Book chapter for Global Catastrophic Risks, 2008

Biotechnology and Biosecurity

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1. Introduction

Biotechnological power is increasing exponentially, reminiscent of the increase in computing power since the invention of electronic computers. The co-founder of Intel Corporation, Gordon Moore, pointed out in 1965 that the number of transistors per computer chip—a measure of how much computation can be done in a given volume— has doubled roughly every eighteen months (Moore, 1965). This exponential increase in computing power, now called "Moore's Law," has continued to hold in the decades since, (Lundstrom, 2003) and is the reason that individuals now have more computing power available in their personal computers than only decades ago was available only to the most advanced nations. Although biotechnology's exponential liftoff began decades after that of computing, its rate of increase, as measured, for example, by the time needed to synthesize a given DNA sequence, is as fast or faster than that of Moore's Law (Carlson, 2003). Just as Moore's Law led to a world of personal computing and home appliance microprocessors, so biotechnological innovation is moving us into a world where the synthesis of DNA, as well as other biological manipulations, will be increasingly available to small groups of technically competent and even individual users.

There is already a list of well-known experiments—and many others that have received less public attention—that illustrate the potential dangers intrinsic to

modern biological research and development. We review several examples of these in some detail below, including: genetic manipulations that have rendered certain viruses far more deadly to their animal hosts (Jackson et al., 2001); the synthesis of polio virus from readily purchased chemical supplies (Cello et al., 2002)—so that even if the World Health Organization (WHO) succeeds in its important task for eradicating polio worldwide, the virus can be reconstituted in laboratories around the world; the reduction in the time needed to synthesize a virus genome comparable in size to the polio virus from years to weeks; the laboratory re-synthesis of the 1918 human influenza virus that killed tens of millions of people worldwide (Tumpey et al., 2005); the discovery of "RNA interference," which allows researchers to turn off certain genes in humans or other organisms (Sen et al., 2006); and the new field of "synthetic biology," whose goal is to allow practitioners to fabricate small "biological devices" and ultimately new types of microbes (Fu, 2006).

The increase in biological power illustrated by these experiments, and the global spread of their underlying technologies, is predicted to lead to breathtaking advances in

medicine, food security, and other areas crucial to human health and economic development. For example, the manipulation of biological systems is a powerful tool that allows controlled analysis of the function—and therefore vulnerabilities of and potential defenses against—disease organisms. However, this power also brings with it the potential for misuse (NRC, 2006). It remains unclear how civilization can ensure that it reap the benefits of biotechnology while protecting itself from the worst misuse. Because of the rapid spread of technology this problem is an intrinsically international one. However, there are currently no good models from Cold War arms control or nonproliferation diplomacy that are suited to regulating this uniquely powerful and accessible technology (Chyba and Greninger, 2004). There are at least two severe challenges to any regulatory scheme (Chyba, 2006). The first is the mismatch between the rapid pace of biotechnological advances and the comparative sluggishness of multilateral negotiation and regime building. The second is the questionable utility of

large-scale monitoring and inspections strategies to an increasingly widespread, small- scale technology.

However, this is not a counsel for despair. What is needed is a comprehensive strategy for the pursuit of biological security—which we take here to be the protection of people, animals, agriculture and the environment against natural or intentional outbreaks of disease. Such a strategy is not yet in place, either nationally or globally, but its contours are clear. Importantly, this strategy must be attentive to different categories of risk, and pay attention to how responses within one category strengthen or weaken the response to another. These categories of risk include naturally occurring diseases; illicit state biological weapons programs; non-state actors and bio-hackers; and laboratory accidents or other inadvertent release of disease agents.

Just this listing alone emphasizes several important facts. The first is that while about 14 million people die annually from infectious diseases (WHO, 2004) (mostly in the developing world), only five people died in the 2001 anthrax attacks in the United States (Jernigan et al., 2002), and there have been very few other modern acts of biological terrorism. Any approach to the dual-use challenge of biotechnology that substantially curtails the utility of biotechnology to treat and counter disease runs the risk of sacrificing large numbers of lives to head off hypothetical risks. Yet it is already clear that humans can manipulate pathogens in ways that go beyond what evolution has so far wrought, so the hypothetical must nevertheless be taken seriously. A proper balance is needed, and an African meeting on these issues in October 2005 suggested one way to strike it. The Kampala Compact declared that while “the potential devastation caused by biological weapons would be catastrophic for Africa,” it is “illegitimate” to address biological weapons threats without also addressing key public health issues such as infectious disease. The developed and developing world must find common ground.

A second important observation regarding biological terrorism is that there have, so far, been very few actual attacks by non-state groups. It is clearly important to understand why this has been the case, and to probe the extent to which it has been due to capabilities or motivations—and how whatever inhibitions may have been acting can be strengthened. Skeptical treatments of the biological terrorism threat, and of the dangers

of apocalyptic dramatization more generally, can place important focus on these issues— though the examples of dual-use research already mentioned, plus recent U.S. National Academy of Sciences studies and statements by the UN Secretary-General make it clear that the problem is real, not hype.[1]

While the focus of this chapter will be on biotechnological capabilities, and how those capabilities may be responsibly controlled, it should be remembered that a capabilities-based threat assessment only provides part of the comprehensive picture that is required. Indeed, it is striking to compare the focus on capabilities in many technology-oriented threat assessments with the tenor of one of the most influential threat assessments in U.S. history, George Kennan's "X" article in *Foreign Affairs* in 1947. In this piece, Kennan crystallized the U.S. policy of containment of the Soviet Union that prevailed for decades of the Cold War. On reading today, one is struck by how little of the X article addressed Soviet capabilities. Rather, nearly all of it concerned Soviet intentions and motives, informed by Kennan's experience in Soviet society, his fluency in Russian, and his knowledge of Russian history and culture. To the extent that the biological security threat emanates from terrorist groups or irresponsible nations, a similar sophistication with respect to motives and behavior must be brought to bear (see also the chapter by Potter and Ackerman, as well as Hughes in this volume).

In this chapter, we first provide a survey of biological weapons in history and efforts to control their use by states via multilateral treaties. We then describe the biotechnological challenge in more detail. Finally, we survey a variety of approaches that have been considered to address these risks. As we will see, there are no easy answers.

2. Biological Weapons and Risks

The evolutionary history of life on Earth has, in some instances, led to

biological weapons in the form of harmful toxins (and their underlying genes) that are carried by simple organisms like bacteria and fungi, as well more complex ones like spiders and snakes. Humans learned that such natural phenomena could be used to their advantage; long before the identification of microbes and the chemical characterization of toxins, humans were engaged in rudimentary acts of biological warfare that included unleashing venomous snakes on adversaries, poisoning water wells with diseased animal flesh, and even catapulting plague-infested human bodies into enemy fortifications (Wheelis, 2002).

As scientists learned to optimize growth conditions for microbes, stockpiling and storing large quantities of infectious living organisms became feasible and dramatically increased the destructive potential of germ warfare. These advances and a better understanding of disease-causing microbes, together with the horror and carnage that was caused by non-conventional weapons during WWI, elevated fears of germ warfare and

[1] One important skeptical discussion of the bioterrorism threat is Milton Leitenberg, *Assessing the Biological Weapons and Bioterrorism Threat* (U.S. Army War College, 2005).

provided the impetus for the 1925 Geneva protocol, an international treaty that outlawed the use of chemical and bacteriological (biological) weapons in war. With the notable exception of Japan (Unit 731 Criminal Evidence Museum, 2005), warring states refrained from using biological weapons throughout WWII—but some continued to engage in offensive weapons programs, which were not prohibited until the Bacteriological (Biological) and Toxins Weapons Convention (BWC) was opened for signature in 1972.

