

Vascular Damage in Neglected Tropical Diseases

A Surgical Perspective

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Introduction

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Introduction

Neglected Tropical Disease: Definition

Neglected tropical diseases were first mentioned as such in the early 2000s, as a group of health disorders highlighted within the Millennium Development Goal. These conditions shared common features, including the fact of being chronic and debilitating infections, in many cases of parasitic aetiology, which mostly occurred among the extreme poor [1]. The phrase “neglected” indicates that they were eclipsed by other diseases such as HIV, tuberculosis and malaria [2].

According to the updated and actual WHO definition, neglected tropical diseases (NTDs) are a diverse group of 20 conditions mainly prevalent in tropical areas, where they affect more than 1 billion people who live in impoverished communities [3]. Specifically, the list includes: Buruli ulcer, Chagas disease, dengue, and chikungunya, dracunculiasis (Guinea-worm disease), echinococcosis, foodborne trematodiases, human African trypanosomiasis (sleeping sickness), leishmaniasis, leprosy

(Hansen's disease), lymphatic filariasis, mycetoma, chromoblastomycosis and other deep mycoses, onchocerciasis (river blindness), podoconiosis, rabies, scabies and other ectoparasitoses, schistosomiasis, soil-transmitted helminthiases, snakebite envenoming, taeniasis/cysticercosis, trachoma, yaws and other endemic treponematoses [4].

The devastating health consequences that characterize each condition usually overlap huge socioeconomic consequences that are due to the reduction of population productivity and are increased by the lack of access to quality healthcare. The marginalization of those populations living in endemic settings, a lack of funding for healthcare systems and inadequate data on disease prevalence and control are also great contributors to the diseases' neglect, making them a public health challenge [2].

Neglected Tropical Diseases: General Epidemiology

The interest in tropical diseases started during the nineteenth century, with the establishment of tropical institutes in countries with large colonial holdings. Only later, the definition of tropical illnesses was integrated with the term "neglected", to better define those conditions affecting populations from resource-poor countries in tropical and sub-tropical regions [5, 6]. People living in these settings experience an inadequate access to safe sanitation, to safe water supply and to government health centres [7]. In this sense, NTDs' epidemiology reflects those health inequities which are main drivers of the NTD burden and shows higher prevalence of these conditions in developing countries compared to developed ones [2]. The global burden of NTDs is reported in the WHO's roadmap 2021–2030, which is available at <https://www.who.int/publications/i/item/9789240010352> and reported in Fig. 1.1.

The African Setting

Africa accounts for about 40% of the global burden of NTDs, with about 600 million individuals requiring treatment. At least one NTD is endemic in each country in the African region, and 79% of African countries are co-endemic with at least five of them [2]. Schistosomiasis, lymphatic filariasis and onchocerciasis emerge among the great challenges. The continent accounts for up to 90% of schistosomiasis cases, with 280,000 deaths estimated yearly due to this parasitosis. For lymphatic filariasis and onchocerciasis, the estimated at-risk population in Africa requiring intervention was 341 and 220 million people, respectively [2, 8].

The Asian Setting

Analysing the Asian setting, it was observed that the first five helminth infections in the WHO list, specifically soil-transmitted helminthiases, schistosomiasis, food-borne trematodiases, lymphatic filariasis and taeniasis/cysticercosis, are still endemic. These infections are mainly reported from eastern Asian countries, where almost 200 million people, mostly indigenous, face extreme poverty, specifically in Indonesia, the Philippines, Myanmar, Viet Nam and Cambodia and among upper



Fig. 1.1 Geographical spread of the NTD burden, by DALY and gross domestic product. Figure from the WHO’s document Ending the neglect to attain the Sustainable Development Goals: A road map for neglected tropical diseases 2021–2030 (who.int) [3]

middle-income countries such as Malaysia and Thailand. As described in the African setting, in Asia, schistosomiasis and lymphatic filariasis are among the most common NTDs, and each helminthiasis is associated with approximately 100 million infections in the region. In addition, more than 10 million people suffer from either liver or intestinal fluke infections, as well as schistosomiasis and lymphatic filariasis [9]. Current conditions and developments in Asia will sustain what was defined as “the yin and yang” of NTDs. In other words, while the reduction of poverty and effective control activities will work towards the decline of NTDs, other factors as urbanization, food insecurity and environmental and climate change will contribute to the persistence of distinct NTDs [9].

The Latin America Setting

Since the start of the twenty-first century, Latin America faced socio-political and economic challenges due to prolonged droughts, intermittent and extreme floods due to climate change, drug trade, food insecurity from agricultural declines, human displacements, urbanization and the marginalization of large indigenous populations. All these factors have shaped the epidemiological scenario of NTD in Latin

America, reducing the public health gains regarding the NTDs in this continent, making this region a global “hotspot” for NTDs [10].

