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Biosecurity: Responsible Stewardship of Bioscience in an Age of Catastrophic Terrorism

GIGI KWIK, JOE FITZGERALD, THOMAS V. INGLESBY, and TARA O'TOOLE

THE NEED FOR BIOSECURITY

BIOLOGICAL RESEARCH has undergone tremendous growth and transformation since 1876, when Robert Koch identified *Bacillus anthracis* as the causative agent of anthrax, since the structure of DNA was solved in 1953, and even since a "rough draft" of the human genome was completed in February 2001. This expansion of knowledge and the powers it brings shows no signs of slowing, and will undoubtedly bring vast benefits in diagnosing, preventing, and curing disease, and in improving agriculture. However, a plentiful array of the same tools, techniques, and knowledge that have beneficent uses could, if misapplied, be used to destroy human life or agriculture on a mass scale. While it is not a new phenomenon that technologies can have positive and negative consequences, biological science is unique in that its powers over both life and death are profound, and the culture of bioscience is open and relatively available, particularly when compared to nuclear weapons research.

In the aftermath of the anthrax attacks of 2001 and the terrorist assaults on the World Trade Towers, policymakers awakened to these inherent powers of biological research and began calling for more governmental controls. The Patriot Act (2001)[1] and the Public Health Security and Bioterrorism Preparedness and Response Act of 2002[2] imposed new regulations on the conduct of research involving "select agents"—the several dozen pathogens that the Centers for Disease Control and Prevention judges to be the most dangerous potential biological weapons. In recent months, the White House Office of Science and Technology Policy has met with representatives of professional science societies, private industry, and others to discuss restricting access to "sensitive homeland security information" generated within government agencies, possibly including data published in scientific journals, lest advances in knowledge and technology inadvertently fuel terrorist attacks using biological weapons.

As debate proceeds about whether or how to more closely govern the practice of biological research, it is critical that the profound stakes are understood for both national security and bioscience: a broad scope of research in the life sciences could conceivably be applied towards biological weapons development, but this same research will be essential to creating the medicines, vaccines, and technologies needed to counter the threat of bioterrorism and naturally occurring disease. Efforts to monitor comprehensively all bioscience research that has potentially destructive applications would subsume huge swaths of science, gravely tax civilian research resources, and could discourage scientists from pursuing advances in fields important to medicine and agriculture, fields we urgently need to advance in order to address the grave vulnerabilities currently imposed by bioweapons.

The problem of biosecurity in an age of bioterrorism is how to constrain malignant applications of powerful bioscience responsibly without damaging the generation of essential knowledge. Over time, we must construct a network of "checks and balances": regulations, incentives, cultural expectations and practices that encourage and enable progress in scientific understanding so that knowledge can be brought to bear on human needs, while simultaneously assuring responsible stewardship of powerful knowledge so that it is not used for malevolent purposes. Such stewardship will have to evolve—rapidly, in concert with the pace of advances in the life sciences—to embrace a network of international agreements, legal regulations, professional standards, ethical mores, and catalogues of "best practices" pertinent to

Gigi Kwik, Ph.D., is a Fellow; Joe Fitzgerald, M.P.H., is a Senior Associate; Thomas V. Inglesby, M.D., is Deputy Director; and Tara O'Toole, M.D., M.P.H., is Director, all at the Johns Hopkins Center for Civilian Biodefense Strategies, Baltimore, Maryland.

various fields and disciplines. Scientists and the scientific community must be integral participants in the design and implementation of such a network.

BIOLOGICAL SCIENCE RESISTS NEAT CATEGORIZATION

It would serve tradition and familiar regulatory precedent to create categories of bioscience, in relation to their impact on national or global security. Strict rules and safeguards against misuse could simply be applied to those categories of research that are "dangerous," leaving scientists working in "beneficent" areas unfettered. However, such categories are by no means distinct in biological science, and in many cases rely upon the intent of the researcher. This is particularly the case when considering research undertaken for defensive purposes (such as reverse-engineering the *Bacillus anthracis* powder used in the October 2001 attacks, in order to determine what manufacturing capabilities were necessary in its creation).[3] Defensive research aside, however, there are many examples of beneficent science that could theoretically be subverted to bioweapons application, lower the intellectual or technical barriers to bioweapons research or production, or enable the creation of more destructive biological weapons. The potential exists for misuse. As a metaphor for the realization of that potential—the misapplication of the powers of bioscience towards biological weapons development and use—we call this the "Persephone effect."

