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## Considerations for infectious disease research and practice

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### ABSTRACT

As the 21st century unfolds, strategies to prevent and control infectious diseases remain an area of vital interest and concern. The burden of disease, disability, and death caused by infectious diseases is felt around the world in both developed and developing nations. Moreover, the ability of infectious agents to destabilize populations, economies, and governments is strikingly apparent. To an unprecedented degree, infectious disease-related issues are high on the agendas of world leaders, philanthropists, policymakers, and the public. This enhanced focus, combined with recent scientific and technological advances, creates new opportunities and challenges for infectious disease research and practice. This paper examines these issues in the context of three countries: China, India, and the United States.

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### 1. Introduction

Only a few decades ago, there was enormous optimism that the threat of infectious diseases was receding. Scientific and technologic advances, such as the development of antibiotics and vaccines, along with improved hygiene, sanitation, and vector control, enabled dramatic improvements in health and led many to predict the end of infectious disease [1]. This was especially true in the industrialized world, but even the poorest nations showed encouraging signs of victory in the battle against infectious disease.

Nonetheless, we know today that such optimism was premature. It did not take into account critical factors such as the extraordinary increase in international travel and trade, and the movement of people into urban settings—many into mega-cities—where the spread of disease is amplified through crowding, poor sanitation, and inadequate hygiene. It also did not recognize that changing agricultural practices and environmental manipulations would dramatically alter disease vectors and opportunities for exposure. That early optimism did not reflect the continuing challenge of how to change behaviors that increase transmission and exposure, including risky sexual practices and intravenous drug use. In addition, it underestimated the extraordinary resilience and ability of microbes to change and adapt, and the continuing difficulty of ensuring that existing medical knowledge and tools translate into real-world care for anyone who needs it, whether because of inadequate resources, ignorance, or complacency. Sadly, it is now apparent that we also live in an era when we must prepare for the possibility of microbial agents being used intentionally as weapons to do harm [2].

### 2. The burden of infectious disease

In our modern world, infectious diseases still claim millions of lives every year. Globally, infectious disease represents the second leading cause of death, and the leading cause of death for children and adults under the age of 50. Infectious

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diseases place a particularly severe burden on the less-developed parts of the world, causing one in every two deaths. Overall, infectious diseases account for about 30% of healthy years lost to illness, as measured by disability-adjusted life years (DALYs) [3].

### 2.1. *Emerging and re-emerging infections*

Within just the last few decades, more than 30 newly discovered infectious disease threats [4] have emerged. The majority of these have been zoonoses, or human diseases that have their origins in animal disease. HIV, severe acute respiratory syndrome (SARS), H5N1 avian influenza, Ebola, and Nipah virus are a few such examples [5]. We have also witnessed the re-emergence or resurgence of old diseases like West Nile disease, monkeypox, dengue fever, malaria, and TB, often in new geographic regions. In some cases, the resurgence of diseases like malaria and TB has come in new and more dangerous forms that are drug-resistant, which is becoming a serious problem worldwide. Unfortunately, the widespread and often inappropriate use of antimicrobials has led to the emergence of resistant strains of many microbes, complicating the management of a wide variety of diseases, and threatening future treatment options [2].

Virtually all nations have been affected by these emerging and re-emerging infectious diseases. In addition, prospects for more emerging diseases will likely increase in coming years due to continuing globalization of trade and travel, urbanization and crowding, inadequate health care, and encroachment on the environment—all leading to new interactions between people and animals and other vectors of disease. While the scope of the problem is vast, the encouraging fact is that we have an opportunity to make enormous improvements in health through new understandings of the threats we face and appropriate applications of scientific and technological advances.

### 2.2. *Infectious component of chronic diseases*

It is important to recognize that there can be a substantial infectious component to chronic disease. In fact, many chronic conditions once thought unrelated to infectious disease are now linked to bacterial, viral, or parasitic agents. This is an area of active exploration and research, and many fascinating examples are emerging in the realm of cancer, cardiovascular disease, neurological disease, ulcers, diabetes, and others, with far-reaching implications for health.