The BWC is the world's first international disarmament treaty outlawing one entire class of weapons—namely, the development, production and stockpiling of biological agents and toxins for anything other than peaceful (i.e. prophylactic)

purposes. Despite 155 ratifications out of the 171 states that are signatory to the convention, the BWC suffers from the lack of a monitoring and inspection mechanism to assess whether a country is engaged in illegal activities. This institutional weakness permitted sophisticated offensive programs to continue long after the convention was signed, such as one in the former Soviet Union. Efforts to develop monitoring and verification protocols within the framework of the BWC began in 1991, but were suddenly terminated 10 years later when the United States withdrew its support in July 2001, arguing that the additional measures would not help to verify compliance, would harm export control regimes and place US national security and confidential business information at risk.[2]

Similarly to what is found in the nuclear and chemical weapons realm, the BWC could also be strengthened by a rigorous verification process. However, the affordability and accessibility of biotechnologies, and the absence of any severe weapon-production bottlenecks analogous to that of the production of plutonium or high-enriched uranium in the nuclear case, renders verification inherently more difficult in the biological realm. This is a distinguishing feature of biological weapons that is obscured by the tendency to include them with nuclear, chemical and radiological weapons as a “weapon of mass destruction” (Chyba, 2002).

3. Biological weapons are distinct from other so-called weapons of mass destruction

Producing a nuclear bomb is difficult; it requires expensive and technologically advanced infrastructure, and it involves uranium enrichment or plutonium production and reprocessing capacity that are difficult to hide. These features render traditional nonproliferation approaches feasible; despite being faced with many obstacles to nonproliferation, the International Atomic Energy Agency is able to conduct monitoring and verification inspections on a large number (over a thousand) of nuclear facilities throughout the world.

These traditional approaches are also reasonably effective in the chemical realm where the Organization for the Prohibition of Chemical Weapons (OPCW) can, inter alia, monitor and verify the destruction of declared chemical stockpiles.

[2] For a statement by Ambassador Donald Mahley, U.S. Special Negotiator for

Chemical and Biological Arms Control Issues, refer to http://www.state.gov/t/ac/rls/rm/2001/5497.htm

But biological weapons proliferation is far more challenging for any would-be inspection regime—and it will only become more so as the underlying technologies continue to advance. In some respects, biological weapons proliferation poses challenges more similar to those presented by cyber attacks or cyber terrorism than to those due to nuclear or chemical weapons. An IAEA or OPCW-like monitoring body against the proliferation of cyber attack capabilities would present a *reductio ad absurdum* for a verification and monitoring regime. Internet technology is so widely available that only a remarkably invasive inspection regime could possibly monitor it. Instead, society has decided to respond in other ways, including creating rapidly evolving defenses like downloadable virus software, and invoking law enforcement to pursue egregious violators. Somewhat similar challenges are presented in the biological realm where the spread of life science research in areas like virology, microbiology, and molecular biology are contributing to a growing number of laboratories worldwide that engage in genetically based pathogen research. In addition, an expanding biotech industry and pharmaceutical sector is contributing to the spread of advanced and increasingly "black box"[3] technologies that enable high consequence research to be carried out by a growing number of individuals; biotechnology is already commonplace in undergraduate institutions, it is beginning to enter high school classes, and is increasingly popular among amateur biotech enthusiasts. Moreover, an increasing number of countries are investing in biotechnology applications to health, agriculture, and more environment- friendly fuels. These trends are contributing to the increasing affordability of these technologies; the initial draft of the human genome cost an estimated $300 million (the final draft and all technologies that made it possible cost approximately $3 billion). Just 6 years later, one company hopes to finish an entire human genome for only $100,000—a 3000-fold cost reduction. Researchers, spurred by government funding and award incentives from private

foundations are now working toward a $1000 genome (Service, 2006).

These are exciting times for biologists; whereas the 20th century saw great progress in physics, the early decades of the 21st century may well "belong" to biology. These advances, however, provide unprecedented challenges for managing biotechnology's risks from misuse, challenges that are compounded by the ease with which biological materials can be hidden and the speed by which organisms can proliferate. Some bacteria can replicate in just 20 minutes, allowing microscopic amounts of organisms to be mass-produced in a brief period of time.

4. Benefits come with risks

[3] Meaning that the scientific or engineering details of what occurs "inside" a particular component or technique need not be understood by the individual investigator in order to make use of it.

Studies that uncovered DNA as life's genetic material and the discovery that genes encode for proteins that govern cellular characteristics and processes ushered in an era of modern molecular biology that saw rapid advances in our knowledge of living systems and our ability to manipulate them. At first, studying gene function involved introducing random mutations into the genomes of organisms and assessing physical and behavioral changes. Soon after, scientists learned to control gene function directly by introducing exogenous pieces of DNA into the organism of interest. Experiments like these began to shed light on the molecular mechanisms that underlie cellular processes and resulted in a better understanding of, and better tools to fight, human disease.

Modern molecular biology continues to develop medical solutions to global

health issues such as newly occurring, re-emerging, and endemic infectious diseases. To address these threats, researchers are working to develop rational-design vaccines and antivirals. Microbiologists are exploring new avenues to counter antibiotic resistance in bacteria, while synthetic biologists are programming microorganisms to mass produce potent and otherwise rare anti-malarial drugs. Biotechnology's contribution to health is visible in medical genomics, where rapid improvements in DNA sequencing technology, together with better characterization of genes, are beginning to unravel the genetic basis of disease. Other advances are apparent in the genetic modification of crops that render them resistant to disease and increase their yield. Biotechnology is even beneficial in industrial applications such as the development of new biological materials, potentially environment-friendly biological fuels, and bioremediation—the breakdown of pollutants by microorganisms.

But the same technologies and know-how that are driving the revolution in modern medicine are also capable of being misused to harm human health and agriculture (NRC, 2003a; NRC, 2003b). Traditional threats created by the misuse of biotechnology involve the acquisition, amplification, and release of harmful pathogens or toxins into the environment. One area of concern, for example, is a potential bioterrorist attack using pathogens or toxins on centralized food resources. Some toxins, like those produced by the bacterium *Clostridium botulinum*, are extremely damaging; small amounts are sufficient to inhibit communication between the nervous system and muscles, causing respiratory paralysis and death. In 2001, the United States found itself unprepared to cope with the intentional spread of anthrax, a bacterium[4] that can be obtained from the wild and amplified in laboratories. Anthrax can enter the body orally, or through cuts and skin lesions, after which it proliferates and releases illness-causing toxins. A more dangerous and deadly infection, however, can result if stable, dormant spores of the bacterium are "weaponized", or chemically coated and milled into a fine powder consisting of small particles that can be suspended in air. These bacterial particles can travel long distances, be taken into the victim's respiratory airways and drawn into the lungs, where the spores germinate into active bacterium that divide and release toxic

[4] Scientifically, one distinguishes between the microorganism, *Bacillus anthracis*, and the disease it causes, anthrax. Here we have adopted the more casual popular usage that conflates the organism itself with the name of the disease, at

the risk of some loss of precision.

substances to surrounding cells. If left untreated, inhalation anthrax infects the lymph nodes, causing septic shock and death in the vast majority of its victims.

