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POLICY

Neglected Diseases, Delinquent Diagnostics

DIAGNOSTIC TESTS CONSTITUTE 3 TO 5% OF HEALTH CARE SPENDING BUT INFLUENCE ~70% of health care decisions (1). Furthermore, less than 5% of annual spending on R&D is allocated to diagnostics for neglected diseases (2)—tropical infections common in underdeveloped countries, such as malaria, leishmaniasis, and tuberculosis (TB) (3).

Last month, the United States and 26 other countries commenced an effort—the Global Health Security Agenda—to prevent and address infectious disease outbreaks before they can spread around the world (4). The effort will focus on improving disease monitoring and developing tests for various pathogens. Although the initiative recognizes the need for new diagnostics, the expenditures for the entire effort are hardly sufficient for the extensive undertaking (\$40 million this year from the U.S. Centers for Disease Control and the U.S. Department of Defense and \$45 million being sought for next year).

Relative to therapeutic R&D, modest investments in diagnostic technology can lead to dramatic improvements in health outcomes, but technology companies need incentives to enter this underfunded arena. Here, I offer recommendations for addressing the challenges facing the diagnostic industry.

PERIL AT THE POINT OF CARE

New diagnostics for neglected diseases permit improved patient outcomes and allow for measurement of the impact of programs designed to deal with neglected diseases. However, disease control often fails because diagnostic tests are unavailable, unaffordable, or too complex to be applied in remote corners of the world. For example, 22 countries have a high incidence of TB (a bacterial disease caused by *Mycobacterium tuberculosis*) despite the existence of antibiotics (5). Control of TB depends on the rapid identification and treatment of active cases. The ability to discern whether individuals are infected with *M. tuberculosis* or have progressed to infection with a multidrug-resistant strain is crucial for establishing the proper therapeutic regimens for infected individuals and for protecting those with whom they come in contact.

Although it can now be accurately detected and effectively treated, malaria remains a global disease threat because many malarial regions of the world lack access to state-of-the-art diagnostics (6). Without the proper molecular tools, rapid diagnosis of malaria is particularly difficult in its early stages because its symptoms cannot easily be distinguished from many other diseases. Nonmalarial febrile illness is responsible for much of the burden of preventable childhood mortality in low-income countries. Progress is hampered by a lack of knowledge about the frequency and distribution of the pathogens involved and a dearth of point-of-care (POC) diagnostics and screening programs to identify them, preventing effective management of these generally treatable conditions.

Diagnosis and subsequent treatment of human African trypanosomiasis (sleeping sickness) remains difficult because the existing analytical tools are ineffective in the remote, impoverished areas where the disease thrives. Because early infection manifests few specific symptoms, cases are rarely detected until they are in advanced stages. By then, treatment requires expensive and highly toxic drugs. The parasitic disease leishmaniasis is endemic in 98 countries and responsible for ~50,000 deaths per year. Nearly 350 million people are at risk of contracting leishmaniasis, and some patients can become reservoirs for transmission. But current diagnostic procedures are highly invasive and expensive, which blocks improvements in clinical outcomes. Untreated Chagas-disease patients remain infected for life. Current diagnostic methods—which help to determine the appropriate medical treatments—are insufficient to address this challenge because they are inaccessible, are unaffordable, and cannot be easily applied in the remote areas where the parasites flourish.

There is no proper health intervention without an accurate diagnosis. Thus, from a world-health perspective, reliable diagnostic tests for neglected diseases are critical. Although governments and private foundations have the goal of providing equitable and timely medical care in low-resource settings, the absence of effective diagnostics still pre-

cludes millions from receiving effective treatment and imposes a greater burden on health costs in those countries that can least afford it.

DELIVERING DIAGNOSTICS

For a diagnostic test to be appropriate in low-resource countries, it must display the characteristics set forth in World Health Organization (WHO) guidelines: affordable, sensitive, specific, user-friendly, robust and rapid, equipment-free, and deliverable (ASSURED) (7). Furthermore, successful introduction of a new test depends on effective collaboration with multiple entities: companies that develop the diagnostic tests, the health care industry, and local governmental health ministries. Add to this weak public health systems with a chronic lack of funding, and one can quickly discern why manufacturers are not racing to make investments in these diagnostics.

For the most part, funding for neglected-diseases diagnostics relies heavily on the public sector and, to a lesser degree, on philanthropy (8). Despite the importance of accurate diagnosis to health outcomes and the economic benefits of reducing the cost of disease management in the developing world, current funding is anemic.

CURES FOR DIAGNOSTIC WOES

Make the case for the economic benefits of diagnostics. Major donors to global-health funding must be better educated on the importance of diagnostics in the fight against neglected diseases. If governments and philanthropic organizations gain a greater understanding of the economic value of diagnostics to world health, they are more likely to step up their investments in diagnostic development. Although potential funders may appreciate the impact of reliable diagnostics on treatment, there is still an underappreciation of the value of diagnostics in reducing the overall cost to health systems in low-resource settings.

Although funding for diagnostics R&D for the developing world increased from \$62 million to \$118 million between 2007 and 2011, this jump is not nearly sufficient to address global health goals espoused by governmental organizations. It is estimated that funding for malaria alone must increase fourfold, to \$50 million per year, in order to address the goals that were established by the global malaria community (8). Although the world-health community focuses on the number of deaths caused by neglected diseases, data on disability-adjusted life years is also a useful measure for calculating disease burden. But well-designed studies must be conducted and statistically valid results disseminated to relevant funding sources, in a digestible format, if we are to show that by the introduction of robust diagnostics, overall healthcare costs can be substantially reduced over a specific period of time.

