Neglected Tropical Diseases: Why should we care?

Presented by:
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Drugs for Neglected Diseases initiative

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Why Neglected?
Common features of Neglected tropical diseases

• Many of the neglected tropical diseases are disfiguring and stigmatizing.
• They affect the poorest of the poor, with few or no commercial markets for drugs and vaccines against them.
• The pharmacopoeia for these diseases has remained essentially unchanged since the middle of the 20th century.
What are NTDs

A group of infectious diseases that affect more than one billion people and cost developing economies billions of dollars every year.

The diseases are found in tropical and subtropical conditions in 149 countries.

Populations living in poverty, without adequate sanitation, and in close contact with infectious vectors and domestic animals and livestock are those worst affected.

3 billion people are at risk of neglected tropical diseases, 1 billion affected.

170,000 people will die by the end of each year from these diseases.

There are 20 diseases in the WHO NTD list including mycetoma, added in 2016, as well as chromoblastomycosis and other deep mycoses, scabies and other ectoparasites and snakebite envenoming which were added in 2017.
Global distribution of NTDs

Approximately 1 billion people are affected by more than one of NTDs
WHO's List of Neglected tropical Diseases

1. Dengue
2. Rabies
3. Trachoma
4. Buruli ulcer
5. Yaws
6. Leprosy
7. Chagas disease
8. Human African trypanosomiasis (sleeping sickness)
9. Dracunculiasis (guinea-worm disease)
10. Leishmaniasis
11. Onchocerciasis (river blindness)
12. Taeniasis and neurocysticercosis
13. Echinococcosis
14. Foodborne trematodiases
15. Lymphatic filariasis
16. Schistosomiasis
17. Soil-transmitted helminthiases
18. Mycetoma, chromoblastomycosis and other deep mycoses,
19. Scabies and other ectoparasites
20. Snakebite envenoming
Blinding trachoma, caused by a bacterium, chlamydia trachomatis, affects more than 80 million people around the world. Children are mainly concerned by the infection, and every 4 people blind from trachoma 3 are women. Africa is the continent with the greatest number of endemic countries, but America, Middle-East and Asia are also endemic. SAFE strategy (Surgery, Antibiotics, Facial cleanliness, Environmental improvement) has proven its effectiveness in eliminating this scourge from humanity.
Lymphatic filariasis (LF)

Over 120 million people are currently infected and around 1.3 billion people in more than 80 countries are at risk of infection. Drugs used against lymphatic filariasis are either donated – albendazole and ivermectin, or very inexpensive DEC. Albendazole is donated to WHO by GlaxoSmithKline for mass administration to at-risk populations.
Guinea-worm disease

The disease exists only in Africa and is transmitted exclusively by drinking contaminated water.

Global progress in eradication linked to increased availability of safe drinking water in endemic regions.
Leishmaniasis

Leishmaniasis is a parasitic disease caused by the Leishmania parasite. This parasite typically lives in infected sand flies. You can contract leishmaniasis from a bite of an infected sand fly. The sand flies that carry the parasite typically reside in tropical and subtropical environments.
Mycetoma

Mycetoma is a bacterial or fungal infection that can be devastating, and can result in amputation. Research on mycetoma is scarce & incidence unclear. However, prevalence of 14.5 per 1,000 reported in endemic areas.
# Disease Burden of the Neglected Tropical Diseases in Deaths and DALYs

<table>
<thead>
<tr>
<th>Variable</th>
<th>Deaths</th>
<th>DALYs&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schistosomiasis</td>
<td>280,000&lt;sup&gt;b&lt;/sup&gt;</td>
<td>4.5 million&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Hookworm infection</td>
<td>65,000&lt;sup&gt;c&lt;/sup&gt;</td>
<td>22.1 million&lt;sup&gt;c,d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Ascariasis</td>
<td>60,000&lt;sup&gt;c&lt;/sup&gt;</td>
<td>10.5 million&lt;sup&gt;c,d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Leishmaniasis</td>
<td>51,000&lt;sup&gt;e&lt;/sup&gt;</td>
<td>2.1 million&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>Trypanosomiasis</td>
<td>48,000&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1.5 million&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>Chagas disease</td>
<td>14,000&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0.7 million&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>Trichuriasis</td>
<td>10,000&lt;sup&gt;b&lt;/sup&gt;</td>
<td>6.4 million&lt;sup&gt;c,d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Leprosy</td>
<td>6,000&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0.2 million&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>Lymphatic filariasis</td>
<td>0&lt;sup&gt;c&lt;/sup&gt;</td>
<td>5.8 million&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>Trachoma</td>
<td>0&lt;sup&gt;c&lt;/sup&gt;</td>
<td>2.3 million&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>Onchocerciasis</td>
<td>0&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0.5 million&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>Dracunculiasis</td>
<td>ND</td>
<td>&lt;0.1 million&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
<tr>
<td>Buruli ulcer</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Taeniasis and cysticercosis</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Food-borne trematodiases</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>534,000</strong></td>
<td><strong>56.6 million</strong></td>
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https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.0030102
## Comparative Disease Burdens of Communicable Diseases Measured in DALYs