THE FATE OF PERSEPHONE, AND THE KIDNAPPING OF MODERN BIOLOGY

The Persephone of Greek myth was an innocent, who spent her time picking beautiful flowers. One day, as she was wandering in the fields, she spied a flower more elegant than any other: the Narcissus. She could not resist the desire to possess this novel work of Nature's art, and moved to put it in her basket. But at that moment Persephone was kidnapped; Hades carried her off to the Underworld in his gold chariot, where he forcibly made her his queen. Eventually, Persephone's mother persuaded Zeus to force a compromise with Hades: Persephone could return to earth, but for four months of every year, she had to return to the darkness of the Underworld. Persephone "was never again the gay young creature who had played in the flowery meadow without a thought of care or trouble. She did indeed rise from the dead every spring, but she brought with her the memory of where she had come from."[4] And while Persephone was in the Underworld, winter fell upon the earth.

As Persephone gathered flowers, so too has biological science involved the collection of novel observations and alluring concepts. Biological science has been the "good" science, the science of life, of medicine and agriculture, and has remained largely innocent of the intentions and machinations of those who wish to do harm. Yet, as the power and reach of biological knowledge expands, the community of bioscience must consider whether and how their powerful discoveries might be captured and used, as Persephone was, by a modern-day Hades, and what havoc that would bring to the world. Indeed, biological science has already been to the Underworld; for example, the biological weapons programs of Iraq, the former Soviet Union, WWII-era Japan, and the United States' former offensive biological weapons program have taken her there again and again. She has come back from this Underworld and joins once again in the beneficent exploration of Nature; but it should be apparent to all of us that she can always be pulled back under.

THE PERSEPHONE EFFECT IS AN INHERENT RISK IN BIOSCIENCE

The risk of a Persephone effect is inherent in how bioscientific research is conceived, designed, conducted, and communicated—openly, available to everyone, and on a global scale. However, the openness of biology has contributed substantially to progress in understanding the life sciences.

In ideal terms, the practice of bioscience may be thought of as a "natural selection" of ideas, where hypotheses must demonstrate their "fitness" for survival against constant experimental challenges from other scientists.[5] The dissemination of these hypotheses to as many scientists as possible accelerates the process of rejecting hypotheses and proposing new ones, furthering gains in knowledge. The reality of biological research is more complicated, of course. Competition for recognition among individual scientists, and commercial interests are important influences in the world of bioscience. Patents, proprietary knowledge, and new alliances between university researchers and for-profit companies now intervene in the free flow of scientific information.

Nonetheless, much of the data produced in the course of bioscientific research are published openly in thousands of peer-reviewed journals, advancing the general knowledge of scientists everywhere in the world. No scientist wants to reinvent the wheel; having one's novel research published allows it to influence the work of others and shape emerging models of living systems. A central tenet of science is the reproducibility of experimental findings. Accordingly, scientific publications must include sufficient technical detail to allow other investigators to repeat the experiment and verify the reported results.

POTENTIAL SCOPE OF BIOSCIENCE VULNERABLE TO THE PERSEPHONE EFFECT

Examples of beneficent research that could fall prey to the Persephone effect are plentiful. Reviewing small portions of the peer-reviewed literature of the past several years, we have found numerous articles that might be considered useful to would-be bioweaponeers. Published advances in the life sciences that arguably have dual-use applications can be found in many diverse fields, including directed evolution; studies of the mechanisms of virulence in viruses and bacteria including human, animal, and plant pathogens; gene therapy technology; aerosol technology; biomanufacturing; and others. If one considers that small pieces of information in a variety of fields can be combined to devastating effect, and that the techniques and information gleaned about an innocuous biological organism can provide crucial information about modulating a more dangerous pathogen, the scope of bioscience vulnerable to a Persephone effect is very large, indeed.

