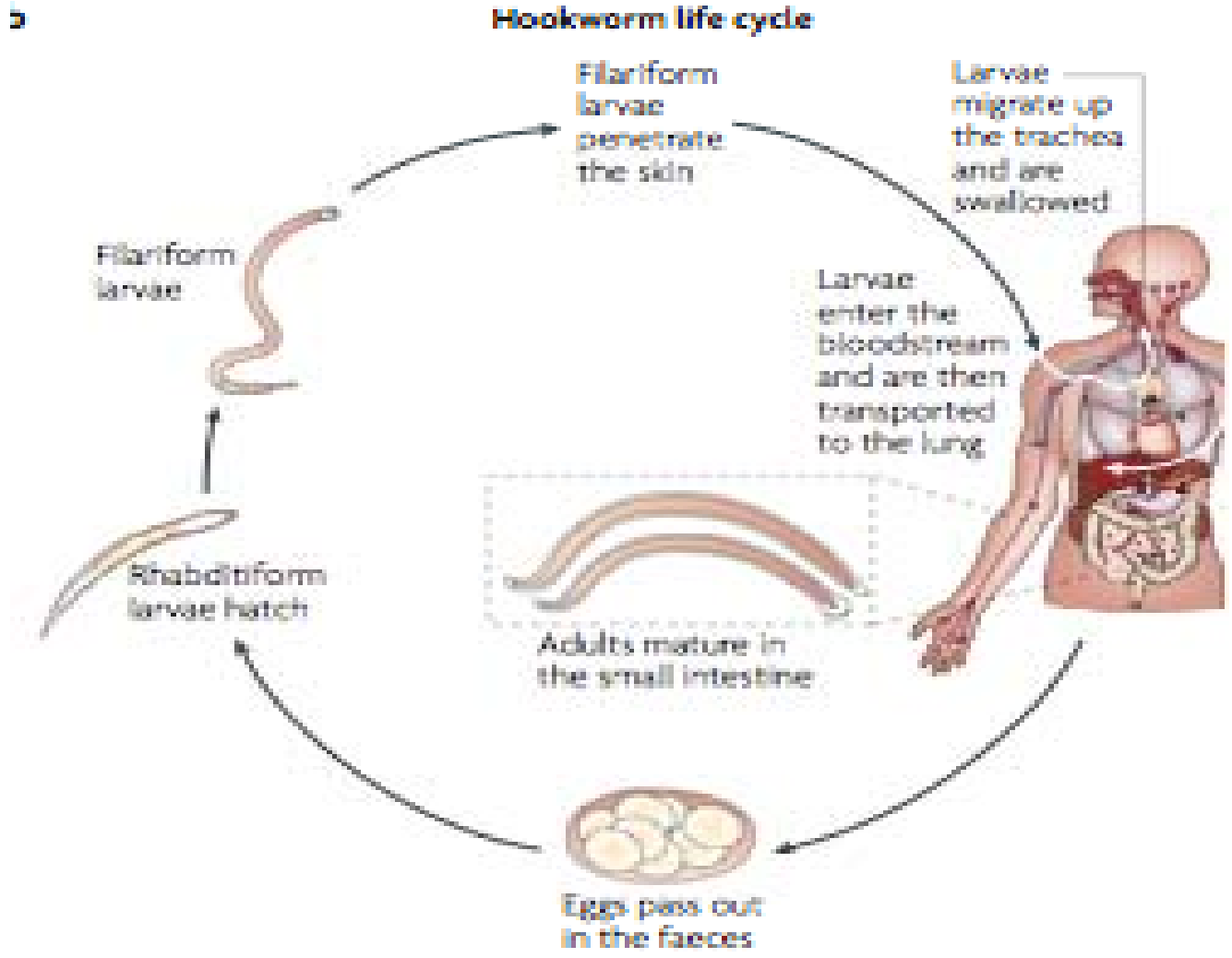
- East Asia:
  - Hookworm, Ascaris and trichuriasis
  - Schistosomiasis
- South Asia
  - Hookworm, lymphatic filariasis, amebiasis
- Latin America & Caribbean (LAC)
  - Hookworm, schistosomiasis, Chagas disease, Leishmaniasis
- Sub-Saharan Africa
  - Hookworm, Shistosomiasis, Lymphatic filariasis, Buruli ulcer

Helminthiasis: Hookworm infection & Schistosomiasis



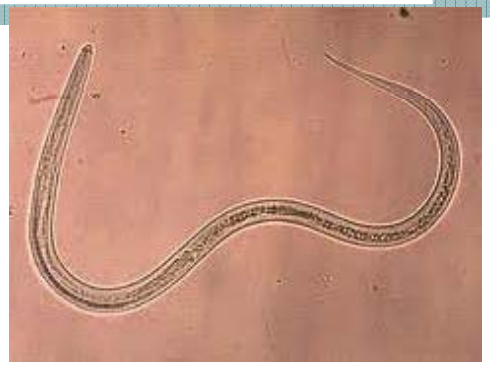
Hotez et al, Nature Microbology 2010;

Life cycles of hookworm: *Necator americanus*



Hotez et al, Nature Microbiology 2010; 8:817

Hookworm infection



- The most common STH infection, the most common NTD in Sub-Saharan Africa.
- A roundworm infestation in the phylum Nematoda
- 600-700 million infected.
- 90% of school going children are at risk.
- Hookworm most prevalent in coastal regions & areas of extreme temperatures (<37°C)
- *Necator americanus* (85%) and *Ancylostoma duodenale* are the most common species.
- Cause intestinal blood loss leading to iron deficiency anemia esp. in pregnant women and children.
- Diagnosis by finding parasite eggs on stool.

