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Neglected tropical diseases – the present and the future

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Neglected tropical diseases are a diverse group of diseases that predominantly but not exclusively affect people in tropical and subtropical climatic zones. The collaboration between the WHO, non-governmental organisations, local stakeholders and pharmaceutical companies, among others, is key to achieving control and elimination of these diseases.

The term ‘neglected tropical diseases’ was coined by Peter Hotez and colleagues in 2003 to counterbalance the attention given to HIV/AIDS, tuberculosis and malaria (1). Neglected tropical diseases have been termed a ‘chronic pandemic’ (2) and are largely associated with lower socioeconomic status. The diseases are highly prevalent both in rural and poor urban settings, mainly in low- and middle-income countries (3). It is, however, not well defined which diseases fall under this category, as indicated by the different lists of diseases included in the WHO and PLOS definitions (Table 1) (4, 5).

Table 1

Major neglected tropical diseases adjusted from the expanded list of PLOS NTD (5). The 20 diseases recognised by the WHO (4) have been underlined.

Protozoan infections	• Amoebiasis • Balantidiasis • Chagas disease • Giardiasis • Human African trypanosomiasis • Leishmaniasis
Helminth infections	• *Taenia solium* (neuro)cysticercosis/taeniosis • Dracunculiasis • Echinococcosis • Foodborne trematodiases • Loiasis • Lymphatic filariasis • Onchocerciasis • Schistosomiasis • Soil-transmitted helminthiases (ascariasis, hookworm diseases, trichuriasis, strongyloidiasis) • Toxocariasis and other larva migrans diseases
Bacterial Infections	• Bartonellosis • Bovine tuberculosis in humans • Buruli ulcer • Cholera • Diarrhoeal diseases (shigella, salmonella, *E. coli*) • Leprosy • Leptospirosis • Relapsing fever • Trachoma • Treponematoses (endemic syphilis (=bejel), pinta, syphilis, yaws)
Viral Infections	• Dengue and chikungunya fevers • Japanese encephalitis • Jungle yellow fever • Other arboviral Infections • Rabies • Rift Valley fever • Viral haemorrhagic fevers
Fungal Infections[1]	• Mycetoma, paracoccidiomycosis, chromoblastomycosis, other deep mycosis
Ectoparasitic[1] Infections	• Scabies, myiasis

Venom[1]	• Snakebite envenoming

[1]Have been added recently in 2017 on the occasion of the 10th meeting of the Strategic and Technical Advisory Group for Neglected Tropical Diseases

Neglected tropical diseases are characterised by a high burden of disease, measured in disability-adjusted life years (6). Estimates vary from 26 million to 48 million years lost to the diseases. Compared to tuberculosis (49 million years), malaria (83 million years) and HIV/AIDS (82 million years), the disease burden of neglected tropical diseases is also substantial (7). An estimated one billion people are currently affected by neglected tropical diseases worldwide and approximately 350 000–500 000 die from them each year (2), (8–10). Exact numbers are, however, unknown as most diseases progress slowly. Signs and symptoms are often insidious or unspecific and are commonly not diagnosed until late stages of disease progression. As affected individuals tend to be poor and lack the necessary information and financial resources to access health care, many cases go unreported.

Parasites cause more than 50 % of all neglected tropical diseases and include both protozoan and helminthic infections, and of late also ectoparasites (scabies), followed in order of frequency by bacterial, viral and fungal infections. In endemic areas, especially in sub-Saharan Africa, individuals often suffer from more than one neglected tropical disease. For possible symptoms and signs that patients may suffer from, refer to Box 1. Moreover, areas endemic for neglected tropical diseases tend to be endemic for HIV/AIDS, tuberculosis and malaria, and co-infection, especially with soil-transmitted helminths and schistosomes, has been shown to exacerbate the progression of the aforementioned diseases (2, 8, 11).

Importantly, neglected tropical diseases are not only confined to the tropics. Increase in prevalence has been observed in southern Europe (e.g. dengue fever, Chagas disease, leishmaniasis, opisthorchiasis and schistosomiasis). This may be due to increased poverty, migration and climate change (12).

Management of the diseases

Integrated intervention-centred approaches to management of neglected tropical diseases focus on outreach to poor and marginalised communities through preventive chemotherapy, intensified case management, vector control, veterinary public health as well as safe water, sanitation and hygiene (2, 13). Preventive chemotherapy through mass drug administration refers to distribution of disease-specific medication to individuals in endemic areas, without the need for individual diagnosis, at low cost (between USD 0.30 and USD 0.50 per person treated) (14). It is therefore at the core of programmes that fight neglected tropical diseases.

