

The more Neglected Tropical Diseases



Alan Fenwick
Department of Infectious Disease
Epidemiology,
Faculty of Medicine
Imperial College, London



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The “more” Neglected Tropical Diseases

- The poor relations in terms of people who are infected and the funding available to treat those people
- Will doctors in UK ever see cases like these ?
- But how important are they to people in the developing world

The Neglected Tropical Diseases

A growing Core Group of 15 – MDA for

7

- Protozoan Infections

- Human African Trypanosomiasis (HAT)
- Chagas Disease
- Leishmaniasis

- Bacterial Infections

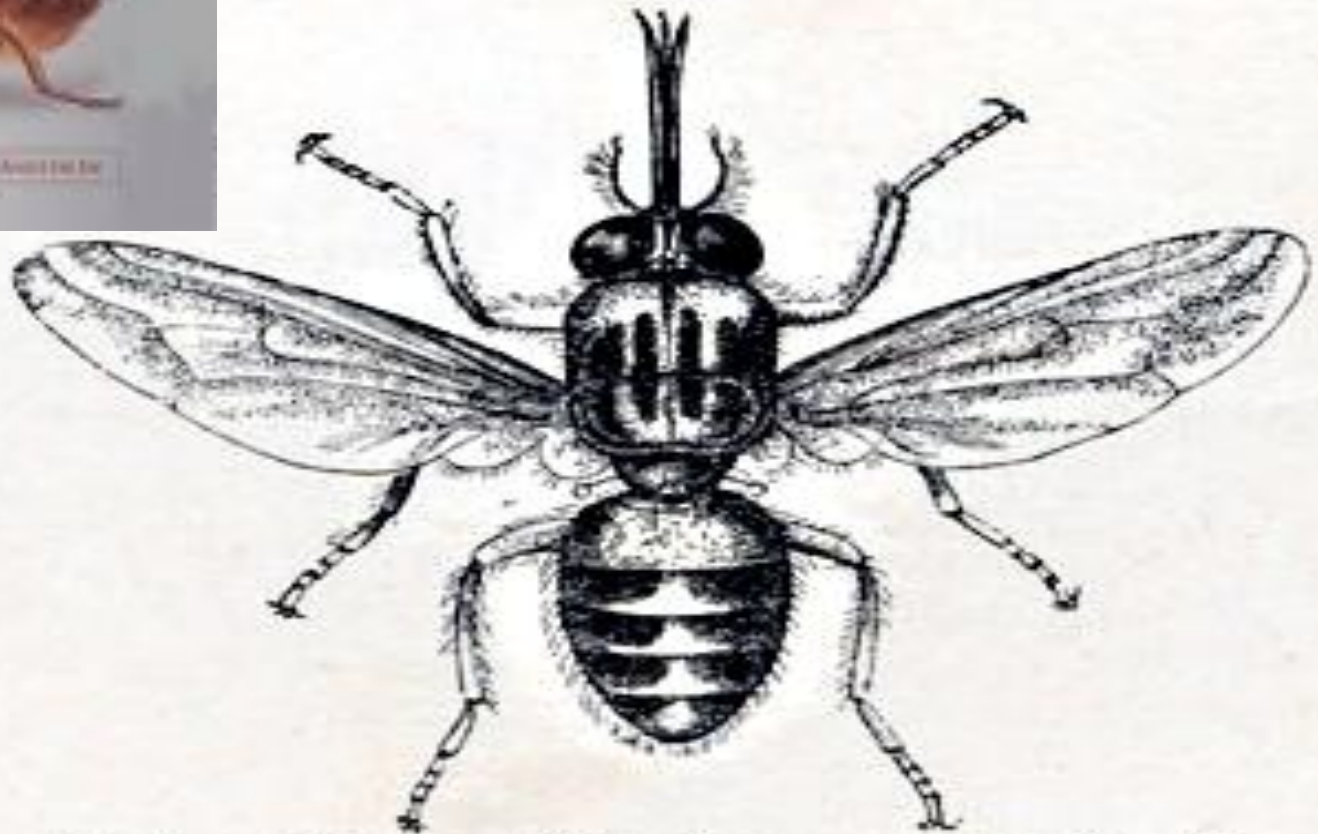
- Buruli Ulcer
- Leprosy
- **Trachoma**

- Helminth Infections

- **Ascariasis**
- **Hookworm Infection**
- **Trichuriasis**
- **Schistosomiasis**
- **Lymphatic Filariasis**
- **Onchocerciasis**
- Dracunculiasis
- Cysticercosis

+ Podoconiosis

Tsetse fly – sleeping sickness



Tsetsefliege (*Glossina morsitans*). ³/₁.
(Art. *Tsetsefliege*.)

Trypanosomiasis – sleeping sickness can be an acute killer

In humans

- *Trypanosoma brucei gambiense* (*T.b.g.*) is found in west and central Africa. This form represents more than 90% of reported cases of sleeping sickness and causes a chronic infection. A person can be infected for years without symptoms of the disease. When symptoms do emerge, the patient is often already in an advanced disease stage when the central nervous system is affected.

Trypanosomiasis – sleeping sickness an acute killer

Trypanosoma brucei rhodesiense (*T.b.r.*) is found in eastern and southern Africa. This form represents less than 10% of reported cases and causes an acute infection. First signs and symptoms are observed after a few months or weeks. The disease develops rapidly and invades the central nervous system

Transmitted by the Tsetse fly

Which has a sharp bite but fortunately a very limited distribution (max 70,000 infected)

Chaga's Disease

– the South American form of
Trypanosomiasis

Trypanosoma cruzi is found in parts of South America, and causes major heart problems.

