

Review

Neglected tropical diseases need more than drug

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For centuries, there have been forgotten diseases among forgotten people including the endemic communities in Nigeria. Neglected populations living in poverty and in areas highly marginalized by the health sector throughout the world (e.g., slum and shanty-town dwellers, numerous indigenous groups and small ethnic groups, and the rural poor including migratory workers in agriculture, miners, and fishers) are often heavily burdened by neglected diseases. These neglected diseases constitute major public health problem and therefore can no longer be taken for granted. Fortunately, some drugs developed and donated by pharmaceutical companies are now effective in controlling morbidity and reducing the transmission of many of these neglected diseases. With these donated drugs and low-cost drugs such as praziquantel and diethylcarbamazine (DEC), it is feasible to control or eradicate seven of the neglected diseases through mass drug distribution. Notwithstanding the successes achieved by the international community in the use of drugs to control the neglected diseases, there is need for re-channelling of government expenditures toward activities to protect and promote health for all as well as convincing donors to also invest a major part of their financial contribution to address the persistent conditions of poverty (unsafe water, poor sanitation and refuse disposal) which, sustain the transmission and spread of neglected diseases. Also addressing the problem of lack of access to health services, low levels of literacy, inadequate nutrition and poor personal hygiene will help to synergistically support drug administration in the control/prevention and eradication of neglected diseases.

Key words: Neglected tropical diseases, control, drug.

INTRODUCTION

Many millions of people living in the tropic are cut off from the mainstream of social and economic progress by a combination of harsh economic circumstance, poor living conditions as well as poor environment and a heavy burden of disease. No wonder the Millennium Declaration, adopted by world leaders at the United Nations in September 2000, established eight millennium development goals to eliminate extreme poverty, hunger, and disease by 2015. The sixth goal, "to combat HIV–AIDS, malaria and other diseases," specifically addresses the health and economic impact of infectious diseases. This goal has led to considerable and welcomed large-scale financial support through strong initiatives sponsored by the Group of Eight (G8) governments to fight HIV–AIDS, tuberculosis and malaria (Hotez et al., (2007).

There is currently strong and huge global support put in place to control the most serious problems facing health planners, the big three: HIV/AIDS, tuberculosis and malaria. These control efforts are yielding impressive results. However, programs to combat many of the "other diseases," particularly the neglected tropical diseases, have not yet benefited from such support (Molyneux, 2004; Molyneux et al., 2005; Hotez et al., 2006 a; Hotez et al., 2006 b; Hotez, 2006). As a result, biomedical scientists are urging policy makers and health economists to also recognize that there are other diseases which have been neglected and which can be addressed at realistic cost effective interventions (Molyneux et al., 2005).

The World Health Organization (WHO) estimates that diseases associated with poverty are responsible for 45% of the total disease burden in developing countries (Brooker et al., 2006). These neglected diseases are found in 100 of the poorest countries in Africa, Asia and Latin America. They affect more than 750 million people and kill at least 500,000 every year (Hotez, 2005). Each

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year, these neglected tropical diseases strike millions of the world's poorest people in sub-Saharan Africa, Asia and Latin America.

NEGLECTED DISEASES (NDs)

The Millennium Development Goals (MDGs), as well as several other global initiatives have focused exclusively on the control of major communicable diseases with high mortality rates, such as HIV/AIDS, tuberculosis, and malaria. However, this focus has left out a considerable list of "other diseases" that have been aptly coined the **"neglected diseases" (NDs)** (Molyneux et al., 2005). These diseases have been given relatively little attention by national governments and are considered to be low priority international public health issues (Hotez, 2005).

