Neglected Tropical Diseases

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Disease	Control strategy	Elimination target
Schistosomiasis	MDA, health education, sanitation, snail control	Yes (in some countries)
Onchocerciasis	MDA, (vector control)	Yes (in Americas)
Lymphatic filariasis	MDA, vector control	Yes (as a PH problem)
Trachoma	MDA, water and sanitation, health education	Yes (as a PH problem)
Yaws	MDA	Yes
Soil transmitted helminths	MDA	No
Guinea worm	Safe water, health education	Yes
African trypanosomiasis	Case finding and treatment, (vector control)	Yes (*T.b. gambiense*)
Visceral leishmaniasis	Case finding and treatment	Yes (subcontinent)
Leprosy	Case finding and treatment	Yes
Cysticercosis	Sanitation, meat inspection, vaccination of pigs	No
Echinococcosis	Abattoir control, treatment of dogs, education	No
Fascioliasis	Treatment of sheep, health education	No
Chagas disease	Vector control, blood screening	Yes (some countries)
Buruli ulcer	Case finding and treatment	No
Rabies	Vaccination of dogs, health education	No
Dengue	Vector control	No

35 year old English man

- Unwell for 3 days
- Fever
- Cough
- Itchy rash
- Holiday in Malawi for 2 weeks
- Returned 5 weeks ago
- What else would you like to know?

Travel History is important

Where exactly has the patient been?

- **Which countries?**
- **Rural or urban?**
- **Dates of travel, when did symptoms begin?**

What exactly has the patient been doing?

- **New sexual partner(s)?**
- **Fresh water contact?**
- **Exposure to sick people?**

Immunisations before travel?

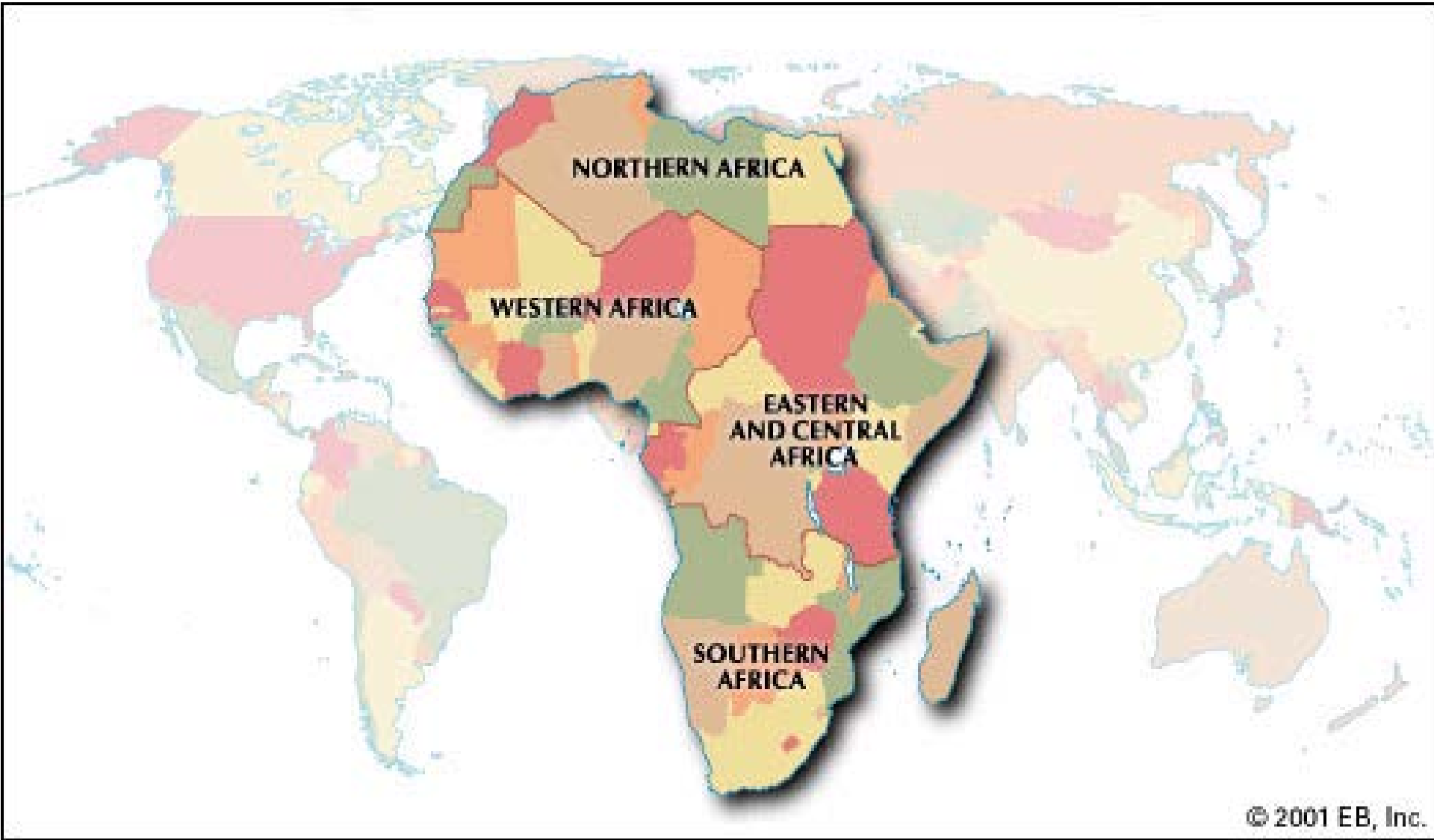
Malaria prophylaxis?

Any other medication or past medical history?

Travel History

- Had all recommended immunisations before travel
- Took malarone malaria prophylaxis
- Travelled with his wife
- Visited friends in Blantyre
- Swam in Lake Malawi several times

Africa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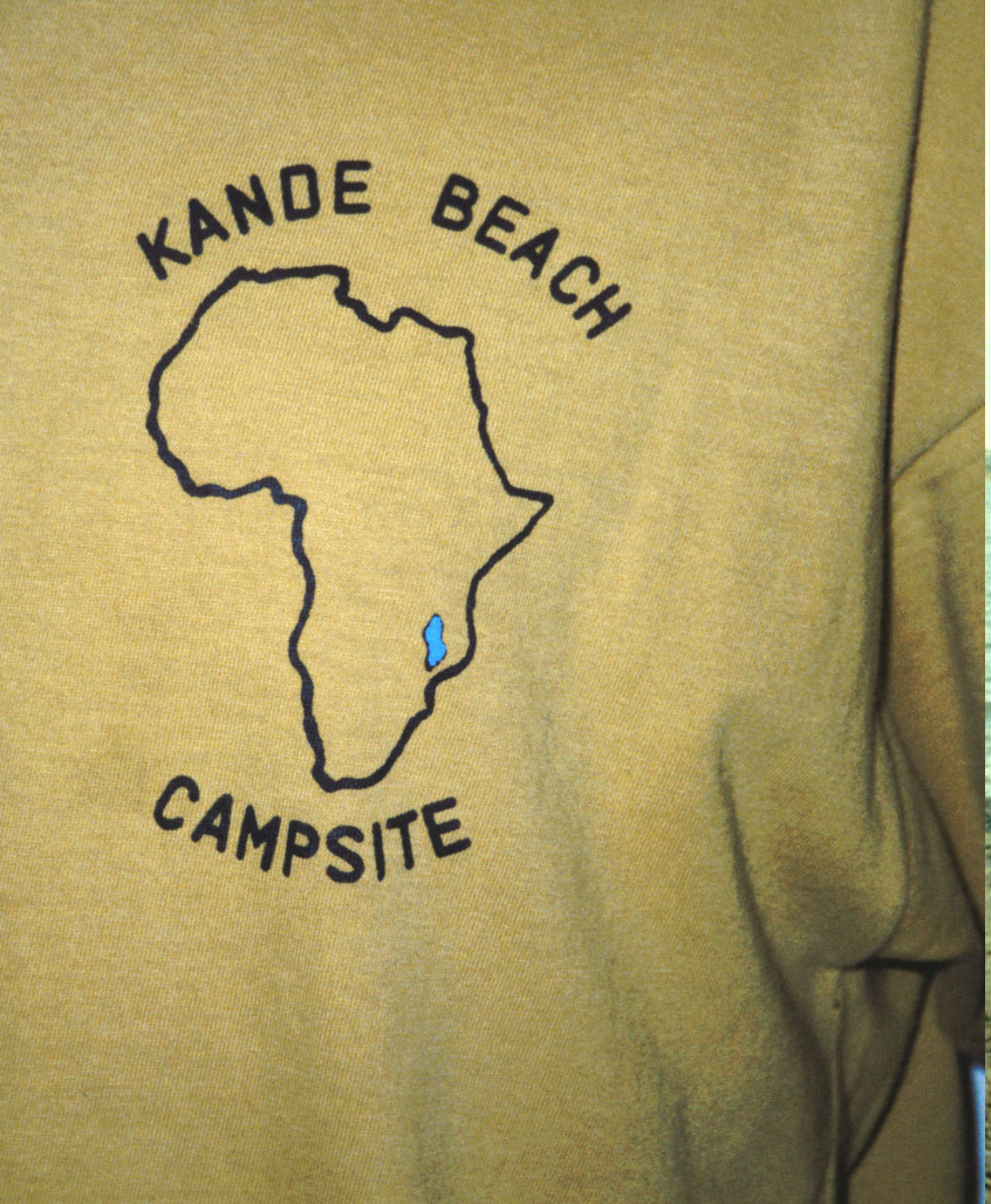
Lake Malawi


KANDE BEACH
CAMPSITE

Physical Examination

- Temp 39^0C
- Generalised rash
- Chest: Scattered rhonchi
- Liver palpable 1cm below costal margin

Investigations?

