Neglected Tropical/Infectious Diseases

17 NTDs listed in WHO

- Buruli ulcer
- Dengue
- Dracunculiasis
- Endemic treponematoses (yaws/bejel)
- Human African trypanosomiasis
- Leishmaniasis (visceral and cutaneous)
- Leprosy
- Lymphatic filariasis
- Onchocerciasis
- Rabies
- Schistosomiasis
- STH
- Trachoma
- Cysticercosis
- Echinococcosis
- Fascioliasis
- (Chagas)

18th added May 2016

- Mycetoma

Key research questions and role of EDCTP2
Disease burden ... & the vicious cycle

>1 billion affected incl. 500 million children

<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Deaths/year</td>
<td>150,000 350,000</td>
</tr>
<tr>
<td>DALYs</td>
<td>27 million 48 million</td>
</tr>
</tbody>
</table>

- Disease is both cause and consequence of poverty
- Poorest of the poor
- Living in remote areas
- Socioeconomic burden on family and community
- Marginalized & voiceless patients
Africa concentrates over 90% of NTD burden

Source: Uniting to Combat NTDs, 2012
### Ranking of NTDs in SSA by prevalence and distribution

<table>
<thead>
<tr>
<th>Disease</th>
<th>Estimated Population Infected in SSA</th>
<th>Estimated % of SSA Population Infected</th>
<th>Estimated % Global Disease Burden in SSA</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hookworm</td>
<td>198 million</td>
<td>29%&lt;sup&gt;a&lt;/sup&gt;</td>
<td>34%&lt;sup&gt;b&lt;/sup&gt;</td>
<td>[3, 24]</td>
</tr>
<tr>
<td>Schistosomiasis</td>
<td>192 million</td>
<td>25%</td>
<td>93%</td>
<td>[21]</td>
</tr>
<tr>
<td>Ascariasis</td>
<td>173 million</td>
<td>25%&lt;sup&gt;a&lt;/sup&gt;</td>
<td>21%&lt;sup&gt;b&lt;/sup&gt;</td>
<td>[3, 24]</td>
</tr>
<tr>
<td>Trichuriasis</td>
<td>162 million</td>
<td>24%&lt;sup&gt;a&lt;/sup&gt;</td>
<td>27%&lt;sup&gt;b&lt;/sup&gt;</td>
<td>[3, 24]</td>
</tr>
<tr>
<td>Lymphatic filariasis</td>
<td>46–51 million</td>
<td>6%–9%</td>
<td>37%–44%&lt;sup&gt;c&lt;/sup&gt;</td>
<td>[25–28]</td>
</tr>
<tr>
<td>Onchocerciasis</td>
<td>37 million</td>
<td>5%</td>
<td>&gt;99%</td>
<td>[15, 29]</td>
</tr>
<tr>
<td>Active trachoma</td>
<td>30 million</td>
<td>3%</td>
<td>48%</td>
<td>[30]</td>
</tr>
<tr>
<td>Loiasis</td>
<td>≤13 million</td>
<td>1%–2%</td>
<td>100%</td>
<td>[31, 32]</td>
</tr>
<tr>
<td>Yellow fever</td>
<td>180,000</td>
<td>0.02%</td>
<td>90%</td>
<td>[33, 34]</td>
</tr>
<tr>
<td>Human African trypanosomiasis</td>
<td>50,000–70,000 (17,000 new cases annually)</td>
<td>&lt;0.01%</td>
<td>100%</td>
<td>[39, 40]</td>
</tr>
<tr>
<td>Leprosy</td>
<td>30,055 (registered prevalence); 21,037 new cases in 2007</td>
<td>&lt;0.01%</td>
<td>14%</td>
<td>[35]</td>
</tr>
<tr>
<td>Leishmaniasis (visceral)</td>
<td>19,000–24,000 new cases annually in Sudan and Ethiopia</td>
<td>&lt;0.01</td>
<td>ND</td>
<td>[41–44]</td>
</tr>
<tr>
<td>Dracunculiasis</td>
<td>9,585</td>
<td>&lt;0.01%</td>
<td>100%</td>
<td>[36]</td>
</tr>
<tr>
<td>Buruli ulcer</td>
<td>&gt;4,000</td>
<td>&lt;0.01%</td>
<td>57%</td>
<td>[37, 38]</td>
</tr>
</tbody>
</table>


<sup>b</sup>Calculated from global burden data from [48].