Recent research indicates that viruses are a causal factor in 15–20% of all human cancers [1]. For example, human papilloma virus causes almost all cases of cervical cancer, a major killer of women worldwide. Liver cancer is the third leading cause of cancer death in the world, and hepatitis B and C account for about 80% of all liver cancers. In many of these cases, viral genes are necessary for the initial development of the tumor as well as for the continuing survival of tumor cells in the final malignant stage. This suggests there may be opportunities to prevent or possibly cure certain cancers through control of either the initial viral infection or through the inhibition of viral functions [6]. In fact, the use of hepatitis B vaccine has already resulted in a decreased incidence of liver cancer in certain populations [1].

### 2.3. *Infectious disease in the US, China, and India*

No nation is immune to the complex challenges of infectious disease. In more developed countries such as the United States, but also in China and India, the burden of infectious disease is less pronounced but still severe. The US has demonstrated the greatest progress in the struggle against infectious disease, with a 10-fold decrease in the number of infectious disease deaths over the first half of the twentieth century, thanks to improvements in sanitation, hygiene, and the introduction of antibiotics and vaccines. In the following decades, there were continuing improvements—although less dramatic—until the 1980s, when infectious disease rates actually began to increase because of emerging and re-emerging infectious diseases, including HIV/AIDS. However, even when deaths from HIV/AIDS are excluded, there is still a general upward trend in the number of deaths from infectious disease [2].

Both China and India have made enormous strides in improving the health and curbing the spread of infectious diseases, reflecting the remarkable economic progress of these two nations [7]. However, people in these countries remain at a higher risk of developing infectious diseases and dying from their illness than people in the US, largely due to poor sanitation, unhygienic living conditions, and inadequate access to quality healthcare.

India suffers the greater burden of infectious disease. India is estimated to have the second highest number of HIV/AIDS cases in the world (second only to South Africa), with over 4.58 million infected people. Half a million people are projected to die from AIDS in India next year, and 600,000 are in urgent need of antiretroviral therapy [8]. Tuberculosis, including multi-drug resistant-tuberculosis (MDR-TB), also represents a major challenge for India. Cholera and dengue fever have been longstanding health problems in India; however, outbreaks of both of these diseases have increased significantly of late. Acute respiratory infections, diarrhea, and neonatal infections remain major childhood killers, despite significant improvements in immunization rates in recent years [8].

China is better off than most of the countries to its south. The toll of many infectious diseases, including sexually transmitted disease, malaria, schistosomiasis, and vaccine-preventable diseases, was substantially reduced over past decades, although recent reports from China indicate continuing problems with increasing trends for some areas [9,10]. The most prevalent disease is tuberculosis, followed by hepatitis B, dysentery, syphilis, and gonorrhea. According to official

reports, these five diseases account for almost 88% of all reported cases [11]. Although overall prevalence remains relatively low, HIV/AIDS is fast becoming a major problem. As of the end of 2005, the Chinese Ministry of Health estimated that 650,000 people in China were infected, with an estimated 70,000 new HIV infections and 25,000 deaths that year [12]. The joint United Nations Program on HIV/AIDS (UNAIDS) predicted that by 2010 over 10 million people could become infected, and it termed this HIV epidemic as “China’s titanic peril” [13].

China is highly vulnerable to other emerging infectious diseases as well. Animal husbandry practices in China have led to close contacts between animal and human populations. In fact, China has more people, pigs, and poultry (1.3 billion, 508 million, and 13 billion, respectively) living in close proximity to people than any nation in the world—or in history [14]. With high levels of avian flu circulating within the country, China is now dangerously positioned to become the source of a new pandemic flu. Such conditions also raise significant concerns about the emergence of another serious zoonotic disease like the SARS outbreak, which began in China.

### **3. The widening context of infectious disease threats**

Addressing the problems of serious endemic infectious disease is a fundamental and urgent requirement. However, the increasingly transnational nature of emerging infectious diseases constitutes one of the greatest challenges of our modern era. In today’s highly interconnected world, a disease that occurs in one part of the world can travel around the globe in less than 24 hours. In recent years, avian flu, SARS, and HIV/AIDS have received prominent coverage, but they are only three on a list of infectious diseases that require a global response.

