DNDi
Drugs for Neglected Diseases *initiative*

Raising the Profile of Neglected Tropical Diseases by Bernard Pécoul

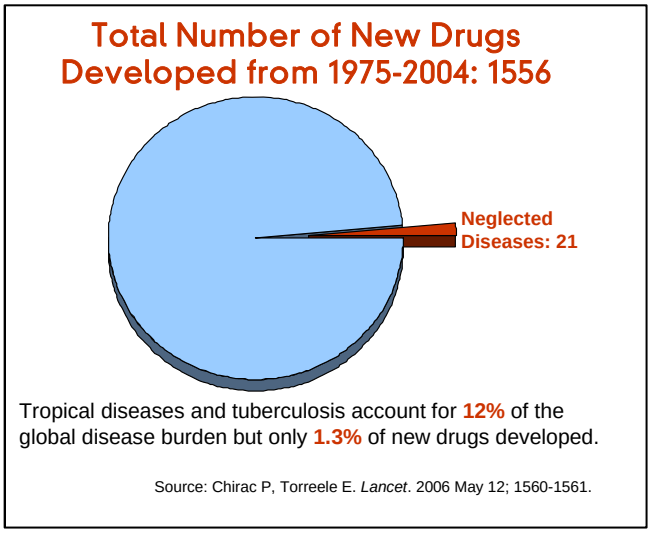
What is the problem?

Despite the phenomenal changes in medicine over the past half-century, with therapeutic advances saving many millions of lives, adequate drugs are not available for many diseases affecting poor, neglected populations in the developing world.

While much attention in the past decade has focused on combating the 'Big Three' neglected diseases (HIV/AIDS, malaria, and tuberculosis), many other tropical diseases have failed to attract adequate resources. Neglected tropical diseases (NTDs) kill millions of people each year and aggravate poverty in the developing world. The world's sixth leading cause of disability-adjusted life years (DALYs), NTDs exact a worldwide cost that is greater than road traffic accidents or tuberculosis.[1]

For NTDs that can be effectively diagnosed and treated with existing tools, enormous challenges must be overcome with regard to access – getting treatments to those who need it. Additional challenges stand in the way of combating NTDs for which the drugs being used often date back to colonial period and are simply inadequate by today's standards.

For example, deadly parasitic diseases such as sleeping sickness, leishmaniasis, and Chagas disease cause substantial morbidity and mortality worldwide; yet, because of a combination of market and public policy failures, no adequate tools exist to diagnose and treat these fatal conditions. In 2007, less than 5% of USD 2.5 billion in total funding for neglected diseases R&D went to these deadly diseases.[1] And, in the US, where billions of dollars are spent by the government on medical research, only USD 17 million was spent on R&D for desperately needed new treatments for these diseases.[2]



Existing therapies are often toxic, prohibitively expensive, and need to be administered for long periods by injection – characteristics that are inappropriate for resource-poor environments. In the case of sleeping sickness, diagnostic tools are inadequate, and the few drugs that are available are toxic (i.e. melarsoprol, which kills 1 in 20 patients), difficult to use, and increasingly ineffective in preventing death (up to 60% resistance). For visceral leishmaniasis, another disease that is fatal when left untreated, major obstacles include invasive diagnostics, long treatments (30 days), and drug resistance (up to 65% in India). Meanwhile, no drugs exist at all to treat patients with Buruli ulcer or chronic Chagas disease.

What can be done? A new model for drug development is delivering results…

Several non-profit product development partnerships (PDPs) are working to fill the gaps in essential health tools for diseases that have been neglected by the "profitable market"-driven R&D system. At the end of 2004, 75% of active drug development projects for neglected diseases were conducted by PDPs, with 8-9 new drugs expected in the market by 2010.[3] These emerging PDPs offer a valuable alternative model to the traditional one: R&D is no longer financed by a product's sale price. Thus the cost of R&D and the product price are separated, making medicines more affordable and accessible to those who need them.

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DNDi is one such PDP that is currently developing new treatments against sleeping sickness, leishmaniasis, Chagas disease, and malaria. DNDi's objective is to deliver six to eight new treatments by 2014 for these diseases and to establish a robust R&D pipeline for additional new medicines. In doing so, DNDi also works to use and strengthen existing capacities in disease-endemic countries, and to raise awareness and advocate for the need to develop new treatments for the most neglected diseases.

Established in 2003 by Doctors Without Borders/Médecins Sans Frontières and Institut Pasteur along with four publicly-funded research organizations in neglected disease-endemic countries – the Indian Council for Medical Research (ICMR), the Kenya Medical Research Institute (KEMRI), the Oswaldo Cruz Foundation (Fiocruz) in Brazil, and Malaysian Ministry of Health – DNDi works in partnership with industry, academia, other PDPs, NGOs, and governments to advance on its objectives.

DNDi's delivered products represent examples of needs-driven innovation that provides patients in resource-poor settings with important improvements in treatment options. However, PDPs alone cannot meet the urgent needs of neglected patients.

What else needs to be done?
The changes seen in the past decade offer a new landscape in which to collaborate and to advance essential health, but greater investments (complemented with new and adapted funding mechanisms) are needed from both governments and the private sector to ensure that these efforts are sustained and strengthened.

For example, DNDi requires a total of USD 350 million in order to achieve its objectives of building a robust pipeline and delivering 6-8 new treatments by 2014. To date, a diversified group of public and private donors has contributed to DNDi delivering new products to the patients most in need. However, **USD 200 million more is needed for DNDi** to fully realize its goals.

DNDi's main accomplishments into 2009

- **Largest-ever R&D portfolio** for potential new treatments for sleeping sickness, visceral leishmaniasis, and Chagas disease
- **Clinical research capacity** established in extremely difficult, resource-poor, rural settings in Africa
- **Two fixed-dose antimalarials** (**ASAQ** and **ASMQ**) **delivered** to patients in Africa and Latin America, respectively
  - The first pediatric strengths in such a fixed-dose combination
  - **Millions of these child-friendly, easy-to-use products have been delivered**
- **Improved sleeping sickness treatments**
  - **NECT**, a simpler, safer, shorter treatment for stage 2 sleeping sickness has successfully completed phase III clinical trials
  - **Fexinidazole**, a new sleeping sickness drug candidate, begins clinical trials in 2009

Public leadership is needed to implement policy changes that will support development of new, essential health tools, to ensure equitable access for affected populations, and to contribute to the development of innovative needs-based measures such as IP management policies to encourage needs-driven R&D, technology transfer, and strengthening of research capacities in developing countries. The private sector, including the corporate and philanthropic communities, must devote additional resources, both funding and expertise.

Together, we can make a difference in the lives of the most neglected – the time to act is now – patients are waiting.

[1] Hotez et al. *N Engl J Med.* 2007. 357:10.
[2] The World Can't Wait: More Funding Needed for Research on Neglected Infectious Diseases. Washington, DC: Families USA: 2008.
[3] Moran et al. *The New Landscape of Neglected Disease Drug Development. London, UK: Pharmaceutical R&D Policy Project, London School of Economics. 2005*