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Introduction to the Neglected Tropical Diseases: the Ancient Afflictions of Stigma and Poverty

The age of hypocrisy has been succeeded by that of indifference, which is worse, for indifference corrupts and appeases: it kills the spirit before it kills the body. It has been stated before, it bears repeating: the opposite of love is not hate, but indifference.

ELIE WIESEL, *A JEW TODAY*, P. 17

It is a trite saying that one half the world knows not how the other lives. Who can say what sores might be healed, what hurts solved, were the doings of each half of the world's inhabitants understood and appreciated by the other?

MAHATMA GANDHI

Since the beginning of the 21st century, we have seen unfold a new sense of urgency about the plight of the world's poorest people in developing countries. Today, the average well-educated layperson living in “the North” (North America, Europe, and Japan) is far more aware than ever before about the suffering of the people living in “the South” (the developing countries of sub-Saharan Africa, Asia, and the Americas). Almost certainly, the human catastrophe of HIV/AIDS in sub-Saharan Africa, known as the “plague of the 21st century,” and epidemics or pandemics from Ebola virus and Zika virus infections, and most recently coronavirus disease 2019 (COVID-19), have helped to focus world attention on health threats from infectious diseases, especially problems in the world's low- and middle-income countries (LMICs).¹

Simultaneously, an unprecedented and extraordinary advocacy effort led by some highly influential international leaders and celebrities has helped to fuel a 21st-century global health movement. Throughout the decade of the 2000s, Bono, Angelina Jolie, Brad Pitt, George Clooney, Oprah Winfrey,

Annie Lennox, Bob Geldof, and other actors, celebrities, and musicians; Bill Gates, Melinda French Gates, Warren Buffett, Carlos Slim and his family, and other philanthropists; Jeffrey Sachs; Chelsea Clinton; Prime Ministers Tony Blair, Gordon Brown, David Cameron, Theresa May, and Boris Johnson of the United Kingdom; and Secretaries of State Hillary Clinton and John Kerry and Presidents Jimmy Carter, Bill Clinton, George W. Bush, and Barack Obama of the United States have donated their time and energy to advocate for the health of the world's poorest people. These efforts captivated world attention and have even infused an element of glamour into solving global health problems. Between 2005 and 2006 alone, Bono, Bill Gates, and Melinda Gates were named *Time* magazine Persons of the Year; the Time Global Health Summit in New York was branded the "Woodstock of global health"; Brad Pitt narrated a 6-hour-long documentary, *Rx for Survival, a Global Health Challenge*, for PBS; former President Clinton featured global health issues at his annual Clinton Global Initiative; and Bono and Bobby Shriver launched Product RED to support HIV/AIDS, malaria, and tuberculosis relief at the 2006 World Economic Forum in Davos, Switzerland.

As a university professor and now as a dean, I can attest that these activities stimulated an unprecedented level of interest in global health issues from both undergraduates and graduate public health and medical students. With the important exception of our 2020–2021 years of COVID-19, almost every week during the academic year I have been visited by one or more young persons who request advice on how they can help solve a health problem in an LMIC. I am not the only faculty member to have this experience—today, new university-wide global health institutes are springing up at Duke, Baylor, Brown, Yale, Vanderbilt, Harvard, Emory, Washington University in St. Louis, the University of California campuses, University of Washington, and elsewhere, as university deans and presidents scramble to keep up with student interest.

Like any movement, the one in global health that I benchmark as beginning in 2000 was stimulated by a *manifesto*, which is defined by Webster as "a public declaration of motives and intentions by a government or by a person or group regarded as having some public importance."¹ For the global health movement, we can point to at least three landmark 21st-century policy documents that have effectively served as manifestos.

The first had its origins in January 2000, when then-World Health Organization (WHO) Director-General Gro Harlem Brundtland launched the Commission on Macroeconomics and Health (CMH) and appointed the international macroeconomist Jeffrey Sachs to serve as its chair. Jeff and his colleagues were charged with analyzing the impact of health on development. Their *Report of the CMH*, illustrated with examples of how health investments translate into economic development, elegantly articulated a profound relationship between disease and chronic poverty. As a result, the world's most influential finance ministers and policymakers began to regard improvements in global health as an important tool for poverty reduction. A second initiative was also launched in 2000 when the General

Table 1.1 The MDGs

1. Eradicate extreme poverty and hunger
2. Achieve universal primary education
3. Promote gender equality and empower women
4. Reduce child mortality
5. Improve maternal health
6. Combat HIV/AIDS, malaria, and other diseases
7. Ensure environmental sustainability
8. Develop a global partnership for development