Investigations

- Malaria rapid test negative
- Blood film negative
- FBC: Eosinophils 3.5 (normal < 0.4)
- CRP, ESR, LFTs, U&E normal
- Urinalysis: Normal
- Stool microscopy negative
- Serology for schistosomiasis negative

Katayama Fever

- Acute schistosomiasis
- Occurs 4-6 weeks after infection, when worms have matured and started to lay eggs
- Immune mediated
- Fever, rash, cough
- Urticarial rash
- May be chest signs (wheeze) and hepatomegaly
- Diagnosed clinically as eggs are not found and patients are usually seronegative

Human host

Population of mature adult worms

Production of eggs

Exposure:

Between people and water infected with cercariae from snails

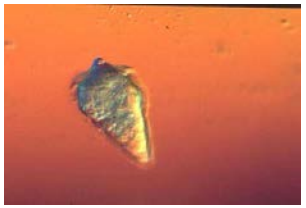
Contamination:
by man of water with faeces or urine containing schistosome eggs that hatch to produce miracidia to infected snails

Cercarial population

Susceptible snails

Miracidial population

Latent snails



Shedding snails

Schistosomiasis

Schistosoma haematobium:
Adult worms in blood vessels of bladder and kidney
Endemic in much of Africa
>100 million people infected
Snail host: *Bulinus* spp.

Schistosoma mansoni:
Adult worms in intestinal blood vessels
Endemic in much of Africa and Americas
> 50 million people infected
Snail host: *Biomphalaria* spp.

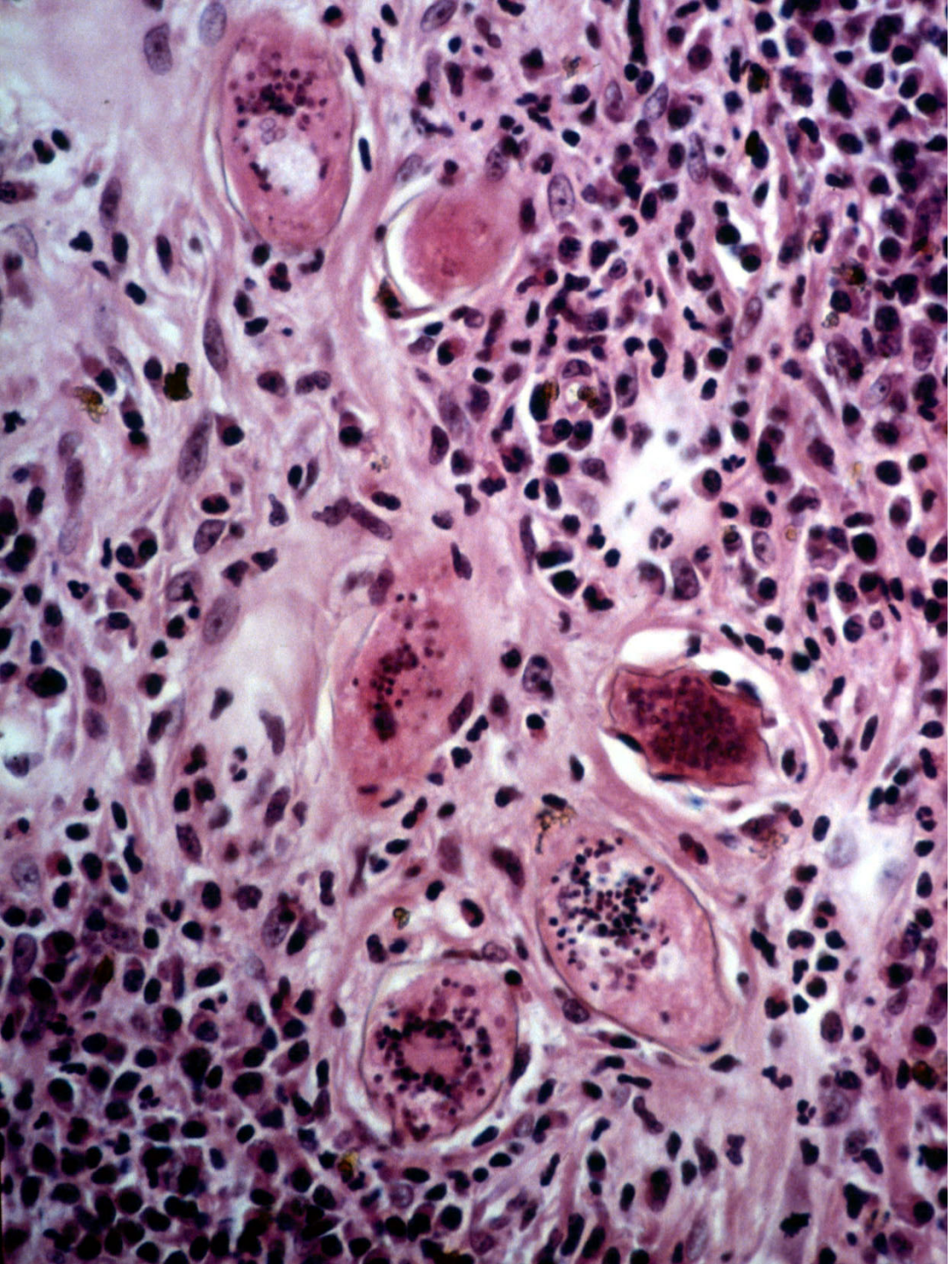
Schistosoma japonicum:
Adult worms in intestinal blood vessels
Endemic in China, Indonesia, the Philippines
Snail host: *Oncomelania* spp.

***Schistosoma mekongi*:**
Adult worms in intestinal blood vessels
Endemic in Lao PDR and Cambodia
Snail host: *Neotricula aperta*

Schistosoma intercalatum:
Adult worms in intestinal blood vessels
Endemic in west and central Africa
Snail host: *Bulinus* spp.

Schistosomiasis

- Pathology caused by eggs passing through the wall of the bladder (S. *haematobium*) or to the liver (other species)
- Severity depends on intensity of infection , usually measured as the number of eggs per ml of urine or gram of faeces