Aerosol technology

Consider a recently published breakthrough in aerosol technology that permits large molecules to escape the respiratory system's usual defenses and be inhaled into the deep lung.[6,7] This advance could allow insulin to be inhaled rather than injected, a development that could increase compliance among diabetics and improve their quality of life. Yet this same breakthrough could theoretically make it easier for an aerosolized bioweapon such as anthrax to be deposited into the lower airways, evading the immune system and causing disease.

Antibiotic resistance

While it is apparent that antibiotic resistance and gene transfer between organisms occurs in the wild at much greater frequencies than in the laboratory,[8] routine laboratory procedures are also used to generate antibiotic-resistant bacteria. Scientists generate antibiotic-resistant bacteria for many important purposes. It is important, for example, to determine whether a bacterial strain *can* become resistant to an antibiotic, a feature that could affect its recommended use. It was discovered during laboratory tests that *Bacillus anthracis* sometimes produce beta-lactamases, which inactivate antibiotic penicillins and cephalosporins. It is this propensity that prompted the CDC recommendation that penicillin not be used in the 2001 anthrax attacks.[9]

Antibiotic resistance is also used widely as a molecular biology tool for the selection of bacteria that have "taken up" plasmids, pieces of circular DNA. In order to insert a gene of interest on a plasmid into bacteria, a gene for antibiotic resistance on that plasmid is included (the NIH Guidelines for Recombinant DNA Research require external review and approval for the use of antibiotics that are given to people).[10] Bacteria that do not include the plasmid with the gene of interest, and the coupled antibiotic resistance gene, will be killed by the application of that antibiotic. In the hands of a bioweaponeer, however, the generation of an antibiotic-resistant strain of pathogenic bacteria could be a step towards the creation of a bioweapon that is resistant to the usual therapies. Indeed, the Soviet biological weapons program is believed to have developed antibiotic resistant forms of plague, anthrax, and tularemia.[11]

Novel pathogens

It is probable that bioscientists will make novel, more virulent strains of pathogens, either by design or by accident. Published examples of this are few, as laboratory manipulation rarely results in a pathogen that is more dangerous than "wild-type." However, the experience of the Australian researchers who modified mousepox virus is instructive.[12] These researchers added a single gene to the mousepox virus, the gene for mouse IL-4, and they reported that this new form of mousepox shut down a mouse's ability to fight the virus with the right immunological defense, and could kill even vaccinated mice. It was speculated that a similar transference of IL-4 into the genome of smallpox, a close cousin of mousepox, could result in a virus capable of overwhelming the protective effects of smallpox vaccine in humans. This appears to be unlikely,[13] but the point remains: laboratory manipulation can inadvertently render strains of viruses more virulent than nature has evolved.

In spite of the mousepox study, some scientists argue that nature has already created the most fearsome human pathogens possible and that researchers are unlikely to inadvertently or deliberately "improve" upon the danger of naturally occurring infectious diseases. Of course, the experiment to test this theory cannot be done. However, modern and forthcoming techniques for manipulating the mechanisms of immunity or altering genomes could very likely allow individuals to accomplish experiments that nature would not pursue. It would be unlikely, for example, that a mousepox virus would acquire the IL-4 gene in nature; it would be highly unlikely for anthrax to acquire resistance naturally to all available antibiotic therapies in the National Pharmaceutical Stockpile.

It must also be remembered that in nature, pathogens are evolutionarily selected for their ability to propagate and spread to new hosts, but in warfare, other delivery mechanisms are possible. Nature may be "red in tooth and claw,"[14] but She is not a thinking enemy.