Assembly of the United Nations convened in New York City to adopt a resolution known as the UN Millennium Declaration. The Declaration was a renewed call for sustainable development and for the eradication of poverty, and its core was a set of eight specific Millennium Development Goals (MDGs) along with a set of specific targets for the year 2015. As shown in Table 1.1, three of the goals (MDGs 4, 5, and 6) specifically emphasize health. Finally, a third manifesto was *Our Common Interest: Report of the Commission for Africa*, commissioned by British Prime Minister Tony Blair to provide specific recommendations on how to accelerate development and reduce poverty in Africa. The report served as an important blueprint for commitments by the Group of Eight (G8) nations at their 2005 summit in Gleneagles, Scotland.

Unlike many UN and international declarations, which too often are forgotten by the global community almost as soon as they are written, the CMH report, the MDGs, and the *Report of the Commission for Africa* continue to exert a major influence on global policymakers. Although the MDGs ended in 2015, they have since continued under a new set of Sustainable Development Goals (SDGs), sometimes just referred to as the “Global Goals.” Equally important, together with the new advocacy by leaders and celebrities, the global health manifestos have stimulated high-level efforts to invent innovative financial instruments for supporting disease control, including some very substantial funding initiatives from both the G7 nations and some prominent private philanthropic organizations such as the Bill & Melinda Gates Foundation.

MDG 6 (to “combat HIV/AIDS, malaria, and other diseases”) has been a particular target of these new funds, with approximately US\$90 billion committed so far by the U.S. Congress for HIV/AIDS through the U.S. President’s Emergency Plan for AIDS Relief (PEPFAR),² together with more than US\$6 billion for malaria through the U.S. President’s Malaria Initiative (PMI). Internationally, the Global Fund to Fight AIDS, Tuberculosis, and Malaria now commits more than US\$4 billion annually to support interventions against these infections (<http://theglobalfund.org>), while the Gates Foundation has also committed vast sums. Practically speaking, these extraordinary new financial commitments mean that unprecedented numbers of poor people in Africa and elsewhere are receiving lifesaving

antiretroviral medications for the treatment of HIV/AIDS or drugs and bed nets for the treatment and prevention of malaria. Such interventions are producing significant positive changes to the global health landscape under the auspices of the SDGs.

Unfortunately, with the exception of some important support from the Gates Foundation, the flurry of global health advocacy and resource mobilization occurring over the past few years has, until recently, largely bypassed the third, “other diseases” component of the original MDG 6. This neglect is particularly true for a group of exotic-sounding tropical infections that represent a health and socioeconomic problem of extraordinary dimensions but one that world leaders and global health advocates are only now waking up to. Beginning in 2005, an original core group of the 13 major so-called neglected tropical diseases, or NTDs, was proposed,³ which has since been expanded by the WHO to a list of 20 diseases and conditions (Table 1.2).

Table 1.2 The NTDs (core group of 20)^a

Infection type	Disease or pathogen name (common name)
Helminth (worm) infections	
Soil-transmitted helminth infections ^b	Ascariasis (roundworm infection)
	Hookworm infection
	Trichuriasis (whipworm infection)
	Others: Strongyloidiasis (threadworm) and toxocariasis
Other helminth infections	Schistosomiasis (snail fever)
	Lymphatic filariasis (elephantiasis)
	Onchocerciasis (river blindness)
	Food-borne trematode infections (liver fluke, lung fluke, intestinal fluke)
	Cysticercosis
	Human echinococcosis (hydatid cyst)
	Dracunculiasis (guinea worm infection)
Protozoan infections	Leishmaniasis
	Chagas disease
	Human African trypanosomiasis (sleeping sickness)
Ectoparasitoses	Scabies and other ectoparasitoses
Bacterial and fungal infections	Trachoma
	Buruli ulcer
	Leprosy (Hansen’s disease)
	Yaws and endemic treponematoses
	Mycetoma, chromoblastomycosis, and other deep mycoses
Snakebite envenoming	Snakebite envenoming
Viral infections	Dengue ^c
	Rabies

^a Data from the WHO (<https://www.who.int/teams/control-of-neglected-tropical-diseases>).

^b Five major soil-transmitted helminth infections are listed, although they are typically considered as a single entity by the WHO.

^c Some modify “dengue” to include “dengue and severe dengue” or “dengue and other arbovirus infections,” which might include Zika virus, yellow fever, and West Nile virus infection, among others.

