The global challenge of NTDs: The classic interface of poverty, health and development

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Professor David Molyneux is a Senior Professorial Fellow and Emeritus Professor at The Liverpool School of Tropical Medicine and in the Centre for Neglected Tropical Diseases, supported by UK Department for International Development (DFID) and GlaxoSmithKline (GSK). His major research interests were initially in trypanosomiasis and leishmaniasis and in particular, the interaction between parasites and vectors. More recently he has become involved in parasitic and vector borne disease control programmes advising the World Health Organization (WHO) on trypanosomiasis, onchocerciasis, lymphatic filariasis and malaria control. Professor Molyneux has also been involved on several aspects and initiatives on the impact of climate change on the distribution of vector borne diseases. He has acted as a consultant to many bilateral and multilateral agencies and has chaired several WHO Advisory Groups and Committees. He has been one of the key advocates in raising the profile of Neglected Tropical Diseases to the extent that they are now one of the priorities of the WHO.
1. Introduction

The concept of neglected tropical diseases (NTDs) emerged more than a decade ago and has been recognised as a valid way to categorise diseases that affect the poorest individuals in poor populations. Substantial progress in control and elimination has been achieved and policy momentum has been generated through continued bilateral, philanthropic, and nongovernmental development organisation (NGDO) support, together with huge donations of drugs from pharmaceutical companies. Some 70 countries are implementing programmes—with varying levels of dependency on donor support. WHO has defined a Roadmap to reach 2020 targets, which was endorsed by member states in a World Health Assembly Resolution in 2013.

NTDs are addressed through five strategies as defined in a World Health Assembly Resolution of 2013:
- preventive chemotherapy,
- intensified disease management,
- vector control,
- veterinary public health measures for zoonotic neglected diseases, and
- improved water and sanitation.

The research agenda has also defined the need for affordable products (diagnostics, drugs and insecticides). However, challenges, such as insecurity and weak health systems, continue to prevail in the poorest countries, inhibiting progress in scaling up and also in achieving Roadmap goals.

More information on the most common NTDs can be found in Annex 1 on page 8.

2. Challenges and “endgame” targets

The continued drive for the control or elimination of NTDs has had many successes, but to address challenges in reaching ‘end game’ targets of elimination and eradication, there is a need for adaptive approaches as well as multi-disciplinary collaboration and intersectoral action.

This requires greater engagement of endemic countries through the recognition of the burden of NTDs and their role as drivers of poverty, as impediments to socio economic development, and the cost-effectiveness and cost-benefit of interventions. The advent of the NTD movement has resulted in massive up-scaling of the delivery of essential and quality medicines to around a billion people annually. Recipients are often the poorest of the poor, thus forging the global aspiration that universal health coverage is possible, equitable, and affordable, as reflected within the 2030 Sustainable Development Goals (SDGs). However, significant challenges remain, including profound socio-political upheavals (conflict, migration), dynamic epidemiological settings (climate change, environmental degradation, urbanization), and a need for innovative approaches to programme delivery as well as scientific and technological advances.

To reach ‘end game’ targets, the NTD community will need to continue to adapt to these global events and changing policy environments to support the development of responsive and resilient programmes that can sustain progress toward NTD targets in the ever-changing world. Innovative
thinking will need to be embedded within regional and national health systems. Policy makers, health managers, and front health workers are the mediators between challenge and change at the global and local level. The health system is the critical mediator of the interactions between these key challenges and opportunities.

We have suggested that NTDs represent “a global pandemic” and question why only 0.6% of Official Development Assistance for health is devoted to a group of infections that kill circa 350,000 people annually and inflict poverty on over a billion people, especially when compared to the response to Ebola which killed “only” 12,000 in a year. The NTD community can focus on successes (one BILLION annual treatments; elimination successes), but the challenges to achieving WHO Road Map targets are less prominent in debates and need to be addressed by a reappraisal of what is possible with the limited resources. We ask, is the glass half full or half empty?