The Neglected Diseases (NDs) are largely comprised of infectious tropical diseases. Today, NDs can be usefully considered as a group because they are concentrated almost exclusively among impoverished populations living in marginalized areas. Nearly all the people devastated by these diseases live in countries with less than US \$400 per capita income per year, where Governments are so poor that they spend an average of only US \$4 per person per year on health (WHO, 1990) or where health services are understaffed, under-funded and unevenly distributed. According to Molyneux et al. (2005) and Hotez et al. (2006 a), thirteen infectious diseases (parasitic and bacterial) known as the neglected tropical diseases include three soil-transmitted helminth infections (ascariasis, hookworm infection, and trichuriasis), lymphatic filariasis, onchocerciasis, dracunculiasis, schistosomiasis, Chagas' disease, human African trypanosomiasis, leishmaniasis, Buruli ulcer, leprosy, and trachoma. Furthermore Hotez et al. (2006b) noted that this could be expanded to include dengue fever, the treponematoses, leptospirosis, strongyloidiasis, food-borne trematodiasis, neurocysticercosis, and scabies, as well as other tropical infections.

Though the phrase "neglected tropical diseases" is commonly used in the literature today, we have instead chosen the broader phrase "neglected diseases" because some of the infectious diseases of concern in the Americas, such as plague and leptospirosis, are not geographically limited to the tropics and sub-tropics.

The infectious diseases identified as being neglected are among some of the most common infections in the estimated 2.7 billion people who live on less than \$2 per day (Hotez et al., 2007). These diseases according to Hotez et al. (2007) occur primarily in rural areas and in some poor urban settings of low-income countries in sub-Saharan Africa, Asia, and Latin America (Table 1).

These scourges cause tremendous pain and suffering ranging from ulcers, internal organ damage and disabling anaemia, to gross deformities of face and limb, blindness, brain damage and death (Lammie et al., 2006; Alvar et

al., 2006). In the words of the Director General of WHO, Dr. Hirashi Nakajima "beyond their toll of individual illness and death, these tropical diseases have insidious effects on the society. They impede national and individual development, make fertile land inhospitable, impair intellectual and physical growth and exact a huge cost in treatment and control". They cause some of the most intense human suffering, often among the poorest people on earth, and rob people of their dignity, independence and hope (WHO, 1992). Young victims according, Hotez et al. (2007) are stunted physically and cognitively, and their education suffers. Environmental conditions make vulnerable people particularly prone. Engels, and Molyneux (2010) noted that costly or unavailable treatment means that disease keeps them in poverty. There is incalculable social and psychological devastation (Weiss, 2008). In fact, "these diseases create a hitherto unrecognized burden of mental illness not only for sufferers but also for caregivers".

PROSPECTS OF CONTROLLING NEGLECTED DISEASES

It is clear from our discussion that these neglected diseases constitute major public health problem and therefore can no longer be taken for granted.

Since the late 1980s, biomedical scientists have worked insidiously to identify and develop new drugs and methods to control/eradicate these ancient diseases. Fortunately, four of these drugs developed by pharmaceutical companies are now effective in controlling morbidity and reducing the transmission of many of these neglected diseases.

These four drugs: Mectizan®, albendazole®, mebendazole® and zithromax® are not only effective but they are currently being donated free of charge to those in need by Merck & Co. Inc., GlaxoSmithKline, Johnson & Johnson and Pfizer respectively (Table 2). Together with low-cost drugs: praziquantel and diethylcarbamazine (DEC), it is feasible to integrate efforts to control or eradicate seven of the neglected tropical diseases through mass drug distribution.

These diseases are trachoma, hookworm infection, ascariasis, trichuriasis, onchocerciasis, schistosomiasis, and lymphatic filariasis.

With these new drugs, in sub-Saharan African, including Nigeria, where more than 500 million people are afflicted by neglected diseases, total annual treatment could be achieved for US \$ 200-400 million, a fraction of what it could cost to treat any of the big three: malaria, HIV/AIDS and tuberculosis. By comparison, the treatment for HIV/AIDS exceeds US \$ 200 per year per person for life of the individual while anti-tuberculosis treatment costs at least US \$ 200 per treatment (WHO, 2006).