They include the major parasitic worm infections of humans, such as the major soil-transmitted helminth infections, e.g., ascariasis (roundworm infection), hookworm infection, and trichuriasis (whipworm infection); and lymphatic filariasis (LF or elephantiasis), schistosomiasis (snail fever), onchocerciasis (river blindness), food-borne trematode infections (liver fluke, lung fluke, and intestinal fluke), cysticercosis, echinococcosis, and dracunculiasis (guinea worm infection). In addition, the NTDs include an important group of infections caused by single-celled protozoan parasites, such as Chagas disease, leishmaniasis, and human African trypanosomiasis (sleeping sickness). Several nonparasitic infections are also prominent, including some atypical bacterial infections, such as trachoma, yaws, and endemic treponematoses; the mycobacterial infections Buruli ulcer and leprosy; mycetoma and related fungal diseases; and selected viral infections, such as dengue and rabies. More recently, snake envenomation and ectoparasitic conditions, especially scabies, were added. Still other tropical infections can also be considered NTDs, and there is an expanded list of these conditions included in the appendix.

While many educated people have since learned something about HIV/AIDS and malaria, and their impact in Africa and elsewhere in the developing world, far fewer have heard about this core group of NTDs. Therefore, it may come as a surprise to learn that the NTDs represent some of the most common infections of the world's poorest people. Today, of the almost 8 billion people living on our planet, an estimated 750 million people (10%) live on less than US\$1.90 per day, which is considered the World Bank poverty threshold. Paul Collier, the Oxford University economist, helped to popularize the term "the bottom billion" to describe this group of people living in extreme poverty at the beginning of this century, a number now declining due to a global assault on poverty. Over the last 2 decades, China has accounted for some of the greatest reductions in those living in extreme poverty.

As shown in Table 1.3, most of the world's population living below World Bank poverty levels suffers from at least one NTD. The most common include worm infections, also known as helminth infections, led by ascariasis, trichuriasis, or hookworm infection—parasitic worm infections that are transmitted through the contaminated warm and moist soil of tropical developing countries (and are known as the soil-transmitted helminth infections)—and schistosomiasis. Essentially all of the "bottom 750 million" (to borrow from Paul Collier) are affected by one or more of the seven most common NTDs currently listed by the WHO.^{3,4}

Shown in Fig. 1.1 are the countries in which the NTDs occur.³ The extensive geographic overlap of these conditions means that many of the NTDs are *coendemic* and that it is common for poor people to be simultaneously infected with multiple NTDs. NTDs occur globally wherever poverty is widespread. While sub-Saharan Africa, South Asia, and Latin America dominate in terms of endemic NTDs, these diseases also occur in areas of poverty in the United States, especially in Texas and the Gulf Coast states,

Table 1.3 The WHO 20 NTDs ranked by prevalence^a

Disease	Estimated global prevalence	Regions of highest prevalence
Soil-transmitted helminth infections		
Ascariasis	446 million	LMICs globally
Trichuriasis	360 million	LMICs globally
Hookworm disease	173 million	LMICs globally
Scabies	187 million	LMICs globally
Schistosomiasis	140 million	Africa and Middle East
Lymphatic filariasis	72 million	Africa and LMICs in Asia
Dengue	57 million ^b	Global
Food-borne trematode infections	34 million	East Asia
Onchocerciasis	19 million	Africa
Animal envenomation ^c	17 million	LMICs globally
Chagas disease	6–7 million	The Americas, including southern United States
Leishmaniasis	5 million	LMICs in Middle East, South Asia, Africa, and the Americas
Cysticercosis	5 million (with epilepsy)	LMICs globally
Trachoma	2 million ^d	LMICs globally
Cystic echinococcosis	0.9 million	LMICs globally
Leprosy	0.5 million	LMICs globally
Rabies	<0.1 million ^c	LMICs globally
Human African trypanosomiasis	<0.01 million ^c	Africa
Mycetoma and other mycoses	Not determined	LMICs globally
Buruli ulcer	Not determined	Africa
Yaws and endemic treponematoses	Not determined	LMICs globally
Dracunculiasis	Near eradication	Africa

^a Data from Global Burden of Disease Collaborative Network, 2020 (<http://ghdx.healthdata.org/gbd-results-tool/result/c1466642d6e4379c7465508afd12d904>).

^b Incidence figures used instead of prevalence estimates because of the acute nature of the illness.