Whereas many bacterial pathogens, like anthrax, are free-living organisms that require proper conditions and nutrients for growth, other bioterrorism agents, like viruses, are parasitic and rely on their hosts' cellular machinery for replication and propagation. Viral propagation in laboratories involves propagating viruses in cells that are often maintained in incubators that precisely mimic the host's physiological environment. A trained individual, with the proper know-how and the wrong intentions, could co-opt these life science tools to amplify, harvest and release deadly pathogens into the environment. This threat is compounded by advances in microbiology, virology and molecular biology, which enable directed changes in the genomes of organisms that can make them more stable, contagious and resistant to vaccines, antibiotics (in the case of bacteria), or antivirals.

Unless it is properly used, biotechnology's dual-use nature—the fact that beneficial advances can also be used to cause harm—poses a potential threat to human health and food security. But risk management measures aimed at minimizing these threats should not excessively impede biotechnology's benefits to health and food security, and should also take care not to unnecessarily hinder scientific progress; inhibiting a developing country's access to health tools that are used in vaccines and pharmaceutical drug production would pose a serious ethical dilemma. Even if humanitarian arguments were set aside, solely from the perspective of self-interest in the developed world, restricting access to biotechnology could undermine desired security objectives by encouraging secrecy and impeding collaborative exchanges among different laboratories.

Biology's dual-use challenges extend beyond technology and include knowledge and know-how: better understanding of the molecular mechanisms that underlie cellular processes expose the human body's weaknesses and sensitivities, which can be exploited by those who intend to harm. Consider immunology research, which has characterized the interleukins, proteins that participate in the body's immune response to an infection. Foreign pathogens can disrupt the normal activity of these proteins and result in a defective immune response, serious illness, and death. A set of experiments that inadvertently illustrated some dual-use applications of this knowledge involved a group of Australian researchers who, in an attempt to sterilize rodents, added one of the interleukins, interleukin-4, to a mousepox virus (among other genetic modifications),

hoping to elicit an autoimmune reaction that would destroy female eggs without eliminating the virus (Jackson et al., 2001). However, the virus unexpectedly exhibited more generalized effects; it inhibited the host's immune system and caused death—even in rodents that were naturally resistant to the virus or had previously been vaccinated. In a separate study, researchers showed that mice resistant to mousepox, if injected with neutralizing antibodies to the immune system regulator, IFN-
, become susceptible to the virus and exhibit 100% lethalilty (Chaudhri et al., 2004).

Although there are genetic variations and different modes of infection between mousepox and its human counterpart, smallpox, these published experiments provide a possible road map for creating a more virulent and vaccine-resistant smallpox virus—a chilling notion given that the virus has been a major killer throughout human history (Tucker, 2001). Although the United States has enough supplies to vaccinate its entire population (assuming the vaccine would be effective against a genetically modified virus), current world supplies can only cover 10% of the global population (Arita, 2005). (However, a "ring vaccination" strategy, rather than a "herd immunity" strategy, might be able to stop an outbreak well before complete vaccination were required.) Fortunately, smallpox has been eradicated from the natural world. The only known remaining stocks are located in U.S. and Russian facilities. Although the WHO's decision-making body, the World Health Agency, had initially called for the destruction of these stocks by the end of 2002, it later suspended its decision, allowing smallpox research with the live virus to continue (Stone, 2002). Currently, researchers are using a variety of approaches to study the biology of smallpox, including research projects that involve infecting animals with the live virus (Rubins et al., 2004).

In addition to fears that smallpox could be accidentally or intentionally released or stolen from research facilities, there are also concerns that the smallpox virus could be regenerated from scratch. The latter requires piecing together the different fragments of the genome, which would be a difficult task, requiring knowledge of molecular biology, a standard molecular biology laboratory with appropriate reagents and equipment, and the skills and substantial time for trial and error. While synthesizing the smallpox virus from scratch in the laboratory is theoretically possible, it is fortunate that this challenge

is both quantitatively and qualitatively much harder than for some other viruses, like polio. Advances in the life sciences, however, are beginning to remove these hurdles.

5. Biotechnology risks go beyond traditional virology, micro- and molecular biology

To date, complete genomes from hundreds of bacteria, fungi, viruses and a number of higher organisms have been sequenced and deposited in a public online database. While many of these genomes belong to inert microbes and laboratory research strains that cannot infect people or animals, others include those from some of the most pathogenic viruses known to humans, such as Ebola and Marburg, and even extinct ones like smallpox and the 1918 Spanish influenza virus. Alongside better DNA sequencing, biotechnology research has also seen the evolution of *de novo* DNA synthesis technologies; it is now possible to commercially order pieces of DNA as long as 40,000 bases[5]—longer than the genomes of many viruses; SARS for instance is roughly 30,000 bases, while the Ebola genome is less than 20,000 bases long. Moreover, the coming rapid improvement of the technology over the next several years should enable even the synthesis of bacterial genomes, many of which are around 1 million bases long. For example, just recently, scientists at the Venter institute transplanted an entire genome from one bacteria species into another, causing the host cell to effectively become the donor cell (Lartigue et al., 2007). The study demonstrates how a bacterial cell can be

[5] A base, or a nucleotide, is the fundamental unit of a DNA molecule

used as a platform, in which to create new species for specialized functions (provided their genomes are available). The donor and host bacterial species that were chosen for the study are highly related to each other and contain relatively small genomes, features which facilitated the success of the

transplantation experiment. Nevertheless, the study does point the way to more general applications, including transplantation of synthesized pathogen genomes, for the creation of otherwise difficult-to-obtain bacterial pathogens.

Automated DNA synthesis removes much of the time-consuming and technically difficult aspects of manipulating DNA; using commercial DNA synthesis, a researcher can copy a sequence of interest from an online public database and "paste" it into the commercial DNA provider's website. Within days or weeks (depending on length of the sequence) the fragment, or even the entire genome of interest, is artificially synthesized and mail-delivered. For many viruses, a synthesized viral genome could then be introduced into a population of cells, which would treat the foreign DNA as if it were their own: "reading" it, transcribing the genes into RNA molecules that are processed by the cell's internal machinery and translated into proteins. These proteins can then assemble themselves into infectious viral particles that are ejected from the cell, harvested and used in infection studies.[6]

In the wrong hands or in laboratories that lack proper safety precautions, this technology poses a serious security risk as it renders some of the traditional regulatory frameworks for the control of biological agents obsolete. A number of countries control the possession and movement of these substances. In the United States these are referred to as "select agents" and include a number of bacteria, viruses, fungi and toxins that are harmful to humans, animals or plants. Conducting research on these high risk organisms and toxins require special licenses or security clearances. The ability to order genomes and create organisms *de novo*, however, necessitates revisiting these regulations. As we have seen, experiments have already been published in the highest profile international scientific journals that describe the re-creation of the poliovirus as well as the Spanish influenza virus, the agent that killed 50 million people in 1918. This virus, which was previously extinct, now exists and is used in research facilities in both the United States and in Canada. The ability to synthesize genomes and create organisms from them has spurred a U.S.-based biosecurity advisory board to call for regulating the possession and movement of pathogen genomes, rather than pathogens themselves (Normile, 2006).