<sup>c</sup>The lower value is from [3, 26, 27]; the higher value from [25].

doi:10.1371/journal.pntd.0000412

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A Decade Ago, Neglected Disease R&D at a Standstill: The ‘Fatal Imbalance’

1.1% of 1393 new products for NTDs + malaria & TB (†) despite their global disease burden of 12%

Illustration of the ‘10/90 Gap’

Source: Fatal Imbalance: The Crisis in Research and Development for Neglected Diseases, MSF, 2001
Putting NTDs on the political agenda (1)

- 2005 creation of WHO Department of Control of Neglected Tropical Diseases
- 2011 WHO roadmap
- 2012 Endorsed at London Declaration including increased commitments for donations
- 2013 WHA Resolution 66.12, endorses Roadmap, strategies for NTDs with targets
  - eradication of dracunculiasis (2015) and yaws (2020)
  - global elimination of blinding trachoma, leprosy, HAT, and lymphatic filariasis by 2020;
  - regional elimination of selected diseases (e.g. onchocerciasis, schistosomiasis in several African

London Declaration
- Pharmaceutical companies
- World Bank
- Donor countries (UK, USA, UAE)
- BMGF and other private donors
- Endemic country MoHs
- DNDi
Putting NTDs on the political agenda (2)

- 2015 GFATM Board opens funding for co-morbidities
- 2015 G7 Heads of State recognise NTDs as a major challenge emphasising need to support research and interventions
- 2014 EDCTP adds NTDs in its new business plan
- 2015 Inclusion in SDGs

SDG 3.3: “By 2030, end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases and combat hepatitis, water-borne diseases and other communicable diseases”

SDG 3.8: “Achieve universal health coverage, including financial risk protection, access to quality essential health care services, and access to safe, effective, quality, and affordable essential medicines and vaccines for all”

Coverage of NTD interventions are a tracer for universal health coverage
Increased Investment in NTDs

Key research questions and role of EDCTP2
New partnerships
But Despite Progress, Fatal Imbalance Remains

- 3.8% of new products (reformulations, combinations) for neglected diseases
- 1.2% of NCEs for neglected diseases
- 1.4% clinical trials (of nearly 150,000 trials) focus on neglected diseases
- Only 1% of global health investment for neglected diseases*


Reality In The Field:  
Treatment Limitations for Neglected Diseases

- Ineffective (resistance)
- Toxic
- Expensive
- Painful when administered
- Difficult to use
- Not registered in endemic regions
- Restricted by patents

We Need Safe, Effective, Affordable and Easy-to-Use Drugs
Identification of key gaps (awaiting R&D Observatory)

A proxy assessment for gaps

- **0** = no critical R&D gaps: existence of either:
  - interventions to prevent infection or
  - at least 2 field adapted treatments
- **1** = critical R&D gaps but some ongoing clinical research
- **2** = critical R&D gaps but no ongoing clinical research

<table>
<thead>
<tr>
<th>Critical gaps but ongoing research (WHO-NTDs-AFRICA)</th>
<th>Critical gaps and NO ongoing research (ALL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>STHs</td>
<td>Food borne trematodes</td>
</tr>
<tr>
<td>Schistosomiasis</td>
<td>(Buruli ulcer)</td>
</tr>
<tr>
<td>LF</td>
<td>Leprosy</td>
</tr>
<tr>
<td>Onchocerciasis</td>
<td>Leptospirosis</td>
</tr>
<tr>
<td>Taeniasis-cysticercosis</td>
<td>Bartonellosis</td>
</tr>
<tr>
<td>Leishmaniasis</td>
<td>Bovine tuberculosis</td>
</tr>
<tr>
<td>Dengue Fever</td>
<td>Relapsing fever</td>
</tr>
<tr>
<td>Rabies</td>
<td>Mycetoma</td>
</tr>
<tr>
<td></td>
<td>Paracoccidiomycosis</td>
</tr>
<tr>
<td></td>
<td>Podoconiosis</td>
</tr>
<tr>
<td></td>
<td>Loiasis</td>
</tr>
<tr>
<td></td>
<td>Tungiasis</td>
</tr>
<tr>
<td></td>
<td>Myasis</td>
</tr>
</tbody>
</table>