^c GBD 2019 does not specifically list snake envenomation, but reports this information as “animal envenomation,” which includes snake envenomation as well as other causes.

^d Only includes those with blindness or visual impairments.

and in Australia among aboriginal populations. Africa stands out because it accounts for 100% of the world’s few remaining cases of dracunculiasis, 99% of the cases of onchocerciasis, more than 90% of the world’s cases of schistosomiasis, approximately 40% of the cases of LF and trachoma, and one-third of the world’s hookworm infections.⁵ The impoverished areas of Asia, especially Southeast Asia and the Indian subcontinent, account for more than one-half of the world’s cases of hookworm, ascariasis, and LF. Hookworm, schistosomiasis, LF, and onchocerciasis also remain endemic in focal regions of American tropics and subtropics, especially in Venezuela and elsewhere in Central Latin America and Brazil, where it has been suggested that these NTDs represent a living legacy of the transatlantic slave trade.⁵ Today, these NTDs still primarily afflict the poor and marginalized people living in the region.⁵

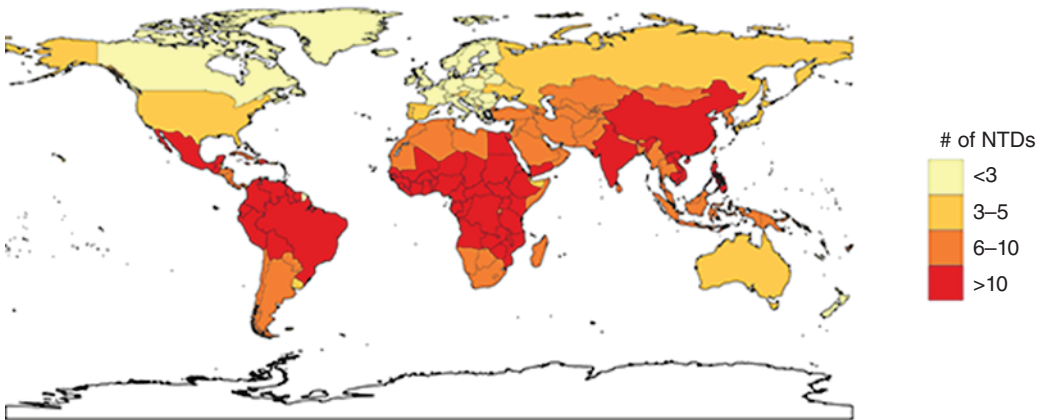


Figure 1.1 Map of the world's coendemic NTDs. (Drawn by Ashish Damania, National School of Tropical Medicine, Baylor College of Medicine. Data from Global Burden of Disease Collaborative Network, 2020.)

In addition to their geographic overlap and coendemicity, the major NTDs exhibit a remarkable set of common features, all of which adversely affect the health and socioeconomic status of the world's poorest people (Table 1.4).⁶

To summarize these common features:

1. *The NTDs have high prevalence.* As discussed above, today the NTDs rank among the most common infections of the poorest people in developing nations or LMICs.³ A new trend is the observation that NTDs are not only found in poor nations, but are surprisingly common in the Group of 20 (G20) countries. In this case, the NTDs still mostly strike people who live in poverty. For example, NTDs such as hookworm infection, toxocariasis, trichomoniasis, and Chagas disease are common among the poor living in impoverished areas of the U.S. Gulf Coast states.³
2. *The NTDs are linked to rural poverty—but this situation may be shifting.* The high prevalence of the NTDs is frequently not widely appreciated by policymakers or sometimes even by many government officials from the countries where NTDs are endemic. An important reason for the lack of awareness about these conditions is that the NTDs are seldom noticed in capital cities, where the government officials work and live. Instead, the NTDs are widespread in poor rural and agricultural areas, particularly in regions where subsistence farming is practiced.⁶ Therefore, unlike HIV/AIDS or other better-known infections, the NTDs are frequently both out of sight and out of mind. They truly are forgotten diseases afflicting forgotten people. There are important exceptions, such as dengue fever and leptospirosis, which are also found in urban slums. These conditions will be addressed separately (in chapter 8), but historically the NTDs occur in the setting of rural poverty. Along those lines, a new trend may be emerging. Increasingly, urban foci of

Table 1.4 Major attributes of the NTDs

Most prevalent among poor people
Endemic in rural areas (some poor urban areas) of low-income countries
Ancient (“the biblical diseases”)
Chronic
Disabling (growth delays, blindness, or disfigurement)
Associated with high disease burden but low mortality
Stigmatizing
Poverty promoting

soil-transmitted helminth infections, schistosomiasis, leishmaniasis, and other NTDs are being reported.⁶ This parallels observations that for the first time the majority of the world’s population lives in urban areas. What remains uncertain is whether urbanization of NTDs reflects some type of reporting bias versus true adaptation of parasites or their insect vectors or snail hosts. However, the confluence of expanding slums and urban poverty and NTDs is a worrisome trend. Some demographers predict that the world’s poor will eventually coalesce into massive “mega-cities” across Africa, Asia, and Latin America, and increasingly NTDs will be the predominant infections found in those areas.

