Introducing the Neglected Tropical Diseases: The Unknown Afflictions of the Developing World

Justin Dhat-Ming Tilak, BSc

KEY POINTS
- The neglected tropical diseases (NTDs) are a group of chronic infections that affect more than one billion people living in some of the most impoverished regions of the world.
- The NTDs perpetuate poverty among those that they affect through physical disability and disfigurement, decreased economic productivity, and social stigma.
- Funding dedicated to controlling the NTDs is disproportionately low relative to their burden.
- Treatment options for many NTDs are limited, and often plagued by major shortfalls. Unfortunately, the development of new drugs for NTDs is often considered economically unprofitable by the pharmaceutical industry.
- Increased awareness of the NTDs and their effects is necessary to ensure that the most vulnerable people in the world do not go unspoken for.

INTRODUCING THE NEGLECTED TROPICAL DISEASES

Over the past two centuries, advances in the understanding of communicable diseases have led to considerable reductions in their global burden. Due to advances in sanitation, germ theory, vaccination, antimicrobial drugs, and other factors, infectious disease is no longer the leading cause of death in the developed world.1 In poor areas of the world, however, infectious disease persists as a major cause of morbidity and mortality.1,2 A significant proportion of the global infectious disease burden can be attributed to a group of poorly understood tropical infections, collectively known as the neglected tropical diseases (NTDs).

The NTDs are a diverse group of chronic and debilitating infections, linked by their high prevalence in impoverished and marginalized communities, their overlapping geographic distribution, and their capacity to cause physical disability and disfigurement.3 International health organizations have designated 13 conditions, including ten parasitic and three bacterial infections, as the core NTDs though many other tropical infections share similar characteristics (Table 1).4-7 Transmission of these diseases occurs in areas of poor sanitation through contaminated food, water, and soil, as well as through bites from arthropod vectors that thrive in tropical climates.4 The consequences of these infections are not only medical, but also economic and social.8,9 Despite their significant global burden, the control of the NTDs is hampered by a lack of awareness of their existence and impact, and by limited efforts to develop and implement effective treatments.

THE DEVASTATING IMPACT OF THE NEGLECTED TROPICAL DISEASES

While relatively unknown in the developed world, NTDs negatively impact the developing world. Over a billion people across the globe are affected, particularly in sub-Saharan Africa, the Middle East, Latin America, the Caribbean, and Asia.10-17 In these regions, rates of parasitic infection are so high that many affected communities display polyparasitism rates exceeding 50%.18-20 While the 13 core NTDs cause an estimated 534,000 deaths per year worldwide, their real burden lies in their morbidity (Table 1).21 When taking into account not only years of life lost, but also years lived with disability, the burden of the NTDs is estimated at 56,600,000 disability-adjusted life years (DALYs); this is greater than the
burden of both malaria and tuberculosis (Figure 1). Furthermore, it is widely believed that current figures grossly underestimate the true burden of NTDs.2,22,23

Table 1. The 13 Core Neglected Tropical Diseases

<table>
<thead>
<tr>
<th>Neglected Tropical Disease</th>
<th>Estimated # Infected Worldwide</th>
<th>Estimated Mortality</th>
<th>Estimated Burden (DALYs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ascariasis (roundworm infection)</td>
<td>807,000,000 - 1,221,000,000</td>
<td>60,000</td>
<td>10,500,000</td>
</tr>
<tr>
<td>Trichuriasis (whipworm infection)</td>
<td>604,000,000 - 795,000,000</td>
<td>10,000</td>
<td>6,400,000</td>
</tr>
<tr>
<td>Hookworm infection (ancylostomiasis and necatoriasis)</td>
<td>576,000,000 - 740,000,000</td>
<td>65,000</td>
<td>22,100,000</td>
</tr>
<tr>
<td>Schistosomiasis (bilharzia)</td>
<td>200,000,000</td>
<td>280,000</td>
<td>4,500,000</td>
</tr>
<tr>
<td>Lymphatic filariasis (elephantiasis)</td>
<td>120,000,000</td>
<td>0</td>
<td>5,800,000</td>
</tr>
<tr>
<td>Trachoma</td>
<td>84,000,000</td>
<td>0</td>
<td>2,300,000</td>
</tr>
<tr>
<td>Onchocerciasis (river blindness)</td>
<td>37,000,000</td>
<td>0</td>
<td>500,000</td>
</tr>
<tr>
<td>Chagas’ disease (American trypanosomiasis)</td>
<td>15,000,000</td>
<td>14,000</td>
<td>700,000</td>
</tr>
<tr>
<td>Leishmaniasis (kala-azar)</td>
<td>12,000,000</td>
<td>51,000</td>
<td>2,100,000</td>
</tr>
<tr>
<td>African sleeping sickness (African trypanosomiasis)</td>
<td>&lt;100,000</td>
<td>48,000</td>
<td>1,500,000</td>
</tr>
<tr>
<td>Leprosy (Hansen’s disease)</td>
<td>400,000</td>
<td>6,000</td>
<td>200,000</td>
</tr>
<tr>
<td>Dracunculiasis (guinea worm disease)</td>
<td>2,000</td>
<td>Unknown</td>
<td>&lt;100,000</td>
</tr>
<tr>
<td>Buruli ulcer</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>Total</td>
<td>&gt;1,000,000,000</td>
<td>534,000</td>
<td>56,600,000</td>
</tr>
</tbody>
</table>

Further, NTDs also have significant effects on maternal and reproductive health.37 Schistosomiasis has been associated with infertility, both in males and females.38-40 In women, severe helmint infections result in anemia during pregnancy, which is associated with premature delivery, low infant birth weight, and poor infant health.41-45 Additionally, congenital infection due to mother-to-child transmission occurs with several NTDs.46,47 The best-known example is Chagas’ disease, which occurs in more than 5% of children born to infected mothers.48-50

