### NTDs in Global Health

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### Case: Malnutrition & Anemia

HPI: Jose is a 2 ½ yo Honduran boy brought in for a check up at a clinic in Honduras. Mom is concerned because Jose doesn't seem hungry. He was hospitalized once at the age of 6 months for pneumonia. He had two episodes of diarrhea last year.

SH: Mom is raising Jose, as well as his 3 older brothers and sister alone. Their father went to the US to work, but they haven't seen much money come back yet. There is sometimes not enough money to buy food.

PE: VS: Height: 86 cm, Weight 10 kg (Wt for Age z-score: -2.0). Temp 99.1. He is sitting on mom's lap, alert; poor appearing, barefoot. His hair is thin but normal in color. His conjunctiva appear mild pale. His abdomen is distended, but nontender. Remainder of exam is unremarkable.

### Case: Malnutrition & Anemia

- What do you think is the cause of Jose's malnutrition and anemia?
- How would you treat Jose?

### **STHs**

### Roundworm (Ascariasis) (1.2b infected)

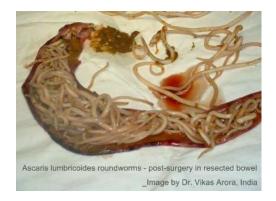
- Ascaris lumbricoides (up to 40cm)
- Fecal-oral (egg lasts up to 6 yrs in soil)
- Abd pain, <u>obstruction</u> (likes jejunum), eosinophilic pneumonitis, CBD obstrxn
- Dx pearl: Prepatent period of 2 months
- Tx: Albendazole\* (better GI absorption and tissue distribution than Mebendazole; Preg Cat C)

### Hookworm (740m infected)

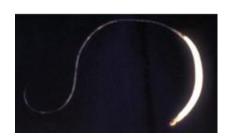
- Necator americanus, Ancylostoma duodenale (1cm)
- Fecal-oral, Skin penetration (larvae "quest" on grass blades)
- Clinical: Ground itch, pneumonitis, abd pain, <u>anemia</u>, impaired cognitive development (IQ decrease of 10 pts), low protein
- Tx: Albendazole

### Whipworm (795m infected)

- Trichuris trichiura (up to 3-5cm, shaped like whip)
- Fecal-oral
- 90% asymptomatic, Growth retardation, <u>rectal prolapse</u> (likes cecum)
- Tx: Mebendazole (high dose) OR Albendazole 3 days OR
   Oxantel-Pamoate w/ Albendazole single dose







## The Helminths

#### Nematodes

#### "Roundworms"

- Intestinal
  - Roundworm
  - Hookworm
  - Whipworm
  - Pinworm
  - Threadworm
- Filarial
- Other Tissue

#### Examples:

Ascaris lumbricoides

Necator americanus, Ancylostoma duodenale

Trichuris trichiura

Enterobius vermicularis Strongyloides stercolaris

Examples: Wuchereria bancrofti, Loa loa, Onchocerca volvulus

Examples: Dracunculus medinensis, Trichinella spp, Toxocara spp,

Ancylostoma spp

#### Cestodes

### "Tapeworms"

Examples:

Taenia solium (and other Taenia spp)

**Echinococcus** 

#### Trematodes

#### "Flukes"

#### Examples:

Schistosomiasis (hematobium)

Intestinal Flukes: Fasciolopsis

Liver Flukes: Opisthorchis, Clonorchis

Lung Fluke: Paragonimus

### Helminths - Treatment

### "Roundworms" → Benzmidazoles (Albendazole)

#### **Examples:**

Ascaris lumbricoides

Necator americanus, Ancylostoma duodenale

Trichuris trichiura (Albendazole + Oxantel Pamoate OR high-dose/longer course Benzmidazoles)

Enterobius vermicularis

Strongyloides stercolaris (Ivermectin)

**Examples:** Wuchereria bancrofti, Loa loa, Onchocerca volvulus

**Examples:** Dracunculus medinensis, Trichinella spp, Toxocara spp, Ancylostoma spp

### "Tapeworms" → Benzmidazoles (Albendazole)

#### **Examples:**

Taenia solium (and other spp)

**Echinococcus** 

#### "Flukes" → Praziquantel

#### Examples:

Schistosomiasis

Intestinal Flukes: Fasciolopsis (Triclabendazole)

Liver Flukes: Opisthorchis, Clonorchis

Lung Fluke: Paragonimus

# Case: Leg wound

- A 38y man presents to you with a painful leg wound that started as a blister then ulcerated (pictured)
- What's your DDX for ulcers in the tropics?
- What prevention interventions may be especially important in this region?





# Dracunculiasis (Guinea Worm Disease)

- 16,000 infections (2007), now 126 (2014)
- Cause: Dracunculiasis medinensis
- SSA: Sudan, Mali, Ethiopia, Chad
- CLINICAL: Painful cutaneous blisters that ulcerate w/ emergence of worm as white filament
- GOAL: Targeted for Eradication. GWEP (Carter Center 1986): Community Health approach, keeping water sources clean, using boiled/filtered water