Attract new funding sources. Funding sources for diagnostics development is concentrated in the public sector, with the philanthropic sector being limited, for the most part, to the Bill and Melinda Gates Foundation (8). Scientists and policy-makers must devise ways to bring more foundations into the diagnostic arena and to attract other sources of capital. For example, the mineral industry in South Africa and other endemic countries has an economic interest in protecting the health of its employees. One can make a strong case that investing in infectious disease diagnostics is in a company's interest. For example, a test that can easily discern whether employees have TB would benefit a company by preventing the spread of the disease among its workforce.

Governmental bodies in countries that have endemic diseases such as TB must be convinced to contribute to diagnostic development efforts for the benefit of their citizens. Contributions can consist of direct funding or donation of resources in kind, such as clinical trial support in facilities controlled by governmental entities. Even when seeking to promote its own industries, direct government support can be a relevant source of funding. For example, the Chinese government—in order to assist local companies to compete with their Western counterparts—awarded \$83 million worth of molecular, biochemical, and immunological diagnostic reagents as well as physical laboratory space and indicated that it will spend an additional \$103 million on basic research.

Create incentives to attract manufacturers. Diagnostics manufacturers also must be incentivized to enter the market for neglected diseases. The fact that diagnostic development costs generally are more modest as compared with therapeutics or vaccines has not been sufficient to attract manufacturers to this marketplace. By providing manufacturers with scientific and regulatory expertise and funding, diagnostics-focused product develop-

ment partnerships (PDPs) can help these craftsmen reduce the cost and time of diagnostics development. This assistance would enable the less well capitalized or nascent manufacturers to introduce their products to the world market on an accelerated timeline.

As has been done with therapeutics for neglected diseases, advanced market commitments for diagnostics for low-resource settings create a larger market for manufacturers beyond the developed world. Donors agree to pay for new diagnostics when they are developed at predetermined prices. Such an agreement would create incentives for firms to identify and pursue innovative technologies. For donors, there would be no cost unless the diagnostic is developed.

Leverage funding by focusing on PDPs. Funding should be directed toward PDPs (or other entities) that have successfully developed diagnostics for neglected diseases so as to leverage their expertise and resources (such as disease specimen banks, clinical trial expertise, and mentoring services) to manufacturers. POC diagnostics must overcome multiple obstacles to achieve adoption in the developing world, and an eventual successful roll-out requires effective collaboration with numerous parties, from the initial design of a diagnostic test to its ultimate adoption in an endemic country. PDPs have the coordination mechanisms and experience to deal with these complexities.

Foster collaboration among PDPs. Collaborations among various PDPs could help to leverage their respective expertise and thus enhance diagnostics development. The Global Alliance for TB Drug Development (www.tballiance.org) and FIND already have initiated such efforts, which recognize that the coupling of new TB drugs with innovations in diagnostics holds greater promise for improving patient outcomes.

Enhance funding coordination among donors. Funding for diagnostic development should be better coordinated among donors in order to avoid having small grants result in underfunding projects or duplicated research efforts, with the net effect that product development is slowed or abandoned for lack of resources. It is also difficult to undertake projects if the funding through completion is uncertain.

One way to achieve coordination is for governments, foundations, and other donors to be part of global networks that establish the relevant funding priorities for diagnostics and make recommendations to the participants for the funding of programs within the purview of the network. This approach will help to avoid multiple grant applications by an organization, underfunding of projects, and duplicative research. The network can share information so as to make better funding decisions and could also serve as a vehicle for attracting additional donors. An example of such a network is the PDP Funders Group, which was created by public and private organizations as an informal network that provides financial support for PDPs developing new health-related technologies.

– Mark Kessel

1. X. Mao, T. J. Huang, Microfluidic diagnostics for the developing world. *Lab Chip* **12**, 1412–1416 (2012).
2. BioVentures for Global Health, *The Diagnostics Innovation Map: Medical Diagnostics for the Unmet Needs of the Developing World* (BioVentures, Washington, DC, 2010). www.bvgh.org/LinkClick.aspx?fileticket=-a1C6u2LE4w%3D&tabid=91.
3. WHO, Neglected diseases. www.who.int/neglected_diseases/diseases/en.
4. Global Health Security Agenda (2014); www.hhs.gov/news/press/2014pres/02/20140213a.html.
5. WHO TB report. www.who.int/tb/publications/global_report/2011/gtbr11_main.pdf.
6. FIND diagnostics report. www.finddiagnostics.org/export/sites/default/about/annual_reports.
7. M. Urdea, L. A. Penny, S. S. Olmsted, M. Y. Giovanni, P. Kaspar, A. Shepherd, P. Wilson, C. A. Dahl, S. Buchsbaum, G. Moeller, D. C. Hay Burgess, Requirements for high impact diagnostics in the developing world. *Nature* published online 22 November 2006 (10.1038/nature05448).
8. FIND, *factsheet*. www.finddiagnostics.org/export/sites/default/media/news/pdf/g-finder-factsheet_dx-rxd-neglected-diseases.pdf.