In addition to risks arising from the intentional misuse of these pathogens, there are serious laboratory safety considerations; many facilities worldwide lack the expensive safeguards needed for handling highly pathogenic organisms—even though they may have the technology to create these

organisms. Moreover, the ease with which genomes

[6] Once they are inside their target cells, viruses hijack cellular proteins to convert their genomes into viral particles. However, viruses that contain negative strand RNA genomes, like Marburg and Ebola, cannot be turned into mature viruses with host proteins alone. Conversion of such genomes into virus particles also requires proteins that are normally packaged within the virus itself. Thus, the Ebola and Marburg genomes are not infectious on their own.

can be synthesized raises the concern that highly pathogenic viruses and bacteria will become increasingly distributed in laboratories and among researchers interested in high consequence pathogen research. The accidental contamination of workers, and the subsequent escape of viruses from highly contained laboratories, has occurred a number of times. In one such case, a researcher at the National Defense University in Taipei was, unknowingly, infected with the SARS virus, after which he left Taiwan for a conference in Singapore. The event prompted quarantine of 90 individuals with whom the infected researcher had come into contact (Bhattacharjee, 2004). Although there were no known secondary infections in this particular case, the escape of pathogenic viruses or bacteria from contained laboratories could have serious consequences.

6. Addressing Biotechnology Risks

Dual-use risks posed by biotechnology may be addressed at a number of points. Efforts may be made to oversee, regulate, or prevent the most dangerous research altogether, or the publication of that research, or to restrict certain lines of research to particular individuals. One may also focus on recognizing disease outbreaks quickly whether natural or intentional when they occur, and responding to them effectively. This requires both improvements in surveillance and response capacity and infrastructure. Finally, one may encourage research,

development, and production of appropriate vaccines, antibiotics, antivirals, and other approaches to mitigating an outbreak—along with the required infrastructure for meeting surges in both drug requirements and numbers of patients. Of course, none of these approaches is exclusive. Perhaps their one commonality is that each faces important drawbacks. We consider a variety of suggested approaches to each, and their challenges.

6.1. Oversight of Research

The U.S. National Research Council (NRC) has recommended a variety of oversight mechanisms and guidelines for federally-funded, high-risk research (NRC, 2003a). These "experiments of concern" would be subjected to greater scrutiny at the funding stage, during the research phase, and at the publication stage.[7] They would include experiments that could make pathogens impervious to vaccines and antibiotics, allow pathogens to escape detection and diagnosis, increase the transmissibility or host range of a pathogen, and experiments that aim to "weaponize" biological agents and toxins. But the NRC guidelines would only extend to laboratories that are funded by the National Institutes of Health, and therefore required to follow governmental guidelines. A comprehensive approach would take into account the commercial sector as well as increased funding from philanthropic and private foundations like the U.S-based Howard Hughes Medical Institute, or the Welcome Trust of England, which annually distribute

[7] The U.S. federal advisory group, NSABB, has called for self-regulation within the scientific community. Under the proposed plan, scientists themselves decide whether their research constitutes dual-use experiments of concern. For a discussion of NSABB's proposal, refer to Jocelyn Kaiser, 2007. "Biodefense: Proposed Biosecurity Review Plan Endorses Self-Regulation" *Science*. 316 (5824), p. 529

500 million, and over 1 billion research dollars, respectively (Aschwanden, 2007). Comprehensive oversight mechanisms would also include governmental laboratories, including those involved in biodefense research. Finally, the biotechnology challenge is inherently global, so an effective research oversight regime would have to be international in scope.

To this end, John Steinbruner and his colleagues at the Center for International and Security Studies at Maryland (CISSM) have proposed a global system of internationally agreed rules for the oversight of potentially high-consequence pathogens research (Steinbruner et al., 2005). Although dedicated non-state groups would not be likely to be captured by such a system, they are unlikely to conduct forefront research. Instead, they might attempt to co-opt discoveries and techniques that are reported in the scientific literature. By overseeing certain high-risk research and its publication, society might therefore head off some of the worst misuse. A limited model for what oversight of the highest consequence biological research might look like is provided by the World Health Organization's international advisory committee that oversees smallpox research; it is important that this committee demonstrate that it is capable of real oversight.

The CISSM model oversight system calls for an International Pathogens Research Authority with administrative structures and legal foundations for participation of its states-parties. It is unlikely that such a system could be negotiated and ratified in the current climate, although plausibility of possible oversight mechanisms could change rapidly subsequent to a laboratory-engineered pandemic; better that careful thinking be done now before the urgency and fear that would be pervasive in that post-attack world. Other international approaches to provide some level of oversight have also been envisioned, including the creation of additional UN bodies, or the establishment of an "International Biotechnology Agency" (IBTA) by analogy to the International Atomic Energy Agency. The IBTA could be established in a modular way, with initial modest goals of helping BWC states-parties meet their reporting ("confidence building measures") requirements, and promoting best practices in laboratory safety. All of these approaches require the creation of new international oversight bodies, a politically challenging requirement.

6.2. "Soft"

Oversight

At the other end of the spectrum from the CISSM oversight model are efforts at what might be called "soft" oversight of high-risk research. Some of the most common among these are efforts to promote codes of ethics (or the more demanding, but rarer, codes of conduct or codes of practice) for scientists working in the relevant fields.[8] Many

[8] For a discussion of codes of conduct in the case of biodefense research, see Roger Roffey, John Hart, and Frida Kuhlau, September 2006 "Crucial Guidance: A Code of Conduct for Biodefense Scientists," *Arms Control Today*. For a review and critical discussion of the broader need for codes applicable to all life scientists, see *Globalization, Biosecurity and the Future of the Life Sciences*, (Washington, DC: National Academies Press, 2006), pp. 246-250.

national and international groups have made efforts in this direction. If coupled with education about the possible misuse of scientific research, such codes would help provide the scientific community with tools to police itself. To this end, a U.S. National Academy panel has recommended establishing a global internet-linked network of vigilant scientists to better protect against misuse within their community (NRC, 2006).

6.3. Multistakeholder partnerships for addressing biotechnology risks

The failure of the negotiations for a compliance protocol to the BWC shows some of the challenges now facing treaty negotiation and ratification. (This protocol, while it would have provided valuable transparency into certain high-end biological facilities, would not have—nor was it meant to—directly addressed the challenge of dual-use biotechnology.) One general result has

been increasing interest in alternative policy models such as multi-stakeholder partnerships. Indeed, the international relations literature has seen a growing body of work devoted to the mismatch between important global problems and the absence of international mechanisms to address them in a timely and effective way.[9] Means of international governance without formal treaties are being sought. In the biological security realm, efforts to forge multi-stakeholder partnerships are bringing together the academic science sector, commercial industry, the security community, and civil society, in order to raise awareness and facilitate feasible risk- management solutions to biology's dual-use problem. The former UN Secretary-General, Kofi Annan, recognized that the increasing distribution of biotechnology requires solutions that have an international dimension and called for a global forum to help extend the benefits of biotechnology and life science research, while managing its security risks. The Secretary-General's unique convening power to bring together a diverse number of players from the appropriate sectors is instrumental for a successful bottom-up approach that aims to address biotechnology's challenges. This, together with other efforts by Royal Society, the InterAcademy Panel on International Issues, the International Council for the Life Sciences, the International Consortium for Infectious Diseases and a number of others, are beginning to work toward an international framework in the absence of a formal, government-driven treaty process.