Synthetic viruses

Technologies used to study viruses are also potential Persephone effect candidates. By creating a virus from scratch, scientists are now able to change parts of the genetic material of a virus, thereby facilitating beneficent investigation of specific viral functions such as virulence or transmissibility.[15,16] To do this, the sequence of the virus must be known, and the pieces of the virus genome either created with the use of a DNA synthesizer (a piece of programmable laboratory equipment that performs the necessary chemical additions to synthesize chains of DNA oligonucleotides), or through use of a noninfectious "library" of the genetic material of the virus (a mix of copies of the genetic material of a virus, without the viral proteins required for infection). These pieces of DNA are then inserted into replicating circular DNA plasmids, which are transferred into a cell line. Once the plasmids are inside the cell, they will produce the protein and genetic components of the virus, assembling complete viral particles. These lab-generated viruses contain everything required for the virus to infect more cells. Researchers have used this or similar techniques to create polio (entirely from synthesized DNA),[17] Ebola,[18] and pandemic flu,[16] as well as other viruses.

Generally, the purpose of using such techniques is to introduce specific genetic alterations and thereby precisely map which parts of the virus allow it to get into cells, which are responsible for virulence, and what parts might become a component of a vaccine. This type of research is necessary in order to develop new mechanisms to prevent or treat infection. An editorial in a prestigious scientific journal reporting on the successful decoding and manipulation of the genetic sequence of the influenza A virus noted that "one can only speculate as to how quickly our knowledge . . . will progress, now that every nucleotide of the viral genome can be mutated and engineered back into the genome, in nearly endless combinations with other mutations."[19] Clearly, the commentator had in mind the potential for medical applications of such knowledge, but it is easy to imagine how such technologies, allowing the creation of infectious viruses from noninfectious material, could share Persephone's fate. Using such technologies, which have been utilized to investigate Ebola, pandemic flu, influenza, hantaviruses, lassa, rabies, and Marburg viruses, there is no need for a bioweaponeer to isolate the virus from an infected patient, acquire it from a germ bank, or culture it from nature. All the required starting materials, such as cell lines and DNA synthesizers, are widely available and used for many beneficent purposes. And the sequences for a growing variety of viruses that infect humans, animals and plants, including Ebola,[20] pandemic influenza,[21–23] and smallpox, are published in the open literature.

ACCESS TO SOPHISTICATED KNOWLEDGE, TECHNIQUES WILL INCREASE OVER TIME

These examples of bioscience technologies that could result in the Persephone effect are all possible *now*. Technologies designed to save lives could be used for malevolent purposes by bioweaponeers, potentially causing an untreatable epidemic and mass casualties. History suggests that as technology becomes increasingly accessible and easier to use, these procedures will get easier to perform over time. Common laboratory techniques such as the polymerase chain reaction (PCR) and mammalian cell transfections (the introduction of new genetic material to a mammalian cell) used to be time-consuming and laborious, and yielded uneven results even in the hands of highly skilled technicians. Now such techniques require much less skill and time, thanks to the development of specialized "kits" purchased from biotechnology companies. Researchers can now pay commercial firms, or in-house "core facilities," to sequence or synthesize DNA and peptides, a practice that reduces the technical and temporal burdens to complete experiments. Future processes and techniques available for purchase will no doubt make advanced biotechnologies more accessible to a determined terrorist, which could lead to the creation of new and more dangerous bioweapons.

TRADITIONAL REGULATORY APPROACHES NOT WELL SUITED TO BIOSECURITY CONCERNS

Concern over the implications of bioterrorism, as well as the Persephone effect, may lead some to propose a governance system for biology much like the "command and control" regulatory regimes placed on nuclear weapons research. This type of governance depends on being able to assign crisp edges to what is and is not subject to regulation, and the ability to define explicitly what is allowed and what, precisely, is prohibited. While command and control regulatory regimes have had reasonable historic success in governing occupational safety hazards, environmental pollution, and nuclear safety, they are less effective where the target and scope of regulation are not easily defined. Command and control approaches are also difficult to implement or enforce when the institutional behavior to be influenced is complex, diffuse, and rapidly changing—all traits that characterize the diverse bioscience community.