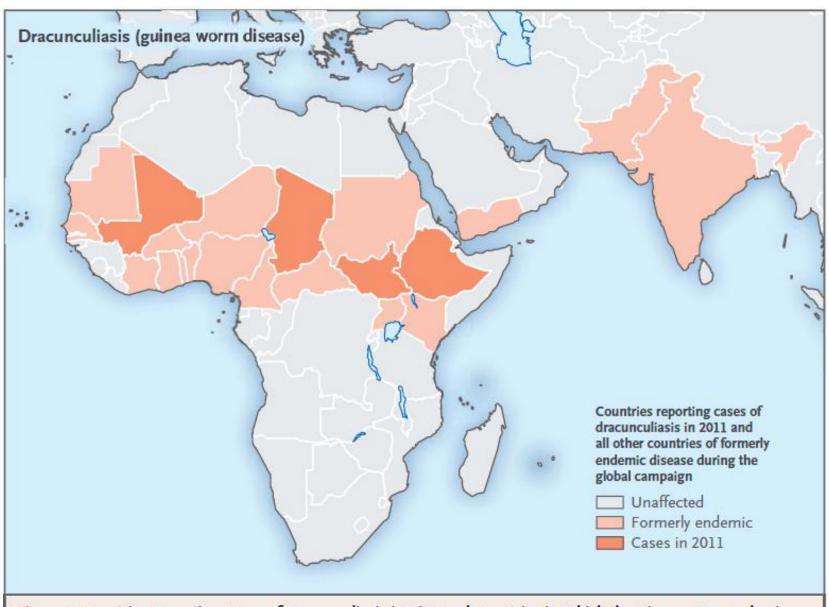
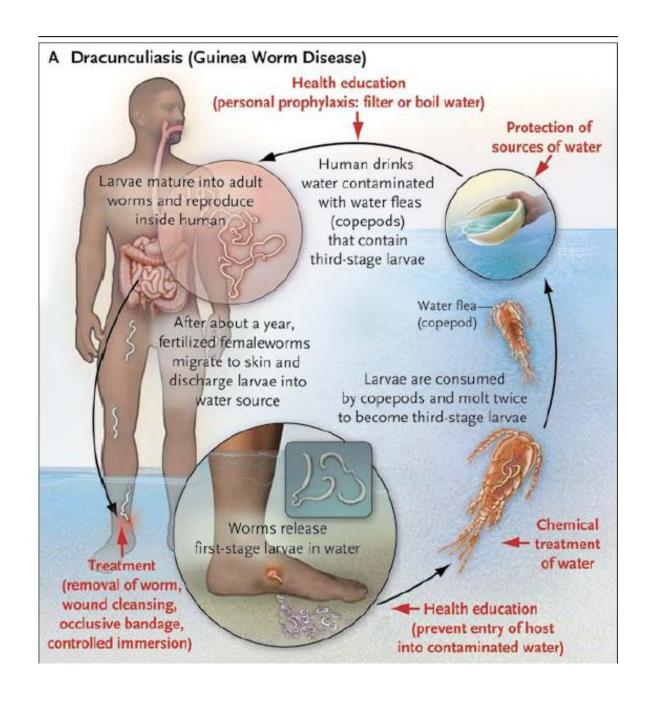
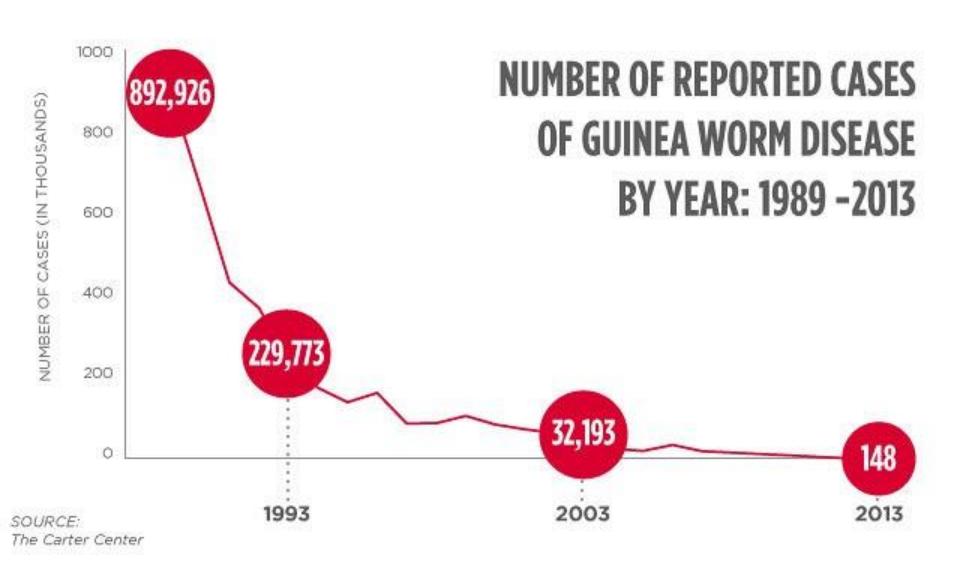


Figure 2. Countries Reporting Cases of Dracunculiasis in 2011 and Countries in Which the Disease Was Endemic in 1980.





# Skin Ulcer DDX (in tropics)

- Buruli Ulcer (pictured)
  - M. ulcerans (Toxin: Mycolactone)
  - Usually <15yo</li>
  - Painless, undermined border, legs/arms
  - Can erode bone, deform
  - Tx: Rifampin+Streptomycin (or Clarithromycin or FQ)
- Tropical Phagedenic Ulcer (TPU)
  - Bacterial/treponemal
  - Painful, enlarging; smelly; usually on leg
  - Hot & humid climate

### Others:

- Anthrax
- Leprosy
- Tick Bite Eschar
- Dracunculiasis (rare)



# Case: Swollen Leg

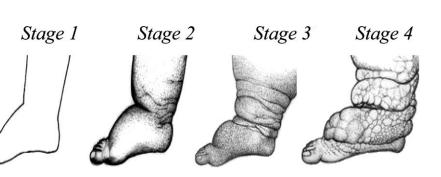
HPI/PE: A 52 year old Rwandan man presents to the FMC for resettlement screening and is noted to have non-pitting edema of the right leg on physical exam. The remainder of your exam is normal. The patient states the problem has been present for >20 years with gradual worsening and is bothersome but not painful. He recalls an episode of acute swelling and pain in the leg as a teenager.

