Evolving Infectious Disease Risks Call for New Collaboration Models

— BY REYNOLDS M. SALERNO and RENEE DEGER[1]

The revolution in biotechnology reached a major threshold last year with the creation of the world's first synthetic life form. Craig Venter and Hamilton Smith built the genome of a bacterium from scratch and incorporated it into a cell, creating a living creature with no ancestor.[2] As with most scientific accomplishments, this incredibly exciting development poses both great promise and potential problems. Advanced biology, in all its various forms, will likely improve our quality of life significantly in the future. However, these new capabilities in manipulating biological materials, accompanied by profound geographic, demographic, economic, and political changes, have also created a more dangerous infectious disease environment around the world.

The challenge for national and international policy makers is how best to address this new reality. How can we mitigate the risk of infectious disease outbreaks without stifling the science that, ultimately, is our best defense against those diseases? We argue that the answers to this question must be explicitly international and collaborative, requiring the United States government and many international organizations to change their traditional ways of doing business in this field.

INDUSTRY, SCIENCE UNDER TRANSFORMATION

Biotechnology is widely accepted as the transformative field of science of the 21st century, just as physics was in the 20th. Already, the first decade has produced an explosion of new developments. In 2003, for example, sequencing of the human genome was completed by a consortium of international scientists who worked for more than 13 years on the project. The Human Genome Project cost U.S. taxpayers approximately $2.7 billion.[3] Today, fewer than ten years later, it costs less than $20,000 to sequence an entire human genome, and some experts predict that cost to fall to less than $1,000 by 2020.[4]

Alongside genetic sequencing, the field of chemical synthesis has advanced at astronomical rates as well. In 2002, researchers at State University New York at Stony Brook produced a genetically engineered version of the poliovirus – the world's first synthesized virus. Since then, scientists have synthesized a variety of increasingly complex viruses, including the 1918 influenza virus, the Marburg virus, and the severe acute respiratory syndrome (SARS) virus.

These achievements help illustrate how capabilities that were once nonexistent and impossible have become almost commonplace, relatively speaking, among biological researchers. At the same time, the globalization and industrialization of the life sciences has fueled the growth and investment in biotechnology capabilities in every corner of the globe, but especially across Asia.

China, for example, has made biotechnology a national priority – not only for economic growth, but also as a source of fuels, food, and materials for its rapidly expanding population. China expects biotechnology to account for 5 percent to 8 percent of its gross domestic product by 2020. In Malaysia, biotechnology accounted for none of that country's GDP in 2005, but it was 2.5 percent in 2010.[5] The government of Singapore recently invested more than U.S.$3.9 billion (S$5 billion) to build Biopolis, a premier biological sciences research campus, and is expected to spend another US$12.5 billion (S$16.1 billion) to support its national biotech industry over the next five years.[6]

The level of sophistication among new biotechnology concerns is often cutting edge, even in the developing world. Noted author and consultant Rob Carlson conducted a study of the global distribution of commercial DNA foundries, and found a large number of suppliers of oligos across Latin America and Asia, as well as North America and Europe. India, for example, supports at least three commercial synthesis foundries.[7] More than 75 genome centers, many located in Latin America and throughout Asia, are currently involved in sequencing at least one of the 183 microbial genomes listed in GenBank, a database of publicly available DNA sequences operated by the U.S. National Institutes of Health.[8]

Also, the number of high-containment laboratories worldwide designed to support research or vaccine manufacturing that involves the most deadly of pathogens has skyrocketed. A decade ago, only a handful of Biosafety Laboratory Level 4 (BSL4) facilities, the highest level of biocontainment, existed worldwide. Today, there are dozens and more are planned.[9] India, for example, is in the process of tripling its BSL4 capacity from what it was only a few years ago.