Global Network on Neglected Tropical Diseases Control (GNNTDC), formed in 2006 is a partnership designed to

Table 1. The major neglected tropical diseases ranked by prevalence.

Disease	Global prevalence (millions)	Population at risk	Regions of highest prevalence
Ascariasis	807	4.2 billion	East Asia and Pacific Islands, Sub-Saharan Africa, India, South Asia, China, Latin America and Caribbean
Trichuriasis	604	3.2 billion	Sub-Saharan Africa, East Asia and Pacific Islands, Latin America and Caribbean, India, South Asia
Hookworm infection	576	3.2	Sub-Saharan Africa, East Asia and Pacific Islands, Latin America and Caribbean, India, South Asia
Schistosomiasis	207	779 million	Sub-Saharan Africa, Latin America and Caribbean
Lymphatic filariasis	120	1.3 billion	India, South Asia and Pacific, Sub-Saharan Africa
Trachoma	84	590 million	Sub-Saharan Africa, Middle East and Caribbean
Onchocerciasis	37	90 million	Sub-Saharan Africa, Latin America and Caribbean
Leishmaniasis	12	350 million	India, Sub-Saharan Africa, Latin America and Caribbean
Chagas disease	8-9	25 million	Latin America and Caribbean
Human African Trypanosomiasis	0.3	60 million	Sub-Saharan Africa
Leprosy	0.4	ND	India, Sub-Africa, Latin America and Caribbean
Guinea worm disease	0.01	ND	Sub-Saharan Africa
Buruli Ulcer	ND	ND	Sub-Saharan Africa

ND = Not determined

Source: Hotez et al, 2007, The New England J. Med, 357: 1018-1027.

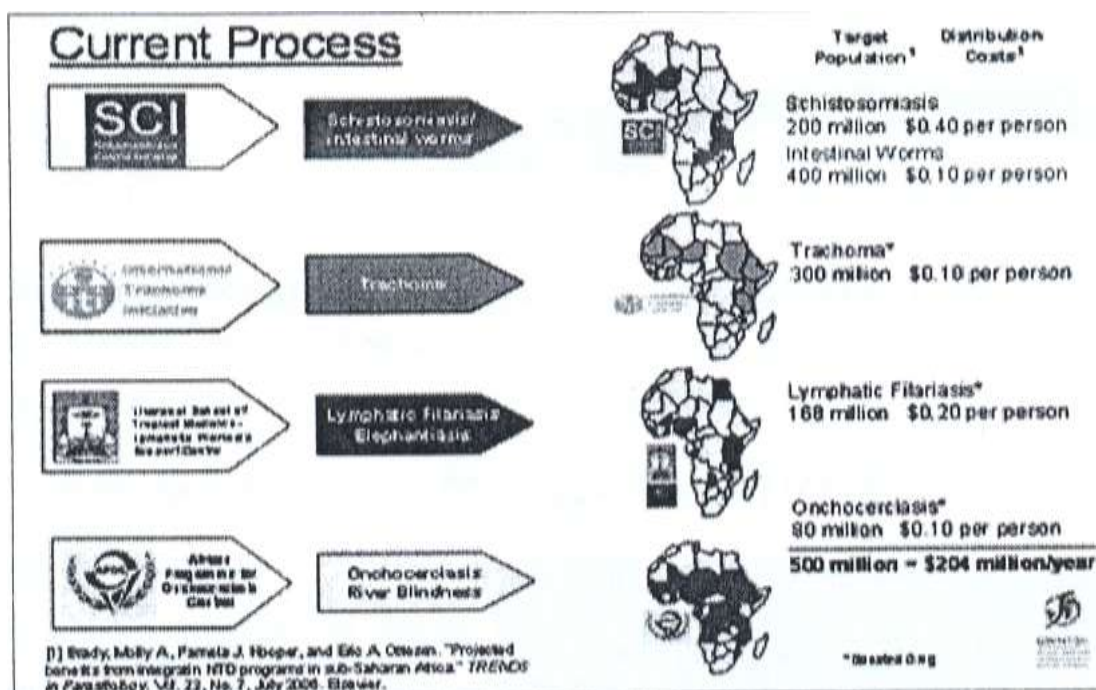
Table 2. Drugs currently being donated free of charge to those in need.