In addition to recognizing the urgency to address biotechnology's risks, some of these efforts have also highlighted the importance of risk-management strategies that don't hinder free flow of scientific communication and that don't impose excessively intrusive oversight mechanisms that would hurt scientific progress. An example of an effective risk-management strategy that manages risks without impacting potential benefits is a proposal that specifically addresses *de novo* DNA synthesis technology. The

[9] For key publications in this literature, see Wolfgang Reinicke, Global Public Policy: Governing Without Government? (Washington, DC: Brookings Institution, 1998); J. F. Rischard, High Noon: Twenty Global Problems, Twenty Years to Solve Them (New York: Basic Books, 2002); Anne-Marie Slaughter, A New World Order (Princeton: Princeton Univ. Press, 2004).

successful adoption of the proposal in the academic and commercial science sectors merits further attention, as the risk-management strategy might be applicable to some of biology's other dual-use areas.

6.4. A risk management framework for de novo DNA synthesis technologies

Currently, *de novo* DNA synthesis technologies capable of making complete pathogen genomes are concentrated in a relatively small number of companies. In 2004, the Harvard biologist and biotechnology developer, George Church, proposed a safeguards strategy to ensure that the technology is not used for the illegitimate synthesis of potentially harmful genomes (Church, 2005). This involves companies agreeing to install automated screening software that "reads" the DNA sequence of incoming customer orders and compares them to genomes of a known list of pathogens (and, potentially, to a list of other potentially dangerous sequences, e.g. those for particular genes). An exact match, or more likely a certain degree of sequence similarity, would elicit further inquiry and possibly result in the notification of proper authorities. Software in the synthesis machines could be installed, and updated, to make it impossible for the machines to synthesize certain sequences of particular concern.

This kind of DNA screening has already been adopted by a number of the DNA providers and has won endorsement within the synthetic biology community, which is a heavy user of DNA synthesis technologies (Declaration of the Second International Meeting on Synthetic Biology, 2006). Successful implementation of the protocol is in large part due to the proposal's non-intrusive nature; rather than requiring formal oversight structures, which many scientists oppose for fear that progress might be hindered, the screening tool allows the laboratory to go about business as usual as the computer software engages in the invisible detective work. The automated nature of DNA screening is also appealing to industry because it enables the protection of customer information. MIT synthetic biologist Drew Endy, together with George Church and other

colleagues, like John Mulligan, CEO of a leading DNA synthesis company, are now working to extend the screening proposal to companies oversees. Indeed, lack of unity among the various DNA providers would risk jeopardizing the entire venture since it only takes a single non-compliant company to provide harmful materials to all interested customers. Possible strategies to address this deficiency include licensing all DNA providers, or establishing a centralized international clearinghouse that receives and screens all DNA orders from the various providers (Bugel et al., 2006).

6.5. From voluntary codes of conduct to international regulations

While adopting safeguard strategies such as DNA screening exemplifies corporate responsibility, implementation of these measures is purely voluntary and without a legal framework. The UN Security Council Resolution 1540 provides the impetus to strengthen and globally extend such measures. Resolution 1540 requires UN member states to strengthen national legislation in order to address a number of issues, including biological terrorism. The legally binding implementation of the DNA screening protocol by countries that are users or providers of the technology could be cast in terms of a step

in the implementation of resolution 1540. Alternatively or additionally, other international mechanisms such as the BWC could be adapted to carry out the operations of a centralized international clearinghouse for DNA synthesis screening.

6.6. Biotechnology risks go beyond creating novel pathogens

As biotechnological tools improve, the various methods that can be used to create novel organisms should be assessed further in order to make informed policy decisions regarding the risks. For example, a combination of virology and

molecular biology could be used to create novel pathogens like hybrid viruses that are composed of inert laboratory strains loaded with additional toxic genes. Once inside its host, the hybrid virus would enter its target cell population, where viral genetic material would be converted into toxic proteins that disrupt normal cellular processes and cause disease (Block, 1999).

Similarly, viruses can be created that have the ability to shut down essential cellular genes (Block, 1999). Consider small interfering RNA (siRNA) technology, whose beneficial applications were recognized by the 2006 Nobel Prize for physiology or medicine. siRNA molecules turn off a gene by inactivating its RNA product (Sen and Blau, 2006). A highly contagious virus, supplemented with siRNA, or other “gene knockdown” technologies, could shut down essential genes in particular cell populations of its host (Block, 1999). Theoretically, this could set off a novel epidemic for which no known vaccine or cure exists. Even more alarming is the ease with which commercial DNA sources can automate the synthesis of these novel pathogens, relieving even the novice from the laborious and methodical task of splicing genes into viral genomes (Tucker and Zilinskas, 2006). Thus, it is important that DNA screening safeguards encompass more than just naturally occurring pathogenic genomes and gene-encoding toxins.

6.7. Spread of biotechnology may enhance biological security

The spread of novel biotechnologies such as large-DNA synthesizers could, paradoxically, provide an opportunity to decrease the probability of misuse. If costs associated with commercial synthesis of large DNA fragments continue to decline, research laboratories will increasingly look to outsource the laborious task of manipulating DNA sequences to more centralized, automated sources. Similar trends have been observed for DNA sequencing; laboratories that carried out sequencing operations in-house now outsource their needs to commercial sources that perform the task faster and at a fraction of the cost. A similar outcome for DNA synthesis could eventually replace a large number of diffuse and difficult-to-regulate DNA laboratories with more centralized DNA providers whose technologies are automated and more safeguard-friendly.

Not all dual-use issues will be addressed through technical solutions. But where possible, technologies that can be safeguarded should be promoted.

This requires innovators and users of new biotechnologies identify potential risks and develop

appropriate safeguards. Biological security gatherings that bring together scientists and policy makers are useful for creating the right mechanism for this but they cannot replace hours of brainstorming by students searching for technical and feasible risk management solutions. Stronger communication links between the security community and biologists and more formal interdisciplinary education programs should be fostered. Fortunately, some scientists at the forefront of fields such as synthetic biology have also been at the forefront of addressing the ethical and security implications of their research (Church, 2005; Endy, 2007).

7. Catastrophic biological attacks

It is difficult to forecast mortality figures resulting from potentially catastrophic bioterrorist incidents—however important such predictions may be for designing defensive public health measures. Unpredictability in human behavior, for example, would impact morbidity and mortality figures, particularly if contagious agents are involved. For aerosolized pathogens, factors like wind speed and direction, as well as other environmental fluctuations, could result in very different attack outcomes. Limitations in our understanding of the biology of pathogens and their interaction with their hosts (i.e. precise mode of infection and, for transmissible pathogens, mode of spread) also render accurate predictions difficult. And as with any major disaster, it is difficult to know in advance the efficacy of emergency response plans and the competence with which they will be carried out (Clarke, 1999).