3. *The NTDs are ancient conditions.* Another interesting feature of the NTDs is their nonemerging character. By this phrase, I mean the NTDs are just the opposite of better-known *emerging infections*, such as avian influenza, SARS (severe acute respiratory syndrome), COVID-19, Ebola, Lyme disease, and HIV/AIDS, which have either newly appeared in the population or have rapidly increased in incidence or geographic range. Instead, the NTDs have been around seemingly forever, as they have plagued humankind for centuries. This historical link is well documented through the accounts and descriptions of some of the dramatic clinical manifestations of the NTDs, particularly leprosy, dracunculiasis, schistosomiasis, hookworm infection, and trachoma, in ancient texts including the Bible, Talmud, Vedas, writings of Hippocrates, and Egyptian medical papyri.⁷ One exception to this persistent state is selected NTDs that can sometimes reappear because of public health breakdowns resulting from civil or international conflicts. Later (in chapter 7), we will see how this situation has tragically unfolded in Angola, the Democratic Republic of the Congo, and Sudan and has resulted in the rise of human African trypanosomiasis and kala-azar.
4. *The NTDs are chronic conditions.* Another distinguishing feature of the NTDs is that unlike many infectious diseases with which we are familiar, they are mostly chronic infections lasting years and sometimes even decades. In some cases, poor people can suffer from NTDs for their entire lives.⁶ The viral NTDs—dengue and related arbovirus infections and rabies—represent important exceptions to this feature.
5. *The NTDs cause disability and disfigurement.* Even though they are infectious diseases because they are caused by microbial or

multicellular pathogens, which are transmitted either from person to person or through contact with contaminated soil or water or through exposure to arthropod vectors (e.g., mosquitoes, sandflies, assassin bugs, and copepods), the NTDs frequently do not exhibit the classic features of most infections. That is to say, they do not typically cause acute febrile illnesses, which either resolve or kill. Instead, the NTDs mostly cause chronic conditions that lead to long-term disabilities and, in some cases, disfigurement.⁶ I will highlight the specific disabling features of each of the NTDs when they are treated separately (in chapters 2 to 9), but to provide some specific examples here, the long-term effects of chronic hookworm infection and schistosomiasis in childhood produce a long-standing anemia, which is associated with physical growth retardation, impaired memory, and cognitive growth delays; in pregnant women, the anemia from hookworm infection and from schistosomiasis results in poor birth outcomes such as low neonatal birth weight and increased maternal morbidity and mortality. Onchocerciasis and trachoma cause impaired vision and blindness. Chagas disease causes a chronic and severely disabling heart condition. LF, onchocerciasis, guinea worm infection, leishmaniasis, Buruli ulcer, and leprosy cause either limb disuse or profound disfigurement (including genital deformities), which often prevent afflicted individuals from either obtaining or maintaining employment (Fig. 1.2).

6. *The NTDs have a high disease burden but low mortality.* An estimated 100,000 to 200,000 people die annually from the NTDs.⁸ These numbers are derived from the Global Burden of Disease Study (GBD) 2019, an initiative led by the Institute for Health Metrics and Evaluation of the University of Washington, Seattle. Throughout this book, we will refer frequently to GBD 2019 estimates of disease prevalence and geographic distribution. While this number of people is significant and approximates the number estimated to have perished in the 2004 Christmas tsunami that hit the beaches of Thailand, Sri Lanka, and Indonesia, for example, the reality is that these numbers pale in comparison to the number of annual deaths from HIV/AIDS or malaria. Therefore, placing NTDs on the global health radar screen of world leaders and policymakers and motivating them to tackle these conditions in a substantive way require focusing advocacy efforts on something more than simply looking at deaths as an endpoint. While it is obvious that the individuals shown in Fig. 1.2 are having their lives ruined by the long-term consequences of their NTDs, these compelling images by themselves do not provide an obvious metric that we can use to justify to the global community investments either in this group of diseases or in the people who suffer from them. Instead, we need another mechanism to convince policymakers that the “other diseases” deserve the same international attention as HIV/AIDS and malaria.