Donor Company	Drug Donation	Treatment	Donation Website
 MERCK	Mectizan™	River Blindness Lymphatic Filariasis	www.mectizan.org
 Pfizer	Zithromax™	Trachoma	www.trachoma.org
 gsk GlaxoSmithKline	albendazole	Intestinal worms and Lymphatic Filariasis	www.gsk.com/filariasis
 MedPharm	Praziquantel™	Schistosomiasis	www.medpharm.net
 Johnson & Johnson	Mebendazole™	Intestinal worms	www.jnj.com

Source: GNNTDs, Liverpool School of Tropical Medicine

raise the profile of neglected tropical diseases and to stimulate a paradigm shift in neglected diseases' control (Table 3).

For the first time, the neglected tropical diseases family is coming together in a large-scale effort to rapidly make impact on the most prevalent neglected tropical diseases

Table 3. Global Network on Neglected Tropical Diseases (GNNTDs).

Source: GNNTDs, Liverpool School of Tropical Medicine.

that afflict the world's poorest population. "Never before have many of these diseases been targeted for action, with time-limited goals supported by stable and committed partnerships. Never before have so many high-quality interventions been made available at low or no cost. Never before have such large numbers of people been protected or cured from crippling diseases. Supported by these trends, the international community is now close to eliminating or vastly reducing the burden of such ancient companions of poverty...." These public-private partnerships devoted to disease-specific control programmes have agreed to work together, in collaboration with World Health Organization, to design an integrated drug administration platform that addresses these neglected tropical diseases.

In January 2012, WHO (2012) published a road map setting target for the prevention, control, elimination and eradication of 17 neglected tropical diseases: lymphatic filariasis, onchocerciasis, dracunculiasis, schistosomiasis, Chagas' disease, human African trypanosomiasis, leishmaniasis, Buruli ulcer, taeniasis/cysticercosis, echinococcosis, endemic treponematoses, food borne trematodiasis, trachoma, dengue, rabies, leprosy, trachoma and soil-transmitted helminth infections. By the roadmap, WHO (2010) set target for the eradication of guinea worm infection (2015) and yaws (2020). With the WHO (2010, 2012) elimination/eradication roadmap, the London Declaration on Neglected Tropical Diseases, endorsed by partners and stakeholders, in January 2012 pledged to sustain, expand and extend control,

elimination and eradication and to ensure that the necessary supply of medicines and other interventions are supported (London Declaration on Neglected Diseases, 2012). The Second WHO Report of 2013, *Sustaining the Drive to Overcome the Global Impact of Neglected Tropical Disease* further elaborated the roadmap and described the need for sustainability of the control, elimination and eradication strategies and programmes (WHO, 2013).

On the issue of Private and Public partnership in the control, elimination and eradication of NTDs, 13 pharmaceutical companies, as well as the United States., United Kingdom and United Arab Emirate governments, the Bill & Melinda Gates Foundation, the World Bank and other global health organisations announced a new, coordinated push to accelerate progress toward eliminating or controlling 10 neglected tropical diseases (NTDs) by the end of the decade (by 2020) (WHO, 2012). "Uniting efforts with NTD-endemic countries, partners pledged to bring a unique focus to defeating these diseases and to work together to improve the lives of the 1.4 billion people worldwide affected by NTDs, most of whom are among the world's poorest".