Moreover, outbreaks of these diseases have the potential to cause profound economic damage, as well as social and political instability. India learned this lesson in 1994 when there was an outbreak of pneumonic plague in Surat. The national and international response led to the closure of airports and dramatic disruptions in tourism and trade, at an estimated cost to India of approximately \$1.7 billion [15]. More recently, this lesson was brought home to China when SARS emerged in Guangdong Province in 2003 and spread rapidly throughout China and around the globe. Health authorities were unprepared, and serious deficiencies were revealed in China’s ability to mount an effective, coordinated response. Early on, official efforts to conceal the extent of the emerging epidemic exacerbated the situation and critical time for disease identification and containment was lost. The consequences were devastating for China and the world; more than 8000 people were infected and some 800 died; cities were paralyzed for months; travel was disrupted; and the direct economic impact on other countries in the region was estimated to be as high as \$30 billion [8]. China was forced to reassess its ability to control communicable disease, and to make new commitments to strengthen its systems for infectious disease control.

### **4. Critical role of infectious disease research**

As new attention and concern is directed to the challenges of global health and infectious disease, extraordinary advances in life sciences research and biotechnology have already begun to drive a global transformation in the design, development, and delivery of new tools to combat infectious diseases. In addition to basic research into how infectious organisms cause disease, and how the human immune system responds—both of which will enable new understanding into the nature of disease and how to address it—new opportunities have appeared. These include rapid and effective strategies for early detection of microbes, antibiotic sensitivity profiles, targeted efforts to improve drugs and therapeutics to manage or cure infectious disease, new and improved vaccines for prevention and control of disease, and new systems to more efficiently deliver therapeutic and preventive interventions. Other technology advances with important implications for infectious disease and public health include enhanced systems for disease surveillance and early recognition, as well as opportunities to more meaningfully analyze and model disease outbreaks and develop strategies for their control.

The emergence and rapid expansion of fields such as recombinant biology, genomics and proteomics, systems biology, synthetic biology, information technology (including computer and mathematical modeling), genetic epidemiology, and nanotechnology underlie much of these new understandings, capabilities, and opportunities [16]. For example, the application of functional genomics and proteomics enables a deeper understanding of the etiology of disease and its manifestations. Synthetic biology offers important new strategies for drug discovery and design. Work at the intersection of these fields and cross-disciplinary approaches are increasingly critical. For example, because many important pathogens persist in animal reservoirs or may be transmitted to human hosts through other vectors, examination of important aspects of infectious disease transmission in these systems, including animal and human host resistance and susceptibility, vector efficiency, genetic variabilities, and population dynamics, will be essential.

At the same time that advances in science offer new tools to analyze information and better understand disease, they also offer opportunities to greatly enhance the speed of progress. For example, continuing technology advances in DNA sequencing will make it possible to rapidly characterize more and more genomes, offering greater insights into basic composition and individual variation in both human and pathogen populations. The ability of genomics to support the development of increasingly rapid and reliable assessment tools like microarrays will be a huge asset to the swift diagnosis of infectious disease agents. Applications from the fields of robotics and informatics will facilitate rapid, high-throughput

screening for new potential antimicrobial drug candidates. Information technology will enable large quantities of data to be rapidly mined, with a goal of more effective disease identification or trend tracking in real time that enables swift response.

Continuing advances in technology will make a range of important tools, techniques, and assays increasingly accessible to those with less training and expertise, which will greatly broaden their utility and impact. However, as these advances move forward, parallel efforts must be undertaken to reduce costs. Cost remains a major barrier to effective application of these tools, whether for research, for clinical care, or for public health disease control interventions. Correspondingly, the link between infectious disease research, and health care needs, services, and training must be strengthened in order to ensure that the appropriate research agenda is addressed and implemented. Moreover, without a commitment to some minimal level of infrastructure for healthcare, the benefits of scientific advances will not translate into meaningful care for those in need.