Schisto granuloma in bladder wall

Clinical consequences: *S. haematobium*

Haematuria

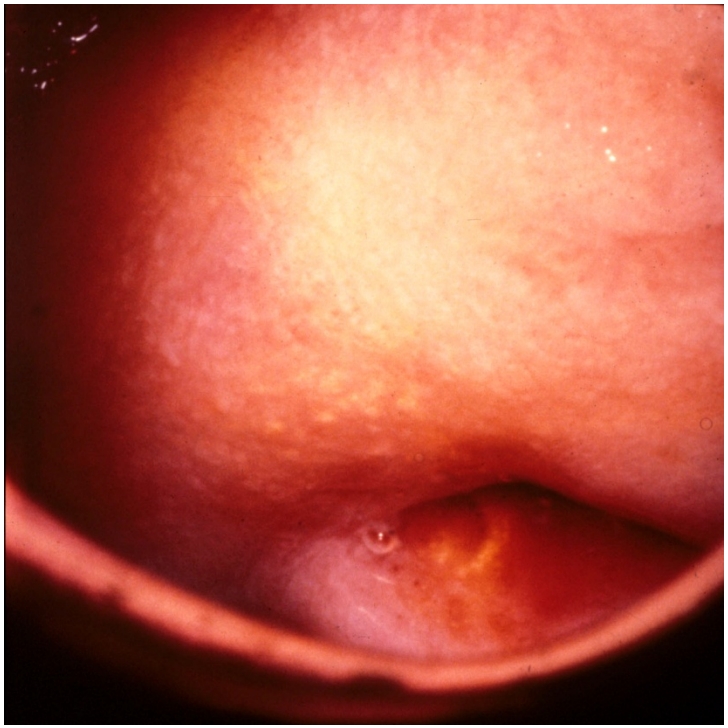
Bladder pathology

Bladder cancer

Kidney failure

Anaemia

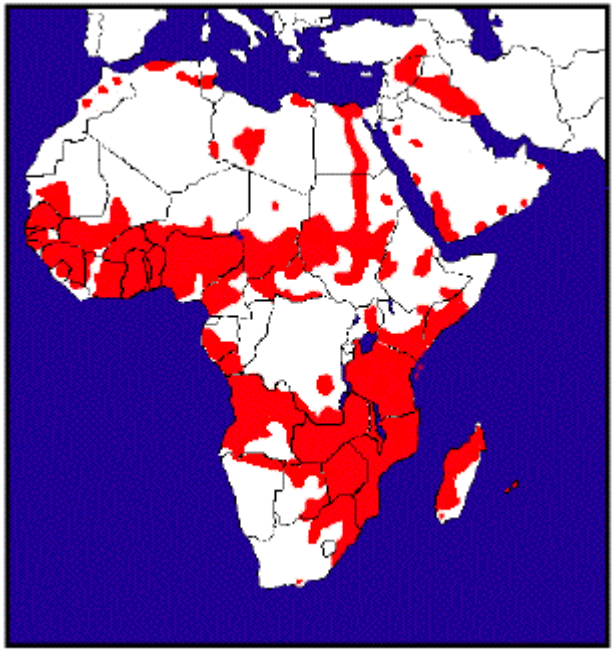
Female Genital Schistosomiasis



Genital schistosmiasis and HIV

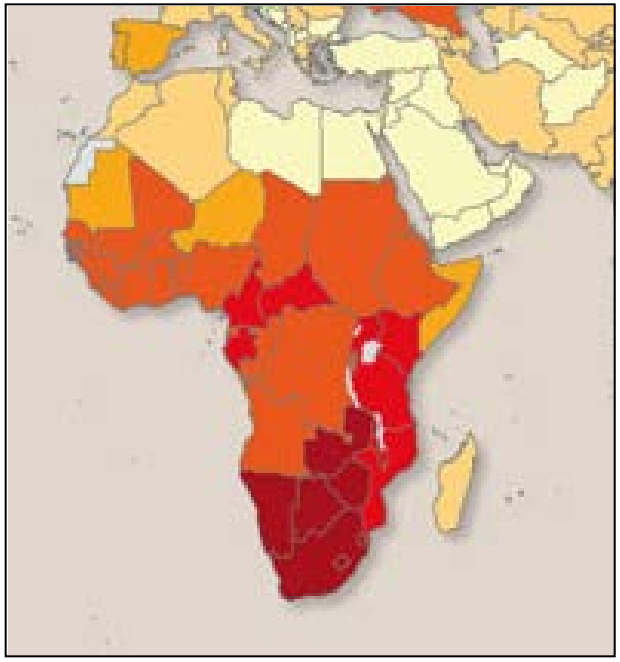
Geographic overlap

Urinary schistosomiasis



Source: www.stanford.edu

HIV



Source: UNAIDS

Clinical consequences of *S. mansoni*, *S. japonicum* and *S. mekongi*

Bloody stool & diarrhoea

Hepatic fibrosis

Portal hypertension

Liver failure

Ascites

Haematemesis

Anaemia

Advanced hepatic fibrosis

Diagnosis of Schistosomiasis

Parasitological diagnosis: the detection of eggs in faeces (e.g. Kato-Katz method) or urine (filtration method)

Immunological tests: the detection of antibodies or antigens. Experimental, simplified dipstick/card tests have been developed and are increasingly available. Antibodies remain detectable for life so antibody tests cannot be used as test of cure

Schistosome eggs

S. haematobium

S. mansoni

Treatment

- Praziquantel 40mg/kg stat, or 20mg/kg, two doses 6 hours apart
- Mass treatment (whole communities, or schoolchildren) for control/elimination
- China plans to eliminate schistosomiasis

Treatment of Katayama Fever

- Short course of steroids may be beneficial
- Treat schistosomiasis with praziquantel 20mg/kg x2, with doses 6 hours apart
- Praziquantel is not effective against immature works so treatment should be repeated 3 months after exposure

Schistosomiasis in London

- **1107 consecutive cases seen at HTD**
- **50% asymptomatic**
- **commonest symptom tiredness (cough)**
- **diagnosis**

urine dipstix blood	**21%**
eosinophilia	**44%**
sero-positive	**86%**
schistosome ova seen	**45%**

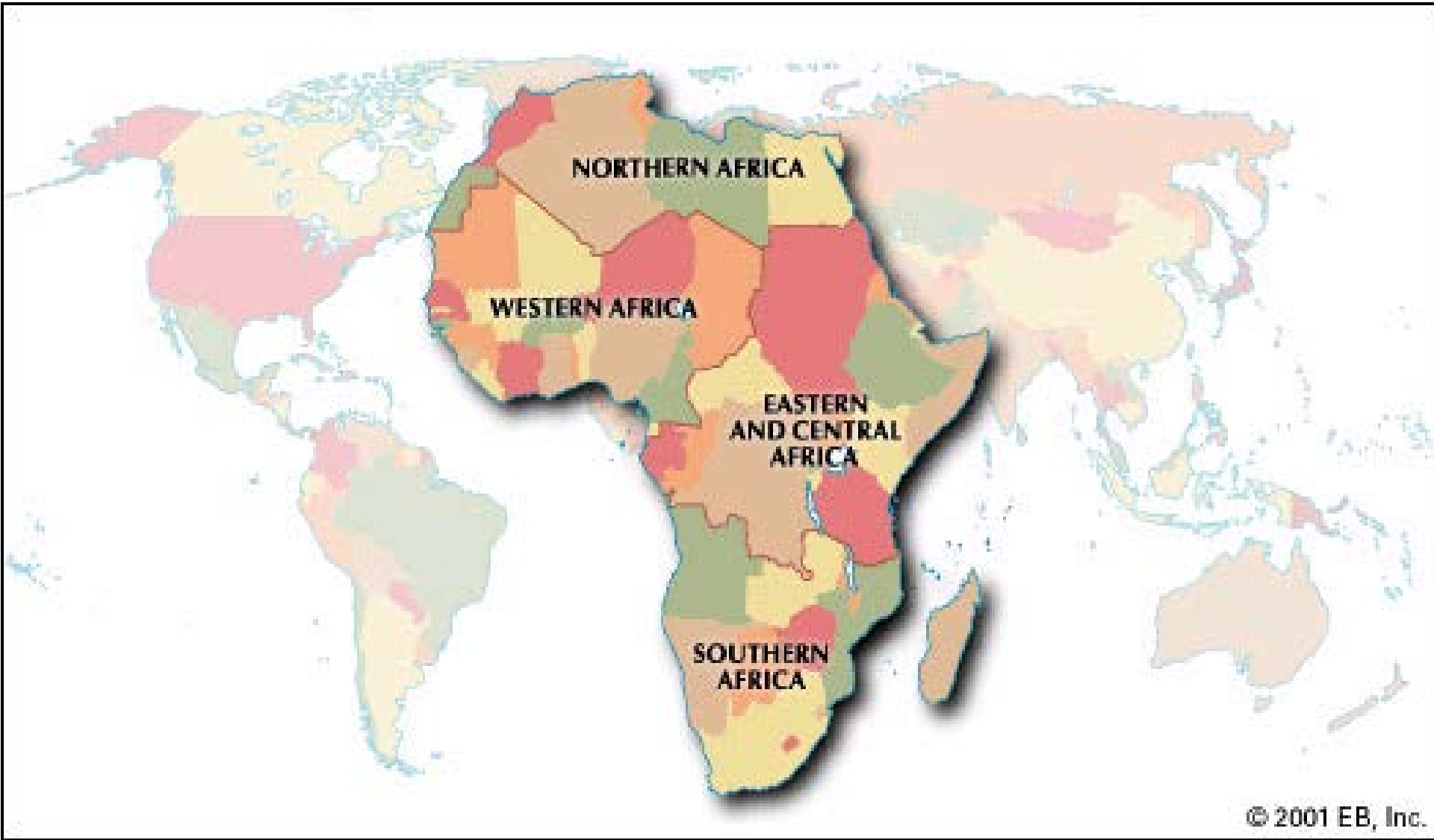
-
- **Whitty et al 2000**

Onchocerciasis ("River blindness")