Moreover, modern society's experience with bioterrorism has, fortunately, so far been limited to a small number of events that were either not intended to, or did not result in high mortality figures, so may not serve as good indicators for

what a successful major attack would look like. The 2001 U.S. Anthrax scare that caused 5 deaths, for instance, involved a non-contagious pathogen, and although milled into a fine powder, the bacterial spores were initially contained within envelopes that resulted in only local dissemination. By contrast, the Aum Shinrikyo cult, seeking to stage a mass-casualty attack in order to realize a prophecy, attempted to disperse *Bacillus anthracis,* from a building rooftop onto the dense urban population of Tokyo. The Aum, which later succeeded in dispersing Sarin nerve gas in Tokyo subways, was, fortunately, unsuccessful both in efforts to procure a pathogenic strain of *Bacillus anthracis*, and in its attempts to efficiently disseminate the bacterium. But a more rudimentary dispersal technique was successfully used by another group, the Rajneeshees, whose actions were motivated by a desire to keep a large block of individuals away from voting polls, in order to influence local elections. In 1984, members of the Oregon-based cult successfully spread the enteric bacterium, *Salmonella typhimurium,* onto salad bars, causing illness in over 750 Oregonians and sending many to hospitals. Had the Rajneeshees used a more virulent pathogen, or had the U.S. Anthrax been more efficiently dispersed, major public health disasters may have ensued. In 1993, estimates from the US Congress' Office of Technology Assessment found that a single 100 kg load of anthrax spores, if delivered by aircraft over a crowded urban setting could, depending on weather conditions, result in fatalities ranging between 130,000 and 3 million individuals. However, these sort of dramatic results have been viewed as overly alarmist by those claiming that such high

casualties would require optimal conditions and execution by the perpetrators, and that there would in fact be a very wide range of possible outcomes (Leitenberg, 2005).

Besides the Rajneeshees and the Aum Shinrikyo, another non-state group[10] that appears to have pursued biological weapons is Al Qaeda, apparently making use of one doctoral-level biologist and perhaps several with undergraduate degrees. It is difficult from the open literature to determine either

the level of sophistication or accomplishment of the program, but what is available suggests that the program was more aspirational than effective at the time that Al Qaeda was expelled from Afghanistan (National Commission on Terrorist Attacks Upon the United States, 2004; Commission on the Intelligence Capabilities of the United States Regarding Weapons of Mass Destruction, 2005).

While intentional biological attacks have yet to result in catastrophic scenarios, natural disease outbreaks can serve as proxies for what such events might look like. Consider smallpox, which infected 50 million individuals—annually—even as late as the early 1950s (WHO, 2007). Procuring (or creating), and releasing a vaccine-resistant or more lethal strain of this contagious virus in a dense urban environment might well be a cataclysmic event.

Whereas smallpox kills up to a third of its victims, certain strains of the hemorrhagic fever viruses, like Ebola-Zaire, can kill up to 90% of the infected—within several days after symptoms surface. Since 1976, when Ebola first appeared in Zaire, there have been intermittent outbreaks of the disease, often along Sub-Saharan African rainforests where the virus is transmitted from other primates to humans. The remoteness of these regions, and the rapid pace by which these viruses kill their human host, have thus far precluded a global pandemic. However, if these pathogens were procured, aerosolized, and released in busy urban centers or hubs, a catastrophic pandemic might ensue—particularly because attempts to generate vaccines to Ebola have, thus far, proven unsuccessful. In 1992, the Aum Shinrikyo sent a medical team to Zaire in what is believed to have been an attempt to procure Ebola virus (Kaplan, 2000). While unsuccessful, the event provides an example of a terrorist group apparently intending to make use of a contagious virus.

In addition to the toll on human life, biological attacks can inflict serious psychological damage, hurt economies, cause political fallout and disrupt social order. A 1994 natural outbreak of pneumonic plague in Surat, India, provides a glimpse into what such a scenario might look like[11]. Pneumonic plague is an airborne variant, and deadliest

[10] We define “sub-state” groups to be those that receive substantial assistance

from a state or state entities; “non-state” groups by contrast are those that do not. The Rajneeshees and Aum Shinrikyo were non-state groups. Because of its accommodation by the Taliban in Afghanistan, Al Qaeda arguably was, at least for a time, a sub-state group. [11] The implication of plague in Surat has been somewhat controversial. A number of studies, however, including Shivaji et al., (2000), have used DNA forensics to show that the causative agent of the disease outbreak was, in fact, *Yersinia pestis*.

form, of the “black death”—the disease caused by the bacterium, *Yersinia pestis*, believed to have wiped out a quarter of Europe’s population in the fourteenth century (Anderson and May, 1991). The 1994 outbreak in Surat resulted in an estimated 300,000 individuals fleeing the city (Hazarika, 1995a), and even led to closure of schools, universities, and movie theatres in cities hundreds of miles away (The New York Times, September 20, 1994). Shock waves were felt globally as India faced increasing international isolation: its exports were banned; its tourism industry drastically declined (Hazarika, 1995b); and its citizens were subjected to scrutiny and surveillance at foreign airports (Altman, 1994).

But while much attention has been paid to human pathogens, threats to agriculture, livestock and crops, which can cause major economic damage and loss of confidence in food security, should not be overlooked. In 1997, for example, an outbreak in Taiwan of the highly contagious foot-and-mouth disease, caused the slaughter of 8 million pigs and brought exports to a halt, with estimated costs of $20 billion (Gilmore, 2004). Crops can be particularly vulnerable to an attack; they inhabit large tracts of difficult-to-protect land, and suffer from low levels of disease surveillance, sometimes taking months, even years, before disease outbreaks are detected. In 2001, in an effort to contain a natural outbreak of *Xanthomonas axonopodis,* a bacterium that threatened Florida’s citrus industry and for which there is no cure, two million trees were destroyed (Brown, 2001). There are well defined steps that may be taken by

countries (assuming the resources and capacity are available) to protect against such threats (NRC, 2003b).

In addition to actual attacks on human health and food security, biological "hoaxes" can also exact an important societal toll. Between 1997 and 1998, as media attention to bioterrorism grew, the number of hoaxes in the United States increased from 1 to 150 (Chyba, 2001). In October and November of 2001, following the US Anthrax attacks, 750 hoax letters were sent worldwide, 550 of which went to US reproductive health clinics by a single group (Snyder and Pate 2002). The high rate of these hoaxes requires defensive systems that can quickly distinguish a real attack from a fake one. This involves vigilance in disease detection and surveillance, as well as forensic discrimination. The remainder of this chapter explores such public health systems, as well as other strategies to defend against biological outbreaks.

8. Strengthening disease surveillance and response

The need to recognize and respond to disease outbreaks is the same regardless of whether the outbreak occurs naturally, by accident, or through an act of terrorism. Therefore, appropriate defense measures should include a strong public health sector that can react to the full spectrum of risks—whether they are relatively common infectious disease outbreaks or less familiar events like bioterrorist attacks.

Defense against biological attacks requires rapid detection of disease, efficient channels of communication, mechanisms for coordination, treating the infected, and

protecting the uninfected. The World Health Organization's deliberate epidemics division provides specific guidelines in these areas.[12]

8.1. Surveillance and detection

Efficient response to a disease outbreak begins with disease surveillance. Early detection can greatly minimize the numbers of infected individuals—particularly when contagious pathogens that can cause secondary infections are involved. Clinicians and medical personnel are indispensable for diagnosing and detecting disease, but they can be complemented by improved surveillance of air, food and water supplies. The United States employs BioWatch in 30 cities; BioWatch employs a device that concentrates outside air onto filters that are routinely tested for the presence of various bioterrorism agents. More advanced systems include the Autonomous Pathogen Detection System (APDS), an automated diagnostic device that conducts PCR (a method that amplifies DNA sequences) as well as other forensic analysis within the device itself. In addition to rapidly recognizing disease agents, the effective use of these automated diagnostics also allows human capacity and laboratory resources to be spent in other areas of need. Although they are partly effective for detecting aerosolized agents, automated diagnostics suffer from high rates of false positives, mistaking background and normal levels of pathogens for biological weapons (Brown, 2004). In addition to focusing future research on improving sensitivity and accuracy of detection devices, the range of pathogens that are surveyed should be broadened beyond the high probability bioterrorism agents— especially because novel technologies allow the synthesis of a growing number of organisms.