The decline in health systems resulting from political and economic instability likely accounts for the scarce public health achievements in the prevention and control of NTD in this vulnerable setting. Additionally, because of Central America’s vulnerability to climate change, the recent formation of a dry corridor in central regions can also promote the susceptibility of this region to vector-borne tropical diseases. This adds to the interruption of vector control activities, which has been detrimental, leading to a significant rise in Chagas disease, leishmaniasis, dengue and the emergence of chikungunya and *Zika virus* infections. Schistosomiasis increases have also been noted in endemic hotspots [10].

Non-Endemic Setting

In recent years, factors such as climate change, migrations and travel and the presence of local conflicts in the endemic regions can additionally challenge the epidemiological context of NTDs by moving diseases outside the limit of the endemic regions of the tropical belt. As a result, these diseases can now be more frequently diagnosed in industrialized countries with temperate climates [5–7].

Because most NTDs do not require hospitalization and several cases of illegal migrants might remain undiagnosed, the prevalence of these conditions in non-endemic countries might be underestimated [5]. This fact emphasizes the importance of increasing global awareness of NTDs among healthcare professionals to improve clinical management and control of such diseases also in non-endemic settings [5].

Prevention and Control Strategies. The Need for Morbidity Management

To address this specific global health issue, WHO set the first NTD road map (2012–2020) [4]. According to it, NTDs are approached through five strategies: preventive chemotherapy, intensified disease management, vector control, veterinary public health measures for zoonotic neglected diseases and improved water and sanitation [6]. A vertical approach through massive drug administration (MDA), the distribution of preventive chemotherapy during prevention and control campaigns, is central to WHO’s prevention and control strategy for many NTDs [7].

As a result of the implementation of the prescriptions of the first road map, the population requiring NTD interventions decreased by 25% between 2010 and 2021, from 2.19 to 1.65 billion. As of the end of 2022, 47 countries have eliminated at least one NTD; more than 1 billion people were treated for at least one NTD each year from 2015 through to 2019 [4].

Still, notwithstanding interventions in place, the burden of NTDs continues to have an unequal global impact, with 80% of this burden affecting 16 countries. The progress in high-burden countries was slower than expected and uneven across certain of the 20 diseases and disease groups, while persistent risk factors such as

poverty, climate change and rapid population growth emerge as threats to achieving the 2030 targets within the defined timescales [11].

Additionally, the dominant vertical approach to the prevention and control of NTDs showed some limits.

One of the major concerns related to the vertical approach to NTDs is the unavailability of drugs donated for prevention and control of these conditions in healthcare centres for clinical practice use outside the setting of the intervention campaigns, thus leaving untreated the infected patients that are not the target of the distribution [12]. Additionally, chronic conditions can go well beyond the active infection, and the public health impact of NTDs is not limited to mortality, but can extend to disability and morbidity [7, 13]. Because of the primary focus of NTD policy on disease elimination, chronic NTDs and their associated morbidity impact have only recently been recognized [14]. These concepts were well described and emphasized in a comprehensive paper by Chami et al., which focused on how a vertical approach is sub-optimal to address all issues related to NTDs because it can't guarantee equitable access to treatment nor comprehensively address morbidity issues outside the prevention and control goal [7].

The need for chronic morbidity management in NTDs urgently calls for a new comprehensive strategy, combining MDA with on-demand access to treatment within local health systems [7]. This new perspective moves from the disease-specific management to a cross-cutting approach of coordinated and multi-disciplinary NTD programmes that could finally be integrated into national health systems [6, 15].

In this sense, the new roadmap for 2021–2030 sets out key actions and programmatic shifts to drive progress towards a world free of NTDs by 2030 [4] and supports the vision of universal health coverage, in which all individuals and communities receive the health services they need without suffering financial hardship [3]. Among the 2030 targets and milestones, special importance is given to disease control, in terms of reduction to locally acceptable levels not only of the incidence and prevalence but also of their morbidity and/or mortality [3].

Different targets have been set to define a successful disease control, according to different diseases. For some of the conditions included in this text, as in the case for filariasis, the goal is to eliminate the condition as a public health threat, with the infection sustained below the thresholds of transmission for at least 4 years after stopping mass drug administration, together with the availability of an essential package of care for patients affected by morbidity due to previous infection sequelae. Different parameters are considered for schistosomiasis: the elimination as a public health problem is currently defined as <1% proportion of heavy-intensity schistosomiasis infections [3]. For other conditions, the goal includes intensifying control (such as in the case of echinococcosis in hyperendemic areas); the incorporation of management in the universal health coverage package of care, as in the case for ectoparasites as scabies, or the reduction of mortality by 50%, as for the neglected frequently fatal snakebite envenomation [3].

Independently from the specific target set for disease control, a better understanding of disease epidemiology and pathology, together with the availability of