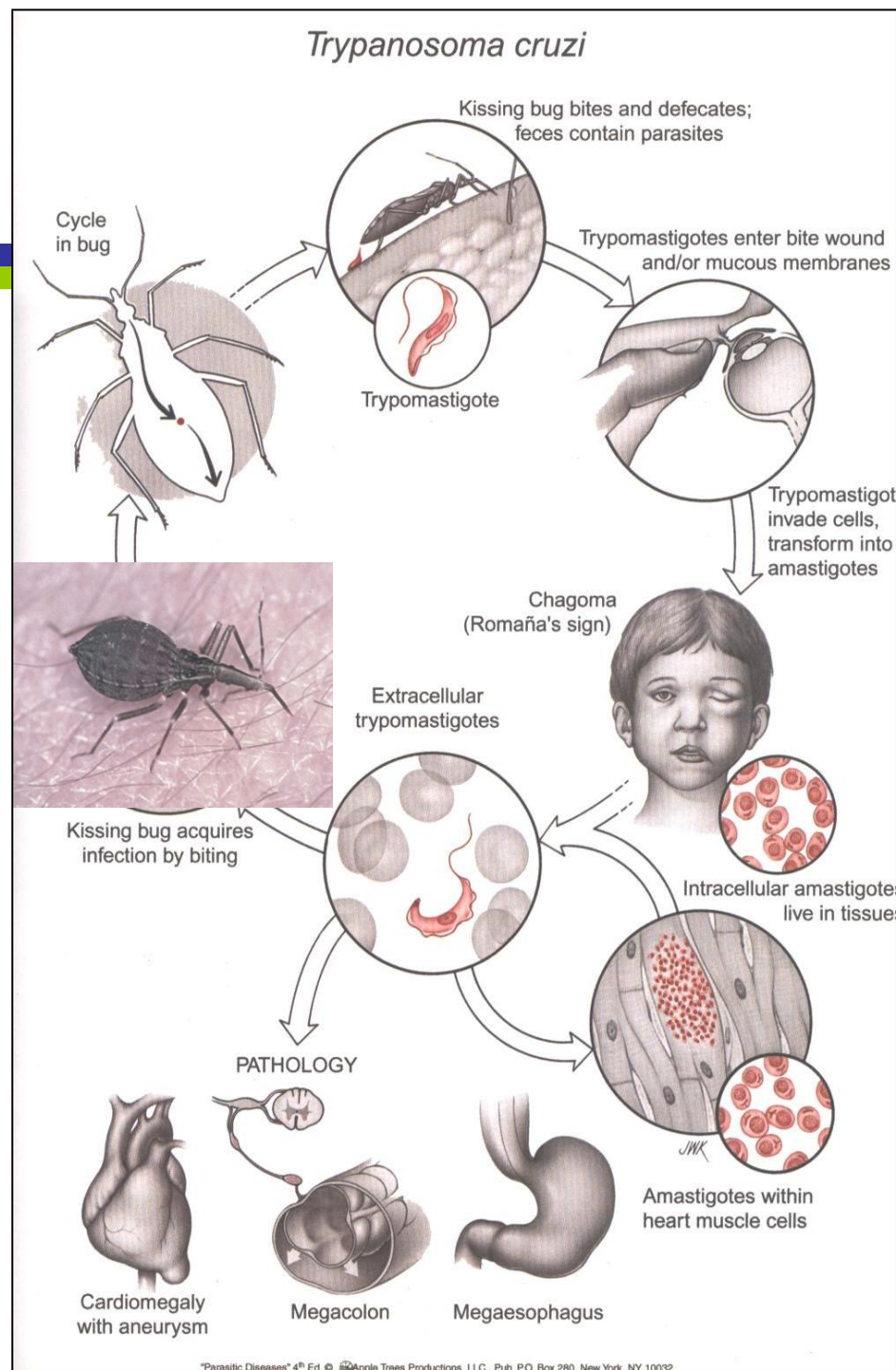
It is transmitted by bed bugs and therefore is confined to people with poor quality housing

Recently it has spread into Europe via immigrants who sell blood

Chagas disease

(*American Trypanosomiasis*)

- 3,000 to 1 million cases
- Unknown burden of heart disease
- Contamination of U.S. blood supply
- Transmission documented in Louisiana and Texas



The sandfly and dermal leishmaniasis



Leishmaniasis – two distinct diseases

In humans

- Dermal – nasty superating wound at the site of the bite which self heals in 6 months
- Visceral – leads to fever, weight loss, and an enlarged spleen and liver. P will have low red blood cell count (anemia), low white blood cell count, and low platelet count.

Transmitted by sandflies – small enough to go through a mosquito net – pin prick bite

Leishmaniasis – two distinct diseases

- Over 90 percent of the cases of **cutaneous leishmaniasis** occur in parts of Afghanistan, Algeria, Iran, Iraq, Saudi Arabia, and Syria (in the Old World) and in Brazil and Peru (in the New World);
- Over 90 percent of the cases of **visceral leishmaniasis** occur in parts of India, Bangladesh, Nepal, Sudan, and Brazil.

Buruli Ulcer

- Buruli ulcer, a disease caused by infection with *Mycobacterium ulcerans*, is one of the most neglected but treatable tropical diseases.

M ulcerans is from the family of bacteria which causes tuberculosis and leprosy but Buruli ulcer has received less attention than these diseases.

30 countries in Africa, the Americas, Asia and the Western Pacific, mainly in tropical and subtropical regions.

In Côte d'Ivoire, approximately 24 000 cases have been recorded between 1978 and 2006. In Benin, nearly 7000 cases have been recorded between 1989 and 2006; in Ghana more than 11 000 cases have been recorded since 1993. In Australia, more cases of BU are being reported recently – 25 in 2004, 47 in 2005 and 72 in 2006.

Buruli Ulcer

Infection leads to extensive destruction of skin and soft tissue with the formation of large ulcers usually on the legs or arms.