Not only are the NTDs common in poverty-stricken areas, but they may also perpetuate poverty. Direct health care costs for the prevention and treatment of the diseases themselves, as well as lost labour time and decreased worker productivity, can both negatively affect the economy.9 NTD sequelae resulting in decreased productivity include blindness due to onchocerciasis or trachoma, and chronic lower limb lymphoedema due to lymphatic filariasis.51,52 These effects are particularly detrimental to communities that rely heavily on manual labour.8 Lost opportunity is a major contributing factor to the economic consequences of the NTDs, particularly in affected children. Chronic hookworm infection in children often produces impairments in cognition, which have been associated with significant reductions in future earning potential.33,34 The worldwide economic losses caused by the NTDs are difficult to estimate, but are believed to amount to several billion dollars every year.55,56

Figure 1. The burden of infectious diseases and funding allocated to their control.21,67,72
The social stigma associated with the NTDs is a major contributor to their burden, as it leads to societal exclusion of affected individuals. Reasons for stigma include cultural factors, the avoidance of disfiguring, and fear of contracting disease. Social isolation and rejection make it difficult for affected individuals to obtain employment, find friends or marriage partners, and seek social services. They may also develop feelings of shame and fear of being seen in public places, leading to self-imposed isolation. Social stigma affects the health outcomes of people with NTDs in many ways. Difficulties in obtaining employment or social services perpetuate poverty and contribute to social inequality, while feelings of fear and shame cause many to delay seeking health care for their conditions. Social stigma has been well-studied in leprosy, but has also been demonstrated for many other NTDs.

CONTROL OF THE NEGLECTED TROPICAL DISEASES

Though their combined burden is comparable to that of HIV/AIDS, malaria, or tuberculosis (Figure 1), NTDs continue to receive minimal attention from the scientific and international communities. Among scientific publications, journal articles about NTDs are substantially less numerous than those about conditions with similar disease burdens, a trend that has worsened in recent years. Furthermore, articles about NTDs are less likely to be published in high impact journals. Research and development funding for the NTDs is also disproportionately low. In 2007, only 7.29% of funding allocated to research and development into neglected diseases was dedicated to the core NTDs (Figure 1). The lack of research into the NTDs is of particular concern given that their burden is widely considered to be underestimated.

Interventions for the prevention and treatment of several of the core NTDs have been developed, most of which involve the use of antimicrobial drugs. Examples include treating soil-transmitted helminthiases with albendazole, treating schistosomiasis with albendazole and praziquantel, and preventing lymphatic filariasis with yearly doses of albendazole and ivermectin. Mass drug administration projects, such as The Global Programme to Eliminate Lymphatic Filariasis, have shown considerable success in recent years. Despite these efforts, the majority of people in need of treatment for NTD infections are still not receiving the drugs that they need. This is, in large part, due to a lack of funding to purchase and distribute drugs. Unfortunately, financial support from developed countries to assist in NTD control remains low. In 2007, a mere 0.6% of official development assistance for health funding provided to developing countries was dedicated to the control of the NTDs, while funding dedicated to several other infectious diseases was disproportionately higher (Figure 1).

Management options for other NTDs are limited by more than just a lack of funding. Many of the available drug treatments are of limited efficacy, are associated with severe adverse effects, and are plagued by rising rates of antimicrobial drug resistance. The need for new and more effective antimicrobial agents to treat many NTDs is clear, but has been largely overlooked by the pharmaceutical industry. Between 1974 and 2009, the number of new chemical entities approved and marketed by the pharmaceutical industry was in excess of 1,550. Of these, just 15 (<1%) were for the NTDs, and only one of them was approved after 2000. A further five entities for NTDs were in clinical development as of July 2009. As the NTDs affect mainly poor people in poor areas of the world, the development of new drugs for these conditions is often viewed as economically unprofitable by the pharmaceutical industry, and ignored in favour of developing drugs for conditions affecting wealthier populations.

CONCLUDING REMARKS

While some progress has been made in controlling the NTDs, further efforts are needed. NTDs persist as a major burden to the developing world, where they continue to devastate some of society’s poorest and most vulnerable people. NTDs cause significant physical disability and disfigurement, impair normal child growth and development, and are harmful to pregnant women. Economic and social consequences occur as a result of physical impairment and social stigma. The control or elimination of NTDs would improve the health of hundreds of millions of people, helping lift them out of poverty and social isolation.

Unfortunately, the burden of NTDs tends to remain hidden from all but those who suffer from them. Though the reach of NTDs is widespread in developing world, people living in poor and remote communities have no public voice. In addition to a lack of awareness, the control of NTDs is hindered by limited research, a scarcity of funding, and a shortage of effective treatments.

Controlling NTDs is a challenging task. Though different NTDs share many common characteristics, there is also considerable diversity in their causative agents and clinical features. As such, each of the NTDs presents its own unique challenges. More research into NTDs is needed to improve our understanding of how these conditions can be effectively diagnosed and controlled. Increased funding is needed to scale up the implementation of existing treatments and to stimulate the development of novel interventions. In addition, efforts are necessary to render the development of such interventions more appealing and profitable for pharmaceutical companies. Above all, increased public awareness of the neglected tropical diseases is essential to ensuring that the concerns of the poorest and most vulnerable people in the world do not go unspoken.
REFERENCES

Author Biography

Justin D. Tilak is a second-year medical student at the Michael G. DeGroote School of Medicine at McMaster University. He received his Bachelor of Science degree at Queen’s University.