## 5. The changing context of life sciences research

The field of infectious disease is being transformed by advances in new fields of science. While US scientific research in the life sciences and biotechnology sectors still leads the world, the US no longer stands alone in its levels of research productivity or research funding [16,17]. Both China and India are becoming major players, which has important implications for the conduct and content of infectious disease research and practice.

With booming economies and new spending power, both India and China see enormous opportunities to invest in key areas of emerging scientific activity, such as genomics and proteomics, information technology, and nanotechnology, and are placing an increasing premium on innovation in their scientific enterprise [18,19]. Clearly, advances in these fields are vital for addressing some of the most pressing disease challenges in those countries and beyond, but investment is also seen as a critical component of their national economic development strategy.

One indicator of the growing role of China and India can be seen in the reversal of the “brain drain.” With considerable new investments to strengthen educational institutions, research facilities, and research funding, growing numbers of talented Indian and Chinese scientists are choosing to stay in their home country to undertake scientific training and careers. In addition, the number of Western scientists seeking research opportunities in Chinese and Indian institutions is on the rise. Many foreign companies, including large multinationals, are deciding to establish sites or launch ventures in China and India because of the large and relatively inexpensive talent pool and the lower costs of doing business [16].

While China and India are well positioned to become powerful players in the infectious disease arena, rapid expansion of their life sciences research and the associated pressures to produce economy-boosting science have led to concerns about quality control, ethics, and the adequacy of research and production oversight [20]. Continued success and the ability to compete at the global level will require sustained investment to strengthen and extend the scientific research infrastructure in these countries, including improving the quality of higher education, regulatory oversight, adherence to ethical and biosecurity regulations, and open, transparent collaboration.

It is in all our best interests to strengthen the cooperative nature of these scientific endeavors. Enriching scientific links and forging far-reaching scientific collaborations will have many benefits. For one thing, a large share of the serious infectious disease problems of global concern currently exist or are likely to emerge from regions that include China and India. Research and development in those areas has special value because it is generally easier and more economical to study diseases where they are endemic. With respect to public health, such collaboration becomes imperative because of the transnational consequences of many of those infectious diseases. Fundamental knowledge about the nature of certain organisms and the diseases they cause, as well as opportunities for early detection, response, and control, can most effectively be achieved through broad-based collaboration. Such collaboration builds confidence and transparency and promotes sharing of data in a timely manner. This will strengthen the science base and opportunities for discovery, and amplify resources for meaningful action. Open scientific collaboration among these nations will also help to support quality research of the highest scientific and ethical standards.

## 6. Potential for misapplication

In an era of terrorism, such collaboration takes on additional importance. It is evident that growth in biotechnology and the explosion of knowledge about the fundamental building blocks of life—and how to manipulate them—bring with it staggering and unpredictable power. While advances in modern biology offer great hope to improve health and prevent disease, they also offer tools that can be used—through malevolence, misapplication, or sheer inadvertence—to create new and more dangerous organisms, and effective mechanisms for delivery. From a scientific perspective, managing this threat is a complex challenge. No one wants to impede the progress of legitimate and important science. However, we must recognize a set of real concerns. Meaningful solutions will require the full engagement and support of the scientific community, as well as a mix of strategies that include professional standards and codes of conduct, national rules and regulations, international guidelines and agreements, and a fundamental shift in understanding and accountability about how science is done.

The potential threat of bioterrorism is felt most profoundly in the US, where the anthrax attacks in 2001 heightened attention and concern. In recent years, new initiatives have been undertaken to examine the implications of advances in life

sciences research and biotechnology, and the government has tightened its ability to monitor the procurement and use of dangerous pathogens [16]. Other countries have indicated concern about this threat as well. For example, the Chinese government and its scientific leaders have developed codes of conduct and other regulations to address biosecurity and reduce the risk of bioterrorism [21]. India has also begun to address this threat through policy and programs now underway [22]. Many cross-national initiatives have also been undertaken to engage these and other nations, and to develop a scientific awareness and ethos to foster adequate and appropriate oversight of biosecurity, including the responsible stewardship of research activities, knowledge, and materials. International cooperation will be essential to achieving these goals.

