Overcoming the global burden of neglected tropical diseases

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Neglected tropical diseases (NTDs) are a broad group of communicable diseases that have proliferated in tropical and subtropical climates, mainly across the developing world, where inadequate sanitation, constant contact with vectors and livestock, and inadequate healthcare services prevail.[1] NTDs are called "*neglected*" because they have been wiped out of the most developed societies, while they have persisted in the poorest and most marginalized ones. If left untreated, they can cause illness, suffering, impairment, and stigma, preventing children from attending schools and hampering adult productivity. As a result, families, communities, and countries remain trapped in a cycle of disease and poverty.[2]

The World Health Organization (WHO) recognizes 20 major NTDs, of which 19 are infectious diseases: American trypanosomiasis or Chagas disease, Buruli ulcer, dengue and chikungunya, dracunculiasis or Guinea-worm disease, echinococcosis, foodborne trematodiases (clonorchiasis, fascioliasis, opisthorchiasis, and paragonimiasis), human African trypanosomiasis or sleeping sickness, leishmaniasis, leprosy or Hansen's disease, lymphatic filariasis or elephantiasis, mycetoma, chromoblastomycosis and other deep mycoses, onchocerciasis or river blindness, rabies, scabies and other ectoparasites, schistosomiasis or snail fever, soil-transmitted helminthiases (ascariasis, ancylostomiasis and trichuriasis), taeniasis/cysticercosis, trachoma, and yaws. Only one non-infectious disease, snakebite envenoming, has made it in the list due to its burden and impact.[1]

Together, NTDs affect nearly 2 billion people, including 0.5 billion children, and are responsible for causing approximately 200,000 deaths per year. On the Global Burden of Disease Study published in 2013 and reviewed by Herricks *et al.* in 2017, soil-transmitted helminthiases (ascariasis 804.4 million cases, trichuriasis 477.4 million cases, and hookworm 471.8 million cases), schistosomiasis (290.6 million cases), and food-borne trematodiases (80.2 million cases) were identified as the most common NTDs worldwide. On the other hand, visceral leishmaniasis (62,500 deaths), rabies (23,500 deaths), and Chagas disease (10,600) were recognized as the most common causes of death related to NTDs worldwide.[3] Together they represent a loss of 25.1 million disability adjusted-life years, 16.9 million years lived with disability, and 8.21 million years of life lost.[3] However, the lack of accurate and available data may underestimate their real number.

NTDs cause a wide range of clinical manifestations, which vary from disease to disease. Some of them may produce unspecific symptomatology in people who suffer from them, leading to wrong diagnosis. Other NTDs may remain asymptomatic until life-threatening complications have developed, leading to late diagnosis.[4] Therefore, epidemiological background and clinical manifestations should be considered in the field, but laboratory and imaging studies are required to confirm their presence, and to offer an integrated approach to the patients. The problem arises when most NTDs appear in resource-limited areas, where appropriate diagnostic tools are not affordable and therefore are not available. Commitment and investment are still required for early case detection to map, treat, and prevent further cases.[5]

Effective control can be achieved when proper public health measures are taken in consideration. The WHO recommends the implementations of

five key interventions to overcome the burden of NTDs: preventive chemotherapy, innovative and intensified disease management, vector ecology and management, veterinary public health services, and safe water, sanitation, and hygiene.[6] Among them, the availability of affordable and safe preventive chemotherapies has led to the reduction of the prevalence of many NTDs. Most people requiring a package of essential medicines can be reached by the "rapid impact" package, which contains up to four drugs (albendazole or mebendazole, azithromycin, ivermectin or diethylcarbamazine citrate, and praziquantel) that are administered twice a year in a single oral dose. The package can be accessed for less than US$0.50 per person,[7] because pharmaceutical companies have been donating these drugs for more than a decade, but the lack of reliable distribution systems has often kept people that need them the most without it.[8] On the other hand, there are other NTDs that are still treated with drugs that have poor effectivity and low security profile, leading to treatment detachment and worsening of the outcome of those who suffer from them. The formulation of new chemical entities is still needed, as most advances of the last decade entail repurposing or reformulating existing drugs.[9] New research and development incentive mechanisms and innovative financing instruments, as well as improved global priority-setting and coordination will be critical to ensure that treatments are brought out of the pipeline and put into the hands of neglected patients.[10]

Currently there are no preventive nor therapeutic vaccines available for the vast majority of NTDs. However, international companies have compromised with advancing and introducing new vaccines due to the publication of several studies showing their cost-effectiveness or cost-savings.[11–13] Nevertheless, further engagement and commitment of the major pharmaceutical companies are still required. New risk-reducing approaches integrating preventive measures for other common infectious diseases, such as dengue, malaria or Zika could make investments more attractive to the pharmaceutical industry and partnering with Developing Country Vaccine Manufacturing Networks for industrial-scale production may enhance the response.[7]

To enhance the response, in 2011, the WHO Strategic and Technical Advisory Group for NTDs drew a roadmap purposed to guide the implementation of policies and strategies set out in the *Global Plan to combat neglected tropical diseases 2008–2015*[14] and developed in *Working to overcome the global impact of neglected tropical diseases*.[15] The ultimate roadmap destination is the reduction of their impact to levels at which they are no longer considered public-health problems or even their eradication, if possible.[16] In 2012, governments, pharmaceutical companies, and non-governmental organizations, endorsed the *London Declaration on Neglected Tropical Diseases* to commit themselves to enhance a more effective response by working in alliance.[17] Since then, many advances have been made and several goals have been reached, allowing new projections for the eradication of dracunculiasis and yaws, the interruption of transmission of leprosy, human African trypanosomiasis (*Trypanosoma gambiense*), and onchocerciasis, the elimination as a public health problem of Chagas disease, human African trypanosomiasis (*T. rhodesiense*), leishmaniasis (visceral), lymphatic filariasis, rabies, schistosomiasis, soil-transmitted helminthiases and trachoma, and the control of Buruli ulcer, dengue, echinococcosis, foodborne trematodiases, leishmaniasis (cutaneous), mycetoma, chromoblastomycosis and other deep mycoses, scabies and other ectoparasitoses, taeniasis/cysticercosis and snakebite envenoming by 2030.[18]

As NTDs occur mostly in underdeveloped areas and settings, controlling, eliminating, and eradicating them can also serve as a marker of compliance to achieve the Sustainable Development Goals. To overcome their global burden, we need to invest in their surveillance, in new accessible and reliable diagnostic tools, in new safe and effective treatments, and innovative prevention strategies. No patient should be left behind.

Author contributions

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