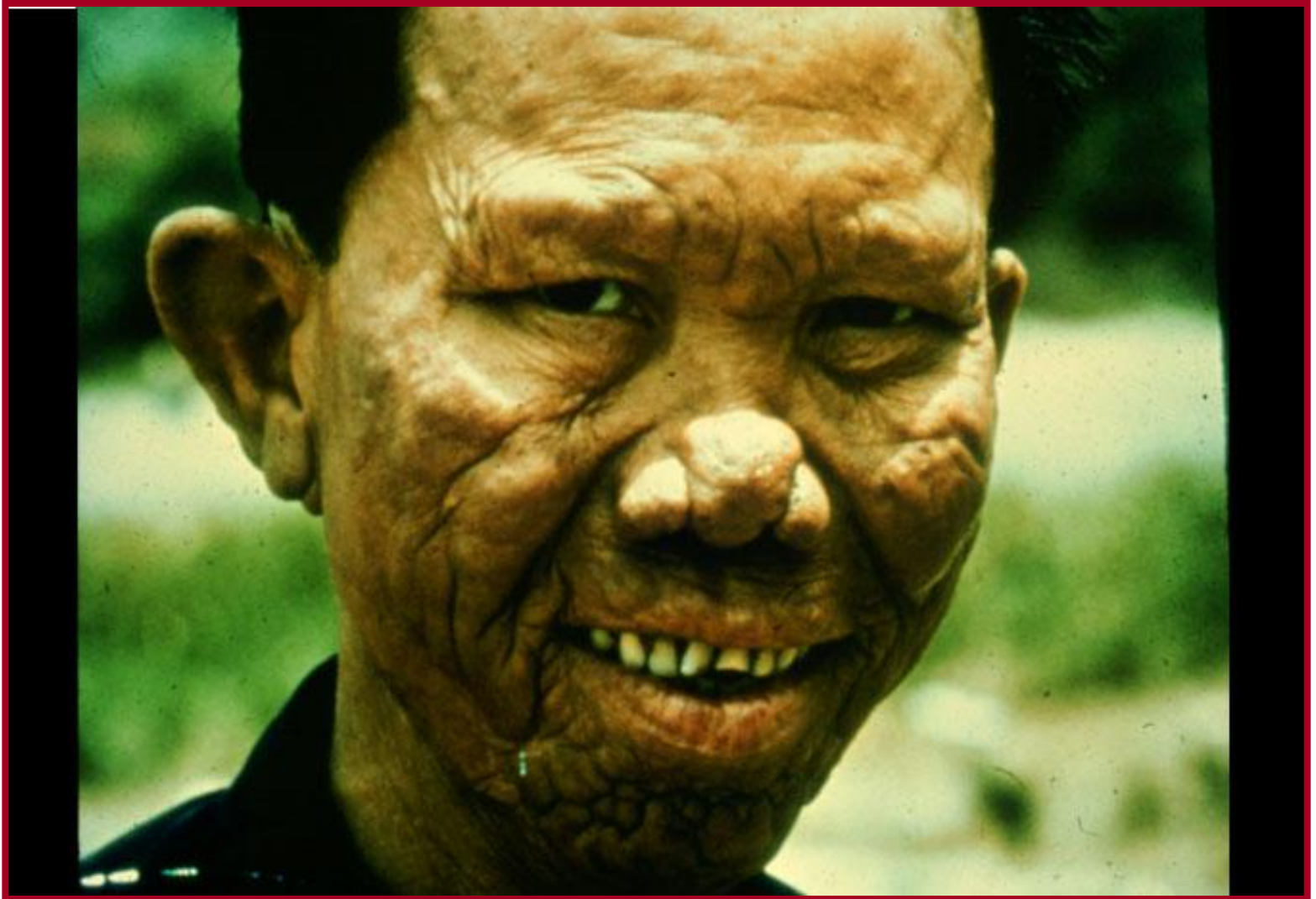
Non treatment leads to long-term functional disability such as restriction of joint movement as well as the obvious cosmetic problem. Early diagnosis and treatment are vital in preventing such disabilities.

Current recommendations for treatment are a combination of rifampicin and streptomycin/amikacin for eight weeks as a first-line treatment for all forms of the active disease.

Nodules or uncomplicated cases can be treated without hospitalization.

Surgery to remove necrotic tissue, cover skin defects and correct deformities.

Leprosy



Leprosy

Leprosy is a chronic disease caused by a bacillus, *Mycobacterium leprae*

M. leprae multiplies very slowly and the incubation period of the disease is considered to be about five years.

Can you believe that 99% of the population have natural immunity

Since 1981, WHO Study Group recommended multi-drug therapy (MDT), a combination of three drugs which effectively kills the pathogen and cures the patient. This is donated by Novartis

Leprosy

In 1991 World Health Assembly passed a resolution to eliminate leprosy as a public health problem by the year 2000 - defined as a prevalence rate of less than one case per 10,000 population.

The global disease burden was reduced from **5.2 million** in 1985 to **805,000** in 1995 to **753,000** by 1999 to **220,000** cases by 2005.

The South-East Asia Region, including India, achieved the elimination goal in December 2005.

The last five major countries to achieve the target were: DR Congo, Madagascar, Mozambique, Nepal and Tanzania
BRAZIL is yet to achieve the elimination goal

CONTROL MEASURES AGAINST DRACUNCULIASIS AT VARIOUS POINTS OF INTERVENTION

Village Based Surveillance

Case containment

[Health education to prevent entry of patients into sources of drinking water, occlusive bandaging, controlled immersion and worm extraction]

Health education

Filter drinking water

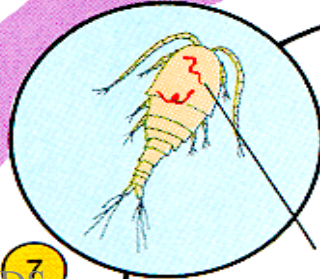
Provision of

safe drinking water

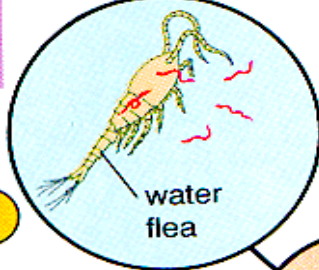
Hand pumps,
boreholes,
wells, etc.

Vector control

COPEPODS



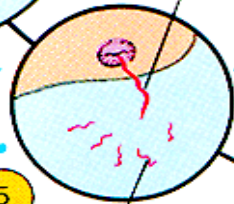
third-stage larva



water flea

6

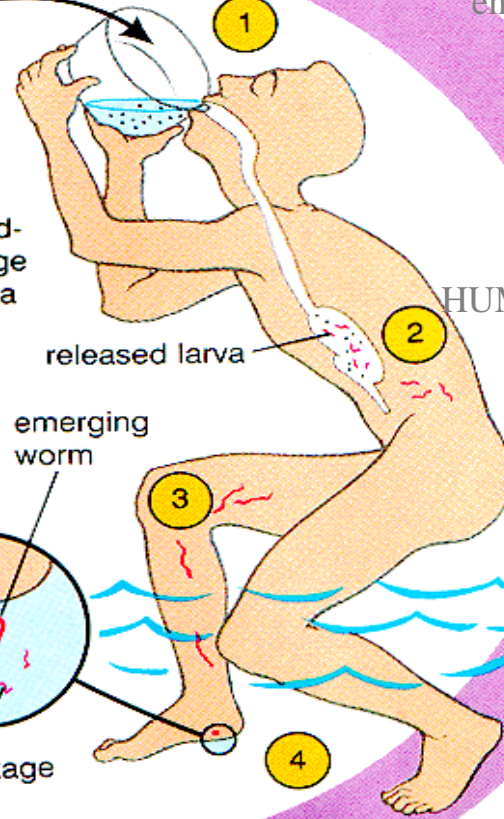
1st STAGE LARVAE



first-stage larva

5

emerging worm



HUMAN

released larva

1

2

3

4

Case Containment Centers

[motivate patient to voluntarily seek care at CCC.]