The challenges of elimination and eradication and the achievement of WHO Road Map Targets-resources (human and financial), effectiveness of available tools, innovation, the role of vector control, accessing remote populations, security and conflict, and the high costs of the “last mile” in elimination and eradication programmes, suggest that realistically such programmes have a 20 year plus time frame which require longer term perspectives often beyond donor horizon.

The impact of the socio-political, geographic, ecological, and climate impacts on NTD epidemiology and the difficulty of treatment and control in rapidly expanding and complex urban settings exemplify major challenges.

Can the health community respond to rapidity of change on epidemiology? Can new products be introduced and resourced in sufficient time to make an impact? WHO imposes rigorous requirements before it recommends introducing new policies to treat or control infectious organisms and vectors. Yet, many organisms have the capacity to respond to selective pressures faster than any policy response. This makes policy guidance and implementation of that policy behind the curve of what is critically needed should problems such as resistance occur.

Country ownership and engagement

It is important that endemic countries are aware of the problems NTDs pose to their populations and the economic and social benefits that accrue from implementing recommended WHO strategies. The value and leverage provided by drug donations of NTD drugs and the low delivery costs at often less than USD$0.50 per person/annum represent huge opportunities to provide essential drugs valued at USD$ 2–3 billion/year. The delivery costs represent a small percentage of per capita national health expenditure even for the poorer countries which have the highest burden of NTDs.

Hence, the pharmaceutical donations play a crucial role as do NGDOs as contributors and implementers of NTD programmes “for as long as needed”. There is also a crucial role of CEO Round table as an advocacy link to Bill Gates, whilst President Jimmy Carter has been an essential advocate for the Guinea Worm Eradication Programme and locally in Nigeria ex-President Yakubu Gowon. There is however a need for a greater country commitment and also more bilateral donors to engage beyond USAID and DFID. The challenge is how this can this be achieved. One of the
challenges within countries is working with other compatible programmes, such as malaria vector control in Africa for filariasis\(^1\); HIV/AIDS and schistosomiasis\(^2\). There are significant opportunities for programme synergies: polio programmes have assisted surveillance for guinea worm and laboratory diagnosis for worms has recently been examining stool samples collected by the global polio programme networks who sample children to detect STH prevalence; bed nets for the prevention of malaria and lymphatic filariasis (LF); and improved WASH for prevention of several NTDs, such as schistosomiasis, STH, trachoma and guinea worm. However, there remains a need for greater appreciation of the benefits of linking country programmes.

The challenge is for the health sector to engage with the WASH and education sectors for soil-transmitted helminths (STH)\(^3\). Similarly, for rabies control via dog vaccination who pays—the health or veterinary sector? Can the “One Health” concept be operationalised?

### NTDS and health systems

The role of NTDs programmes have in strengthening health systems are exemplified by: improved drug and supply chain management; improved surveillance and reporting systems; evaluation and monitoring; enhanced engagement of community with distribution systems (mass drug administration (MDA) programmes reach ‘beyond the end of the road’); empowered communities that are involved in other health issues; improved laboratory capacity; promotion of improved surgery practice; and enhanced cross programme links (see above).

Country ownership of NTD programmes should be recognised as being an integral part of the health system and not separate from it. Populations are entitled to the multiple benefits provided by drug donations—products all on the Essential Medicine List\(^4\) which poor people have a right to access.

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\(^1\) Mosquitoes of the genus Anopheles (in rural areas of Africa and elsewhere) carry the parasite W. bancrofti which causes filariasis. These mosquitos also carry the parasites that causes malaria and thus vector-control programmes aimed at malaria prevention can have beneficial spill over effects on filariasis prevention.

\(^2\) Urogenital schistosomiasis is also considered to be a risk factor for HIV infection, especially in women (WHO, 2018).