In the largest coordinated effort to date to combat NTDs, the group announced at an event at the Royal College of Physicians that they would: sustain or expand existing drug donation programs to meet demand through 2020; share expertise and compounds to accelerate research and development of new drugs; and provide more than US \$785 million to support Research and Development

efforts and strengthen drug distribution and implementation programmes. Partners also endorsed the "London Declaration on Neglected Tropical Diseases," in which they pledged new levels of collaborative effort and tracking of progress (Bill & Melinda Gates Foundation, 2012).

Bill Gates, co-chair of the Bill & Melinda Gates Foundation said "Today, we have joined together to increase the impact of our investments and build on the tremendous progress made to date. This innovative approach must serve as a model for solving other global development challenges and will help millions of people build self-sufficiency and overcome the need for aid." The Gates Foundation announced a five-year, US \$363 million commitment to support NTD product and operational research.

To guide the effort against NTDs, the World Health Organisation launched a new strategy that sets targets for what can be achieved by the end of the decade (WHO, 2012).

During the launching of the roadmap, Dr. Margaret Chan, Director-General of the WHO noted that "The efforts of WHO, researchers, partners, and the contributions of industry have changed the face of NTDs. These ancient diseases are now being brought to their knees with stunning speed," "With the boost to this momentum being made today, I am confident almost all of these diseases can be eliminated or controlled by the end of this decade."

Speaking on behalf of the CEOs of the 13 pharmaceutical companies involved, Sir Andrew Witty, CEO of GlaxoSmithKline, said, "Many companies and organisations have worked for decades to fight these horrific diseases. But no one company or organisation can do it alone. Today, we pledge to work hand-in-hand to revolutionize the way we fight these diseases now and in the future"(WHO, 2012).

These pledges and Declaration came in response to WHO's 2010 report, which called for new resources to overcome NTDs (WHO, 2012). By these declarations, partners pledged to work together towards the achievement of the 2020 goals, to meet up the WHO's roadmap.

NEGLECTED DISEASES NEED MORE THAN DRUGS

Notwithstanding the successes achieved by the international community in the use of drugs to control some of the neglected diseases, our present challenges include the urgent determination of the distribution, levels of endemicity and intensity of these diseases. These will enable us define the high-risk areas/zones in the country where control measures are to be directed. The issue of coverage of the integration strategies are also very important. And because the numbers of affected people

are so great and hard to reach, we must develop ways to expand coverage.

Again, sustainability of control programme is a major challenge. Although great progress has been made in several countries (Molyneux, 2006; Utzinger *et al*, 2005), it is unclear whether existing financial resources and global political commitments are sufficient to reach the World Health Assembly's ambitious resolutions - for the global control or elimination of the neglected tropical diseases with the greatest disease burden as a public health problem by the year 2020 or sooner (Brady *et al*, 2006; WHO, 2006). This means that if we must prevent/control/eradicate these neglected diseases, we need more than drugs.

At this point, it is important to note that these neglected diseases share features that allow them to persist in conditions of poverty where they frequently overlap. These conditions of poverty include:

- Unsafe water,
- Poor sanitation and
- Poor refuse disposal, which sustain transmission cycles and favour the proliferation of vectors that transmit the diseases.

Other conditions, which encourage the incidence and spread of neglected diseases, include lack of access to health services, low levels of literacy, inadequate nutrition and Poor personal hygiene

Unfortunately, in the endemic areas, both physical and biological environmental factors are to the advantage of these neglected diseases. This is compounded by the socioeconomic environment which is reflected in the whole range of factors that affect the general standard of living, attitudes, beliefs and behaviour.

Neglected diseases are most prevalent among neglected populations living in poverty throughout the world (e.g., slum and shanty-town dwellers, numerous indigenous groups and small ethnic groups, and the rural poor including migratory workers in agriculture, miners, and fishers) and highly marginalized by the health sector. In some areas women and children may be considered neglected populations due to their limited access to health and social support services. This hinders their ability to exercise their basic human rights and fundamental freedoms, especially the right to physical and mental health. A reduction in the neglected diseases burden would enable these communities and groups to become more economically active and therefore further reduce the socioeconomic factors contributing to disease. A reduction in the total neglected diseases' burden may not only improve the overall economic performance of families and communities, but of entire nations.