Figure 1.2 Disfiguring effects of the NTDs. (Top) Elephantiasis of the leg due to filariasis, Luzon, the Philippines. (Image from CDC-PHIL [ID#373]/CDC, 1962.) (Bottom) Guinea worm infection, with female worm emerging from the patient's foot. (© The Carter Center.)

One approach to measuring the full health impact of the NTDs is to use the disability-adjusted life years, or DALYs, which consider the number of healthy life years lost from either premature death or disability. Because of the chronic, disabling, and disfiguring components of the NTDs, the DALYs ascribed to them are substantial. Shown in Table 1.5 is a ranking of HIV/AIDS, malaria, tuberculosis, and the NTDs by deaths and DALYs, according to the GBD 2019. One of the greatest values of DALYs is that they facilitate the comparison of one condition with another. The data illustrate that the total disability resulting from the NTDs is almost as great as the disability from HIV/AIDS, malaria, or tuberculosis.⁸

The devastating comparison between the NTDs and the “big three” diseases—HIV/AIDS, malaria, and tuberculosis—has multiple implications for international efforts to control or eliminate infectious diseases. Today, much of the global enterprise targeting infections focuses primarily on HIV/AIDS, malaria, and tuberculosis. The DALY measurements suggest a strong rationale for considering the NTDs an important fourth leg of the chair. The rationale goes beyond merely comparing DALY estimates and pointing out the high disease burden resulting from the NTDs. Instead, an increasing body of evidence indicates not only that the NTDs exhibit geographic overlap and coendemicity with each other but also that the NTDs are coendemic with AIDS and malaria. The geographic overlap and coendemicity between the NTDs and malaria and AIDS will be further elucidated elsewhere (chapter 10). However, to briefly mention it here, there is new evidence that the morbidities resulting from the NTDs are additive with malaria and that some NTDs actually increase susceptibility to HIV/AIDS. The HIV/AIDS and NTD link is especially apparent for a condition known as female genital schistosomiasis, now considered one of the most important gynecologic conditions of adolescent girls and young women

Table 1.5 Ranking of the “gang of four” by deaths and DALYs

Condition	Initial 2006 estimates of DALYs annually ^a	Updated 2019 estimates of DALYs annually ^b
HIV/AIDS	84.5 million	47.6 million
NTDs	56.6 million	16.5 ^c –25.4 ^d million
Malaria	46.5 million	46.4 million
Tuberculosis	34.7 million	47.0 million

^a Data from Hotez et al., 2006a.

^b Data from Global Burden of Disease Collaborative Network, 2020.

^c The lower number is obtained by subtracting the DALYs for malaria from the combined NTDs and malaria total (62.9 million DALYs) provided by the GBD 2019.

^d The higher number is obtained by also including the DALYs from scabies (4.84 million DALYs) and venomous animal contact (4.09 million DALYs, including snakebite envenomation). The GBD 2019 does not currently include these two conditions in their NTDs category, but the WHO does. The WHO and IHME are working to harmonize their disease category assignments.

on the African continent.⁸ Therefore, there is an important rationale for not simply tackling the big three conditions in isolation, as currently advocated by the Global Fund, PEPFAR, and PMI, but also for embracing the NTDs to take on what is really a “gang of four.” This concept of integrating NTD control measures with those for malaria and HIV/AIDS will become clearer when we outline possible intervention strategies for NTD control (in chapter 10) and give the reason why we need to consider bundling treatment strategies for the NTDs together with those for HIV/AIDS and malaria (and even possibly why the Global Fund should incorporate NTD control into its programs).