Onchocerciasis

- Caused by a filarial worm (*Onchocerca volvulus)*
- Transmitted by blackflies (*Simulium* species) which breed in fast flowing rivers
- Adult worms live in subcutaneous nodules
- Microfilaria cause pathology in skin and eyes
- Found in mountainous regions of Africa
- Has been eliminated fom South America

Africa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Diagnosis

- Skin snips

- Serology

Treatment and Control

- Ivermectin (single dose) kills microfilariae but not adult worms
- Has been widely used for community-based mass treatment in endemic areas
- Doxycycline 100mg bd for 3 weeks kills adult worms

Lymphatic Filariasis

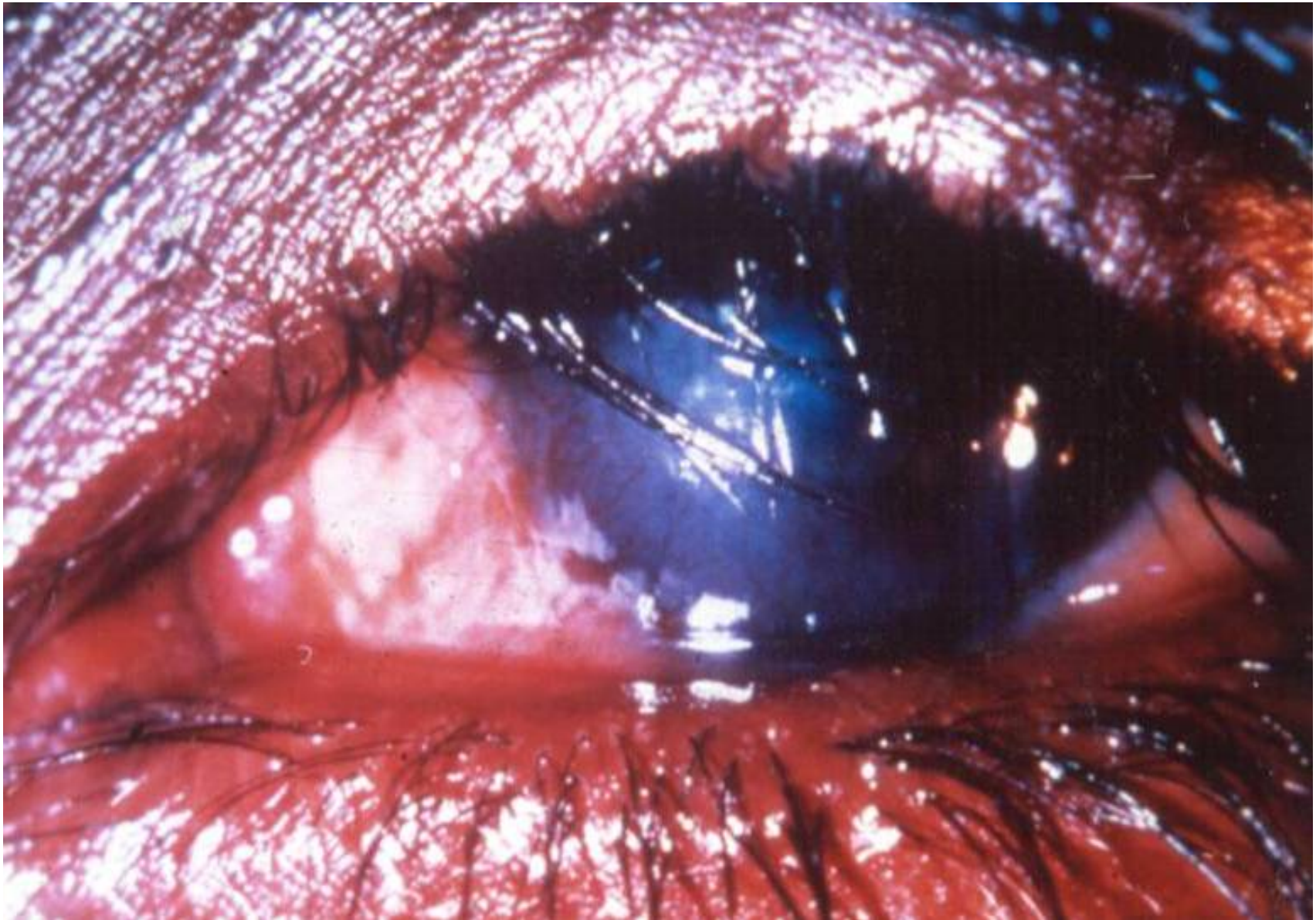
Lymphatic filariasis

- Cause: *Wuchereria bancrofti* or *Brugia malayi*
- Transmitted by culicine mosquitoes
- Found in tropical regions of Asia and Africa
- Adult worms live in lymphatic system
- Microfilariae found in blood at night
- Diagnosis: Midnight blood (microscopy) or serology

Treatment

- Doxycycline 100mg bd for 3 weeks kills adult worms, but lymphoedema usually persists
- Control programmes use mass treatment with single dose albendazole + ivermectin or di-ethyl carbamazine (DEC), but this does not kill the adult worm

Blinding Trachoma



Active Trachoma in a child

Scarring Trachoma

Trichiasis with Corneal Opacity

Trachoma

- Cause: *Chlamydia trachomatis*
- Repeated infections lead to scarring of the conjunctiva lining the upper eyelid, which causes the lashes to turn inward
- Found in poor rural populations in Africa an Asia; ? Eliminated from China
- Treatment: azithromycin 20mg/kg stat
- Surgery for inturned lashes

Soil Transmitted Helminths

Acquired by faecal-oral route

- *Ascaris lumbricoides*
- *Trichuris trichiura*

Acquired through the skin

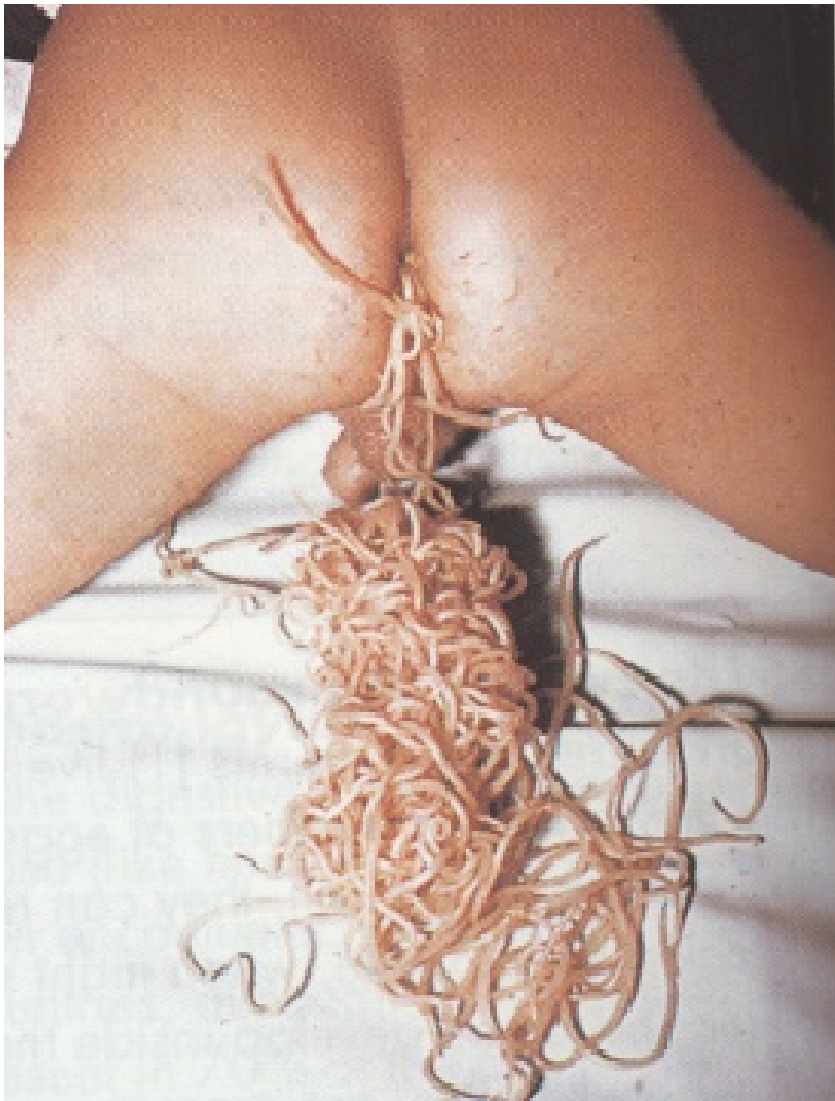
- Hookworm species
  - *Necator americanus*
  - *Ancylostoma duodenale*
- *Strongyloides stercoralis*

