The neglected tropical diseases: a rags-to-riches story
The poorest of the poor have suffered from deadly, painful and disfiguring tropical diseases since ancient times, but the battle against neglected tropical diseases is now being won. Since 2007, WHO has helped streamline delivery of donated drugs and stimulate the development of new ones. In the London Declaration of 2012, leading pharmaceutical companies agreed to donate billions of dollars’ worth of drugs through 2020, guided by a technical strategy devised and managed by WHO. This bold collaboration is providing close to a billion people per year with access to free treatment and helping to put several of these tropical diseases on the path to elimination.

Though medically diverse, the neglected tropical diseases (NTDs) form a group because all are strongly associated with poverty, all flourish in impoverished environments, and all thrive best in tropical areas, where they tend to overlap. Most are ancient diseases that have plagued humanity for centuries. They blind, maim, disfigure, and debilitate their victims, causing untold misery that anchors populations in poverty.

Once widely prevalent, many of these diseases gradually disappeared from large parts of the world as economies developed and living conditions and hygiene improved. Today, the neglected tropical diseases have their hotbeds in the places left furthest behind by socioeconomic progress, where substandard housing, lack of access to safe water and sanitation, chronic hunger, filthy environments, and abundant insects and other vectors contribute to their efficient transmission. In the recent past, the need for control has been hidden from the international community as the diseases themselves rarely travel beyond such deeply impoverished settings.

The situation has changed dramatically over the past ten years, making the control of these diseases one of the best rags-to-riches success stories in modern public health. With more than one billion people affected, efforts to control these diseases are a pro-poor initiative on a massive scale – in effect, a frontal assault on a root cause of poverty. Stepped-up control is based on a deliberate decision not to wait for these diseases to gradually disappear as living conditions improve, but to strike aggressively using a population-wide preventive approach.

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The appeal of viewing the neglected tropical diseases in this way has been compelling for several groups, most notably the pharmaceutical industry. When the first NTD global partners meeting was convened by WHO in 2007, industry was present with commitments to donate large quantities of effective high-quality medicines to suppress common tropical parasitic and bacterial infections. That commitment opened the way for mass drug administration to at-risk populations with the goal of reducing the human reservoir of parasites and pathogens, eventually resulting in the interruption of transmission.

**With large quantities of safe, effective, and free drugs on offer, the goal of immediately expanding access emerged as a moral imperative.** It also threw down the gauntlet: if the world cannot deliver high-quality free drugs to those in desperate need, how will it manage to solve much more complex problems?

Several overarching principles and assumptions underpinned the design and implementation of control programmes. First, as the people in greatest need are the poorest of the poor, interventions – no matter how low the price – are unaffordable and must be made available free-of-charge. Drug donations are the only option.

Second, as most at-risk people live beyond the reach of effective health systems, interventions must be simple, safe enough to be administered by non-health staff, and undemanding, ideally requiring only once-yearly contact with the health services.

Third, diseases that are concentrated in very poor populations carry few market incentives for R&D. Many treatments are old and some have toxic side-effects that can be deadly. The job here is to move forward fast with what already exists while clamouring for better products, using field experience to define the ideal product profile, right down to the price.

Finally, ignorance is the first battle that must be fought in the war against extreme poverty. As these diseases are so deeply dreaded by affected populations, community engagement has huge potential to generate grassroots demand for treatment and reduce the stigma that so often rips away social opportunities, especially for women.

Many of these treatments produce tangible results that communities can readily understand. A person who takes a pill and then expels large numbers of worms provides highly visual evidence of cause and effect. Watching the crippling, stigmatizing signs of leprosy disappear in a community or seeing ugly skin conditions and bloody urine vanish provides powerful proof that physical pain, deformities, and emotional misery are not the inevitable companions of poverty. Instead, they can be deliberately and definitively ended. Hope is a precious gift for the extremely poor.

**A streamlined integrated approach**

As subsequent research would show, drugs for preventive chemotherapy, when distributed according to WHO guidelines, raise no safety issues when administered on a massive scale. Many are effective after a single once-yearly pill, and several can be administered by non-
health staff. For praziquantel for schistosomiasis, for example, a simple “dose pole” lets teachers deliver the right dose to schoolchildren according to their height. Research made two additional contributions: some pills provide protection against several diseases, and several pills can be safely taken together, further simplifying control programmes in the many areas where neglected tropical diseases overlap.

Those findings paved the way for simplified and streamlined approaches that reduced costs and logistical demands on countries. WHO technical guidance for an integrated approach was just one of many operational innovations. As the diseases frequently overlap, delivery systems for one have been used by others. Some programmes ride piggy-back on existing systems to deliver childhood immunization, bednets for malaria, nutrition supplements like vitamin A, and school meals provided by the World Food Programme.

In another boost to control, research pioneered by the Special Programme for Research and Training in Tropical diseases (TDR) showed that community-directed treatment can revolutionize the reach and sustainability of delivery systems: communities themselves take on the responsibility for inclusive drug delivery, supervised by the health services.