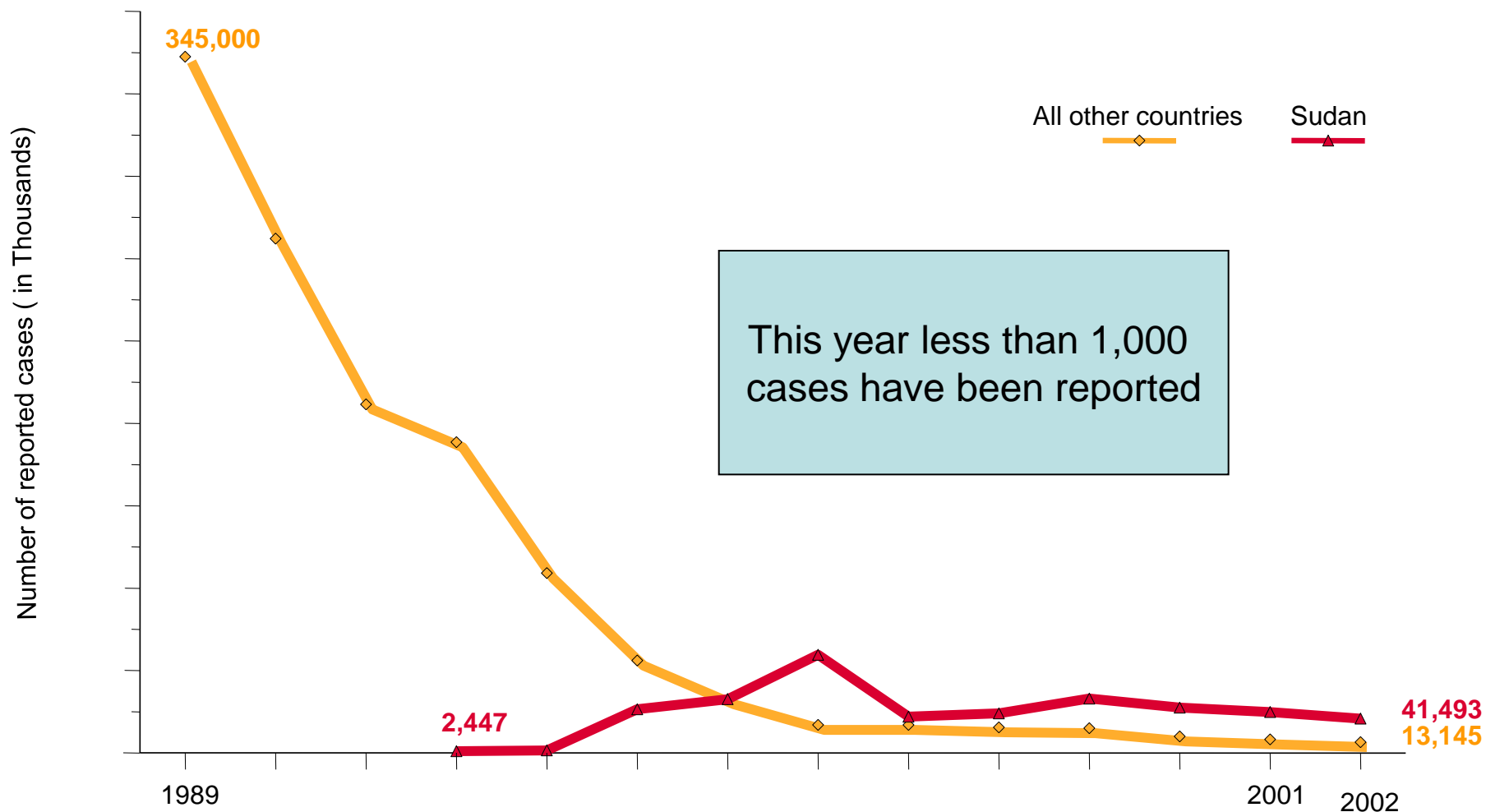
Guinea worm in Ghana



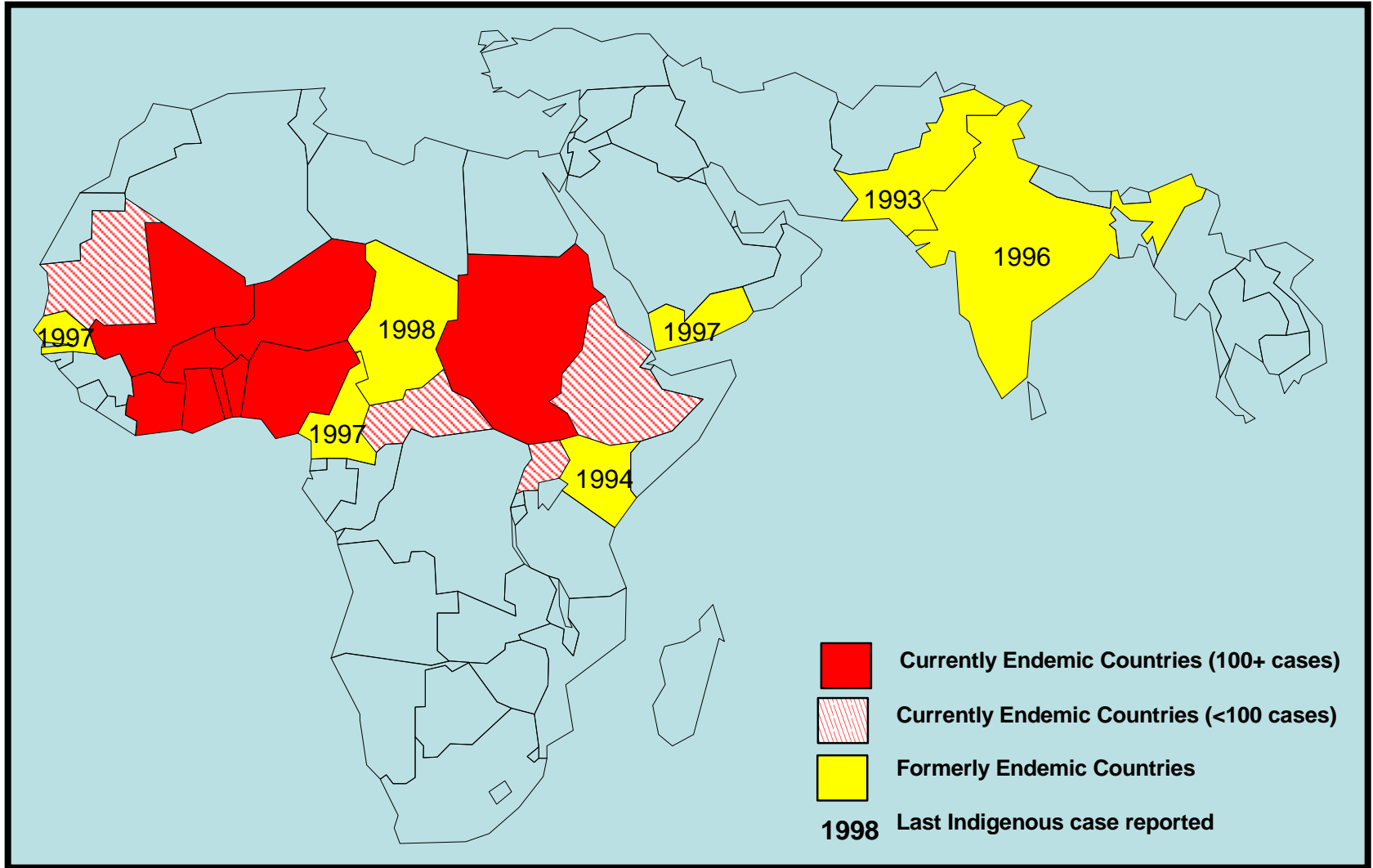
Guinea Worm

- 30 years ago approximately 2 million people suffered from Guinea Worm
- Today less than 1,000 and most of them are in Southern Sudan
- Water and sanitation, case management and health education have