## 7. Conclusion

Looking to the future, all nations share a common need to meet the challenge of more effectively detecting, tracking, treating, and preventing infectious diseases. The scientific research community must respond by identifying critical needs and developing strategies to address them. These challenges will require the integration of cutting-edge science and technology with a complex array of social, political, legal, ethical, and economic realities. Moreover, it will require new partnerships across nations, and a more effective coordination of public- and private-sector efforts. And throughout, it will require a delicate balancing act between competing priorities, including: global health needs; personal, national, and international security; the role of the research enterprise and industry on the economy of a growing number of countries; and support for the advancement of science and its safe application.

## References

- [1] Fauci AS. Infectious diseases: considerations for the 21st century. *Clin Infect Dis* 2001;32:675–85.
- [2] Smolinski M, Hamburg M, Lederberg J. *Microbial threats to health: emergence, detection and response*. Washington, DC: National Academies Press; 2003.
- [3] Fauci AS. Emerging and reemerging infectious diseases: the perpetual challenge. *Acad Med* 2005;80:179–1085.
- [4] Morens DM, Folkers GK, Fauci AS. The challenge of emerging and re-emerging infectious diseases: the perpetual challenge. *Nature* 2004;430:242–9.
- [5] Wolfe ND, Dunavan CP, Diamond J. Origins of major human infectious diseases. *Nature* 2007;447:279–83.
- [6] Ahlquist P. Keynote lecture. GDEST China–US workshop on the genomic revolution: new tools for combatting infectious diseases. 29 March, Beijing, China.
- [7] Bloom B. Passages to China and India. *Harvard Public Health Rev* 2006(Summer/Fall):4–6.
- [8] World Health Organization (WHO) website: <<http://www.who.int/countries/ind>>.
- [9] Koplan J, Xingzhu L, Haichao L. Public health in China: organization, financing and delivery of services. Background paper for World Bank China Rural Health Study; 2005.
- [10] Yu W, Wu M, Garber A. Control of infectious disease: challenges to China's public health system. Presented at the SCID/SIEPR conference: Economic challenges in Asia, Stanford University, May 31–June 3, Palo Alto, CA; 2006.
- [11] Health Ministry issues briefing on infectious diseases in China. Xinhua News Agency 17 July 2003. Retrieved from <<http://www.china.org.cn/english/government>>.
- [12] Ministry of Health, People's Republic of China. Joint United Nations programme on HIV/AIDS, World Health Organization. 2005 update in the HIV/AIDS epidemic and response in China; January 2006.
- [13] Joint United Nations Programme on HIV/AIDS. HIV/AIDS: China's titanic peril; 2002.
- [14] Osterholm M. Preparing for the next pandemic. *Foreign Affairs* 2005 (July/August).
- [15] World Health Organization, World health report, 2007.
- [16] Committee on Advances in Technology and the Prevention of Their Application to Next Generation Biowarfare Threats. *Globalization, biosecurity, and the future of life sciences*. Washington, DC: National Academies Press; 2006.
- [17] Burrill GS. *Biotech 2007. Life sciences: a global transformation*. San Francisco: Burrill Life Sciences Media Group; 2007.
- [18] Lakhan S. The emergence of modern biotechnology in China. *Issues Inform Sci Inform Technol* 2006;3:333–53.
- [19] Biotechnology in India: a promising future. *India Economic News Winter* 2002-03;13:1–2.
- [20] Shetty P. Will Britain be sidelined by the rise of Asian science? *Lancet* 2007;369:813–4.
- [21] Smithson A, editor. *Beijing on biohazards: Chinese experts on bioweapons non-proliferation issues*. Monterey, CA: Monterey Institute for International Studies; 2007.
- [22] Roul A. Biological weapons, infectious diseases, and India's security imperatives. *Society for the study of peace and conflict*. Paper #7; September 2007.

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