\(^3\) Such as roundworm (ascariasis), hookworm (Necator americanus and Ancylostoma duodenale), and whipworm (trichuriasis), which can cause anaemia (particularly in pregnant women and children), vitamin A deficiency, malnutrition and impaired growth, delayed development, and intestinal blockages. (WHO, 2018)).

\(^4\) Essential medicines are those that satisfy the priority health care needs of the population. They are selected with due regard to public health relevance, evidence on efficacy and safety, and comparative cost-effectiveness. Essential medicines are intended to be available within the context of functioning health systems at all times in adequate amounts, in the appropriate dosage forms, with assured quality and adequate information, and at a price the individual and the community can afford. The implementation of the concept of essential medicines is intended to be flexible and adaptable to many different situations; exactly which medicines are regarded as essential remains a national responsibility (WHO, 2017).
NTDs—the disability and mental health dimensions

The burden of NTDs of mortality and morbidity as reflected in global burden of disease studies has been underestimated and inappropriately attributed; misclassification of NTDs which cause cancers (trematodes), injuries (rabies/snakebite), and neurological conditions (epilepsy) mean that published figures do not truly reflect the problems posed by NTDs.

In addition, there is an unrecognised mental health burden of NTDs and co-morbidity and disability including caregivers (see Reading 2) in particular in LF, onchocerciasis, leishmaniasis, Buruli ulcer, leprosy, and trachoma. The morbidity of mental health caused by NTDs has not until recently been recognised either by the NTD community nor by the mental health community whilst the stigma and physical disability caused by clinical conditions directly categorise NTDs as major causes of a range of disabilities.

3. Some future challenges

Social science studies have a key role to play in understanding the community perspectives of MDA and the culture-specific approaches needed to improve drug delivery to different populations.

There is a need for more extensive use of technology in surveillance and communication (mapping, SMS, MMS and photo identification of cases) to ensure targeted delivery of implementation.

A major challenge will be to reaching remote populations in equatorial regions—for example, the Yanomami in Brazil and Venezuela; eastern Congo; Papua New Guinea. These settings are characterised by dense tropical rain forests and limited transport access to isolated communities with limited or no access to formal government health care provision. It is questionable whether elimination can be achieved and verified in these settings.

Greater recognition of the role of insects as vectors and snails as intermediate hosts is often overlooked. Elimination programmes should focus on transmission interruption as the key means of impacting on prevalence. For example, compare the impact of bed nets on malaria mortality from 2000–2015: most of the health gain has been through insecticide treated bed nets. Furthermore, success of river blindness programme from 1974–2000 was due almost entirely to blackfly control. Capacity strengthening for medical entomology is seriously deficient and many NTDs are vector transmitted. The threat of epidemic dengue in Africa, new Chikungunya outbreaks; and the Zika experience are warnings of emergent vector borne viruses given expansion of certain Aedes mosquito populations: Aedes albopictus into Europe and Aedes aegypti in southern USA. Yellow Fever (transmitted by A. aegypti) has the best vaccine against any infectious disease and is produced in Brazil, and yet we have emerging epidemics in Brazil as

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5 The WHO global burden of disease (GBD) measures burden of disease using the disability-adjusted-life-year (DALY). This time-based measure combines years of life lost due to premature mortality and years of life lost due to time lived in states of less than full health. The DALY metric was developed in the original GBD 1990 study to assess the burden of disease consistently across diseases, risk factors and regions (WHO, 2018).

6 The study of insects that cause disease or that serve as vectors of organisms that cause disease in humans.
well as in Africa. Allied to this is the monitoring for insecticide resistance, which will be a pre-requisite but for which few skills are available.

Innovation has been the key to progress and examples of innovation are well documented for NTDs. For example, the Community Directed Treatment for the river blindness programme resulted in increased health delivery of other interventions beyond the reach of the formal health system, such as filters for guinea worm; innovative health education tools (board games, exercise books, and printed cloth); the dose pole for measuring drugs needed as a surrogate for weight; and the use of SMS and MMS for reporting. These types of innovations have had a massive impact. Emerging new tools derived from basic research are limited and unlikely to be deployable in the time frame of 5 years. Innovation is not just the search for a magic bullet (which will be expensive to deploy).