A top-down governance system for biological research runs the risk of being either too heavy-handed and all-encompassing, thereby interfering with critical life-saving research, or of missing work that is vulnerable to the Persephone effect and applicable to potential bioweapon applications. Another drawback to traditional government-based regulatory approaches is that they are expensive to implement—a reality that makes their development a matter of lengthy contention in the commercial world. The costs of regulating scientific research via such approaches may prove formidable and, given the fierce competition for research funds and the uncertain payback of most R&D efforts, possibly unsustainable. In addition, within command and control type regulations which impose "one-size-fits-all" constraints, the "fit" between the hazards subject to regulation and the actual circumstances of application is often imperfect. Enormous effort and expense may be lavished on relatively small risks, while more important issues are neglected.

John Steinbruner and his colleagues at the University of Maryland have pointed out that some types of research activities clearly pose "large inherent dangers" and argue that such research can be defined and subjected to special standards. Research involving particularly lethal biological pathogens would fall into this "dangerous" class, as would any research that has the potential to significantly increase the virulence of an otherwise innocuous biological agent, should one be able to recognize that potential in advance.[24] We agree that a limited number of experiments with especially lethal pathogens might wisely be managed under that form of strict regime that ensures transparency and accountability, as research with smallpox virus is currently managed.[25] But the scope of bioscience that may conceivably contribute to malignant bioweapons work is too broad to submerge in any traditional regulatory scheme. The dual use nature of modern biology must be faced squarely if we are to construct effective biosecurity frameworks without damaging the force and great beneficent potential of scientific inquiry.

BEYOND DANGEROUS PATHOGENS

The Patriot Act (2001)[1] and the Public Health Security and Bioterrorism Preparedness and Response Act (2002)[2] are examples of traditional command and control regulation. Section 817 of the Patriot Act criminalizes possession of biological agents unless justified by a "prophylactic, protective, bona fide research, or other peaceful purpose" and prohibits the possession, transport, and receipt of select agents by convicted felons; foreign nationals from terrorism-sponsoring nations; individuals dishonorably discharged from the Armed Services; and unlawful users of controlled substances. The Public Health Security and Bioterrorism Preparedness and Response Act requires that the Secretary of Health and Human Services maintain a list of select agents; requires research facilities possessing select agents to register their possession to the CDC; requires background checks of those in possession of select agents to ensure that they are not convicted felons, etc.; and requires the "establishment of safeguard and security measures to prevent access for such agents and toxins for use in domestic or international terrorism or for any other criminal purpose."

Some scientists believe that the Patriot Act's requirement that select pathogens be used only for "bona fide research" is too subjective and will have a "chilling effect upon legitimate scientific inquiry."[26] They also worry about the financial burden: no one yet knows what it will cost to implement the select agent security provisions of the Bioterrorism Preparedness and Response Act, but it is feared that significant research funds will be diverted to pay for the laboratory surveillance and facility registration. As John H. Marburger, Director of the Office of Science and Technology, testified, "I am concerned that universities are already taking steps that incur great expense without ensuring a commensurate increase in security."[27] The true costs of such legislation must also take into account the loss of the talented scientists who cannot engage in select agent research because the regulations are too expensive to implement or because it is not feasible to restrict work in their laboratories according to the regulations, even if the scientists themselves would not be prohibited.

For both biosecurity and bio*safety* reasons, there is significant utility to knowing what pathogens are stored in which laboratories. However, the security that is bought by such measures extends only so far: the select agent list does not encompass all pathogens that could be used as weapons, does not account for the official and unofficial repositories of pathogens found in countries around the globe, and obviously cannot inventory pathogens found in the natural environment. In addition, because of the Persephone effect, harmless bacteria and viruses could be made pathogenic through genetic engineering, and pathogenic organisms which are not on the select agent list could be used as weapons, as salmonella was in the 1984 bioweapons attack in Oregon.[28] It is also possible to conduct research on the mechanisms responsible for select agents' virulence or transmissibility, for example, without triggering the law by manipulating fragments of genomes.