Soil Transmitted Helminths (STH)

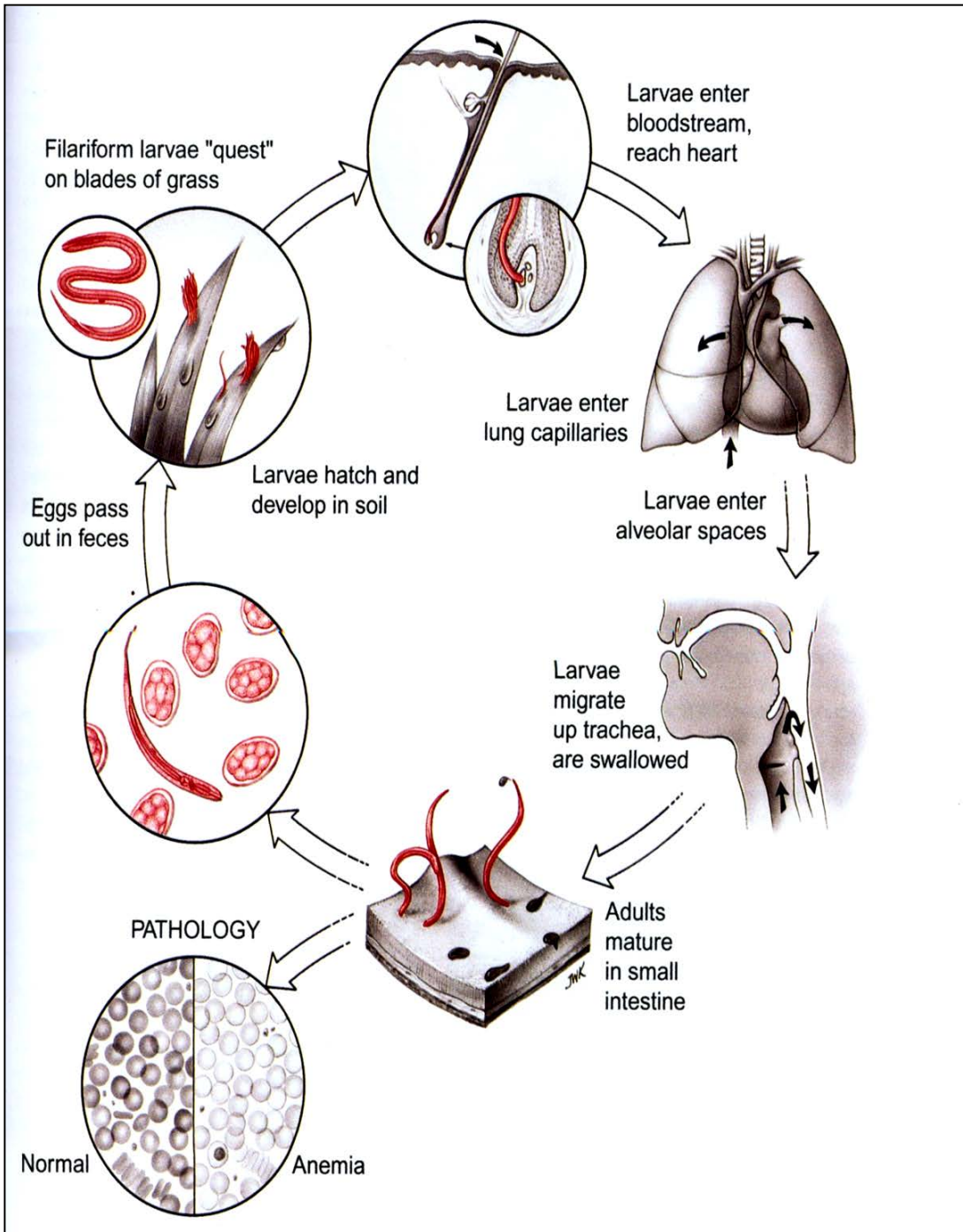
- Most infections cause no symptoms
- *Strongyloides* can replicate in the human host, other STH cannot
- Symptoms and pathology depend on the intensity of infection

Intestinal obstruction due to heavy ascaris infection

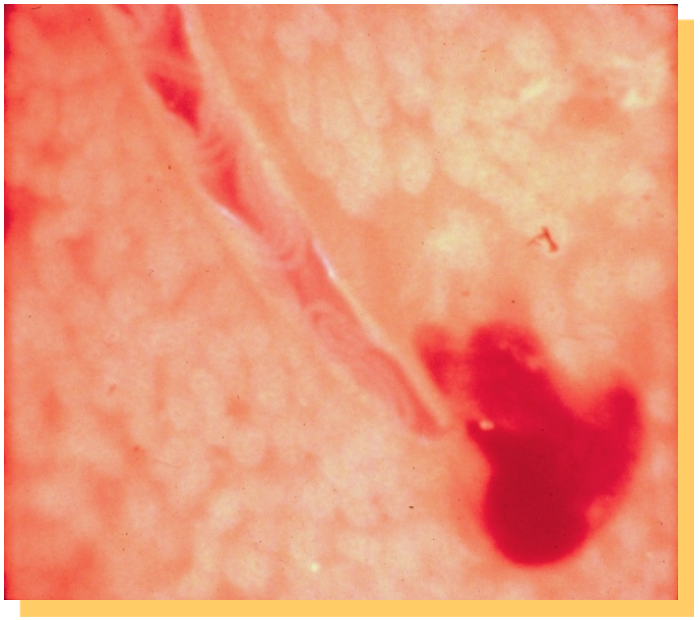
Massive ascaris infection following treatment