7. *The NTDs are stigmatizing.* Not surprisingly, the blinding and disfiguring features of NTDs are stigmatizing and cause individuals to be ostracized by their families, their communities, and sometimes even health care professionals.⁶ In some societies NTDs are considered a sign of a curse or an “evil eye.” The social stigma of the NTDs strikes young women particularly hard, and as a result, these women are frequently abandoned by their husbands, prevented from holding or kissing their children, or unable to marry altogether. In some instances for example, community health workers have accused adolescent girls with female genital schistosomiasis of sexual promiscuity when in fact they acquired the condition by standing in water contaminated with schistosome larval stages.⁸ Specific examples of these stigmatizing consequences of the NTDs will be illustrated in the chapters dealing with schistosomiasis; LF, onchocerciasis, and podoconiosis; Buruli ulcer; leishmaniasis; and scabies, yaws, and mycetoma (chapters 3, 4, 6, 7, and 12, respectively).
8. *The NTDs have poverty-promoting features and other socioeconomic consequences.* The health impact of the NTDs may also represent only the tip of the iceberg in terms of their adverse effects on international development. Because of their chronic and disabling features, the NTDs also produce important and serious socioeconomic consequences that keep affected populations mired in poverty. The NTDs not only occur in the setting of poverty; they also actually promote poverty. For example, the cognitive and intellectual impairments resulting from hookworm-associated iron deficiency and anemia severely affect childhood education in terms of school performance and school attendance. Reduced school attendance leads to reduced future wage-earning capacity, while chronic hookworm infection among agricultural workers reduces worker productivity in Africa, Asia, and the Americas. Similarly, LF has a huge impact on productive capacity and costs a significant percentage of India’s gross national product, trachoma causes US\$5.3 billion in worldwide losses annually, and leishmaniasis is responsible for 0.43% of French Guiana’s social security budget.⁹ We are only beginning to understand the full economic impact of the NTDs, but these nascent studies indicate that the effects are likely to be profound.

However, even a full consideration of the enormous disability, disfigurement, and economic impact does not adequately convey the total devastation wrought by the NTDs. In an interview with a Sri Lankan LF-affected patient suffering from a severe limb deformity, we can get a palpable sense of the enormous shame and stigma from the limb or genital deformities caused by her disease and how they in turn promote an inexorable slide into poverty.¹⁰

I got this big leg when I was engaged to be married. When they heard it was filarial, they backed out of the marriage. I was earning Rs 2,500 (US\$25) a month from sewing, but when the leg got worse, the hospital doctor told me I should not pedal the machine. So I lost my income as well. When my parents died and my sister got married, only my brother and I lived in the house. My brother married and left the house, but my sister become widowed so came to live with me and her child. She had no money to buy a bandage as instructed by the clinic. So I went to a house to cook. When they saw my leg, they asked me not to come there anymore and found fault with me for hiding such a dirty illness from them. When I get fever, I cannot walk to the hospital, so I take paracetamol for 2 days and walk to the hospital when I feel less pain.

According to the Sri Lankan health care team investigating such cases of LF, the woman in this vignette, who previously lived on earnings of approximately US\$1 per day, lost even this meager income and became totally dependent on her brother-in-law.¹⁰ An important theme in the succeeding chapters is how stigma actually contributes to the morbidity of the NTDs and creates not only a medical crisis for the affected individual but also a tragic cycle of social and economic devastation for both the individual and his family. According to Swiss Tropical and Public Health Institute's Mitchell Weiss, the stigma of the NTDs contributes to suffering, delays the seeking of help, promotes nonadherence to treatment, negatively affects families and communities, and ultimately lessens support for services, control, and research.¹¹ Later, we will even see how, with some of the NTDs such as leishmaniasis and schistosomiasis, the stigma is particularly acute for young women, often leading to their verbal and physical abuse (in chapters 3 and 7), or how the stigma associated with Buruli ulcer is linked to beliefs about witchcraft (in chapter 6).

In summary, the health impact of the NTDs reflects their chronic and disabling features. But there are also educational and socioeconomic consequences that may even be greater. Neglect occurs at many different levels: at the community level because the NTDs arouse fear and inflict stigmas, at the national level because the NTDs occur in remote and rural areas and are often a low priority for health ministers, and at the international level because they are not perceived as global health threats equivalent to the high-mortality big three conditions.¹² Paul Hunt, previously the UN Special Rapporteur on the right to the highest attainable standard of health, pointed out that relief from the suffering caused by the NTDs is a fundamental human right, which unfortunately has been largely ignored.¹³ Despite their global importance,

we so far have no Bono equivalent to champion the plight of the 1 billion of the world’s poorest people who suffer from NTDs, and the total dollars thus far committed to NTD control are currently measured in the millions, not the billions.

Fortunately, this picture of neglect may one day turn an important corner, in part because of a new resolve by the WHO and national ministries of health, together with several key public-private partnerships dedicated to NTD control. Further, many of the organizations involved in NTD control have begun to partner through the WHO and new organizations including the END Fund and Uniting to Combat NTDs (discussed in chapter 10).¹⁴ These new organizations work to mobilize resources for the NTDs and to promote high-level advocacy from global leaders and well-placed individuals and organizations. At the same time, student groups are beginning to voice their concerns about the urgency of addressing the NTDs. These important, nascent efforts are about to lead to a modest revolution in global health and to make a huge impact on the world’s poorest people.