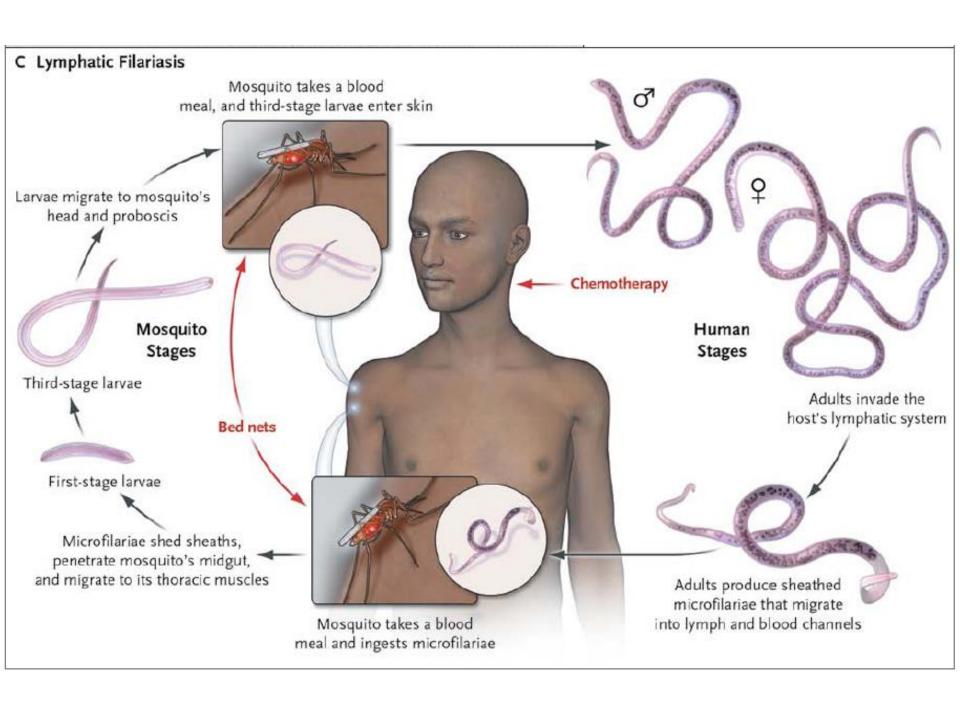
What is the likely diagnosis? What would you do?

# Lymphatic Filariasis (LF)

- Cause: W bancrofti (90%), B malayi, B timori
- Vector: <u>Culex (Asia)</u>, <u>Anopheles (Africa)</u>
- Epid: 120m infected, SSA/Asia
- Clinical: (1/3<sup>rd</sup> of infected)
  - Acute: local swelling 3-12m post-exp (AFL), ADLA/cellulitis, TPE
  - Chronic: lymphedema, hydrocele, elephantiasis
- Dx: Midnight blood smear (Giemsa), Trop Bio Og4C3 Ag, ICT card, IgG, U/S (Filarial Dance Sign)
- Tx: <u>DEC</u>, <u>Ivermectin</u>, <u>Albendazole</u>, <u>Doxycycline</u> (Wolbachia endosymbic lymphedema mgmt; limit secondary bacterial infections
- Program: GPELF







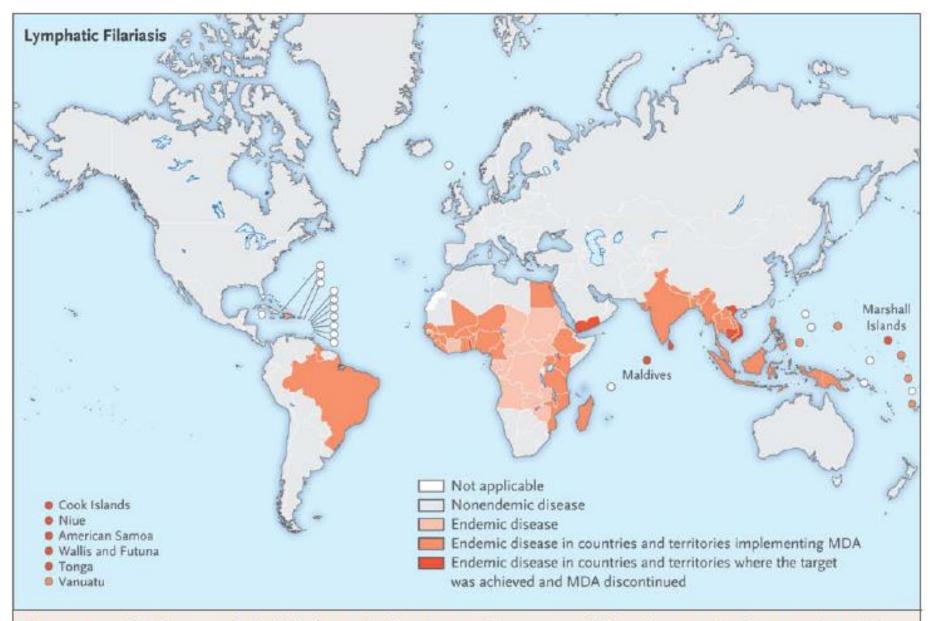


Figure 4. Countries Where Lymphatic Filariasis Is Endemic and Status of Mass Drug Administration (MDA) in Those Countries, 2010.

Adapted from the World Health Organization.<sup>26</sup>

# Case: Hematuria & Hepatomegaly

HPI: A 10 year old boy from Yemen presents complaining of pain w/ urination for 6 months. He also noted some blood at the end of voiding. He described a "piece of meat" following the blood associated w/ lower abdominal pain.