However, is eradication sensu strictu possible given the definition—permanent reduction to zero of the world wide incidence of infection caused by a specific agent as a result of deliberate efforts; intervention measures are no longer needed—?

Polio and guinea worm have recorded, respectively, 12 and 30 cases in 2017, but challenges in certification need to be overcome. Polio in Pakistan and Afghanistan and inability to access insecure areas in Mali, Sudan, and South Sudan in the Guinea Worm Programme demonstrate common challenges. Yaws is another NTD which is believed to be possible to eradication.

Research needs are well-defined and have been for many years; however, few products are in the pipeline and dependence is still on drugs from other sectors (animal health) and the pyrethroids, which were developed for agricultural pest control. Whilst each specific organism requires a specific drug, a single effective new insecticide would have multi-disease impact for vector-borne NTDs as well as malaria, yet far less is being spent proportionately on vector control research than on disease specific drugs. New insecticides or other vector control measures are in the pipeline but time to implementation of new products (from agrichemical sector) will be on a 5–10 year horizon whilst insecticide resistance continues to spread rapidly.

4. The NTDs and SDGs—a summary of links

Maintaining the NTD brand as a key contributor to achieving the SDGs (Reading 6) and challenges of key sector beyond health such as WASH and Education. Most of the SGD’s have an NTD dimension beyond health targets: poverty, partnerships, education, water and sanitation. NTDs will be a ‘litmus test’ of SDG progress given numbers of SDGs relevant to NTDs.

- **SDG 1 End poverty**: NTDs create and drive the medical poverty trap.
- **SDG 2 End hunger – achieve food security – improve nutrition**: Parasitic worms greatly impact nutrition and growth; guinea worm is often called the ‘disease of the empty granary’ because peak transmission coincides with the agricultural season, leaving individuals unable to tend fields.
- **SDG 3 Ensure health lives**: Universal Health Coverage. Goal for NTDs programmes to reach over one billion people with treatments. NTDs have been specified in the health targets along with malaria, HIV, and TB.
• SGD 4 **Education**: NTDs impact the health of school children, their attendance, and educational performance. Children are also affected indirectly because they act as carers and because parents cannot afford fees due to NTDs.

• SDG 5 **Achieve Gender equality**: There is a disproportionate impact of NTDs on girls and women due to anaemia caused by schistosomiasis and hookworm and urogenital schistosomiasis and HIV transmission. Therefore, there needs to be improved access to praziquantel for women and girls.

• SDG 6 **Ensure access to water and sanitation**: Reduce the transmission of worms, schistosomiasis, guinea worm, and trachoma through WASH improvements.

• SDG 11 **Sustainable cities**: Urban transmission of dengue and Zika can be reduced by improving planning to reduce vector breeding.

• SDG 12 **Combat climate change**: Arrest the spread of potential vectors from tropical areas which carry diseases such as dengue, chikungunya, and schistosomiasis (Corsica).

• SGD 15 **Sustainable forests, combat desertification, halt biodiversity loss**: All factors which enhance emergence of vector borne NTDs.

• SDG 17 **Global Partnerships**: NTDs success based on strong multi partner alliances of endemic countries, private sector, bilateral agencies, WHO/World Bank/NGDOs, civil society, academia, and philanthropy.
5. Questions to guide readings

1. NTDs—a global pandemic: Why is only 0.6% of Official Development Assistance for health devoted to a group of infections that kill circa 350,000 people annually and inflict poverty on over a billion? Compare response to Ebola which killed “only” 12,000 in a year.

2. How can we engage the WASH and Education sectors for STH and schistosomiasis to play a key role in provision of services and drug distribution via schools? Similarly, for rabies control via dog vaccination, who pays?