Affordability, availability, and proper implementation of better diagnostic tools represent some of biotechnology's biggest benefits for improving health (Daar et al., 2002). For example, effective diagnosis of acute lower respiratory infection, if followed by proper treatment, would save over 400,000 lives each year (Lim et al., 2006). Equally optimistic predictions can be made for malaria, tuberculosis and HIV (Girosi et al., 2006). Moreover, new generations of technologies in the pipeline, if they become more affordable, could revolutionize the future of disease detection. These include small nanotechnology-based devices that can prepare and process biological samples and determine the nature of the pathogen in real time; effectively serving as an automated laboratory on a small chip (Yager et al., 2006).

Despite technological improvements, traditional methods such as surveillance of blood samples and diagnosis by medical professionals remain of utmost importance, and must not be overlooked in the face of “high-tech” approaches of limited applicability. Diagnosis of anthrax in the 2001 bioterrorist attack, for example, was not made by sophisticated technologies, but by a vigilant clinician. Improvements in human diagnostic skills, however, is badly needed, especially for likely bioterrorist agents; a

[12] Much of the discussion here, regarding disease preparedness and response, has been based on WHO strategies that can be found here: http://www.who.int/csr/delibepidemics/biochemguide/en/index.html

survey of 631 internal medicine residents in 2002-2003 demonstrated that only 47% were able to correctly diagnose simulated cases of smallpox, anthrax, botulism and plague, better training for which increased the frequency to 79% (Cosgrove et al., 2005; Bradbury, 2005). Better diagnostic training, human capacity and laboratory infrastructure, is particularly important for parts of the developing world that suffer most from disease. Improving domestic and international disease surveillance capacity and infrastructure (in areas of human and animal health, as well as communication between the two communities) lacks the glamour of high-tech solutions, but remains one of the most important steps that needs to be taken (Chyba, 2001; Kahn, 2006).

8.2. Collaboration and communication are essential for managing outbreaks

While diagnosis of an unusual disease by a single astute physician can sound the alarm, detecting an epidemic for a disease that normally occurs at low frequencies requires the consolidation of regional surveillance data into a single database that is monitored for unusual trends. Once an outbreak is

suspected or confirmed, it must be communicated to appropriate individuals and departments whose roles and responsibilities must be delineated in advance. Coordination, transparency and timely sharing of information are of great importance, procedures which require oversight bodies and a clear chain of command.

The increasing volume in global trade and travel, and the rapid pace by which transmissible disease can spread, necessitate effective international communication and coordination. Electronic communication tools include the Program for Monitoring Emerging Diseases (ProMed) and the World Health Organization's Global Public Health Information network (GPHIN). PROMED provides news, updates and discussion regarding global disease outbreaks, while the web-based early "disease warning system", GPHIN, scans websites, blogs and media sources, gathers disease information and reports unusual biological incidents. Coordination between countries is facilitated by the WHO's Global Outbreak and Response Network (GOARN), which links over one hundred different health networks that provide support for disease detection and response. During the 2004 SARS outbreak, the WHO established laboratories to link efforts among different countries, which resulted in rapid identification of the disease agent as a coronavirus. The organization is in a position to provide similar support in the event of deliberate pandemics.

Coordination within and between countries is also necessary to facilitate sharing of disease samples, which are used for production of vaccines and treatments. Determining whether an outbreak is intentional or natural can be difficult, unless forensic analysis can be performed on the genome or protein composition of the organism. For example, rapid sequencing of a genome may uncover artificially added pieces of DNA that confer antibiotic resistance or enhanced stability to an organism. Such findings might impact the design of appropriate drugs and therapies, but require the prompt availability of disease data and samples; the US Centers for Disease Control and Prevention, for instance, has been criticized for not sharing flu data with other scientists (Butler, 2005).

8.3. Mobilization of the public health sector

Once disease outbreaks are detected and communicated to the proper authorities, local agencies and individuals must assemble and respond to the public health crisis. Lack of preparation for responding to large-scale biological outbreaks can overwhelm the health care system, negatively impacting not just the disaster sector, but also the greater public health infrastructure. There have been speculations, for example, that Toronto's effective response in curbing SARS placed pressure on other critical health care areas that resulted in a number of preventable deaths (IOM, 2004:34). Emergency relief procedures should be established and practiced in advance, particularly for procedures that deal with surge capacity—the ability to expand beyond normal operations in order to deal with emergencies and disasters. Surge capacity involves enlisting medical personnel from other sectors. The ability to co-opt existing networks of local health care workers to perform disaster relief is an important element of a successful surge-capacity strategy. While local health care providers can address general disaster relief functions, more specialized responders are also instrumental for proper isolation and handling of hazardous biological materials, for selection of appropriate decontamination reagents, and for assessing risks to health and to the environment (Fitch et al., 2003).

8.4. Containment of the disease outbreak

The rapid containment of a disease outbreak requires identification of the "hot- zone"—the area that is contaminated. This is exceedingly difficult for contagious agents, particularly ones with long asymptomatic incubation periods during which disease can be transmitted to others and spread over large areas. Also difficult is containing novel agents whose mode of infection or transmissibility is not known. Both epidemiological tools and computer simulations may be used to help identify, isolate and quarantine affected individuals and to break the chain of infections. [13] This was successfully accomplished during the SARS outbreak with the WHO leadership issuing timely and aggressive guidelines concerning quarantine procedures, curfews and travel advisories.

Halting disease spread also requires provisions to care for large numbers of infected individuals, possibly in isolation from others in mobile hospitals or dedicated hospital wings, gymnasiums, or private homes. The public is most likely to respond well if there is effective dispersal of information through responsible media sources and credible internet sites such as the Centers for Disease Control and Prevention and the World Health Organization. The use of telephone hotlines also proved to be an effective information dispersal tool during the SARS outbreak.

[13] There are a host of legal and ethical issues regarding implementation of quarantines. For a discussion, refer to Cécile M. Bensimon and Ross E.G. Upshur, 2007 **"**Evidence and effectiveness in decisionmaking for quarantine.**"***American Journal of Public Health* Suppl 1, pp. 44-8; Richard Schabas, 2003. "SARS: prudence, not panic" *Canadian Medical Association Journal*. 169 (1) pp. 1432-4

In addition to curbing social contacts, implementing curfews and quarantines, and halting public activities, other types of public health protection measures can be implemented in a disease outbreak. These include the decontamination of high-traffic areas like hospitals, schools and mass-transit facilities and implementing personal precautions such as hand washing and protective clothing, gloves, and masks. Masks should be worn by both the infected and the uninfected; the N-95 masks, so called for its ability to block particles greater than 0.3 microns in size 95% of the time, is particularly effective and provided protection against the SARS virus; even though that virus is smaller than 0.3 microns, SARS travels in clumps, resulting in larger sized particles that become trapped (IOM, 2004:18). Personal protection is particularly important for health care workers and first responders who are in the front lines and more at risk of becoming infected; during the early stages of the SARS pandemic, a single

patient, the “super- spreader”, infected every one of 50 health workers who treated him. Fully contained suits and masks, depending on the nature of the pathogen, might be appropriate for health care workers. In addition, these individuals should also receive prophylaxis and immunizations, when available; the United States, for instance, encourages more than 40,000 medical and public health staff personnel to protect themselves against a potential smallpox outbreak by vaccination (Arita, 2005).