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INFECTIOUS DISEASES RAGING GLOBALLY

This surge in biotechnology and bioscience capabilities across the globe has coincided with a significant increase in the frequency of naturally occurring emerging and reemerging infectious disease outbreaks.[10] Between 1980 and 2007, 87 new human pathogen species were discovered – a rate of over three new diseases per year. Experts have identified 33 "medically significant" new infectious diseases in the last thirty years. Moreover, this emergence of new pathogens reflects a truly global pattern, with multiple incidents reported from every continent except Antarctica.[11]

Scholars agree that the increasing frequency of new and reemerging infectious disease is not a result of improved disease detection and diagnostics, but a consequence of a variety of demographic, globalization, and climatic trends. Agricultural practices have intensified to support the growing human population, leading to larger herds or the commingling of multiple species. Expanding populations have pushed humans to encroach upon more animal habitats, increasing the risk of zoonotic disease transmission, while increasing population densities in urban areas encourage disease incubation and spread. Meanwhile, globalization has led to more rapid and frequent movement of people, livestock, and products around the world, creating fertile opportunities for disease spread. And climate changes have facilitated favorable conditions for disease vectors, mutation, and propagation.[12] None of these trends show any sign of abating, and thus we must assume that the rate of infectious disease outbreaks will continue to accelerate, threatening public and agricultural health, global economies, and international security.[13]

In the last decade alone, the world has experienced major outbreaks with profound impacts on human health and national and international security, including SARS, H5N1 avian influenza, and H1N1 swine influenza.[14] Human behavior has also contributed to the rising risk of infectious diseases. The outbreak of Foot and Mouth Disease in the United Kingdom in 2001, after the virus was accidentally leaked from an infectious disease laboratory, caused an estimated $7 billion (£4.5 billion) in economic damages. The intentionally introduced anthrax in the United States in 2001, which killed five people and sickened 22, cost the U.S. economy more than $500 million just to decontaminate the affected buildings.[15]

All of these issues – the advances in biotechnology, the global expansion of the bioscience community, and the significant increase in the frequency of infectious disease outbreaks around the world – have created a dramatically changed global infectious disease profile. More life scientists are now working in more locations worldwide with more deadly, and potentially dangerous, pathogens and toxins that are now simpler to manipulate with today's readily available equipment. This means there's a much greater potential for accidents, theft, or other kinds of mishandling that could pose a serious public health or global security threat.

POLICY RECOGNITION

U.S. policy recognizes the potential security threats posed by the geographic and intellectual expansion of the biosciences. The *National Strategy for Countering Biological Threats* states: "Advances within the life sciences hold extraordinary potential for beneficial progress, but they also can empower those who would use biological agents for ill purpose."[16] At the same time, the *National Strategy* recognizes that many policy initiatives are necessary to counter the diverse spectrum of biological risks – from preventive measures to response preparedness. Importantly, the *National Strategy* articulates the promotion of "global health security" as its first of seven specific objectives:

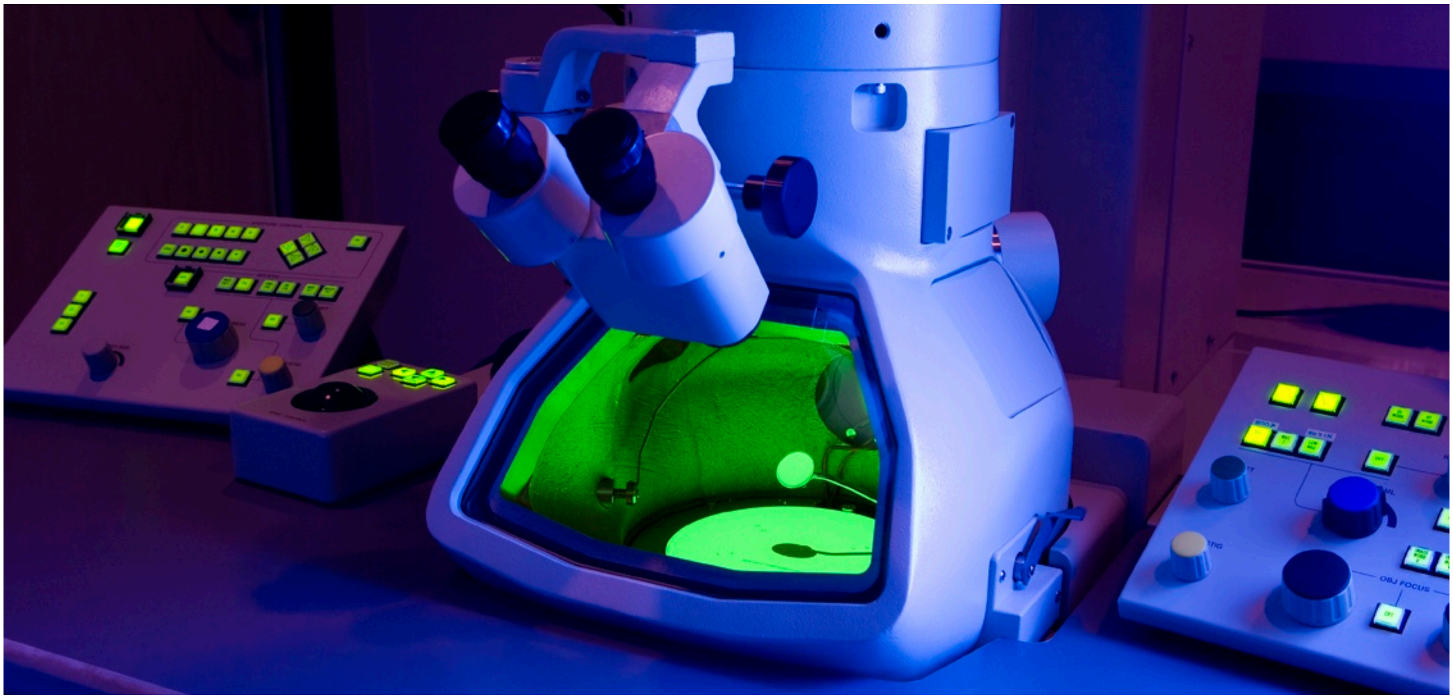
"We will seek to advance access to and effective use of technologies to mitigate the impact from outbreaks of infectious disease, regardless of their cause." This U.S. government intention is laudable, but *how* the U.S. government will build global capacity for disease surveillance, detection, diagnosis, and reporting is particularly daunting.

This challenge is most acute in the developing world – where many of the most dangerous infectious diseases tend to originate. Many developing countries lack the basic tools, expertise, or infrastructure to detect, identify, and contain outbreaks of infectious disease. Others may have the skills to identify disease outbreaks, but they lack the resources to contain and control the illness or monitor its spread. Without the ability to respond, to assure local and global populations an outbreak is contained, nations are reluctant to admit they have an outbreak, seek external assistance, or even to invest in monitoring capabilities. Effective response and monitoring capabilities would risk disrupting international trade or tourism. Further, such isolation and lack of resources help facilitate those with malicious intent and increase the vulnerability of the select pockets of professionals with sophisticated capabilities and equipment.

NEW CHALLENGES, NEW PARADIGM

Elevating or channeling the capabilities in the global life sciences and public health communities requires a new model for engagement. The current approach – exporting technologies and methods, and even containment laboratories, developed and used in the West to regions vulnerable to infectious disease outbreaks – has failed to markedly improve disease surveillance even in limited circumstances. The approach further fails to take into account the growing communities of life sciences professionals who are acquiring capabilities for very sophisticated science, but are not participating in the global public health conversation.

International aid programs that target anthrax detection are a good example. Anthrax has been identified as a disease that terrorists may target for malicious use, but it is not an especially common or consequential disease in much of the world. Still, many threat reduction programs distribute thermal cycler (PCR) machines with reagents for anthrax.



Stories abound of storerooms in developing world facilities filled with unused PCR machines still in their original packaging. In some cases, equipment was given to facilities that lacked trained staff, or trained staff had left the facility (such training is often hoarded and used to further job prospects). In other instances, facilities lacked the necessary reagents or even adequate or consistent power to operate the equipment. But more often than not, the scientific staff at the facility did not believe that modern technology – provided by an outsider and designed to detect a rare disease – could help them conduct their daily work or improve local conditions. They ignored the equipment or stopped using it when outside funding ended.