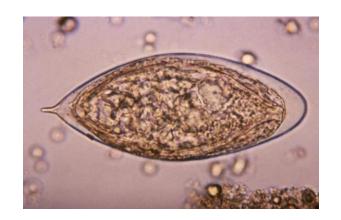
PE: Normal VS. POS suprapubic tenderness. O/w negative exam.

What is the likely Diagnosis?

How would you diagnose and treat this?

## Schistosomiasis

- Cause: <u>Schistosoma haematobium</u> (Fluke)
- Vector: Snails (warm shallow fresh water)
- Epidemiology: 207m people infected, most in SSA
- Clinical:
  - Acute: dermatitis, pneumonitis, fever (+/diarrhea) 4-6wks after infection (<u>Katayama</u> <u>Fever</u>)
  - Chronic: GU tract disease including hematuria, <u>SCC Bladder CA</u>
- Dx:
  - Active: Ova on urine or rectal mucosa scrapes/snips (Kato-Katz Smear)
  - Old: ELISA
- Tx:
  - Praziquantel (1d = 80-85% cure); re-treat 8 wks; f/u testing 3-6mo





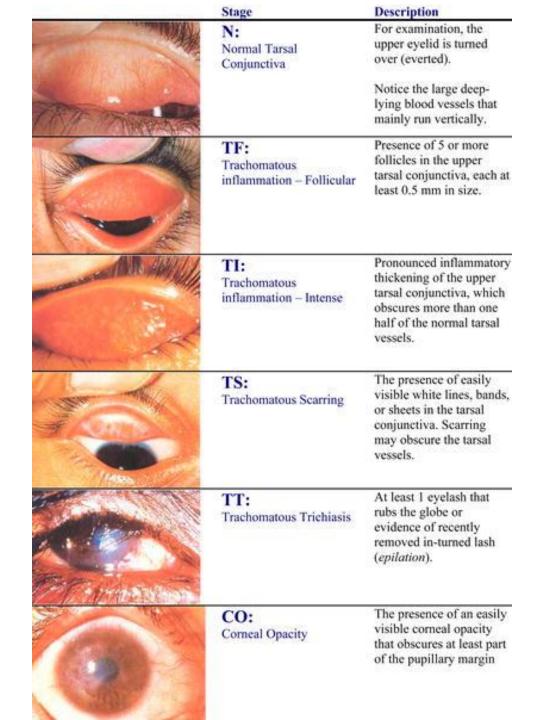
### Case: Blindness

- A 30y woman is brought to your clinic in Nigeria with decreased visual acuity and h/o of recurrent eye problems
- PE: bilateral conjunctival scarring, eyelash entropion, and slight corneal scarring (pictured)
- What's your DDX?
- How would you manage this case at a community health level?



### Trachoma

- Cause: Chlamydia trachomatis
- 21m actively infected (2010)
- Cause of 3% of blindness worldwide
- Multiple re-infections in childhood results in conjunctival scarring, then trichiasis
- Tx: <u>Azithromycin</u>



# Key Strategy for Elimination: SAFE



Surgery

**Antibiotics** 

Facial Cleanliness Environmental Improvements

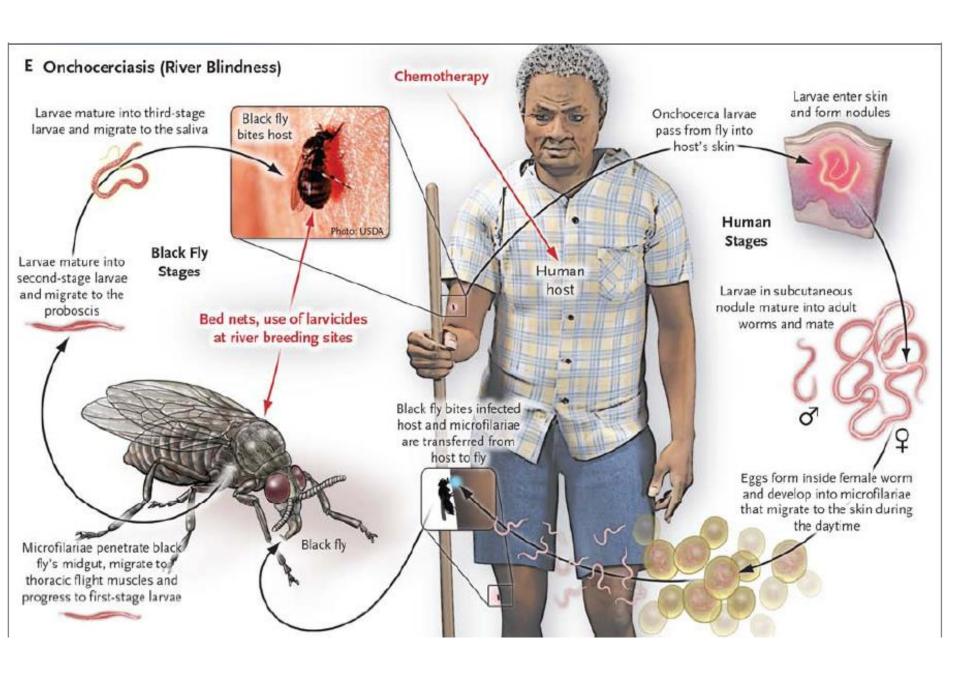
## DDX for Blindness in Global Health

- Cataracts (46%)
- Glaucoma (12.3%)
- AMD (8.7%)
- Corneal Opacities (5.1%)
- Diabetic Retinopathy (4.8%)
- Childhood Blindness/VAD (3.9%)
- Trachoma (3.6%)
- Onchocerciasis (0.8%)
  - 37m infected (99% in Africa)
  - Cause: Onchocerca volvulus
  - Vector: Simulium damnosum
  - Migrate in skin/eye
  - Tx: <u>Ivermectin</u>
  - Programs:
    - OEPA 1992 (L Am) → Eliminated
    - OCP (Afr) → Almost eliminated in 11 countries
    - APOC (Afr) → Expanded OCP in 1995 (reduced from 46.5% 1995 to 28.5% in 2008)



# Onchocerciasis control programmes





# Case: Syncope

HPI: 27y male admitted to hospital for syncope. Had been in excellent health, until day of admission, when he experienced palpitations and dizziness while playing soccer and then passed out. LOC x2-3min.