Life cycle of hookworm

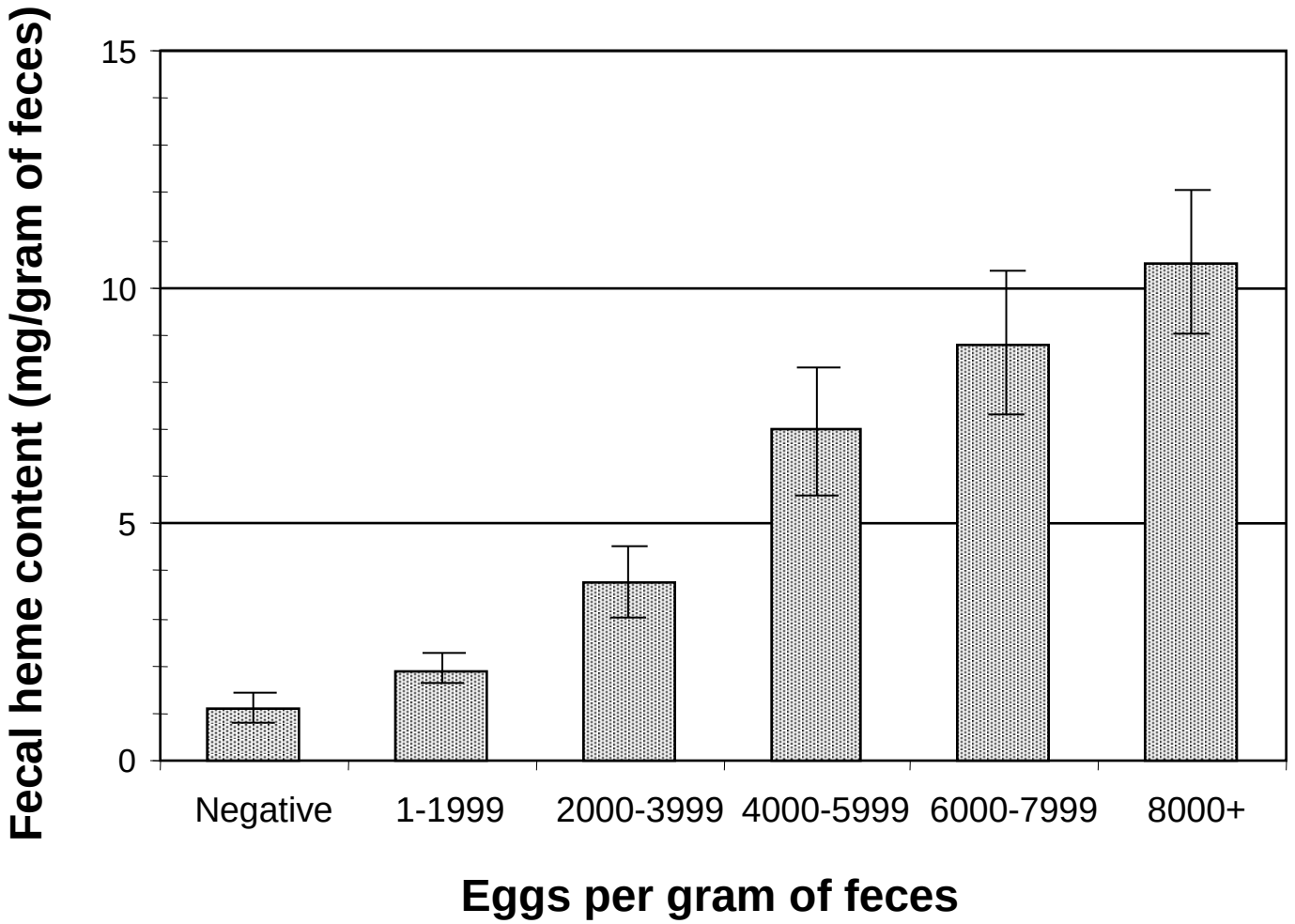


Hookworm-blood Loss



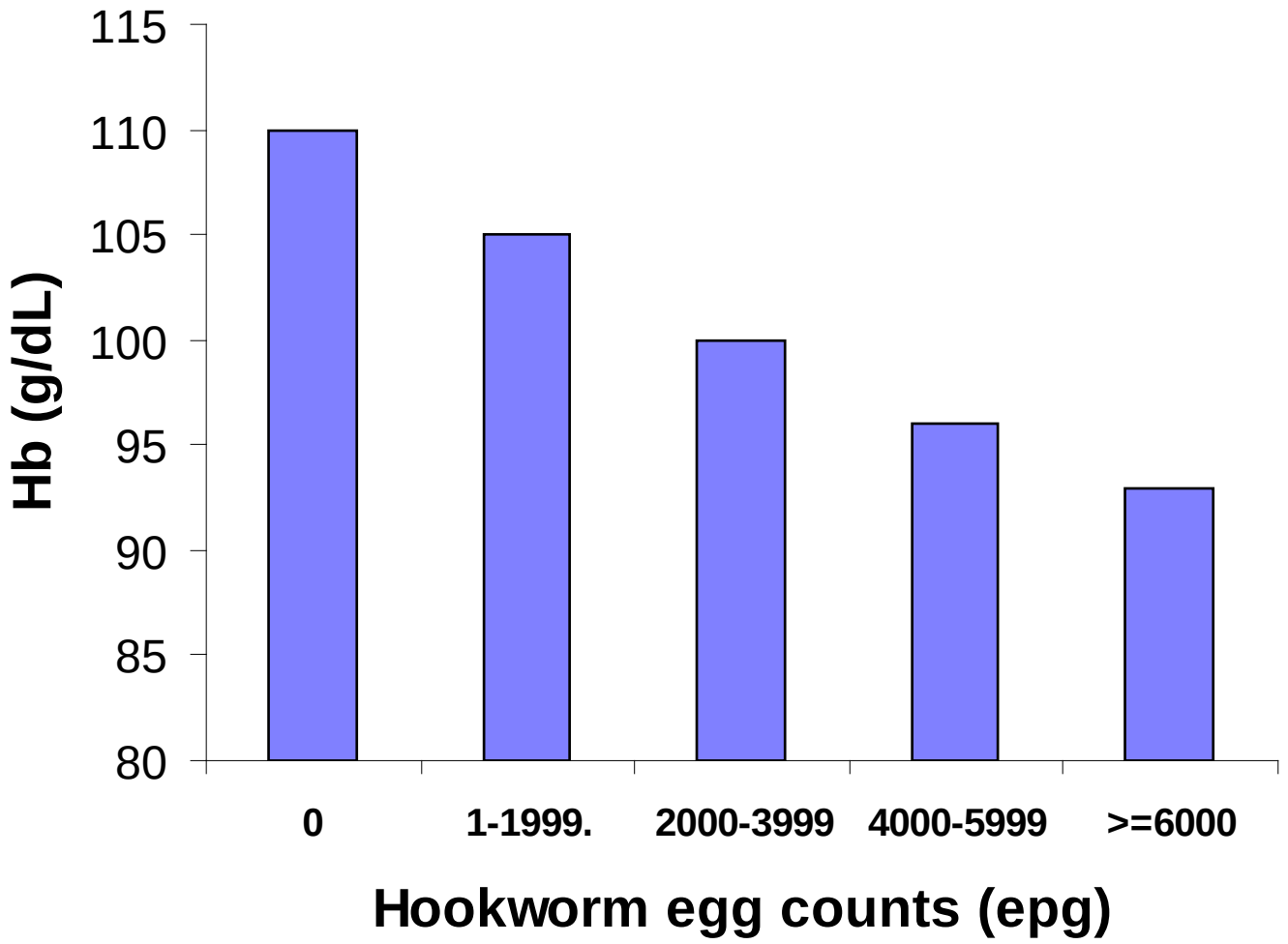
30 to 200 µL blood per day per hookworm

Fecal Blood Loss (Heme Content) and Hookworm Infection Intensity



Stoltzfus et al. 1996

Hookworm intensity and anaemia among Tanzanian schoolchildren (Stoltzfus et al., 1997)



38 year old English man

- Unwell for 4 months
- Progressive fatigue
- Sleeplessness
- Severe headache
- Fevers

Travel History is important

Where exactly has the patient been?

- **Which countries?**
- **Rural or urban?**
- **Dates of travel, when did symptoms begin?**

What exactly has the patient been doing?

- **New sexual partner(s)?**
- **Fresh water contact?**
- **Exposure to sick people?**

Immunisations before travel?

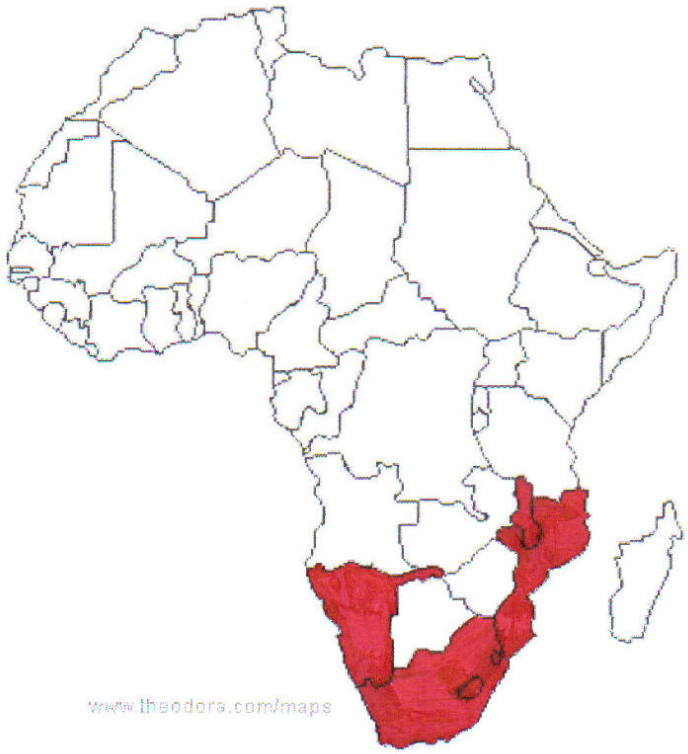
Malaria prophylaxis?

Any other medication or past medical history?