SUMMARY POINTS	<p>Introduction to the Neglected Tropical Diseases</p> <ul style="list-style-type: none"> • The NTDs are among the most common infections of the world’s poorest people, those living on less than US\$1.90 per day. • Nonemerging, ancient conditions • Chronic and disabling features • High morbidity, low mortality • DALYs almost comparable to those for HIV/AIDS, malaria, and tuberculosis • Coendemicity of the NTDs and with HIV/AIDS and malaria • The “gang of four” • Poverty-promoting features that keep populations destitute • Associated with profound stigma • Urgent need for stepped-up advocacy and resource mobilization
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Notes

1. The designation of HIV/AIDS as the “plague of the 21st century” is found in Skolnik, 2007, p. 191. The definition of “manifesto” is from Agnes, 2000, p. 874.
2. Kaiser Family Foundation, The U.S. President’s Emergency Plan for AIDS Relief (PEPFAR), May 27, 2020; <https://www.kff.org/global-health-policy/fact-sheet/the-u-s-presidents-emergency-plan-for-aids-relief-pepfar/>.
3. The original core list of 13 NTDs was shaped and refined by Molyneux et al., 2005; Hotez et al., 2006a; and Hotez et al., 2007. The WHO’s list of 17 NTDs was first reported in World Health Organization, 2010, and later revised to the current list of 20 NTDs; see <https://www.who.int/teams/control-of-neglected-tropical-diseases>. Details of NTDs among the poor in the United States and G20 nations can be found in Hotez, 2016.
4. The numbers of people infected with NTDs are now updated regularly by the Global Burden of Disease Study (GBD) based at the Institute of Health Metrics and Evaluation at the University

- of Washington, Seattle (Global Burden of Disease Collaborative Network. 2020). The latest GBD 2019 and previous estimates can be found at <http://www.healthdata.org>, by going to the GBD Results Tool, or by searching using the terms “GBD 2019” and “disease” and “level 3.”
5. Further details regarding Africa’s disease burden are found in Molyneux et al., 2005; and Hotez and Kamath, 2009. Information about the link between NTDs and slavery from Africa is found in Lammie et al., 2007.
6. Many of these features are excellently summarized in World Health Organization, 2003. The urbanization of NTDs was reported in Hotez et al., 2017.
7. Specific citations of ancient references on NTDs can be found in Hotez et al., 2006b.
8. Details of the overall estimates for deaths and DALYs resulting from malaria and the NTDs can be found in the GBD 2019 at http://www.healthdata.org/results/gbd_summaries/2019/neglected-tropical-diseases-and-malaria-level-2-cause (Global

Burden of Disease Collaborative Network, 2020). The deaths and DALYs combine NTDs and malaria; however, it is possible to delink the NTDs values from malaria by searching for malaria as a level 3 illness, or by going directly to the GBD 2019 by using the GBD Results Tool. This provides a value of 115,000 deaths for NTDs. However, now that snakebite envenomation has been added as one of the newest NTDs, the death estimate is closer to 200,000. The paper by Herricks et al., 2017 reports on some of the differences in DALYs and death estimates between the GBD studies and the community of NTD investigators. Details of female genital schistosomiasis can be found in Hotez et al., 2019.

9. Specific references for these data can be found in Hotez et al., 2007; Hotez and Ferris, 2006; and Hotez et al., 2009.

10. Interviews and qualitative analysis of patients with LF are described in Perera et al., 2007.

11. Some of the details about the relationships between stigma and health are outlined in Weiss and Ramakrishna, 2006. In addition, there are excellent descriptions of the stigmatizing aspects of NTDs in World Health Organization, 2003. In May 2008, a special issue of *PLoS Neglected Tropical Diseases* was devoted to the links between stigma and NTDs, with a lead article by Mitchell Weiss (Weiss, 2008). The effects of NTDs on the general and specific aspects of mental health were recently summarized in Litt et al., 2012.

12. The three levels of neglect are described in greater detail in World Health Organization, 2006, p. 3.

13. Hunt, 2006.

14. Details on Uniting to Combat NTDs can be found at <https://unitingtocombatntds.org/>. Details on the END Fund can be found at <https://end.org/>.

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