ROS: intermittent palpitations w/ CP over last 2 yrs

PMH: o/w neg

Soc: Occas ETOH and MJ; POS h/o prostitute exp

PE: HR 56, o/w nl VS; athletic appearing; CV occas premature beats, "forceful left ventricular lift", S3; nl neuro exam

Scully, RE, et al. Case Records of the MGH, New Eng J Med, 8/12/1993; 329(7).

# Case: Syncope

- What's on your DDX?
- What more would you like to know?
- What further testing would you like to order?

# Case: Syncope

- Pt is Latin-American born in El Salvador
- DDX:
  - Syncope: Cardiovascular vs Neurologic vs Other
  - Cardiac:
    - Arrythmias (Long QT, WPW, PSVT, etc)
    - Valvular disease (AI from Syphilis)
    - CMP (HCOM, other)
    - Myocarditis (Viral, Syphilitic, Protozoal)
- Tests:
  - EKG: RBBB, LAD; Monitor: PVCs, 8b VT
  - CXR: LVH
  - Echo: NI AV, NI EF, POS LV dilation, hypokinesis of apex/septum
  - Cardiac Bx: multifocal fibrosis (neg stains for fungi, toxo, trypanosomes, treponema, and mycobacterium)

# Chagas Disease (American Trypanosomiasis)

- Epidemiology: >20m LAs infected; >300k USA, no txf screening before 2007, 50k deaths/yr, #1 cause of HF in LA
- Cause: <u>Trypanosoma cruzi</u>
- Vector: Reduviid Bug (Triatomine)
- Reservoir: Rodents, Armadillos, Opossums
- Pathophysiology: Infection of autonomic ganglia, striated and cardiac mm
- Clinical:
  - Acute: Rare (1%), Chagoma, Romana's Sign, Giemsa Stain
  - Chronic: 30%, >20yrs after infection, Mega-esophagus, Mega-colon, Cardiac disease (arrythmias, HF)
- Treatment:
  - Acute: Nifurtimox or Benznidazole
  - Chronic: Symptomatic (eg, anti-arrythmics)

## Case: Fever & Headache

HPI: 30y Australian returned home after 4 wk trip to E Africa (Zambia) and 1 day later developed fever, severe headache, and rigors. Initial w/u was negative and pt worsened, developing nausea, vomiting and myalgia.

ROS/PMH o/w noncontributory

PE: T 39.5, HR>100, postural hypotn; enlarged spleen (1cm bcm), 5x6cm macular erythematous lesion on inner right thigh, no LA

### Case: Fever & Headache

- What's on your DDX?
- What more would you like to know?
- What further testing would you like to order?

### Case: Fever & Headache

- DDX: (Fever+HA+Splenomegaly)
  - Malaria
  - Acute Schistosomiasis (Katayama Fever)
  - African Trypansomiasis
  - VL (Kala Azar, "Black Fever")
  - ATBF
- Hx: Multiple insect bites while in Africa, none recalled as painful and did not recall being bitten at lesion site
- Tests:
  - CBC, CMP, Urine Cx normal/neg
  - Multiple malaria smears NEG, but POS for...

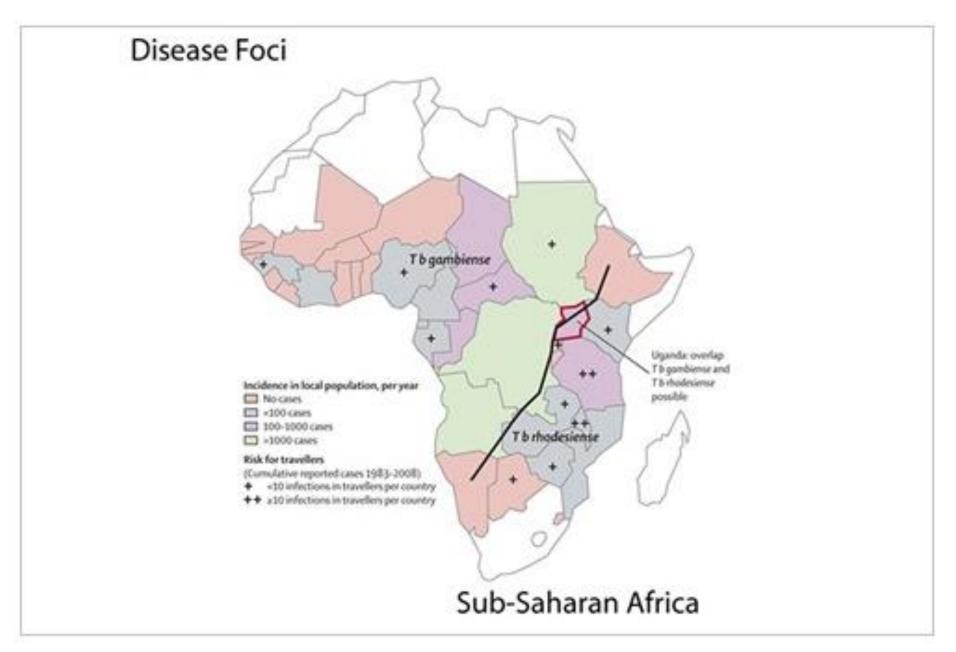
# Human African Trypanosomiasis (HAT)("African Sleeping Sickness")