The persistence of the "vicious circle" between poverty and poor health demonstrates the importance of linking the activities of the health sector with those of other sectors such as education, housing, water and sanitation, labour, public works, transportation, agriculture, environment, and industry and using human rights norms

and guidelines.

As far as this vicious circle persists, the current efforts by national and international organizations and agencies to control/eradicate neglected diseases through mass drug administration will not yield the expected result. This is because none of the health problems that affect a given population can be resolved and sustained exclusively by the health services system itself such as mass drug administration.

We are advocating a shift in policy frameworks from vertical to horizontal, integrated, inter-sectoral approach to neglected diseases prevention, control and elimination. While the mass drug administration should be encouraged to continue, we think that there is need for re-channelling of government expenditures toward activities to protect and promote health for all (including neglected populations) as well as convincing donors to also invest a major part of their financial support in neglected diseases control towards solving environmental health problems identified through integrative and inter-sectoral efforts.

When we put in place integrative and inter-sectoral efforts, persistent conditions of poverty (unsafe water, poor personal hygiene and poor environmental sanitation etc) which sustain the transmission and spread of neglected diseases will be addressed. Also addressing the problem of lack of access to health services, low levels of literacy, inadequate nutrition and poor personal hygiene will help to synergistically support drug administration in the control/prevention and eradication of neglected diseases.

Neglected diseases and the environment in which they flourish are intimately tied with other issues of sustainable development, therefore allowing the neglected diseases agenda to provide an ideal entry point to develop new paradigms of action. The introduction of basic public health measures in communities would significantly reduce the burden of a number of diseases where these elements play an important role. There is also a considerable overlap in the prevention and management of these diseases, permitting useful synergies amongst these efforts. It is now an opportune time to link an integrated neglected disease strategy with the newly emerging global partnerships addressing HIV/AIDS, tuberculosis and malaria, in order to take advantage of the economies of scale that occur during the scaling up process of these global initiatives (Hotez, 2006)

Integrated, inter-programmatic and inter-sectoral approaches are not new phenomena. They represent a working multi-disciplinary framework or strategy for which countries, technical assistance organizations and governments should work toward. In the specific context of the neglected diseases agenda, integrated, inter-programmatic and inter-sectoral approaches to reach marginalized populations or geographic areas, based on stratification of risks, provide added value for several reasons:

- They provide added benefits to the community at large by drawing attention to issues that generally fall outside the purview of the health sector and are intrinsically related with States' human rights obligations (e.g., improved housing and education, provision of clean water, safe disposal of excrement).
- They have the potential to greatly increase the standard of living for the local community by recognizing the economic impact that these diseases have as a result of disability and lost productivity.

Many complex issues, such as housing for the urban poor and local economic development require a wide range of resources and abilities that integration, inter-programmatic and inter-sectoral efforts are the only viable approaches to effectively address them over the long-term and help to reduce the duplication of activities and at the same time control great majority of neglected diseases.

Conclusion: In view of the fact that these neglected diseases are big obstacles to our socioeconomic development, and requires more than drug, efforts by the policy makers and socioeconomic developers in health care delivery system must be directed towards shift in policy framework. That is shifting from vertical to horizontal, integrated, inter-sectoral approach to neglected diseases prevention, control and elimination. While the mass drug administration should be encouraged to continue, we think that there is need for re-channelling of government expenditures toward activities to protect and promote health for all (including neglected populations) as well as convincing donors to also invest a major part of their financial support in neglected diseases control towards solving environmental health problems identified through integrative and inter-sectoral efforts.

These cannot be achieved without partnership. Partnerships are sine qua non for effective work in international health. While individuals, institutes, and agencies comprise the usual coalitions, linkages between research, training, and control activities are also essential in international science and public health, and a balance between these components must be fostered.

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