Research needs: Some examples
## Research needs

1. Regional response to treatment and specific medical needs
2. Co-morbidities
3. Diagnostic and treatment research approach
4. Responding to pediatric needs
5. Pregnant and breast feeding mothers
6. Conducting and running CTs effectively
7. Transitioning from clinical research to implementation
8. New category of NTDs
9. The development of resistance
Regional response to treatment and specific medical needs

a) regional response to treatment

<table>
<thead>
<tr>
<th>Drugs</th>
<th>SSG</th>
<th>Ampho B Liposomal</th>
<th>Ampho B deoxycholate</th>
<th>MIL</th>
<th>PM sulphate</th>
<th>SSG+PM</th>
<th>LAB+SSG</th>
<th>LAB+MIL</th>
<th>PM+MIL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical efficacy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asia</td>
<td>35-95% (depending on areas)</td>
<td>&gt; 97% all regions</td>
<td>&gt; 97%; single dose: &gt; 96%</td>
<td>94-97% (India)</td>
<td>94% (India)</td>
<td>Not documented</td>
<td>&gt; 97%</td>
<td>&gt; 97%</td>
<td>&gt; 97%</td>
</tr>
<tr>
<td>Africa</td>
<td>93% 33 - &gt;97% (depending on areas) Not fully established</td>
<td>72%</td>
<td>84%</td>
<td>91%</td>
<td>87%</td>
<td>79%</td>
<td>Not documented</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resistance</td>
<td>As high as 60% (India) Not documented</td>
<td>Not documented</td>
<td>20% (Nepal)</td>
<td>Lab isolates (easily)</td>
<td>Lab isolates (easily)</td>
<td>Lab isolates</td>
<td>Lab isolates (easily)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Efficacy and resistance of different medicines by geographical areas (modified from van Griensven, 2010)

The treatment of African VL is far from optimal.
Regional response to treatment and specific medical needs

b) disease complexity and regional distribution

Key research questions and role of EDCTP2
PKDL: reservoir of disease

Global incidence

Post-Rx estimates

<table>
<thead>
<tr>
<th>Country</th>
<th>Global incidence</th>
<th>Post-Rx estimates</th>
</tr>
</thead>
<tbody>
<tr>
<td>INDIA (Bihar)</td>
<td>5:10,000</td>
<td>5-10%</td>
</tr>
<tr>
<td>BANG (Fulbaria/Trishal)</td>
<td>6:16-10,000</td>
<td>9.5%</td>
</tr>
<tr>
<td>Sudan</td>
<td>NA</td>
<td>50-60%</td>
</tr>
</tbody>
</table>

PKDL: Post Kala-azar Dermal Leishmaniasis

An immune mediated process: VL (necrotic), PKDL (non-necrotic), cure (healed)

Main clinical differences

<table>
<thead>
<tr>
<th>Main clinical differences</th>
<th>Sudan</th>
<th>India</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most common presentation</td>
<td>polymorphic, papular</td>
<td>monomorphic, macular</td>
</tr>
<tr>
<td>Typical distribution</td>
<td>yes</td>
<td>often not</td>
</tr>
<tr>
<td>(face-arms/chest-lip)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spontaneous cure</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>May occur while on rx for VL</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>Genital lesions</td>
<td>uncommon</td>
<td>common</td>
</tr>
</tbody>
</table>

Main gaps in knowledge

- Infectivity
- Spatial distribution
- Pathogenesis
- Treatment optimization
- Drug skin penetration

DNDI

Zibretta et al., Lancet 00, 2003
Regional response to treatment and specific medical needs

b) disease complexity and regional distribution

\( T. b. \) rhodesiense vs \( T. b. \) gambiense

One disease: two strains

- \( T. b. \) gambiense is endemic in 24 countries of west and central Africa
- Less than 3,000 cases reported in 2015
- Transmission cycle:
  - NECT

- \( T. b. \) rhodesiense is endemic in 13 countries of eastern and southern Africa
- 117 cases reported in 2014
- Transmission cycle:
  - melarsoprol

Geographic distribution of HAT cases

Source: Adapted from WHO

Key research questions and role of EDCTP2
Co-morbidities are frequent

- Schistosomiasis & mycetoma

- HIV-VL: need for treatment and prophylaxis

- Onchocerciasis and nodding syndrome / epilepsy

- Helminths-HIV ...