- Epidemiology: Affects 50m in Africa plus economic damage due to cattle disease (Nagana)
- Cause: <u>Trypanosoma brucei gambiae (90%) & Trypanosoma brucei rhodesiense (10%)</u>
- Vector: <u>Glossina</u> (Tsetse Fly)
- Reservoir: Cattle
- Clinical:
  - Tbg: West/Central SSA, bite lesion, fever 1-3 wks later, <u>lymph node involvement</u> (Winterbottom sign), <u>later</u> CNS involvement (mos-yrs)
  - Tbr: East SSA, bite lesion/chancre (70-80%), fever 1-3wks later, early CNS involvement (wks-mos)
- Treatment: (Fatal if untreated)
  - Pre-CNS: Suramin (Tbr), Pentamadine (Tbg)
  - CNS: Melarsoprol (Tbr), Eflornithine (Tbg)

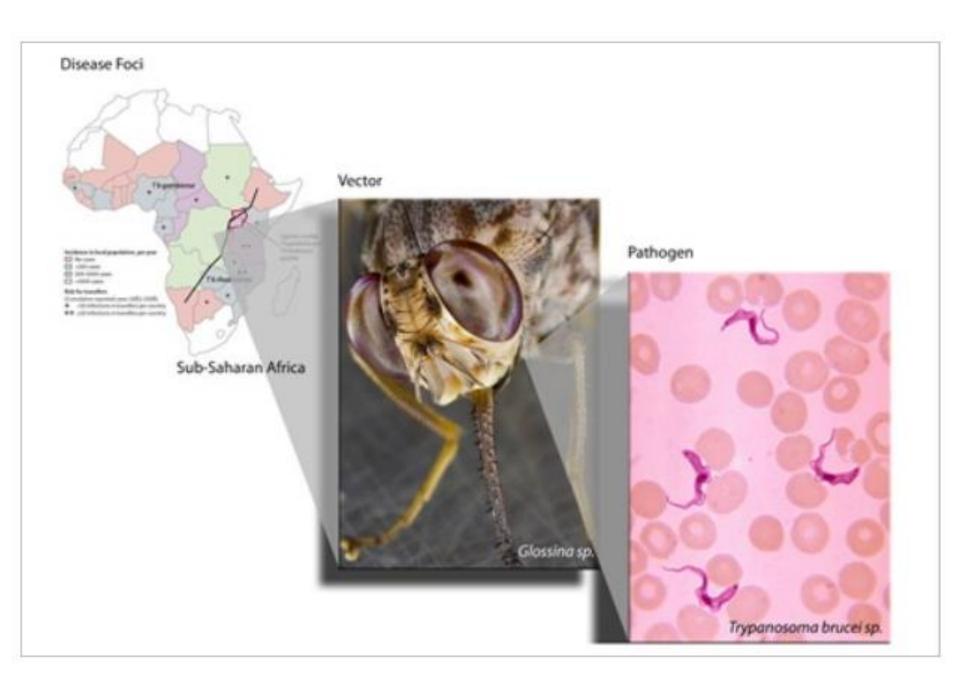




http://publichealth.yale.edu/news/slideshows/hat.aspx



http://publichealth.yale.edu/news/slideshows/hat.aspx





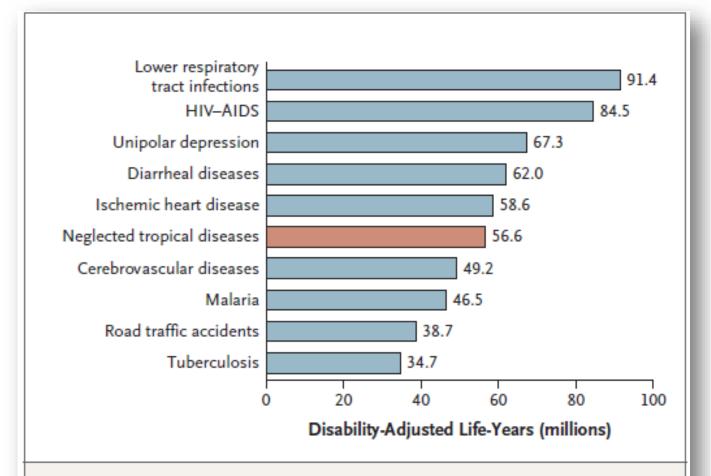


Figure 1. The 10 Leading Causes of Life-Years Lost to Disability and Premature Death.

The number of years lost to disability and premature death (disability-adjusted life-years) for the 13 major neglected tropical diseases were calculated according to a method we described previously. The disability-adjusted life-years for the other conditions are based on data from the World Health Organization. The ranking of disease burdens is based on data in Hotez.

# NTD Geographical Overlap

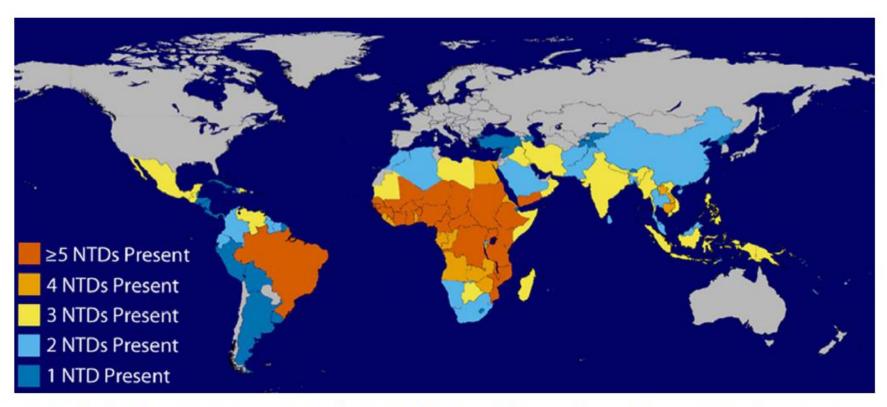


Figure 1 Map showing the significant geographical overlap and global burden of six neglected tropical diseases (specifically guinea worm, lymphatic filariasis, onchocerciasis, schistosomiasis, trachoma and the three major soil transmitted helminth infections). Image courtesy of the Centers for Disease Control and Prevention.