led to this reduction (Credit to WHO and the Carter Centre)

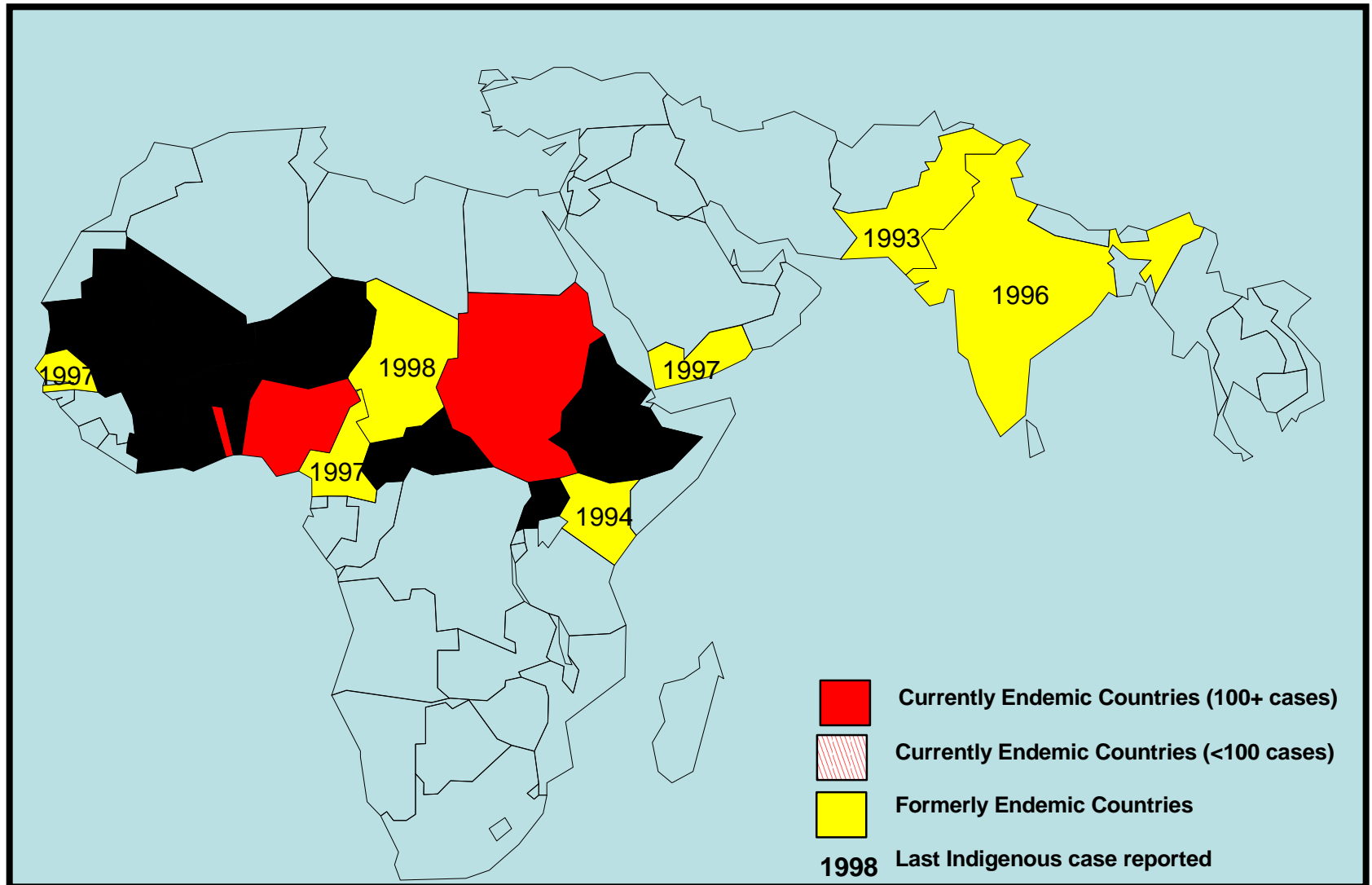
NUMBER OF CASES OF DRACUNCULIASIS BY YEAR: 1989 - 2002



Guinea worm status as at 2004



Guinea Worm eradication is getting ever closer

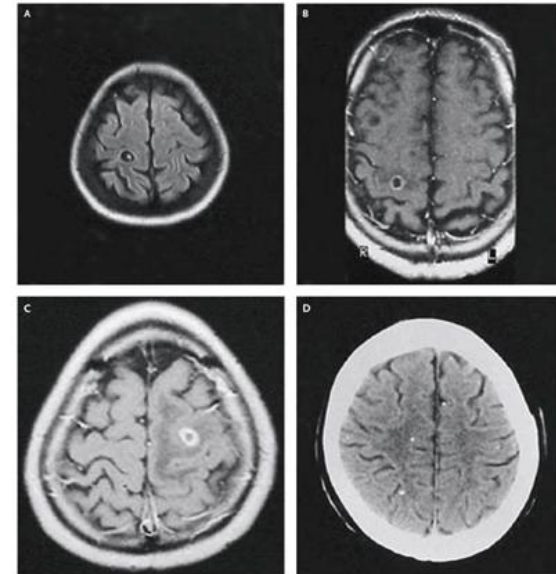


Cysticercosis (*Taenia solium*)