3. Health or veterinary sector. Can the “One Health” concept be operationalised?

4. NTD community focuses on successes (one BILLION annual treatments; elimination successes), but the challenges to achieving WHO Road Map targets are less prominent in debate and need to be addressed by re-appraisal of what is possible with the limited resources: Is the glass half full or half empty?

6. Readings

Reading 1:

Reading 2:

Reading 3:

Reading 4:

Reading 5:

Reading 6:

Key websites

- CDC: Neglected tropical diseases: [https://www.cdc.gov/globalhealth/ntd/index.html](https://www.cdc.gov/globalhealth/ntd/index.html)
- PLOS Neglected tropical diseases: [http://journals.plos.org/plosntds/s/journal-information](http://journals.plos.org/plosntds/s/journal-information)
### Annex 1: Neglected tropical diseases

<table>
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<th>Disease</th>
<th>Key Facts</th>
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| **Chikungunya**| • A viral disease transmitted to humans by infected mosquitoes.  
• Causes fever and severe joint pain. Other symptoms include muscle pain, headache, nausea, fatigue and rash.  
• Joint pain is often debilitating and can vary in duration.  
• Shares some clinical signs with dengue and Zika, and can be misdiagnosed in areas where they are common.  
| **Dengue**     | • Mosquito-borne viral infection.  
• Flu-like illness which occasionally develops into a potentially lethal complication called severe dengue and dengue haemorrhagic fever.  
• Global incidence of dengue has grown dramatically in recent decades. About half of the world’s population is now at risk.  
| **Leishmaniasis**| • There are 3 main forms of leishmaniasis – visceral (also known as kala-azar and the most serious form of the disease), cutaneous (the most common), and mucocutaneous.  
• Leishmaniasis is caused by protozoan *Leishmania* parasites which are transmitted by the bite of infected female *phlebotomine* sandflies.  
• The disease affects some of the poorest people on earth, and is associated with malnutrition, population displacement, poor housing, a weak immune system and lack of financial resources.  
• Leishmaniasis is linked to environmental changes such as deforestation, building of dams, irrigation schemes, and urbanization.  
| **Rabies**     | • Rabies is a vaccine-preventable viral disease which occurs in more than 150 countries and territories.  
• Dogs are the main source of human rabies deaths, contributing up to 99% of all rabies transmissions to humans.  
• Rabies elimination is feasible through vaccination of dogs and prevention of dog bites.  
• Infection causes an estimated 55,000 deaths per year, mainly in Asia and Africa.  
[http://www.who.int/rabies/about/en/](http://www.who.int/rabies/about/en/) |
| **Yaws**       | • Yaws is a chronic disfiguring and debilitating childhood infectious disease caused by *Treponema pallidum* subspecies *pertenue*.  
• It was one of the first diseases targeted for eradication by WHO and UNICEF in the 1950s. WHO renewed global efforts to eradicate yaws in 2012. India has eliminated yaws over a 20 year period.  
• The disease affects skin, bone and cartilage. Humans are currently believed to be the only reservoir, and transmission is from person to person.  
• Yaws is cured with a single oral dose of an inexpensive antibiotic called azithromycin.  
Lymphatic filariasis
- Impairs the lymphatic system and can lead to the abnormal enlargement of body parts, causing pain, severe disability and social stigma.
- 856 million people in 52 countries worldwide remain threatened by lymphatic filariasis and require preventive chemotherapy to stop the spread of this parasitic infection.
- In 2000 over 120 million people were infected, with about 40 million disfigured and incapacitated by the disease.
- It can be eliminated by stopping the spread of infection through preventive chemotherapy with safe medicine combinations, repeated annually for at least 5 years. 6.7 billion treatments have been delivered to stop the spread of infection since 2000.