<table>
<thead>
<tr>
<th>Disease Condition</th>
<th>Disease Burden</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower respiratory infections</td>
<td>91.3 million&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>HIV-AIDS</td>
<td>84.5 million&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Diarrheal diseases</td>
<td>62 million&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Neglected tropical diseases</td>
<td>56.6 million&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Malaria</td>
<td>46.5 million&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>34.7 million&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Measles</td>
<td>21.4 million&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>Annex table 3 in [1]  
<sup>b</sup>Data derived from Table 1 and [8].

DOI: 10.1371/journal.pmed.0030102  
https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.0030102

Economic impact of NTDs

• High endemicity in rural and in impoverished urban areas of low-income countries.
• Significant ability to impair childhood growth, intellectual development, and education.
• Reduced worker productivity.

*In this way, the neglected tropical diseases are poverty-promoting conditions.*
Economic impact of NTDs: filariasis

- Lymphatic filariasis is most prevalent in working aged men, making the economic impact of this disease significant.
- Affected patients lose as much as 11 years of productivity, mainly in the agricultural sector.
- Cost per patient treated is no higher than $2.23 and the economic return is between $20 - $60

Psychosocial burden of NTDs

“Before this disease, I walked around easily and carried out my activities with ease. Nowadays I rarely visit my friends. I don’t want to be a burden to them”
Zainab Ibrahim
Mycetoma Patient

• Discrimination and poverty are both causes and consequence of NTDs.
• The psychosocial burden and stigma associated with lifelong disfigurement of some NTDs is frequently overlooked.
Neglected tropical diseases (NTDs): a right-to-health issue

- NTDs almost exclusively affects poor and marginalized people in low-income countries, in rural areas and settings where poverty is widespread.
- Health interventions and research and development have long been inadequate and under funded and the picture has changed only in recent years.
- Some of the essential drugs against NTD are now available but other are still inadequate or unavailable.
- Addressing NTDs is vital towards attainment of the SDG 3 and others.
What is the relationship between environmental change and neglected tropical diseases?
Environmental change and NTD transmission

Vectors, pathogens and hosts each survive and reproduce within a range of optimal climatic conditions (temperature, humidity etc)
### Predicting the impact of Environmental change and NTD transmission

<table>
<thead>
<tr>
<th>Environmental changes</th>
<th>Example diseases</th>
<th>Pathway of effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dams, canals, irrigation</td>
<td>Schistosomiasis</td>
<td>Snail host habitat, human contact</td>
</tr>
<tr>
<td>Malaria</td>
<td></td>
<td>Breeding sites for mosquitoes</td>
</tr>
<tr>
<td>Helminthiasies</td>
<td></td>
<td>Larval contact due to moist soil</td>
</tr>
<tr>
<td>River blindness</td>
<td></td>
<td>Blackfly breeding, disease</td>
</tr>
<tr>
<td>Agricultural intensification</td>
<td>Malaria</td>
<td>Crop insecticides and vector resistance</td>
</tr>
<tr>
<td>Venezuelan haemorrhagic fever</td>
<td></td>
<td>Rodent abundance, contact</td>
</tr>
<tr>
<td>Urbanization, urban crowding</td>
<td>Cholera</td>
<td>Sanitation, hygiene; water contamination</td>
</tr>
<tr>
<td></td>
<td>Dengue</td>
<td>Water-collecting trash, Aedes aegypti mosquito breeding sites</td>
</tr>
<tr>
<td>Cutaneous leishmaniasis</td>
<td></td>
<td>Proximity, sandfly vectors</td>
</tr>
<tr>
<td>Deforestation and new habitation</td>
<td>Malaria</td>
<td>Breeding sites and vectors, immigration of susceptible people</td>
</tr>
<tr>
<td></td>
<td>Oropouche</td>
<td>Contact, breeding of vectors</td>
</tr>
<tr>
<td></td>
<td>Visceral leishmaniasis</td>
<td>Contact with sandfly vectors</td>
</tr>
<tr>
<td>Reforestation</td>
<td>Lyme disease</td>
<td>Tick hosts, outdoor exposure</td>
</tr>
<tr>
<td></td>
<td>Red tide</td>
<td>Toxic algal blooms</td>
</tr>
<tr>
<td>Ocean warming</td>
<td>Rift valley fever</td>
<td>Pools for mosquito breeding</td>
</tr>
<tr>
<td>Elevated precipitation</td>
<td>Hantavirus pulmonary syndrome</td>
<td>Rodent food, habitat, abundance</td>
</tr>
</tbody>
</table>

↑ increase, ↓ reduction
Can we indeed eradicate neglected tropical diseases?