SCIENTIFIC SELF-GOVERNANCE

The challenge of biosecurity involves striking an acceptable balance between preventing and mitigating the "Persephone effect"—the likelihood of beneficently intended research being applied towards evil ends—and maintaining the imaginative freedom that fuels scientific inquiry. Achieving this balance will require the creation of new systems and institutional forms of governance. Although governance is usually carried out by governments, there are governance practices and models that do not require or rely on governmental authority, resources, or approval. Such governance mechanisms can be employed instead of, or in concert with, more traditional forms of governmental governance to achieve enhanced biosecurity. It is understood from the outset that governance systems that rely on voluntary standards or institutional practices cannot, alone, guarantee the prevention of bioterrorism or protect against malignant uses of biology. But international treaties or national top-down regulation cannot, on their own, deliver such promises either. The nature of the bioscience/biotechnology enterprise and the infrastructure necessary to support it is such that legal sanctions and government-based initiatives are not sufficient to prevent the diversion of legitimate science for malevolent purposes. Given that science is at once an inherently global enterprise and is also a practice and product of individual scientists, national governments are in some ways poorly positioned to influence scientific practice, and reduce the risk of a Persephone effect.

The process of reducing the risk of a Persephone effect therefore requires holding a mirror to the practice of bioresearch, to see what can be done to make bioscience more secure without impeding progress. To start, biological scientists must play critical roles in evaluating what research could be vulnerable to the Persephone effect. Donald A. Frederickson, former head of the National Institutes of Health during the recombinant DNA debate in the 1970's, remarked that "one of the most important lessons to be learned about controversy over use of high technologies . . . is the absolute requirement for expert opinion."[29] Bioweaponeers may make use of information from a variety of beneficent disciplines, such as aerosol science (important for new drug design), biomanufacturing (important for drug production, agricultural products, and vaccine production), and gene therapy (including the creation of "stealth" viruses that do not provoke an immune response), making it exceedingly difficult to discern what research is truly "dangerous." The amount of technical knowledge required to understand the implications of new research makes it challenging even for scientists in distinct disciplines (for example, immunology, virology, microbiology, genetics, neuroscience, bioinformatics, public health, and internal medicine) to evaluate research outside their expertise. Experts in these respective fields therefore need to work together to evaluate critically the potential of misapplications of research discoveries and knowledge, and what is required to counteract those misapplications.

It is likely that efforts to prevent the Persephone effect by screening all scientific experiments would fail, and not just from the logistical nightmare such a tactic would engender. Even if every experiment were followed exactly as planned, the results of those experiments are not predetermined; otherwise, no one would conduct experiments in the first place. Serendipity—the extra reagent added in, or forgotten; the coffee break that turned into a 24-hour incubation—has been notorious for leading scientists to breakthroughs or otherwise unanticipated results.

On the other hand, the inherently collaborative nature of the practice of bioscience presents opportunities to improve biosecurity. Gone are the days when most scientists are self-taught, self-funded, work in relative isolation, and are not unduly pressed for time. Charles Darwin, for example, took decades to publish his *Origin of Species* in 1859. The brisk pace of modern biological research, as well as its complexity, requires that scientists rely on other people, organizations, and the scientific community for their research to continue. Such reliance could lead to innovative solutions for scientists and the organizations with which they work to heighten biosecurity, and block the Persephone effect.

CHARACTERISTICS OF AN EFFECTIVE SELF-GOVERNANCE SYSTEM

Biosecurity cannot be achieved with any single law or program. Similarly, self-governance measures for bioscience should not be viewed as one program, one policy, or one institutional measure, but rather as individual threads of control woven into a network of considerable strength. The Center for Civilian Biodefense Strategies is currently engaged in efforts to detail measures that could be effective for increasing biosecurity, without impeding beneficent scientific research.[30] However, some essential characteristics of an effective self-governance mechanism are already clear:

1. *There must be increased awareness of biosecurity and bioterrorism risks among scientists and the scientific leadership.* Scientists must first be aware that there is a necessity for action. The idea of subjecting biological knowledge to constraints because of security concerns is a new and unwelcome notion within much of the research community. Biosecurity controls or regulations do not have much chance of succeeding unless they achieve the direct and willing engagement of scientists and the scientific community to determine what constitutes dangerous science and how it should be managed. Part of the current lack of awareness stems from the fact that the professional worlds of bioscience and national security do not interact very much or demonstrate a good understanding of each other's concerns; those in the national security community should articulate their analysis and information about the dangers for the misuse of biological re-

search to biologists. A number of other steps might increase bioscientists' awareness of the biological weapons threat. For example, training requirements and accreditation procedures for researchers emphasizing biosecurity issues could be instituted, or grant proposals might require investigators to review briefly the potential for malignant applications of their intended research. Currently, the advantage of biological weapons production and use is to the offense. To reverse this situation, a governance system must be developed that engages biologists to defend against biological threats as well as enhance the security of the research they produce.