## A Summary of the 5 "tool ready" NTDs

Disease	Cause	Prevalence worldwide	Importance	Key Strategy	Goal
Lymphatic Filariasis (Elephantiasis)	Wuchereria bancrofti	120m in 81 countries	Disfigurement, permanent disability	MDA (DEC, Ivermectin + Albendazole)	Elimination by 2020 (GPELF)
Onchocerciasis (River Blindness)	Onchocerca volvulus	37m (99% in Africa)	Eye lesions, blindness, skin disease	MDA (Ivermectin)	Elimination in Americas by 2016
Schistosomiasis (Snail Fever, Bilharzia)	Schistosoma hematobium	200m	Anemia, bladder/ renal/liver/spleen disease	MDA (Praziquantel)	Control
STHs (Roundworm, Whipworm, Hookworm)	Ascaris, Necator, Ancylostoma, Trichuria	1.5-2b	Impaired growth & cognition, malnutrition, anemia	MDA (Albendazole)	Control
Trachoma	Chlamydia trachomatis	80m	Blindness	MDA /"SAFE" (Azithromycin)	Elimination by 2020 (GET)

## Disease Eradication

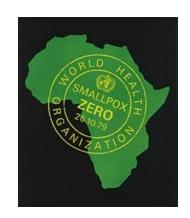
- Definitions (Dahlem Workshop, 1997)
  - Control reduction to locally acceptable level w/ continued intervention
  - Elimination reduction of incidence to zero in defined area w/ continued intervention
  - Eradication permanent reduction of worldwide incidence to zero w/ continued intervention no longer needed



Success: Smallpox (1977)

Failure: Malaria, YF, Yaws

- Current Targets
  - Polio, Guinea Worm (Eradication)
  - LF, Oncho, Trachoma (Elimination)
  - STHs, Schistosomiasis (Control)





# Preventive Chemotherapy in Human

# Mass Drug Administration (MDA)

#### Table 2. Drugs, dosages, implementation thresholds and regimens in preventive chemotherapy interventions

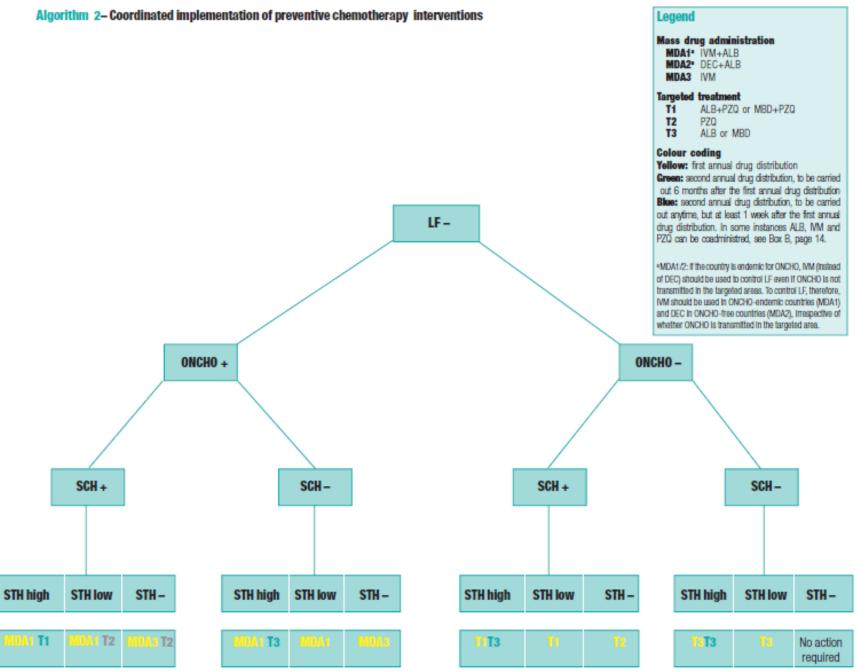
Note: Drug names are given in full in the list of abbreviations at the front of the manual.

Disease	Drugs and dosages	Threshold for implementation of preventive chemotherapy interventions <sup>a</sup>	Frequency of Intervention
Lymphatic filariasis (in countries where onchocerciasis is co-endemic)	IVM according to height (using IVM tablet-pole) <b>plus</b> ALB 400 mg	Prevalence of infection≥1%	Once a year
Lymphatic filariasis (in countries where onchocerciasis is not co-endemic)	DEC 6 mg/kg (using age as criterion for dose) plus ALB 400 mg	Prevalence of infection ≥1%	Once a year
Onchocerciasis	IVM according to height (using IVM tablet-pole)	Prevalence of infection ≥ 40% or prevalence of palpable nodules ≥ 20%	Once a year
Schistosomiasis	PZQ 40 mg/kg (using PZQ tablet-pole)	Presence of infection	According to prevalence of infection (see Annex 2)
Soil-transmitted helminthiasis (ascariasis, trichuriasis, hookworm disease)	ALB 400 mg or MBD 500 mg <sup>a</sup>	Presence of infection	According to prevalence of infection (see Annex 2)
Trachoma	Azilthromycin 20mg/kg (using tablet-pole) max 1g in adults	Active trachoma (TF) prevalence > 5 % in 1–9 years old at district level <sup>c</sup>	Once a year

<sup>\*</sup>LEV 2.5 mg/kg or PYR 10 mg/kg is useful where trichuriasis does not pose a significant problem.