Box 1 Clinical signs and symptoms associated with neglected tropical diseases (1, 3, 11, 14)

- Skin diseases with severe itching, blindness, acute and chronic diarrhoea, anaemia (with potentially severe adverse effects in children and pregnant women), acute and chronic pain, hepatic disease and other end organ damage as well as cancer
- Psychiatric and neurological conditions, including epilepsy
- Malnutrition
- Stunting and cognitive impairment leading to compromised education and loss of productivity in adults
- Stigma and social exclusion due to disability and disfigurement

Repeated mass drug administration aims at morbidity control as it tends to lead to reduction in the force of infection as well as having the potential to break disease transmission, as seen in programmes on river blindness (onchocerciasis). Mass drug administration programmes are carried out by non-governmental organisations in collaboration with national governments. Guidelines for national control and elimination programmes have been developed by the World Health Organization based on expert opinion. In addition, the Neglected Tropical Diseases Non-Governmental Organisations Network, a group of more than 60 non-governmental organisations, has developed a comprehensive 'Behaviour, Environment, Social Inclusion and Equity, as well as Treatment and Care' framework the BEST framework) to facilitate the uptake of this type of holistic and multidisciplinary approach (15).

Overall, progress has been made with regard to the 2020 targets outlined by the World Health Organization in its Roadmap on neglected tropical diseases, including eradication, national/regional elimination and control, see Box 2 (2, 16). This progress has been possible due to strong global partnerships, donations by the pharmaceutical industry, new diagnostic tools, new drug development, commitment by governments to global collaboration and the support of public and private partners (13, 17).

Box 2 WHO Roadmap strategy on control, elimination and eradication of neglected tropical diseases (2, 16).

Control

Dengue fever, Buruli ulcer, cutaneous leishmaniasis, foodborne trematode infections, *Taenia solium* (neuro)cysticercosis/taeniosis, echinococcosis, soil-transmitted helminthiasis

Regional elimination

Lymphatic filariasis, onchocerciasis, leprosy, human African trypanosomiasis, trachoma, schistosomiasis, rabies, Chagas disease, visceral leishmaniasis

Eradication

Guinea worm, endemic treponematoses (yaws)

Nonetheless, efforts are still largely focused on the diseases for which medication and large-scale treatment options are available, including lymphatic filariasis, onchocerciasis, schistosomiasis, soil-transmitted helminthiasis and trachoma. Zoonotic diseases, such as *T. solium* (neuro)cysticercosis/taeniosis, do not necessarily benefit from preventive chemotherapy and need a different, even more cross-sectoral approach, including e.g. environmental studies. Despite vaccines and medication for animals being readily available, zoonotic neglected tropical diseases have received less attention and are sometimes referred to as the most neglected among the neglected tropical diseases (18). Advocacy for and investment in both domestic and wild animal health and community livelihood are key to successful control and elimination of zoonotic neglected tropical diseases.

One promising approach to push this agenda forward would be the integration of management of neglected tropical diseases and that of emerging infectious diseases. These groups of diseases share important characteristics, such as their tendency to affect largely underserved populations, their zoonotic nature and the need for vector control, as well as scarcity of point-of-care diagnostics, drugs and vaccines. Thus, strong and resilient health systems with adequate access to health care and universal health coverage as well as a cross-sectoral 'one-health approach' combining human, animal and environmental health should be given highest priority (2, 10).

Politics and future directions

Important steps have been taken towards reaching the 2020 World Health Organization Roadmap targets on neglected tropical diseases, published in 2012, as shown in Box 2 (16). The number of people treated for neglected tropical diseases is increasing, with one billion people having been provided with preventive chemotherapy in 2015 (19), and some countries having been able to announce the elimination of certain diseases.

Furthermore, this disease group was included in the Sustainable Development Goal agenda, the German G7 summit and G20 communications, which is the result of the hard work of the neglected tropical disease lobby in raising political awareness that this group of diseases clearly deserves (20, 21). It is now imperative to go beyond the focus on the preventive chemotherapy of neglected tropical diseases and to address the zoonotic neglected tropical diseases that do not yet benefit from the pharmaceutical and governmental support that the others enjoy. The one-health approach needed to tackle zoonotic neglected tropical diseases provides an important opportunity to link these diseases with emerging infectious diseases and can thereby create leverage for resources and political attention. In addition, and most urgently, strengthening global health systems is required in order to prevent, diagnose, treat and eventually eliminate neglected tropical diseases.

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