2. *Security provisions should be organic to the culture and practices of biological research.* In order to be effective, controls should not be haphazardly thrown onto research. Rather, security provisions should be integrated into the research process and not unduly warp the "natural" process of research. There are several natural "control points" for research, based upon the way bioscientific research is conceived, designed, conducted, and communicated, as shown in Figure 1. Care must be taken to not only avoid impeding bioresearch progress, but to avoid impeding the careers and professional rewards of bioscientists, so that people continue to enter the field. Currently, particularly among academic biologists, one must "publish or perish." This runs counter to classification schemes. It also runs contrary to the recent actions of the government: "the White House asked the American Society for Microbiology . . . to limit potentially dangerous information in the 11 journals it publishes" and "eliminate the sections of articles that give experimental details researchers from other laboratories would need to replicate the claimed results, helping to prove their validity."[31] The American Society for Microbiology is opposed to this, and at their request, the National Academy of Sciences will convene a meeting in 2003 of scientific publishers to determine how to "strike a balance that will enable the free flow of scientific information without providing information that would be useful to bioterrorists."[32] Presumably, legitimate researchers could directly contact the authors to get details withheld from "Methods" sections of articles, but should entire articles have to be withheld from public access, other systems must be set up so that bioscientists can advance in their careers and learn from their peers.