Research needs
Understanding morbidity impact
Assessing combined treatment needs
Testing field use
Onchocerciasis and Loa-loa

LF and onchocerciasis co-endemic in 18% of endemic districts in Africa (28%).

Loiasis coendemic with onchocerciasis or LF in 18%.

In areas of *Loa loa* coinfection, SAEs (encephalopathy) with high load of microfilariae (that can be fatal) limits MDA.
Diagnostic and treatment research approach: HAT
Diagnostic and treatment research approach: HAT

15 years ago:
- Eflornithine
- Melarsoprol

Since 2009:
- NECT & first generation RDTs

2018 and beyond:
- Oral treatment & second generation RDTs
Diagnostic and treatment research approach: HAT

Objectives DiTECT-HAT project:

- To evaluate accuracy and feasibility of new, ready to implement diagnostic tools, and to propose algorithms for HAT diagnosis in 3 contexts:

1. Passive case detection in peripheral health centres
2. Post-elimination monitoring for detection of disease re-emergence
3. Early test of cure in therapeutic trials

DNDi clinical sites (SCYX7158)
## Responding to pediatric needs

### Table 1. Responses to questions of target population for mass drug administrations (MDAs).

<table>
<thead>
<tr>
<th></th>
<th>Lymphatic Filariasis</th>
<th>Onchocerciasis</th>
<th>Trachoma</th>
<th>Schistosomiasis</th>
<th>Soil-transmitted Helminths</th>
<th>P-value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elimination possible from indirect effects of MDAs, N (%)</td>
<td>8/26 (30.8%)</td>
<td>2/22 (9.1%)</td>
<td>12/22 (54.6%)</td>
<td>28/85 (32.9%)</td>
<td>16/48 (33.3%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Elimination possible by targeting…*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-school children</td>
<td>2/22 (9.1%)</td>
<td>2/17 (11.8%)</td>
<td>9/17 (52.9%)</td>
<td>11/65 (16.9%)</td>
<td>7/38 (18.4%)</td>
<td>0.006</td>
</tr>
<tr>
<td>School children</td>
<td>5/22 (22.7%)</td>
<td>3/17 (17.7%)</td>
<td>6/17 (35.3%)</td>
<td>30/65 (46.2%)</td>
<td>11/38 (29.0%)</td>
<td>0.10</td>
</tr>
<tr>
<td>Those with clinical signs</td>
<td>7/22 (31.8%)</td>
<td>3/17 (17.7%)</td>
<td>3/17 (17.7%)</td>
<td>11/65 (16.9%)</td>
<td>6/38 (15.8%)</td>
<td>0.59</td>
</tr>
<tr>
<td>Targeting not effective</td>
<td>10/22 (45.5%)</td>
<td>12/17 (70.6%)</td>
<td>3/17 (17.7%)</td>
<td>26/65 (40.0%)</td>
<td>19/38 (50.0%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Other</td>
<td>4/22 (18.2%)</td>
<td>2/21 (11.8%)</td>
<td>5/17 (29.4%)</td>
<td>9/65 (13.9%)</td>
<td>5/38 (13.1%)</td>
<td>0.55</td>
</tr>
</tbody>
</table>

*Respondents were allowed to provide more than 1 response; therefore, percentages within an NTD do not sum to 100%.
†Chi square test.

Responding to pediatric needs: the case of VL

Strong Epidemiological Data:
Visceral Leishmaniasis: 50% of cases are below the age of 12

Age distribution of leishmaniasis patients

11484, 38%
12647, 41%
4637, 15%
1939, 6%

<2 years 2-11 years 12-17 years ≥18 years

Responding to pediatric needs

In onchocerciasis IVM is not registered < 5 years and doxycycline contra-indicated < 8 years

Schistosomiasis: children under five could also be vulnerable to schistosomiasis and in the absence preventive chemotherapy they could be at risk of severe morbidities
Responding to pediatric needs

Children and adults differ in:

- Absorption
- Distribution
- Renal function (excretion)
- Hepatic function (metabolism)
- Pharmacodynamics:
  - therapeutic response
  - adverse reactions
  - mechanisms of disease