- Leading cause of epilepsy among Hispanic Americans

41,400-169,000 cases

- 10% of seizures presenting to ED in Los Angeles



Podoconiosis (non LF elephantiasis)

- Podoconiosis ('dust in the feet') presents as bilateral asymmetrical swelling of the feet and lower legs. It is seen in susceptible families of bare-footed farmers in well-defined fertile volcanic highland zones of Africa, Central and South America, and Indonesia, and also in the lowlands irrigated by rivers from these highlands.
- It is due to the absorption of silica particles from the soil, through the feet of someone from a susceptible family.
- This causes the patient's lymphatics to fibrose, and obstruct, and his femoral nodes to enlarge. This in turn makes the legs and feet swell, and progress through stages which are described as 'water bag', 'rubbery', and 'wooden'.
- Treatment – choose another occupation !!!



The even more Neglected Tropical Diseases

Helminth infections

strongyloidiasis;

Toxocariasis and larva migrans;

loiasis;

food-borne trematodiasis;

Taeniasis; cysticercosis; echinococcosis

Protozoan infections

Leishmaniasis;

amoebiasis;

giardiasis;

balantidiasis

The even more Neglected Tropical Diseases

Bacterial infections

Bartonellosis;
Bovine tuberculosis;
buruli ulcer;*
leptospirosis;
relapsing fever;
Rheumatic fever;
treponematoses

The even more Neglected Tropical Diseases

Fungal infections

Mycetoma;
paracoccidiomycosis

Ectoparasitic infections

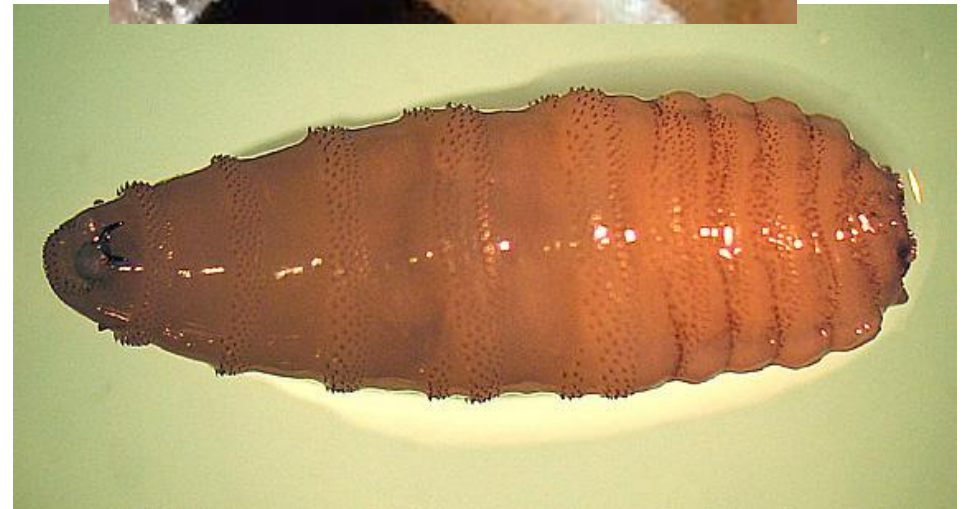
Scabies;
myiasis; tungiasis

Viral infections

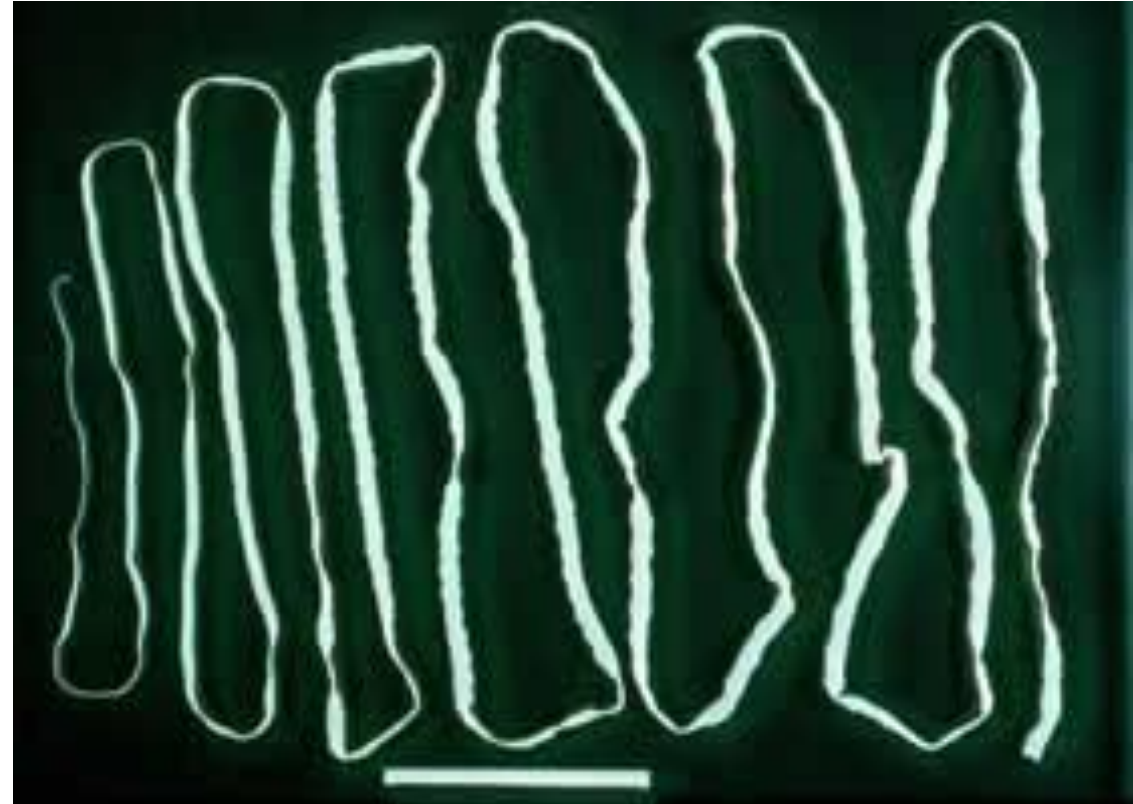
Dengue fever;
yellow fever;
Japanese encephalitis;
rabies;
haemorrhagic fevers

Screw worm

The fly and larvae



Tapeworm 4 metres long



Loa Loa

Distributed around west and central Africa not important as far as pathology in itself

A filarial worm transmitted by Tabanids – horseflies

Important because mass ivermectin treatment of LF and onchocerciasis with albendazole and ivermectin can cause serious side effects in people infected with *Loa Loa* and onchocerciasis in certain areas of west and central Africa,

especially in patients who have high *Loa loa* microfilarial densities.