Beyond health workers, determining who should receive treatment can be difficult to assess, particularly when supplies are limited or when there are detrimental side effects of receiving treatment. These difficult choices can be minimized and avoided through aggressive drug and vaccine research, development and production strategies.

8.5. Research, vaccines, and drug development are essential components of an effective defense strategy

Defending against likely disease outbreaks involves the stockpiling of vaccines, antibiotics and antivirals in multiple repositories. But for outbreaks that are less probable, cost and shelf-life considerations may favor last-minute strategies to rapidly produce large quantities of drugs only when they are needed. Drug and therapy development strategies require coordination between public health experts, life scientists, and the commercial sectors. Equally important is investing in basic science research, which is the cornerstone to understanding disease; decades of basic science research on viruses, bacteria and other organisms has been instrumental for rapid identification and characterization of novel biological agents, and for developing appropriate treatments and cures. (It is, of course, also this research that may bring with it the danger of misuse.) Efforts are needed to generate and promote a stronger global research capacity. This requires better funding mechanisms worldwide so that local scientists can address local health needs that are neglected by pharmaceutical companies that focus on expensive drug markets in the industrialized world. Encouraging industry to address infectious diseases includes providing incentives such as advance market commitments. The United States uses the “orphan drug legislation” to provide tax credits to companies to invest in rare diseases that are otherwise not deemed profitable.

Efforts to improve funding for addressing infectious and neglected diseases include those by The Bill and Melinda Gates Foundation, which provides grants with the precondition that any eventual product would be patent-free and publicly available. In the same spirit, the pharmaceutical giant Sanofi-Aventis and a non-profit drug development organization funded by “Doctors Without Borders” have combined to create a cheap, patent-free Malaria pill (New York Times, March 5, 2007).

8.6. Biological security requires fostering collaborations

Due to the low availability of drugs and diagnostic tools, high population densities, and pre-existing health issues, developing countries may suffer the greatest consequences of a biological attack. In some places this is exacerbated by inadequate human resources and infrastructure, which contribute to less effective planning; more than 150 countries do not have national strategies to deal with a possible flu pandemic (Bonn, 2005). Based on current public health capabilities, it is estimated that were the 1918 Spanish Influenza to take place today, 95% of deaths would occur in the developing world (Murray, 2006). Moreover, global trends of increasing urbanization create high population densities that are breeding grounds for human pathogens and attractive targets for bioterrorists.

Improvements in disease surveillance, together with better communication and coordination, should be a global priority. In an increasingly interconnected world, small- scale outbreaks can rapidly turn into pandemics, affecting lives and resources worldwide. The SARS outbreak, a relatively small pandemic, is estimated to have cost $40 billion in 2003 alone (Murray et al., 2006). Even local or regionally confined outbreaks can result in a decrease in the trade of goods, travel, and tourism that is felt globally. Strengthening global tools to fight disease

outbreaks, therefore, is sound governmental and inter- governmental policy for humanitarian reasons as well as for national and international security.

9. Toward a biologically secure future

In addition to defensive measures like improved disease detection and response, a comprehensive biological security strategy must safeguard potentially dangerous biotechnologies. Despite some of the current difficulties in identifying and implementing safeguards, there are historical reasons for optimism regarding the response of the scientific community. In the past, when confronted with potentially hazardous research involving recombinant DNA technology[14], biologists took precautions by adopting guidelines and self-regulatory measures on a particular class of experiment. One reason for this success was that from the beginning biologists enlisted support from prestigious scientific academies (Chyba, 1980). These continue to provide a powerful tool today.

[14] Recombinant DNA technology facilitated the exchange of genetic material between vastly different organisms and opened new frontiers for molecular biology research, but it also brought with it a number of safety concerns regarding potential harm to laboratory workers and to the public.

A greater challenge for biotechnology nonproliferation will be the expansion of safeguards throughout the academic, commercial, and governmental scientific sectors, as well as the international implementation of these measures. Traditional nonproliferation conventions and arms control treaties predominantly address nation states and do not provide adequate models for dealing with the non-state aspects of the biotechnology dilemma (Chyba, 2006). But despite these shortcomings, novel and innovative efforts that safeguard biotechnology

are beginning to take shape. Together with better disease detection and response, if accompanied by political will, these efforts may provide a multi-pronged approach of preventative and defensive measures that will help to ensure a more biologically secure future.

Suggestions for further reading

1. Christopher F. Chyba, October 2006. Biotechnology and the Challenge to Arms Control. *Arms Control Today*. Available at http://www.armscontrol.org/act/2006_10/BioTechFeature.asp

This article deals with dual-use biotechnology, which, due to its increasingly accessible and affordable nature, provides unprecedented challenges to arms control. The article also reviews a number of strategies that are aimed at managing biotechnology risks, paying particular attention to proposals that have an international dimension.

2. Institute of Medicine of the National Academies. 2004. *Learning from SARS, Preparing for the next disease outbreak.* Washington, DC: National Academies Press.

Learning from SARS, Preparing for the next disease outbreak explores the 2002-2003 outbreak of a novel virus, SARS. The rapidly spreading virus, against which there was no vaccine, posed a unique challenge to global health care systems. The report examines the economic and political repercussions of SARS, and the role of the scientific community, public health systems, and international institutions in the halting of its spread.

3. Lederberg, Joshua. 1999. *Biological Weapons: Limiting the Threat*. Cambridge, Ma: The MIT Press.

This book is a collection of essays that examine the medical, scientific, and political aspects of the BW threat, and strategies aimed at mitigating these threats. These essays explore the history of the development and use of offensive biological weapons, and policies that might be pursued to contain them.

4. Leitenberg, Milton. 2005. Assessing the Biological Weapons and Bioterrorism Threat. U.S. Army War College.

The spreading of Anthrax through the U.S. postal system, and discoveries in Afghanistan that al-Qaeda was interested in procuring biological weapons, have contributed to shifting

the context within which biological weapons are considered, to one that almost exclusively involves bioterrorism. This transformation in threat perception, together with a $30 billion, 4-year government spending package arrived with inadequate threat assessments, which this book begins to provide.

5. National Research Council. 2006. *Committee on Advances in Techology and the Prevention of their Application to Next Generation Biowarfare Threats, Globalization, Biosecurity, and the Future of the Life Sciences*. Washington, DC: National Academies Press.

Globalization, Biosecurity, and the Future of Life Sciences explores the current status and future projections of biomedical research in areas that can be applied to the production of biological weapons. The report explores and identifies strategies aimed at mitigating such threats.

6. National Research Council. 2003. *Biotechnology research in an age of terrorism: Confronting the 'dual use' dilemma.* Washington, DC: National Academies Press.

The report addresses dual-use biotechnology and proposes a greater role for self- governance among scientists and journal editors. Other findings include identification of “experiments of concern”, which would be subjected to an approval process by appropriate committees. Proposals are put forward for the creation of an international forum aimed at mitigating biotechnology risks

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