Kearns et al. NEJM 2003. 349:1157-1167
Responding to pediatric needs in VL
LEAP 0208 – Miltefosine PK and clinical outcome

Miltefosine concentration over time

Adult
Pediatric

Miltefosine concentration at end of treatment

Adult
Pediatric

D210 Efficacy by age group

<table>
<thead>
<tr>
<th></th>
<th>AmBisome® + Miltefosine</th>
<th>Miltefosine monotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Final number of patients</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7-12</td>
<td>27</td>
<td>22</td>
</tr>
<tr>
<td>13-60</td>
<td>22</td>
<td>29</td>
</tr>
<tr>
<td><strong>Final number cured, n (%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7-12</td>
<td>20 (74.1%)</td>
<td>13 (59.1%)</td>
</tr>
<tr>
<td>13-60</td>
<td>20 (90%)</td>
<td>25 (86.2%)</td>
</tr>
<tr>
<td><strong>Fisher’s exact test p-value</strong></td>
<td>0.25</td>
<td>0.061</td>
</tr>
</tbody>
</table>

Children had poorer clinical response as compared to adults, which can be explained by the underexposure to the drug.

Allometric dose to be assessed in children

Study was not powered for sub-group analysis.
Pregnant and breast-feeding mothers

1. Females historically less included in CTs, and generally exclude pregnancy, but ....

   ... *Pregnant women get sick and sick women can become pregnant* ...

2. Drug PK is modified by pregnancy (higher acidity, lower GI motility, lower pulmonary exposure, slower renal clearance. Modified immune response....)

3. Pregnancy rates are high (from 3.95–63.9 pregnancies / 100 women-years in HIV)

4. Vertical transmission documented / suspected for some NTDs

5. Some of the current treatments options are contra-indicated during pregnancy:
   
   1. Antimonials and miltefosine for VL, PKDL, HIV-VL
   2. Melarsoprol for tb rhodesiense HAT

Research needs: prospective efficacy
Conducting and running trials effectively

Approval timelines for clinical trials remains a challenge

From submission to import license:
Mean: 8 months
Median: 6 months

Lack of expertise/experience

Capacity strengthening AVAREF ...
Joint reviews ...
Transitioning from clinical research to implementation & impact

PoC  <100  
Phase 3  300-500 +  
Effectiveness  >1000  
Real life  

Key research questions and role of EDCTP2
New category of NTDs: example of mycetoma

Transmission – knowledge gaps

Key characteristics of eu- and actinomyetoma

<table>
<thead>
<tr>
<th></th>
<th>Eumycetoma</th>
<th>Actinomyetoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Causative agent</td>
<td>Fungi</td>
<td>bacteria</td>
</tr>
<tr>
<td>Main endemic area</td>
<td>Africa</td>
<td>Middle- and South America</td>
</tr>
<tr>
<td>Treatment</td>
<td>Antifungal + surgery</td>
<td>antibiotics</td>
</tr>
<tr>
<td>Current regimen</td>
<td>Ketoconazole</td>
<td>amikacin (IV) + cotrim (PO)</td>
</tr>
</tbody>
</table>

Drug Safety Communications

- FDA Drug Safety Communication: FDA levels usage of Nizoral (ketoconazole) oral tablets due to potentially fatal liver injury and risk of drug interactions and adrenal gland problems.
- Treatment: ketoconazole 12 Months + mass removal
- Treatment outcomes: 37% → 25.9% > 90% (in Mexico)

Very low efficacy of treatment in fungal form
## New category of NTDs: example of mycetoma