This fact necessitates the development of more specific diagnostics tests for *Loa loa* to identify high risk areas prior to treatment.

Cholera

- Cholera is an acute intestinal infection caused by ingestion of food or water contaminated with the bacterium *Vibrio cholerae*.
- It has a short incubation period, from less than one day to five days, and produces an enterotoxin that causes a copious, painless, watery diarrhoea that can quickly lead to severe dehydration and death if treatment is not promptly given.
- Vomiting also occurs in most patients

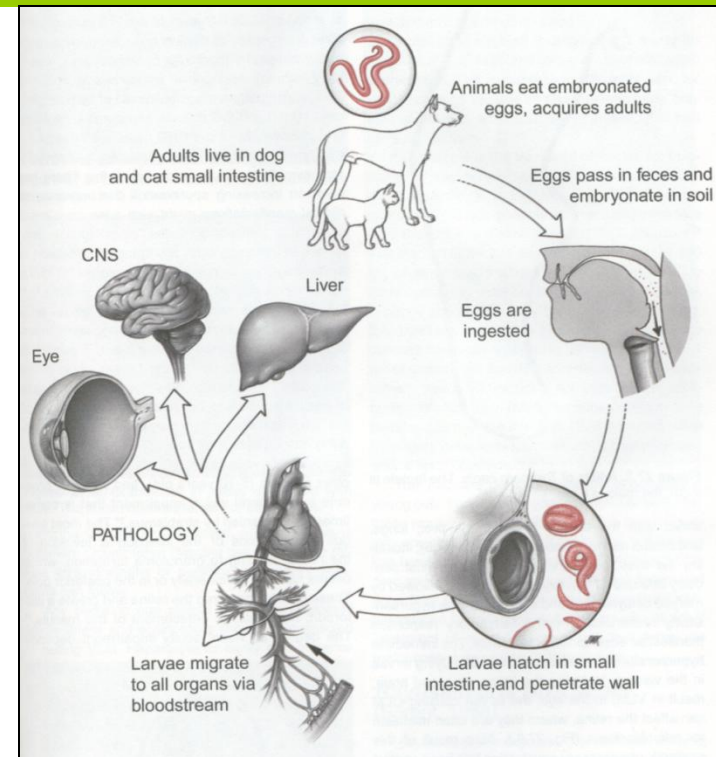
Dengue fever – one of the most common NTDs

Dengue is transmitted by *Aedes* mosquito infected with any one of the four dengue viruses. It occurs in tropical and sub-tropical areas of the world. Prevalence has increased dramatically in recent years and WHO state that 40% of the worlds population are at risk
Symptoms appear 3—14 days after the infective bite.
Dengue fever is a febrile illness that affects infants, young children and adults.

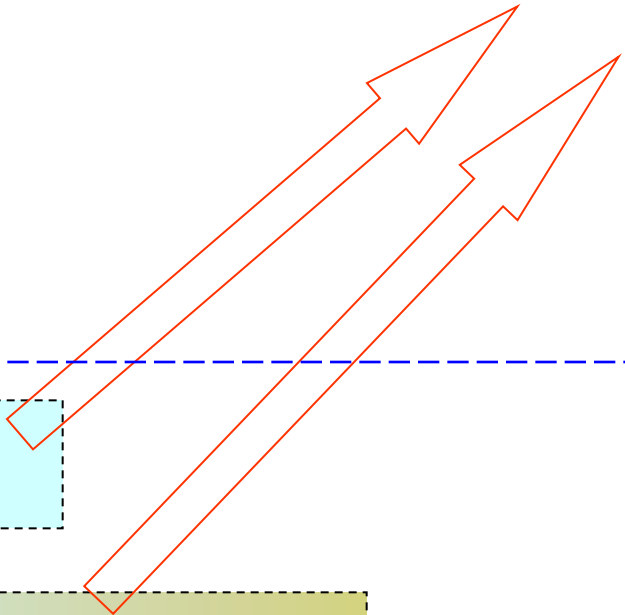
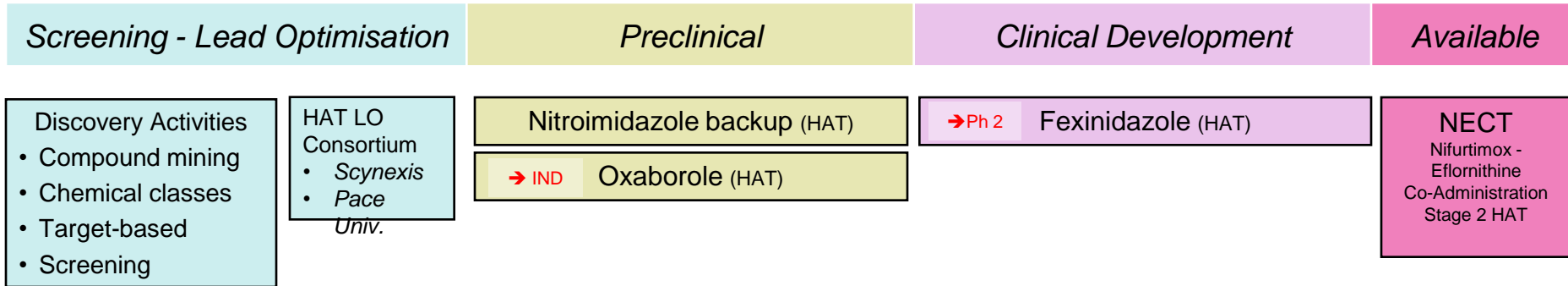
Dengue haemorrhagic fever (fever, abdominal pain, vomiting, bleeding) is a potentially lethal complication, affecting mainly children
50 million cases last year and no treatment

Toxocariasis (*Toxocara canis*)

- 23% seroprevalence among African-Americans
- 50% seroprevalence among some Hispanic groups
- American South & inner cities
- Rise of Asthma?
Developmental delays?