What successes and challenges of current efforts?
Yes it's possible to eradicate NTDs.

Guinea Worm Disease has decreased from 3.5 million cases in 1986 to 22 cases in 2015.
Control with current tools

Diagnostic procedures are not sensitive, cannot be used at field level and are expensive

Treatment is costly, difficult to administer, can have serious side-effects and can become resistant

Need for specialized services

Integration is not possible

Sustained control/elimination is difficult

What do we need?

Simple, efficient and inexpensive diagnostic tools

Oral, inexpensive drugs that do not have side-effects

Integration within existing health structures is possible

Sustained control/elimination is feasible
Preventive chemotherapy

Existing field-applicable tools

Simple, cheap community diagnosis
Large scale treatment of groups or communities in need

Regular "preventive" treatment

Coordinated use of a few drugs will have an impact on many diseases

Sustained control / elimination
Persistence of the fatal imbalance

1975-1999

- 1.1% of new products for NTDs, malaria and TB
- But 12% of global disease burden

2000-2011

- 756 products registered (excluding vaccines & biologicals)
- 1% of 336 new chemical entities approved for NTDs, malaria and TB
- 1% of 148,445 clinical trials registered for neglected diseases

Sources: Fatal Imbalance: The Crisis in Research and Development for Neglected Diseases, MSF, 2001
DNDi’s Response
DNDi, a new model for drug development created in 2003

- Non-profit drug research & development (R&D) organization founded in 2003
- Addressing the needs of the most neglected patients
- Harnessing resources from public institutions, private industry and philanthropic entities

- **8 regional offices working close to patients in:**
  Brazil, Democratic Republic of Congo, Kenya, South Africa, Malaysia, India, Japan, USA

- **Founding Partners**
  Indian Council for Medical Research (ICMR), Kenya Medical Research Institute (KEMRI), Malaysian MoH, Oswaldo Cruz Foundation Brazil, Médecins Sans Frontières (MSF), Institut Pasteur France, WHO/TDR (permanent observer)
DNDi’s Mission

- To develop new drugs or new formulations of existing drugs for **people suffering from neglected diseases**.
- To develop drugs for the **most neglected diseases** (such as sleeping sickness, leishmaniasis, and Chagas disease), while considering engagement in **R&D projects for other neglected patients** (e.g. malaria, paediatric HIV, filarial infections).
- To **strengthen capacities in a sustainable manner**, including through know-how and technology transfers in the field of drug R&D for neglected diseases.
- To adopt a **dynamic portfolio approach**
Responding to the needs of patients suffering from neglected diseases

- Hepatitis C
- Sleeping sickness
- Mycetoma
- Malaria
- Chagas disease
- Paediatric HIV
- Leishmaniasis
- Filarial diseases

+ incubation with WHO of:

...from bench to bedside

DNDi’s PRIORITY: Neglected Patients
DNDi’s success is only possible through innovative partnerships

Over 160 partnerships worldwide

CRITERIA FOR SUCCESS
✓ Share the same vision
✓ Mutual understanding
✓ Involvement throughout the whole process
Some of DNDi’s Open Innovation Projects

NTD Drug Discovery Booster, *Est. 2015*


The Mycetoma Open Source project (MycetOS), *Est. 2017*
8 new treatments delivered since 2007

2007 **ASAQ**
Malaria
>500 million patients reached

2008 **ASMQ**
Malaria
Used in Africa and Asia

2009 **NECT**
Sleeping sickness
100% of stage-2 patients

2010 **SSG&PM**
Visceral leishmaniasis in E Africa
Now 1st line in all countries

2011 **PAEDIATRIC BENZNIDAZOLE**
Chagas disease
**Two sources developed**

2011 **NEW VL TREATMENT ASIA**
Visceral leishmaniasis in Asia
**Support to disease elimination**

2016 **SUPERBOOSTER THERAPY**
Paediatric HIV
**Recommended by WHO**

2018 **FEXINIDAZOLE**
Sleeping sickness
Approved by European Medicines Agency, first all-oral treatment
The R&D landscape for neglected patients has changed but large gaps still remain

1. **R&D priorities** do not sufficiently originate from low- and middle-income countries

2. Patients’ **needs are not prioritized** (e.g. Ebola, mycetoma, etc.)

3. **Innovation is not linked to equitable access** even when there is commercial incentive to drive innovation (e.g. HCV)

4. **Market incentives** aligned with IP/exclusivity do not adequately address health needs in LMICs (e.g. AMR)

These are the **fundamental challenges for the future of biomedical innovation.**
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Thank you for your attention