For details, see Annex 6.

<sup>°</sup>TF>10% at district level; dictrict-wide mass treatment. If TF<5% at district level, some communities might still require community wide treatment.



# Does MDA work? In Theory...

- ALB+DEC:
  - LF  $\downarrow$  from 16.7 to 5.3%
  - Hookworm ↓ from 10.3 to 1.9%
  - Roundworm  $\downarrow$  from 34.5 to 2.3%
  - Whipworm ↓ from 55.5 to 40.3%
- ALB+IVM
  - LF  $\downarrow$  from 12.6 to 4.6%
  - Hookworm ↓ from 7.8 to 0.0%
  - Roundworm  $\downarrow$  from 33.5 to 6.1%
  - Whipworm ↓ from 42.7 to 8.9%
- ALB alone similar to above, except for LF
- AZITHRO for trachoma (TF) no RCTs in MDA

Reddy, M et al, Oral Drug Therapy for Multiple NTDs, JAMA, October 24/31, 2007, 298(16):1911-1924.

# Does MDA Work? In Reality...

Parker and Allen Health Research Policy and Systems 2011, 9:3 http://www.health-policy-systems.com/content/9/1/3



RESEARCH Open Access

Does mass drug administration for the integrated treatment of neglected tropical diseases really work? Assessing evidence for the control of schistosomiasis and soil-transmitted helminths in Uganda

Melissa Parker1\*, Tim Allen2

**Background:** Less is known about mass drug administration [MDA] for neglected tropical diseases [NTDs] than is suggested by those so vigorously promoting expansion of the approach. This paper fills an important gap: it draws upon local level research to examine the roll out of treatment for two NTDs, schistosomiasis and soil-transmitted helminths, in Uganda.

Table 2 Self-reported drug uptake as a percentage at selected villages in Moyo District, 2005-2008

	Olia West	Pakaa West	Pakonira East	Panjala	Paubu	Dufile	Laropi
2008	90	50	92	5	100	15	33
2007	0*	17	38	95	17	88	33
2006	50	8	38	32	17	54	76
2005	30	8	38	26	50	46	29

<sup>\*</sup> No reported distribution.

## NTDs, MDA, & Child Health

## Global child health

Table 1 Number of people requiring preventative chemotherapy and number of people receiving preventative chemotherapy for the seven most common NTDs, 2011

	Number of people requiring preventative chemotherapy	Number of people receiving preventative chemotherapy	% at risk reached
STH infections (hookworm, ascariasis, trichuriasis)	266 million pre-SAC 609 million SAC	100 million pre-SAC 210 million SAC	38% pre-SAC 34% SAC
Trachoma	325 million people (in 2010)	38 million people treated (in 2010)	12% people
Lymphatic filariasis	1.41 billion people	557 million people	40% people
Schistosomiasis	112 million SAC	16 million SAC	14% SAC
All seven NTDs targeted by preventive chemotherapy	1.9 billion people	710 million people	37% people

Data reported for preschool age children (pre-SAC) and school age children (SAC) if available. If no data are available for these groups, the total population is reported. Onchocerciasis, the seventh NTD that is targeted for preventative chemotherapy, is not included in this table as it primarily affects adults. Numbers were calculated using data obtained from the Preventive Chemotherapy Databank, which is maintained by WHO (http://www.who.int/neglected\_diseases/preventive\_chemotherapy/databank/en/index.html). Additional figures obtained from the Weekly Epidemiological Record: Global WHO Alliance for the Elimination of Blinding Trachoma by 2020, published in 2012 by WHO; Sustaining the drive to overcome the global impact of neglected tropical diseases: Second WHO report on neglected tropical diseases, published by WHO in 2013; and From Promises to Progress: The First Annual Report on the London Declaration on NTDs, published in 2013.

NTD, neglected tropical disease; STH, soil transmitted helminth.

# Thank you!

## Disease Eradication

#### Definitions

#### Eradication

Zero disease globally as a result of deliberate efforts

Control measures no longer needed

### Elimination

Zero disease in a defined geographic area as a result of deliberate efforts

Control measures needed to prevent reestablishment of transmission

## Criteria for Assessing the Eradicability of a Disease

## Scientific feasibility

Epidemiologic susceptibility (e.g., no nonhuman reservoir, ease of spread, naturally induced immunity, ease of diagnosis)

Effective, practical intervention available (e.g., vaccine, curative treatment)

Demonstrated feasibility of elimination (e.g., documented elimination from island or other geographic unit)

## Political will and popular support

Perceived burden of the disease (e.g., extent, deaths, other effects; relevance to rich and poor countries)

Expected cost of eradication

Synergy of eradication efforts with other interventions (e.g., potential for added benefits or savings)

Need for eradication rather than control

# History of Eradication, Elimination

## Eradication:

- Smallpox has now been eradicated and programmes are currently under way to eradicate poliomyelitis and guineaworm disease.
- 1993: International Task Force for Disease Eradication evaluated over 80 potential infectious disease candidates and concluded that six were eradicable.

## • Elimination:

- 1997: World Health Assembly passed a res to eliminate LF
- 1997: WHO listed leprosy, onchocerciasis, and Chagas disease as being candidates for elimination
- With this background, the **Dahlem Workshop** on the Eradication of Infectious Diseases was held in March 1997

MMWR, December 31, 1999 / Vol. 48 / Supplement