Travel

2007: Cairo to Capetown

Has spent past 18 months Travelling in Namibia, Mozambique, Malawi and South Africa by himself in an old Land Rover



Examination

- Febrile
- Posterior cervical + axillary lymphadenopathy
- Hepatomegaly
- CNS
  - slow verbal responses
  - bradykinetic

Generalised tonic – clonic seizure in outpatients

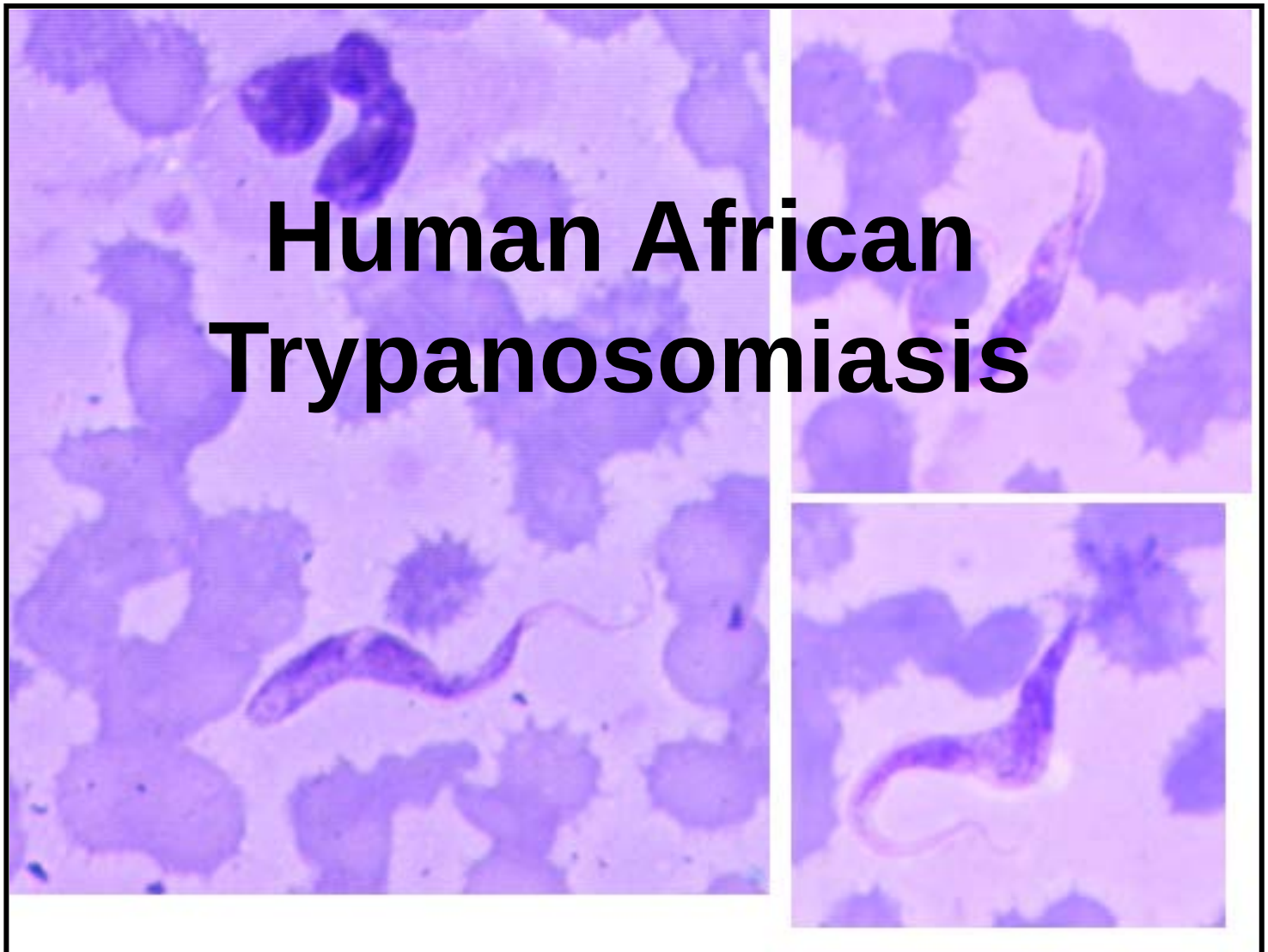
Differential Diagnosis?

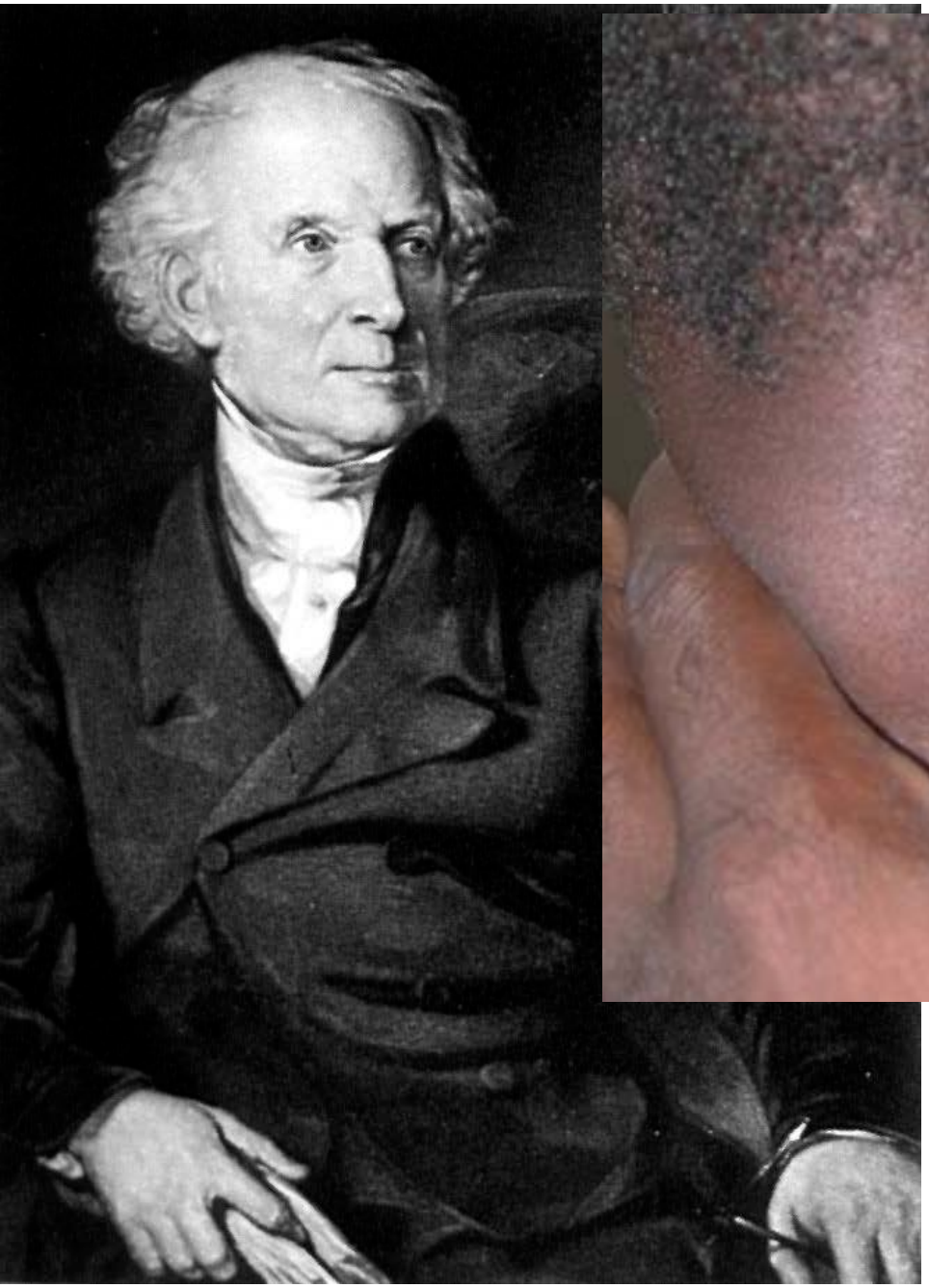
Investigations?

Investigations (1)

- Blood film: No malaria parasites
- CT head normal
- CSF 82 wcc/ mm^3 (lymphocytes),
  prot 1.2 g/ L, gluc 2.1 mmol/ L
- CRP 54 mmol/ L
- ESR 120 mm/ h
- HIV negative