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Hookworm infection

- 3rd stage larvae live in the soil
- Survive for few days/weeks
- L3 infection on skin contact
- Migrate to lungs & mature
- Burrow into mucosa of small intestine, rupture blood vessels
- Intestinal blood loss
- Female & male mate and eggs exit in host faeces & hatch in soil.

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Schistosomiasis

- *Schistosoma haematobium* (67%) & *Schistosoma mansoni.*
- Occurs in school aged children, adolescents, young adults.
- Highest is areas near fresh water bodies contaminated with snail intermediate hosts: rivers, dams, lakes.
- *S. haematobium* causes hematuria, dysuria, renal failure, bowel ulceration.
- Associated with squamous cell carcinoma, sexual dysfunction & infertility.
- Genital schistosomiasis promotes horizontal transmission of HIV.

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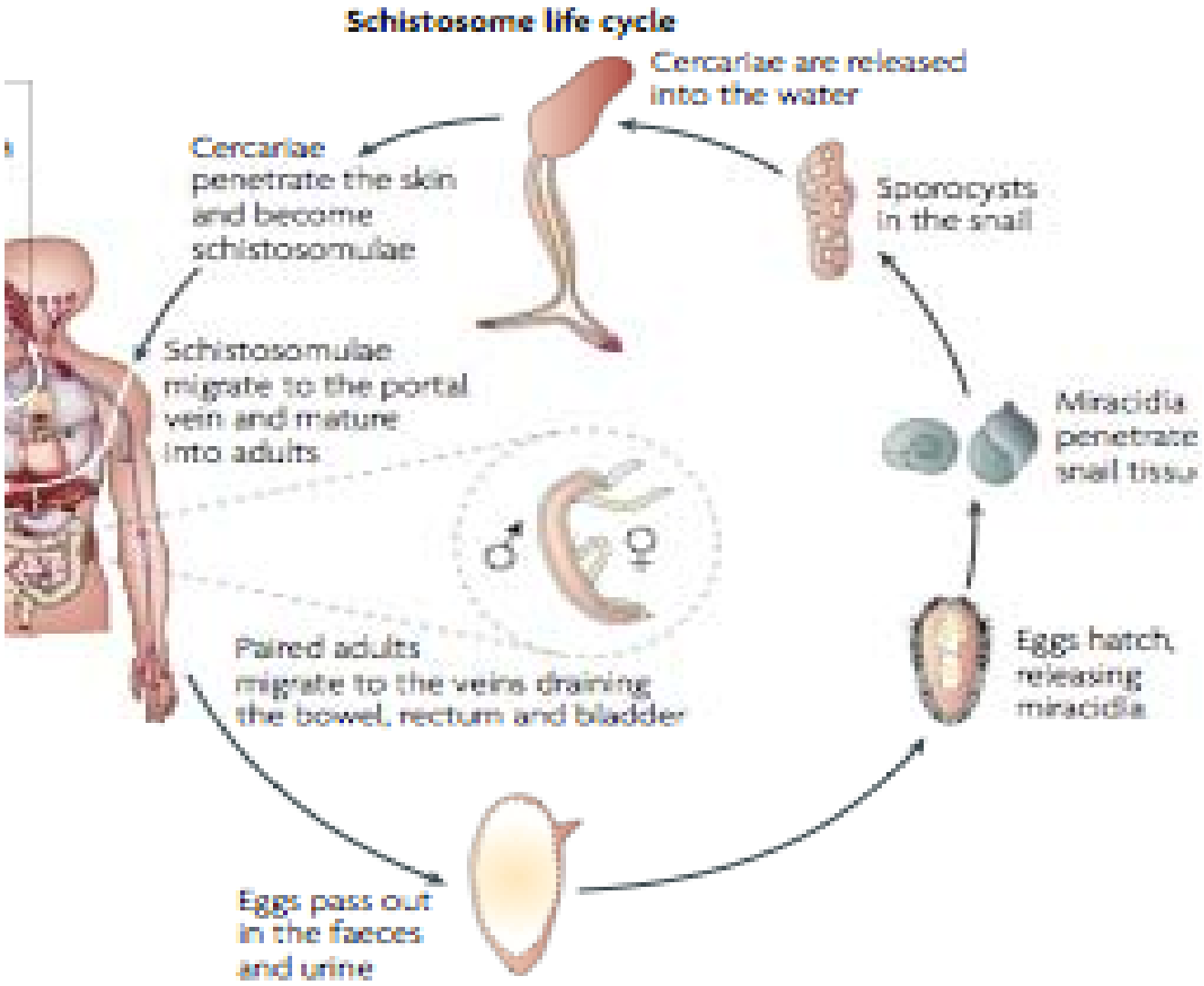
Life cycle