<table>
<thead>
<tr>
<th>Drug</th>
<th>Organism</th>
<th>N</th>
<th>Dose</th>
<th>Outcome</th>
<th>Country</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ketoconazole</td>
<td>M. mycetomatis</td>
<td>13</td>
<td>200 mg OD, 1 year</td>
<td>6 cured; 4 improved, 4 failed</td>
<td>Sudan</td>
<td>Mahgoub ES, 1984</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>400 mg OD, 3 months, then 200 mg, 9 months</td>
<td>Mean treatment response</td>
<td>Sudan</td>
<td>Hay RJ, 1992</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1 cured, 1 improved, 1 failed after surgery; 1 recurrence</td>
<td>India</td>
<td>Porte L, 2006</td>
</tr>
<tr>
<td>Itraconazole</td>
<td>M. mycetomatis</td>
<td>13</td>
<td>400 mg OD 3 months, then 200 mg, 9 months</td>
<td>1 cured; 11 improved, 7 failed</td>
<td>Sudan</td>
<td>Fahal AH</td>
</tr>
<tr>
<td>Terbinafine</td>
<td>M. mycetomatis</td>
<td>23</td>
<td>500 mg BD, 24-48 weeks</td>
<td>4 cured; 11 improved, 7 failed</td>
<td>Senegal</td>
<td>N'Diaye B , 2006</td>
</tr>
<tr>
<td></td>
<td>L. senegalensis (1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other (3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Not known (7)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Voriconazole</td>
<td>S. apiospermum</td>
<td>1</td>
<td>400 mg OD, 18 months</td>
<td>Cured</td>
<td>Ivory Coast</td>
<td>Porte L, 2006</td>
</tr>
<tr>
<td></td>
<td>S. apiospermum</td>
<td>1</td>
<td>Dose not specified, 6 months</td>
<td>Cured</td>
<td>India</td>
<td>Gulati , 2012</td>
</tr>
<tr>
<td></td>
<td>M. grisea</td>
<td>1</td>
<td>Dose not specified, 6 months</td>
<td>Little change</td>
<td>India</td>
<td>Gulati , 2012</td>
</tr>
<tr>
<td></td>
<td>M. mycetomatis</td>
<td>1</td>
<td>200 mg, 3 months, then 300 mg, 13 months</td>
<td>Cured</td>
<td>Mali</td>
<td>Lacroix C, 2005</td>
</tr>
<tr>
<td>Madurella spp</td>
<td>1</td>
<td>200 mg, 12 months</td>
<td>Cured</td>
<td>Senegal</td>
<td>Loulergue P, 2006</td>
<td></td>
</tr>
<tr>
<td>S. apiospermum</td>
<td>1</td>
<td>200 mg BD, unknown duration</td>
<td>Cured, after 3 years follow-up</td>
<td>Brazil</td>
<td>Oliveira F de M, 2013</td>
<td></td>
</tr>
<tr>
<td>Posaconazole</td>
<td>M. mycetomatis (1)</td>
<td>6</td>
<td>800 mg OD</td>
<td>Initially: 5 cured, 1 no improvement; 2 successfully retreated after interval of &gt;10 months</td>
<td>Brazil</td>
<td>Negroni R, 2005</td>
</tr>
<tr>
<td></td>
<td>M. grisea (3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>S. apiospermum (1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liposomal amphotericin B</td>
<td>M. grisea (2)</td>
<td>3</td>
<td>Total dose 3.4, 2.8, 4.2 grams; max. daily dose 3 mg/kg</td>
<td>All showed temporary improvement but relapsed within 6 months</td>
<td>Not specified</td>
<td>Hay RJ, 005</td>
</tr>
<tr>
<td></td>
<td>Fusarium (1)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
New category of NTDs: example of mycetoma

3. Proposed criteria for classifying a condition as an NTD

Disease conditions that

1. disproportionately affect populations living in poverty; and cause important morbidity and mortality – including stigma and discrimination - in such populations, justifying a global response
2. primarily affect populations living in tropical and sub-tropical areas
3. are immediately amenable to broad control, elimination or eradication by applying one or more of the five public health strategies adopted by the Department for Control of NTDs, and/or
4. are relatively neglected by research – i.e., resource allocation is not commensurate with the magnitude of the problem - when it comes to developing new diagnostics, medicines and other control tools

THE WHO STRATEGIC AND TECHNICAL ADVISORY GROUP FOR NEGLECTED TROPICAL DISEASES (WHO STAG)

RECOMMENDATIONS FOR THE ADOPTION OF ADDITIONAL DISEASES AS NEGLECTED TROPICAL DISEASES

28 MAY 2016 / GENEVA - The Sixty-ninth World Health Assembly closed today after approving new resolutions on …… mycetoma; ……
New category of NTDs: Loa Loa?