Not only do initiatives like this fail to target a problem of local concern, they are singular solutions – aimed only at identifying a single disease – that neglect to prepare communities for how to respond. And they often overlook the required supporting infrastructure, from electricity to the storage, handling methods, and transportation for the managing of samples, which developing world communities often cannot afford to maintain. But most importantly, these programs failed to engage local public or animal health professionals in a meaningful way. The local scientists were reduced to being recipients of aid rather than elevated into partners in identifying solutions to meet their immediate needs.

The challenges appear insurmountable, but the solution lies in how Western specialists, from public health experts to engineers, engage global communities. It means embracing a new, more collaborative development model. This new partnership framework would team Western specialists with local government, public and/or animal health, and medical and/or veterinary professionals. The immediate goal would be to develop solutions tailored for the immediate infrastructure that addresses the kind of local challenges that also pose a more widespread threat. The long-term goal would be to build the intellectual capacity within the community. Empowered with greater insight into the impact of an infectious disease outbreak on their communities, these front-line individuals, the doctors, veterinarians, nurses, technicians, and government and public health officials, would become more committed stakeholders in their solutions. Further, they would become more independent.

COLLABORATIVE SOLUTIONS

The "cooperative" concept is not entirely new. The academic community as well as biological threat reduction initiatives regularly partner with local individuals to conduct collaborative research. But these tend to focus on academic studies of a single dangerous, and often rare, disease. Also, the National Academies of Science recommended in 2009 that U.S. threat reduction programs "include broader international cooperation and partnerships, and increased international contributions."[17] But U.S. programs have not yet determined a model for achieving this. They continue to export U.S. or Western technology and expertise, evaluating their performance by the physical quantities of "stuff" they deliver, and not on effectiveness or sustainability.

Going forward, Western programs should endorse collaborative scientific research programs that tap local talent to develop solutions that improve local disease surveillance – detection, diagnosis, reporting, and control. Such partnerships should become the supporting foundation for local communities to identify their unique challenges, and to develop a solution that best suits local needs and resources. Powered by such autonomy, local specialists would become champions of their solutions, making them inherently more sustainable.

There are a number of critical, operational challenges to effective disease response in the developing world that collaborative research could immediately address. Leveraging emerging methods and technologies, such partnerships could target such needs as:

1. Point-of-care diagnostics that are less dependent on reagents, and are rapid, inexpensive, and can identify a range of diseases. Most detection methods require reagents that are disease-specific, expensive, perishable, often hard to come by, and require cold storage – all significant challenges in the developing world.
2. Self-contained sample preparation devices that eliminate the challenges of sample integrity and preservation during transport from the field to clinics and diagnostic laboratories.
3. Secure, remote access to advanced bioinformatics capabilities that would allow developing world laboratories to quickly compare local samples with public data banks to enhance disease detection and identification.
4. Mapping and analysis of historical disease conditions that could facilitate local diagnostic strategies and improve the ability of local health professionals to distinguish between endemic and emerging infectious diseases.
5. Decision support and risk assessment tools that could enable local decision makers to study appropriate response scenarios.

Each of these projects represents a gap in the developing world's disease surveillance needs, and could be addressed through cooperative technical projects staffed by both local and international scientists. Prototype results could be tested in the local community, and modified according to the local needs and shared with other, similar regions. Such collaborative research projects would integrate developing world scientists in the international scientific community, enhance local technical capabilities (regardless of the project's outcome), and potentially create a local solution that ultimately helps solve a global problem.

It may take a long time before the substantial benefits of the asvancing biosciences reach the front lines of the world's battle against infectious diseases. As long as these front lines are weak, the entire world remains vulnerable in the face of an increasingly complex and dangerous infectious disease environment. Western programs can take advantage of the global expansion of biosciences capabilities. But instead of transferring technologies and equipment to the developing world that are difficult for the recipients to use and maintain, Western programs should aim to create new science and technology alongside the scientists and officials on the infectious disease front lines. Adopting genuinely cooperative research and development partnerships that support the local development of tools and capabilities will significantly strengthen global public health communities – communities whose technical knowhow and operational competence are critical to reducing the today's global infectious disease risks. ■

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