HAT Portfolio – Projection for 2010



U. Dundee

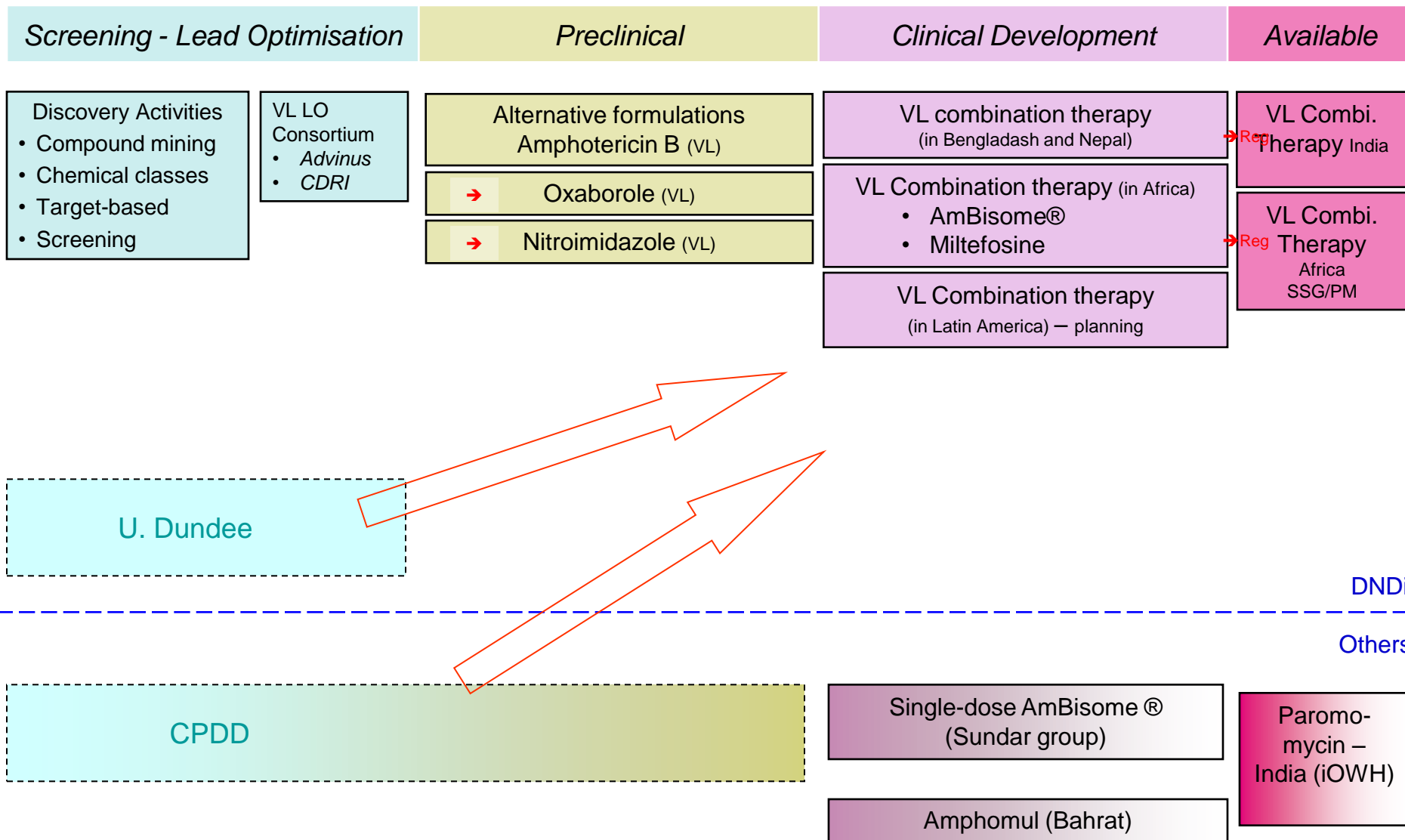
CPDD

3-day pentamidine
Stage 1 HAT (TDR)

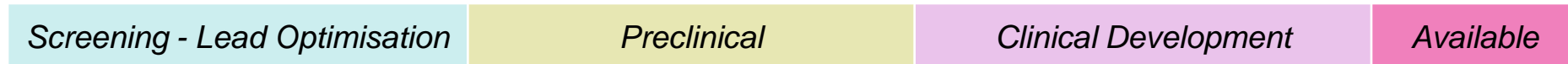
DNDi

Others

VL Portfolio – Projection for 2010



Chagas Portfolio – Projection for 2010



- Discovery Activities
- Compound mining
 - Chemical classes
 - Target-based
 - Screening

- Chagas LO Consortium
- CDCO
 - Epichem
 - Murdoch Univ
 - FUOP

Drug combination (Chagas)

→ Ph 2 Azoles (Chagas)

→ Reg

Paediatric
Benznidazole
Chagas

Cysteine protease inhibitors K777
– UCSF (prio 2)

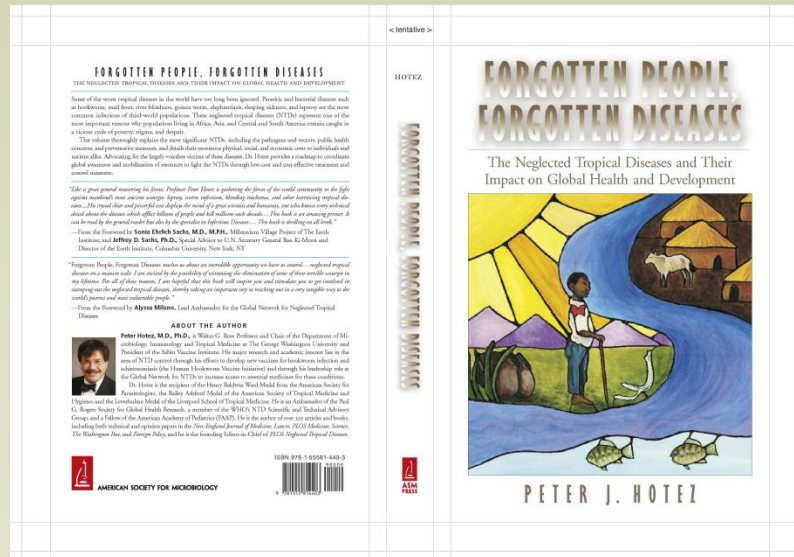
DNDi

Others

Sterol biosynthesis inhibitors



- World's first peer-reviewed, open-access journal devoted to the NTDs
- Launch supported by B&M Gates Foundation
- Magazine section devoted to policy and advocacy
- International editorial board—half of the Associate Editors are from endemic countries



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Alan Fenwick

a.fenwick@imperial.ac.uk



Thank you