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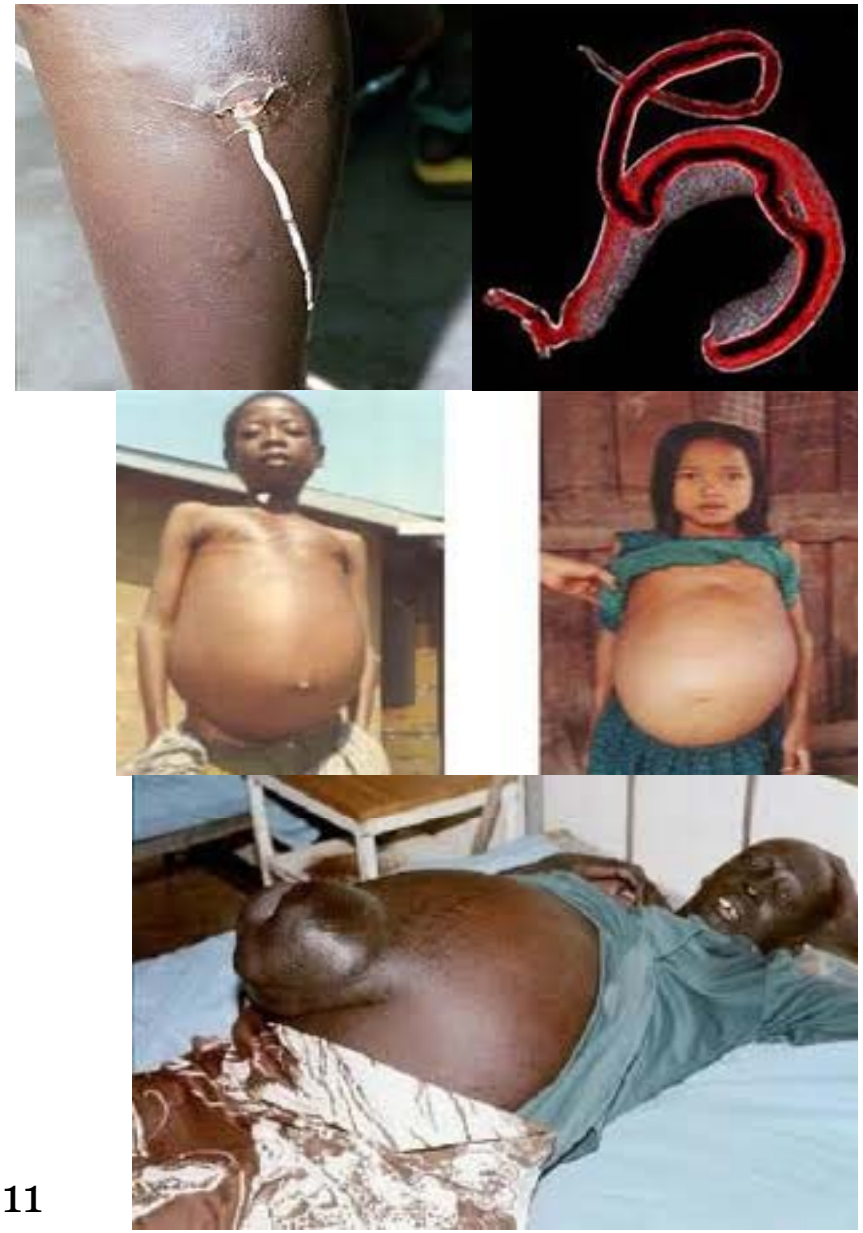
Schistosomiasis

- Free-swimming cercariae penetrate skin
- Larvae shed tails & schistosomes enter vasculature & lungs
- Relocate to venus system & mate
- Produce eggs with spine to penetrate blood vessels into UT, genitals, intestines or liver
- Chronic infection can last 5-7years



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Co-infections

- Both cause chronic anaemia that can cause neurologic impairment, diminished work capacity and adverse outcomes of pregnancy.
- Co-infection with *N. americanus* & *S. mansoni*; Both with *Plasmodium falciparum*
- Anaemias caused by both are additive.
- Controversy: do helminths increase susceptibility to malaria or affect clinical course of disease?
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Helminth-HIV connection

- Increase susceptibility to HIV by undermining host capacity to generate immune response against virus
- Studies inconclusive/controversial
- Female genital schistosomiasis shown to increase acquiring virus 3-fold
- Significant effect of *S. mansoni* on viral load
- Immune suppression of helminths depends on live & viable parasites,elimination=recovery of immune responsiveness
- High prevalence on such helminths in HIV endemic areas
- Schistosome infection induces production of IL4 & 10, & decreased IFNγ

Treatment & Prevention

- Schistosomiasis: Praziquantel & albendazole
- Hookworm: Albendazole & mebendazole
- Benzimidazole drugs used in pregnancy
- Iron supplementation also added
- Deworming is key using albendazole

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