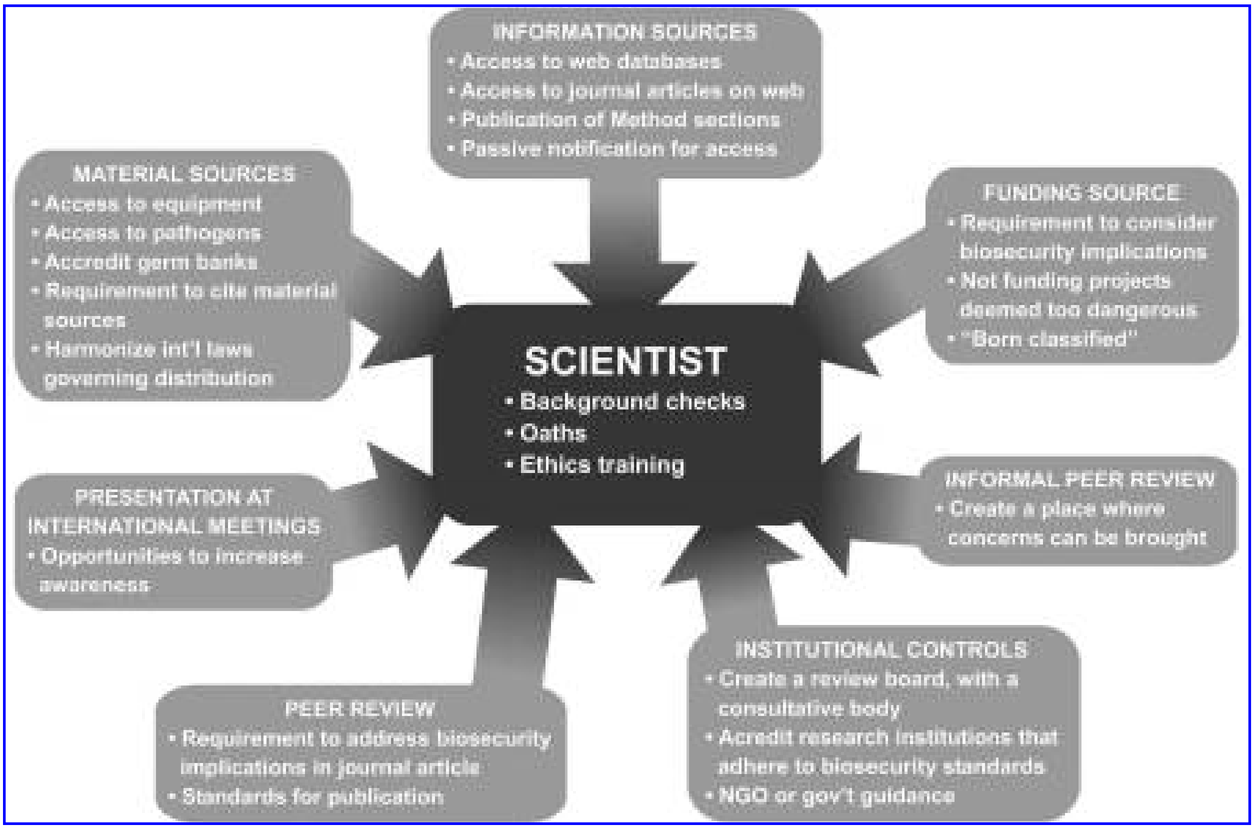

FIG. 1. Bioscience governance spectrum. What combination of these or other proposed mechanisms could enhance biosecurity *without* impairing bioscientific progress remains to be seen.

3. *Biosecurity must be "bottom-up."* A governance system for bioscience should engage the practitioners of science in an integrated management of biosecurity concerns. It is the scientists themselves who are in the best position to recognize the potential misuses of their work, and who best understand the ways in which the craft and business of biological science might be most efficiently governed. Preventing malignant biology cannot be achieved simply by imposing constraints upon scientific research and biotechnology development—it must include a bottom-up approach that is imagined and embraced by scientists, and which evolves as the craft and infrastructure of science itself progresses and is transformed.
4. *Biosecurity must include processes or measures for periodic assessment of how well the system is working.* Measures undertaken to enhance biosecurity will need to balance constraints with scientific freedom; they should not impede biological science to the point that it hampers effective biological weapons defense or lifesaving research. However, achieving this balance is difficult when the issues are complex and evolving, and experience is lacking. The effectiveness and efficacy of biosecurity measures should therefore be subjected to continuous reevaluation. Scientists need to be engaged in designing this assessment process, and should also participate in institutional efforts to capture and apply the lessons that are learned. Institutional mechanisms could be created to monitor the effectiveness of self-governance activities and could provide feedback both to the federal government and to scientists.
5. *Biosecurity systems should provide the means of making applications and test systems increasingly pervasive and global.* Biological research is global, and therefore any governance system that does not expand to the global biological sciences community will not effectively control the development and use of biological weapons. Biosecurity will not be accomplished solely through American laws or practices limited to U.S. laboratories. But the United States is today a clear leader in biological research and biotechnology; students come to the U.S. from all over the world seeking education in the life sciences and postdoctoral experiences in American laboratories. The ethical standards, practice norms, and expectations established in U.S. labs and universities could have widespread effects.

A NEED TO ACT

We find ourselves at a moment when the perils to national security seem to come from many directions, when potential vulnerabilities seem countless. Biological weapons pose a strategic threat mirrored by no other form of attack other than nuclear weapons. There is no simple or immediate solution to the problem of biosecurity. Over time, we must construct the systems of checks and balances needed to assure that the growing power of the life sciences is used to protect life, not to destroy it. Preventing biological knowledge from sharing Persephone's fate will require the bioscience community to actively work with policymakers to identify and establish scientific governance procedures and principles that will prevent or mitigate the exploitation of the life sciences for making bioweapons of mass lethality. Measures contemplated for bioagents and bioscience research must be organic to the methods, culture, and institutions of science itself, and must not impose a burden that alters scientific inquiry in ways that offset any value gained in biodefense. Biosecurity has become a critical aspect of the struggle against catastrophic terrorism. Bioscientists and the bioscience community must make this issue their own.

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Address reprint requests to:
Gigi Kwik, Ph.D.
Johns Hopkins Center for
Civilian Biodefense Strategies
111 Market Place, Suite 830
Baltimore, MD 21202

E-mail: jkwik@jhsph.edu

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