Attention to Innovation

There are impediments to developing drugs to fight emerging diseases

Carol A. Nacy

WHEN new medical threats surface, such as the Ebola virus in Africa, we decry the human toll and ask why pharmaceutical companies don't do more to find medical solutions (Surowiecki, 2014). There are several reasons that innovations are often slow in coming, among them poor economic incentives and bad messaging.

In 2003, after the outbreak in China of Severe Acute Respiratory Syndrome (SARS) that spread to 37 countries and killed 775 people, infectious disease physicians prepared a graphic for the *New York Times* that placed deaths from SARS in context with other global infectious menaces. At the top of the disease-impact list was tuberculosis (TB). Several million people worldwide, most at the peak of their economic productivity, die from TB every year. It is deadly when contracted with HIV/AIDS.

Although we agonize over new, mysterious infections like SARS or Ebola, we long ignored TB, which has killed more people over the last 100 years than any other infectious disease.

If even TB did not attract new drug development efforts until recently, how will research into more localized infections be encouraged? Part of the answer lies in deciding how to finance the enormous development cost, estimated at over $1 billion per drug (PhRMA, 2013), of introducing new and novel treatments for global health threats that affect but a few thousand people. That is, who will pay?

However, it is not just the economics of new product introductions that discourages pharmaceutical industry interest in infections that are prevalent outside advanced economies (*Wall Street Journal*, 2014). Public health messaging also plays an enormous, if unintended, role. Governments and international health organizations, in trying to manage always-scarce public health resources, tend to concentrate their efforts on more efficient use of existing tools. This emphasis on improvements in delivery is frequently interpreted by pharmaceutical manufacturers, rightly or wrongly, as a signal that authorities see no unmet medical need, only efficiency issues.

TB is an excellent example of how public health messaging impeded drug development for decades. For the last 40 years, TB has been treated with four antibiotics that were discovered between 1950 and 1970. The drugs are reasonably effective when taken in combination for many months, but they have unpleasant flulike side effects and toxicities, such as liver damage. The six-month treatment period and the side effects cause many patients to quit taking their drugs before their infection is cured. As a result, the residual TB bacteria develop resistance to the antibiotics.

When this serious treatment problem was recognized, the public health solution was not to call for safer and faster-acting drugs, but to initiate a delivery program that would help patients take the 40- to 60-year-old drugs faithfully for the full treatment period. Nevertheless, patients continued to stop treatment early, and resistance of TB bacteria to the old drugs increased. Some strains of TB bacteria are now resistant to all available antibiotics. Drug-resistant TB is a major global health threat—the World Health Organization estimates that more than 500,000 new cases of multidrug-resistant TB are among the 9 million TB cases reported annually. Drug-resistant TB is at least 10 times more costly to treat, with a worldwide success rate of less than 50 percent.

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In the last 15 years, statistics on drug-resistant TB convinced the pharmaceutical industry that TB is an unmet medical need, and several companies responded with discovery programs for new drugs that are safer and work better than existing drugs. The 10- to 15-year development timeline for new drugs, from discovery to market authorization, means that the industry is just in time to address the growing crisis of multidrug-resistant TB. Two novel TB drugs were recently approved by the EU and U.S. authorities—in 2012 and 2014—and many other innovative TB drugs are nearing completion of clinical development, including two from my company, Sequella.

There are certainly other infectious diseases that we recognize could cause serious disruption of civil society. To encourage industry to develop drugs that could change the trajectory of potential global epidemics, the global public health community must send the right message—asking for innovation not just efficiency, identifying clearly where it wants research resources dedicated, and providing the economic incentives and reimbursement rates that will justify the enormous development costs of such drugs. ■

Carol A. Nacy is Chief Executive Officer of Sequella, Inc., a private company that focuses on commercializing novel treatments for antibiotic-resistant infectious diseases.

References:

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