Funding followed feasibility. In 2008, the US Agency for International Development pledged $350 million for NTD control. In 2011, the UK’s Department for International Development pledged to increase its funding for NTD control from $78 million to $383 million over the next four years.
A watershed event

The event that most decisively rebranded NTD control occurred in January 2012, when Bill Gates, the WHO Director-General, the CEOs of major pharmaceutical companies, senior government officials from endemic and donor countries, and representatives of academic institutions and civil society gathered in London at a meeting entitled “Uniting to combat NTDs: ending the neglect and reaching the 2020 goals”. The 2020 goals, set for a core group of diseases targeted for eradication, elimination, or accelerated control, were spelled out in a WHO roadmap launched before the event.

The London meeting was a landmark in public health cooperation, setting an ambitious agenda for the next decade. It marked a massive expansion of support, including a donation of $363 million by the Bill and Melinda Gates Foundation. In the outcome document, the London Declaration, twelve of the world’s biggest pharmaceutical companies collectively committed to extend their donations through 2020 to help meet the control and elimination goals set by WHO. Some of these donations are open-ended – “for as long as needed” – and most are made through WHO. The value of donated medicines has been estimated at from $2 billion to $3 billion yearly.

The NTDs, so long starved for resources, were getting rich. Equally important was support from foundations and funding agencies, including the Drugs for Neglected Diseases initiative, to promote basic and applied research for the development of new treatments and diagnostic tests. For many diseases, new products are desperately needed.

The most difficult diseases: success against all odds

Unlike diseases amenable to preventive chemotherapy, African sleeping sickness, Buruli ulcer, Chagas disease, and leishmaniasis have been identified by WHO as requiring innovative and intensified disease management. All of these diseases have poorly understood burdens, lack optimal control tools, receive insufficient R&D investment, and affect the poorest of the poor. For decades, their control faced extremely complex challenges. Left untreated, severe permanent disabilities can develop. Fatality rates for sleeping sickness, Chagas disease, and leishmaniasis are the highest of all the neglected tropical diseases. The signs of early illness, when the prospects of treatment are best, are subtle and non-specific. Most poor people will not seek treatment until symptoms become severe. Active screening for cases is required, but difficult to carry out in remote areas.

For a long time, the only treatment options were old, dangerous, and extremely painful. Treatment required specialized care, including extended stays in hospitals, and diagnostic support from well-equipped laboratories. However, this situation has begun to change with the advent of new technical tools, supported by an increasing number of public-private partnerships for product development, which brings the best science to bear on the most neglected diseases. Thanks to these new tools, even these diseases are being beaten back as part of a comprehensive assault on the neglected tropical diseases.
Significant recent progress includes the development of rapid and reliable diagnostic tests, suitable for use in resource-constrained settings, for visceral leishmaniasis, sleeping sickness, and Chagas disease. Research shows that a single dose of the antifungal medication, amphotericin B liposomal (AmBisome), cures up to 96% of cases of visceral leishmaniasis that would otherwise be fatal. For African sleeping sickness, a new treatment combination therapy, nifurtimox-eflornithine, was added to the WHO Model List of Essential Medicines in 2009. Studies have shown that this combination therapy is a highly effective treatment option for one form of second-stage disease.

Attacked on multiple fronts, the burden of sleeping sickness has been reduced from more than 37,000 new cases in 1999 to well under 3,000 cases in 2015, representing the lowest yearly number since reliable records began.

Antibiotic therapy has revolutionized the management of Buruli ulcer, and WHO and its partners have guaranteed an uninterrupted supply of antibiotics to affected countries to ensure that all patients receive free treatment. However, progress remains constrained by the lack of a reliable diagnostic test suitable for use in the field.

In 2007, the control strategy for Chagas disease was scaled up. Donated drugs were secured, the screening of at-risk populations was improved, transmission through blood transfusion and organ transplants was systematically prevented, and new diagnostic tests were introduced.

The emergency response to outbreaks of leishmaniasis has been strengthened. For example, in South Sudan, more than 36,000 cases were treated from 2009 to 2014 with a low case fatality rate. In the Syrian Arab Republic, where the distinctive skin lesions became known as the “Aleppo ulcer”, more than 200,000 cases have been treated over the past three years.

In 2015, the target for the elimination of visceral leishmaniasis was achieved in 82% of sub-districts in India, in 97% of sub-districts in Bangladesh, and in 100% of districts in Nepal. Those countries have adopted single-dose AmBisome as the first-line treatment; WHO supplies the medicines donated by the pharmaceutical industry.