CSF microscopy

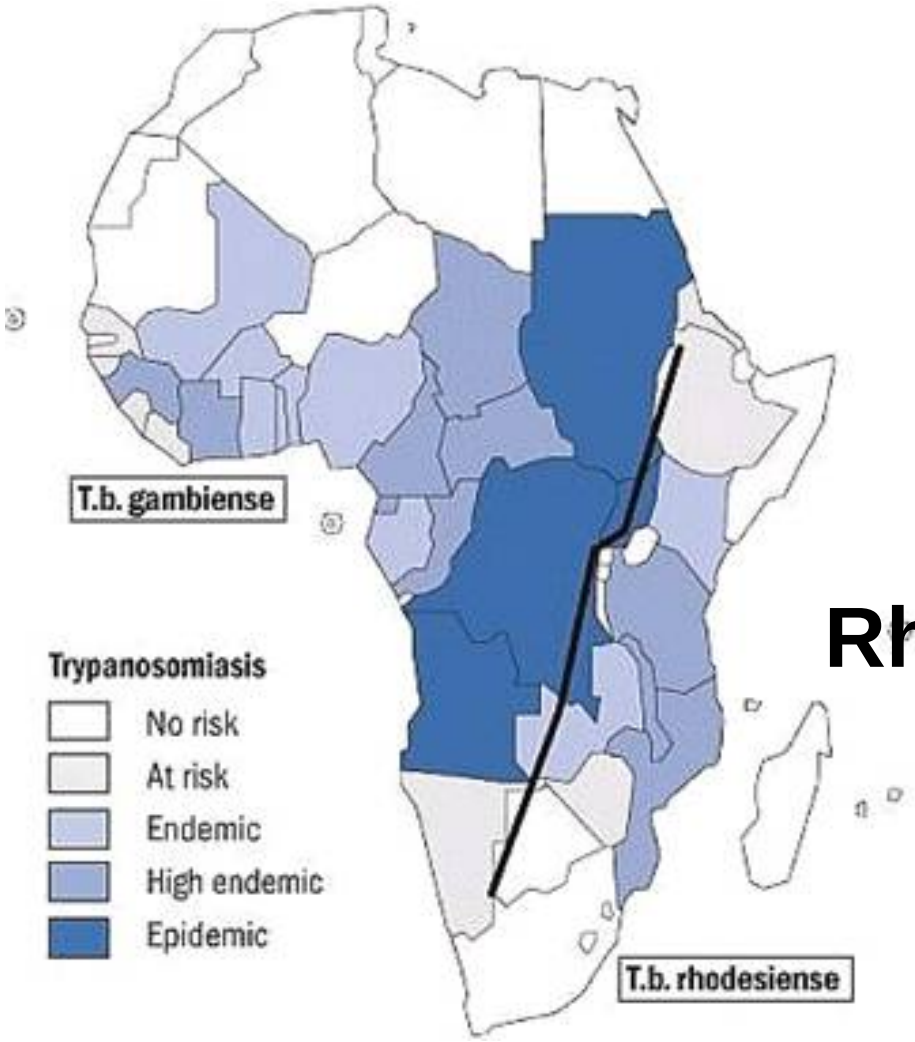




Winterbottom’s sign

East vs West

Gambiense



Rhodesiense

Tsetse fly (Glossina species)

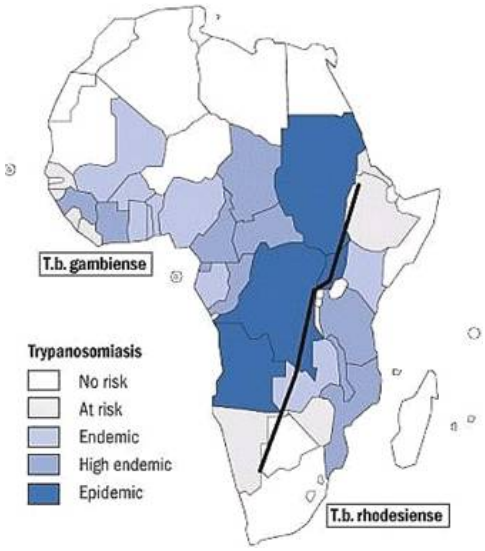
East vs West

Gambiense

- West Africa
- Chronic- months/ years
- Winterbottom's sign cervical lymphadenopathy

Rhodesiense

- East Africa
- Acute- days/ weeks



Treatment

	T. b. Gambiense	*T. b. Rhodesiense*
1st stage haemolymphatic	Pentamidine	Suramin
2nd stage CNS	Nifurtimox/ eflornithine	Melarsoprol

Encephalopathy due to melarsoprol

- 5-10% melarsoprol-treated cases
- 10-70% mortality
- Types convulsive
  progressive coma
  psychotic reactions

Treatment

IV suramin	1g IV od	2 days
IV melarsoprol	WHO regimen	21 days
PO prednisolone	60mg od	

Lumbar puncture 2 weeks later

wcc <1/ mm^3, prot 0.65 g/ L

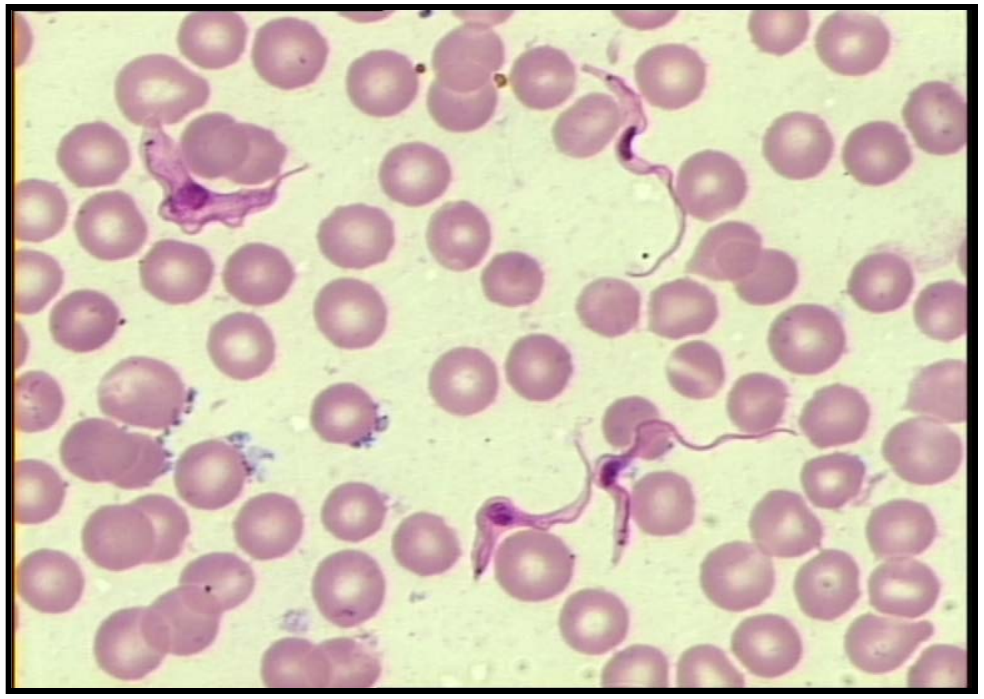
Diagnosis

Microscopy

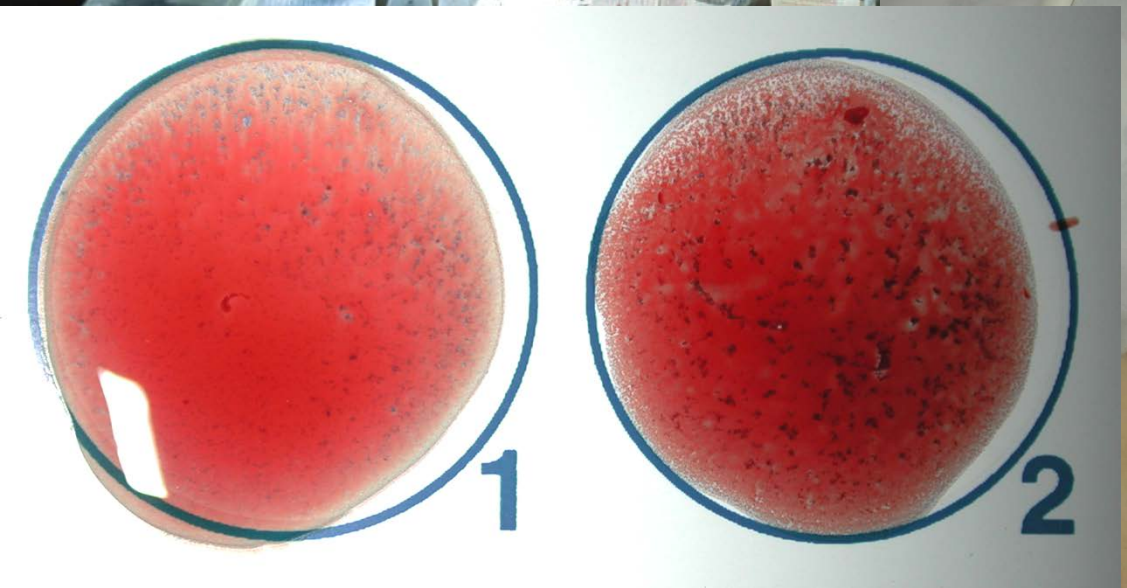
- blood
- lymph nodes
- bone marrow
- CSF → staging

Serology

- CATT
- New POC test



Card Agglutination Test for Tryps (CATT)



Human African Trypanosomiasis

New lateral flow POC (dipstick) test, HAT Sero-K-SeT, is 98% sensitive and 99% specific against a parasite detection gold standard

Buscher P et al. Lancet Global Health 2014; 2: e359

<u>Unmet Needs</u>

- Non-toxic oral treatment
- Non-invasive test to identify CNS involvement (stage 2 disease)