Leprosy
- Leprosy is a chronic disease caused by a bacillus, *Mycobacterium leprae*.
- *M. leprae* multiplies slowly and the incubation period of the disease, on average, is 5 years. In some cases, symptoms may occur within 1 year but can also take as long as 20 years to occur.
- The disease mainly affects the skin, the peripheral nerves, mucosa of the upper respiratory tract, and also the eyes.
- Leprosy is curable with multidrug therapy (MDT).
- Leprosy is transmitted via droplets, from the nose and mouth, during close and frequent contacts with untreated cases.
- Untreated, leprosy can cause progressive and permanent damage to the skin, nerves, limbs, and eyes.

Guinea worm (dracunculiasis)
- A crippling parasitic disease on the verge of eradication, only 30 human cases were reported in 2017.
- The disease is transmitted when people, who have little or no access to improved drinking water sources, swallow stagnant water contaminated with parasite-infected water-fleas (*Cyclops*) that carry infective guinea-worm larvae.
- Of the 20 countries that were endemic for the disease in the mid-1980s, only 2 countries reported cases in 2017 (Chad (15), and Ethiopia (15)).
- From the time infection occurs, it takes between 10–14 months for the transmission cycle to complete when a mature female worm emerges from the body via a painful blistering ulcer.

Buruli ulcer
- Buruli ulcer is a chronic debilitating disease caused by *Mycobacterium ulcerans*.
- It often affects the skin and sometimes bone, and can lead to permanent disfigurement and long-term disability.
- At least 33 countries with tropical, subtropical and temperate climates have reported Buruli ulcer in Africa, South America and Western Pacific regions.
- Most patients in Africa are children aged under 15 years
- The mode of transmission is not known hence there is no preventive strategy for the disease.
- Early diagnosis and treatment with oral antibiotic therapy is the recommended strategy

River blindness (onchocerciasis)
- Caused by the parasitic worm *Onchocerca volvulus*.
- Transmitted to humans through exposure to repeated bites of infected blackflies of the genus *Simulium*.
- Symptoms include severe itching, disfiguring skin conditions, and visual impairment, including permanent blindness.
- More than 99% of infected people live in 31 African countries.
- Community-directed treatment with ivermectin is the core strategy to eliminate onchocerciasis
Schistosomiasis

- An acute and chronic disease caused by parasitic worms.
- People are infected during routine agricultural, domestic, occupational, and recreational activities, which expose them to infested water.
- Lack of hygiene and play habits of school-aged children such as swimming or fishing in infested water make them especially vulnerable to infection.
- Control focuses on reducing disease through periodic, large-scale population treatment with praziquantel; a more comprehensive approach including potable water, adequate sanitation, health education and snail control would also reduce transmission.

http://www.who.int/mediacentre/factsheets/fs115/en/

Polio

- Polio (poliomyelitis) mainly affects children under 5 years of age.
- 1 in 200 infections leads to irreversible paralysis. Among those paralysed, 5% to 10% die when their breathing muscles become immobilized.
- Cases due to wild poliovirus have decreased by over 99% since 1988, from an estimated 350,000 cases then, to 22 reported cases in 2017.
- As long as a single child remains infected, children in all countries are at risk of contracting polio.

http://www.who.int/mediacentre/factsheets/fs114/en/

Soil-transmitted Helminths (STH):

- Soil-transmitted helminth infections of the intestine are caused by different species of parasitic worms.
- They are transmitted by eggs present in human faeces, which contaminate the soil in areas where sanitation is poor.
- Approximately 1.5 billion people are infected with soil-transmitted helminths worldwide.
- Infected children are nutritionally and physically impaired.

http://www.who.int/intestinal_worms/disease/en/

Trachoma

- Trachoma is a disease of the eye caused by infection with the bacterium *Chlamydia trachomatis*.
- It is known to be a public health problem in 41 countries, and is responsible for the blindness or visual impairment of about 1.9 million people.
- Blindness from trachoma is irreversible.
- Infection spreads through personal contact (via hands, clothes or bedding) and by flies that have been in contact with discharge from the eyes or nose of an infected person.

http://www.who.int/trachoma/disease/en/

Source: WHO (2018)
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