Following an intense seven-year campaign based on active case finding and intramuscular injections of penicillin, India eliminated yaws. The last case occurred in 2003, ending a disease that had plagued the country for centuries. Prospects for elimination of the disease elsewhere were considerably increased in 2012, when researchers showed that a single dose of azithromycin, a well-known and safe antibiotic, cures yaws in the same way as intramuscular injections of penicillin. That breakthrough shifted the control strategy to mass drug administration aimed at reaching all people in endemic areas with a single pill. The prospects for yaws elimination in the remaining 13 endemic countries look much brighter as a result.

All of these achievements have benefitted from collaboration with the pharmaceutical industry. Apart from donating supplies of drugs, participating companies provide funds for drug delivery within countries. Drug donations are made to WHO. **WHO is in charge of distributing the medicines, in line with its own technical strategy, for which it has sole responsibility.**
Rapid impact interventions: spectacular progress

For diseases with rapid impact interventions, progress has been spectacular. For example, supplies of praziquantel for schistosomiasis control are now sufficient to blanket every school in sub-Saharan Africa. Donations of praziquantel, albendazole, and ivermectin are being distributed as a rapid-impact package to control schistosomiasis, soil-transmitted helminths, and lymphatic filariasis. Ivermectin, a drug that earned its co-discoverers the 2015 Nobel Prize in Medicine, has already freed 18 million West African children from the risk of blindness and is now being used to shrink the map of onchocerciasis even further. Donations of ivermectin presently amount to about 270 million treatments each year.

Trachoma, the world’s leading infectious cause of preventable blindness, is strongly associated with flies and filth in conditions of extreme poverty. Donations of the antibacterial agent azithromycin are a cornerstone in the WHO four-pronged SAFE strategy to eliminate blinding trachoma (surgery for those with trichiasis, antibiotic treatment to clear conjunctival infection, and facial cleanliness and environmental improvement to reduce transmission). To date, Oman, Morocco, and Mexico have been validated by WHO as having eliminated trachoma as a public health problem.

Success in Morocco followed several decades of community-based interventions and surveillance, supported by government-sponsored training of medical and nursing staff, including training in surgical skills. Beginning in the mid-1990s, all four components of the SAFE strategy were fully implemented. Antibiotic coverage exceeded 80% in each treatment round in each affected province. Beyond demonstrating that the SAFE strategy worked, the initiative brought multiple other benefits to the country’s poorest communities. Household access to potable water increased from less than 20% in 1990 to more than 90% in 2007. A rural electrification system delivered power to more than 2 million households. Simultaneously, extreme poverty virtually vanished.

The incidence of guinea-worm disease, slated for eradication, has been reduced from an estimated 3.5 million cases in 1986 to just 25 cases in 2016. In that year, only three countries reported cases: Chad, Ethiopia, and South Sudan. However, the surprising finding, first in Chad, that dogs can serve as a second mammalian host is likely to delay achievement of the eradication goal, though not derail it. The eradication of guinea-worm disease will mark the first time an infectious disease was vanquished by community engagement and behavioural change, without support from a vaccine or treatment.

The success of these various partnerships makes an additional important point. When all partners work according to an agreed technical strategy, devised and overseen by WHO, the Organization can collaborate with the pharmaceutical industry at no cost to its integrity.

Of the core diseases targeted for eradication, elimination, or accelerated control, lymphatic filariasis is racing fastest towards the finish line. Several external reviews of the programme show strong progress towards the goal of eliminating this disease by within the next few years.

Since WHO established the global programme to eliminate lymphatic filariasis in 2000, mass drug administration and other interventions are estimated to have prevented 97 million cases, averting more than $100 billion in economic losses. A cumulative total of 6.2 billion treatments have
been delivered, covering more than 820 million people with at least one treatment course. To date, WHO has validated the elimination of lymphatic filariasis in ten countries as diverse as China, Cambodia, and Sri Lanka. An additional 12 countries have been able to stop mass drug administration and are now in a surveillance phase.

Haiti, with its well-recognized resource constraints, provides an especially remarkable example. In 2012, the country scaled up mass drug administration to reach all endemic areas. Since then, Haiti has been able to stop treatment in nearly 43% of endemic areas, while extending treatment to 4.2 million people in the remaining targeted areas.

The momentum continues to build. In sub-Saharan Africa, an unprecedented effort to map NTDs has pinpointed areas of endemity, allowing a much more targeted approach to mass drug administration and the surveillance needed to oversee its impact on disease transmission. An extended special project for the elimination of neglected tropical diseases in Africa was launched in 2016.

The stunning success over the past ten years has provoked an intriguing question: can poverty be treated with pills? Not entirely. To make a true dent in extreme poverty, the current frontal assault on the neglected tropical diseases must be combined with the broader attack on the social, environmental, and economic determinants of health called for in the 2030 Agenda for Sustainable Development. Targets set for water supply, sanitation, nutrition, and housing will likely have the largest long-term impact.

On current trends, though, many of these ancient diseases may well be brought to their knees before the 2030 deadline arrives.
This report is available on WHO’s website
www.who.int/publications/10-year-review/en/