MAY 2016 | GENEVA – The Sixty-ninth World Health Assembly closed today after approving new resolutions on neglected tropical diseases (NTDs), and declared that the World Health Organization’s (WHO’s) new strategic advisory group for neglected tropical diseases (WHO-SAG) “…will be established.”

Key research questions and role of EDCTP2

1. Disease conditions that are relatively neglected by the research community are often associated with poverty, and cause major and major disability and mortality. What are the mechanisms to developing new diagnostics?

2. The control or elimination of sleep-walking in tropical areas is usually complex and expensive. What is the role of the EDCTP2 in this process?

3. Proposed criteria for classifying population-based cohort study

Excess mortality associated with loiasis: a retrospective population-based cohort study


37
Preparing for drug resistance? ... 

- Melarsoprol resistance reports in tb rhodesiense
  
  R. Brun et al. Treatment failures in HAT Tropical Medicine and International Health volume 6 no 11 pp 906±914 november 2001

- Ivermectin in onchocerciasis
  

Table 2. Responses to questions about drug resistance.

<table>
<thead>
<tr>
<th></th>
<th>Lymphatic Filariasis</th>
<th>Onchocerciasis</th>
<th>Trachoma</th>
<th>Schistosomiasis</th>
<th>Soil-transmitted Helminths</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is drug resistance a problem...</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>For the NTD?</td>
<td>14/27 (51.9%)</td>
<td>13/20 (65.0%)</td>
<td>4/22 (18.2%)</td>
<td>53/87 (60.9%)</td>
<td>28/46 (60.9%)</td>
<td>0.005</td>
</tr>
<tr>
<td>For another infection?</td>
<td>17/24 (70.8%)</td>
<td>11/17 (64.7%)</td>
<td>16/22 (72.7%)</td>
<td>58/82 (70.7%)</td>
<td>32/41 (78.1%)</td>
<td>0.87</td>
</tr>
<tr>
<td>Best strategy to minimize resistance</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.14</td>
</tr>
<tr>
<td>(1) Annual mass treatment</td>
<td>9/24 (37.5%)</td>
<td>6/16 (37.5%)</td>
<td>14/21 (66.7%)</td>
<td>29/78 (37.2%)</td>
<td>21/42 (50.0%)</td>
<td></td>
</tr>
<tr>
<td>(2) Treatment scattered throughout year</td>
<td>3/24 (12.5%)</td>
<td>1/16 (6.3%)</td>
<td>1/21 (4.8%)</td>
<td>3/78 (3.9%)</td>
<td>5/42 (11.9%)</td>
<td></td>
</tr>
<tr>
<td>No difference between (1) and (2)</td>
<td>12/24 (50.0%)</td>
<td>9/16 (56.3%)</td>
<td>6/21 (28.6%)</td>
<td>46/78 (59.0%)</td>
<td>16/42 (38.1%)</td>
<td></td>
</tr>
</tbody>
</table>

*Chi square test.

Despite many groups involved, R&D for NTDs is largely unfunded ... EDCTP can play a critical role to contribute to WHO elimination goals by supporting:

- **Capacities**: Reinforce/strengthen scientific collaboration btw European and African networks (and existing African networks)
- **Priorities for Innovation**: Support R&D gaps through Disease specific approaches and transversal approaches
- **Regulatory**: Continuation of contribution to AVAREF / AMRH initiatives
- **Clinical Implementation / effectiveness / PV trials**
- **Funding**: increase the available funding given the low success rate and huge demand & leveraging programs funding with other mechanisms/donors
- **African leadership**: Increase African participation (priorities, funding)
- **Process**: improve transparency, decrease time between calls and review
- **Selection criteria**: more focus on scientific excellence and originality, whilst disregarding product development impact (PDPs opinion)
Thank you
EDCTP 2
!!!
THANK YOU
TO ALL OUR
PARTNERS &
DONORS

Bill & Melinda Gates Foundation

Ministry of Foreign Affairs of the Netherlands

Agence Française de Développement

UNITAID

Agenzia dell’Aid alla Cooperazione Internazionale per lo Sviluppo

Wellcome Trust

EDCTP

GFATF

Bill & Melinda Gates Foundation

UK aid

Ministère des Affaires Étrangères

by

KFW

Swiss Confederation

Confédération Suisse

Confederazione Svizzera

UBS Optimus Foundation