Biotechnology and Bioterrorism: An Unprecedented World

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In March 1963, President John F. Kennedy told the American people that he was haunted by the prospect of '15 or 20' nuclear powers by 1975.[1] Come that year, in a world with still only six nuclear states, the strategist Albert Wohlstetter warned that we could nevertheless soon face 'life in a nuclear armed crowd'.[2] Yet the web of measures that comprise the nuclear non-proliferation regime continues to hold that crowd at bay. The number of nuclear weapon states in 2004 stands at only eight or nine, and assertive steps may yet keep this figure from rising.

Barring theft, would-be nuclear proliferators must confront the challenging task of producing highly enriched uranium or weapons-grade plutonium. Even the most proliferation-friendly nuclear materials production technology – gas centrifuge enrichment – remains beyond the capacity of non-state groups. By aggressively confronting centrifuge proliferation and other threats to the non-proliferation regime, we can hope to continue to shape our nuclear future, moving it away from Kennedy's nightmare.

But biological proliferation is a different beast. Biotechnological capacity is increasing and spreading rapidly. This trend seems unstoppable, since the economic, medical and food-security benefits of genetic manipulation appear so great. As a consequence, thresholds for the artificial enhancement or creation of dangerous pathogens – disease causing organisms – will steadily drop. The revolution in biotechnology will therefore almost inevitably place greater destructive power in the hands of smaller groups of the technically competent: those with skills

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sufficient to make use of the advances of the international scientific community. This future is being driven not primarily by military programmes, but rather by open, legitimate private and academic research.

Lessons from the past half-century of relative success in blocking nuclear proliferation cannot be easily applied to the twenty-first century challenge of biological proliferation. Neither Cold War bilateral arms control nor multilateral non-proliferation provide good models for how we are to manage this new challenge. Much more than in the nuclear case, civilisation will have to cope with, rather than shape, its biological future. In the biological realm, we are entering an unprecedented world.

The new biosecurity landscape

Four trends came together in the 1990s to confront civilisation with a new and challenging biological security landscape. Each had earlier manifestations, yet each became salient during that decade.

Emerging infectious diseases. Of course HIV/AIDS and many other catastrophic pandemics preceded the 1990s. But the recognition that over the previous two decades a new disease had emerged into the human population roughly every year, coupled with dramatic outbreaks of diseases, such as ebola overseas and hantavirus within the United States, and the evolution of multi-drug resistant versions of well-known diseases, such as tuberculosis, led to the US National Academy of Sciences and, subsequently, the US government, focusing attention on this threat.[3] The centrality of improving domestic and international disease surveillance and response was embraced intellectually. But the Global Pathogens Surveillance Act, a US Senate initiative to improve capacity in the developing world to detect, monitor, and respond to sudden disease outbreaks, has yet to become law.[4] Somehow the imagination stops at international borders, even after the 2003 SARS epidemic. SARS provided an especially vivid example of an emerging disease that could spread globally on the short timescales of international flight schedules.

Mass-casualty terrorism. There were historical precedents, but with the first attempt, in February 1993, to bring down a World Trade Center tower, the March 1995 sarin nerve-gas attack by Aum Shinrikyo in the Tokyo metro system and the April 1995 Oklahoma City bombing it became clear that a variety of groups aimed at mass murder. Attempts by Aum Shinrikyo to spray the anthrax bacterium throughout downtown Tokyo in 1993 demonstrated that at least some terrorist groups were willing to attempt mass casualty urban biological attacks, even if they were insufficiently competent to succeed. And then came 11 September 2001.

Gross violations of the BWC. Impressive violations of the 1972 Biological and Toxin Weapons Convention (BWC) came to light as a result of the end of the Cold War and the first Gulf War. States parties to the BWC pledge not to 'develop, produce, stockpile or otherwise acquire or retain' biological agents, toxins, or weapons. Yet Iraq, which had signed the BWC (but did not ratify it until 1991) had conducted a covert production programme with anthrax and other agents, and largely hidden it until invasive post-Gulf War UN inspections and high-level defectors revealed many of its details. More disturbing, the Soviet Union had built an illegal programme on a continental scale subsequent to signing the BWC in 1972, employing tens of thousands of people. Certain Russian facilities that had been part of this complex remain closed to outsiders. Equally disturbing were multiple reports that the Soviet programme had weaponised smallpox, a highly contagious agent. For this reason, smallpox had been considered of little interest to military programmes, because of the danger that it might 'boomerang' against one's own troops or populations', but clearly it was of potential interest to apocalyptic terrorist groups.[5] Concern over the ease with which the BWC had been violated for the two decades following its entry into force led to a six-year international negotiation of a compliance protocol to the BWC. In July 2001, the administration of George W. Bush withdrew from these negotiations and has declared the BWC to be 'inherently unverifiable'.[6] Suspicions persist that a number of BWC signatories are involved in illegal activities.[7]

Dramatic advances in biotechnology.[8] Human beings have engaged in genetic engineering for millennia, breeding new strains of both plants and animals. However, the discovery of the structure of DNA in 1953 and, almost 20 years later, the invention of recombinant DNA technology permitted for the first time the direct manipulation of the genomes of organisms to achieve specific goals.[9] Biotechnological inventions, such as the polymerase chain reaction (PCR) in the 1980s, 'DNA shuffling' in the 1990s and other technologies that automate copying, mutating, sequencing and otherwise manipulating DNA, introduced enormous numerical power into molecular biology.[10] The resulting techniques of directed molecular evolution permit investigators to evolve capabilities without having to know beforehand what exact DNA modifications are necessary to achieve the desired result. Instead, it is now possible to engineer via trial and error, in which each step can involve populations of up to trillions of trial DNA molecules.[11] Simultaneously, automation of key techniques has substantially lowered the threshold for performing these experiments. In part as a consequence of these advances, between 1993

and 1999 the biotechnology industry in the United States doubled in size. An industry-sponsored group estimates that by the turn of the century, biotechnology contributed nearly half a million jobs and $47 billion in business revenue annually to the US economy.[12] At the same time, biotechnology has spread rapidly around the world. For example, China now has some 20,000 people working in 200 biotechnology laboratories.[13] In January 2004, a member of the Pakistani Atomic Energy Commission (PAEC) concluded a two-week training workshop on 'advanced techniques in biotechnology' in Faisalabad with the statement that the PAEC is committed to training scientists from Muslim countries in biotechnology.[14] And Singapore is investing billions of dollars in biotechnology, declaring it to be the 'fourth pillar' of its economy.[15]

Automation of key techniques has lowered the threshold for experiments

The globalisation of biotechnology is being driven not only by national decisions, but also by biotechnology firms' growing use of international subcontracting and technological cooperation agreements to further their research – including their biodefence-related research, such as vaccine development for potential bio-terrorist agents.[16]

Necessary and insufficient

By the turn of the twentieth century, the implications of these four trends had led to a re-conceptualisation of the biological terrorism threat, away from misplaced analogies to nuclear or chemical weapons and towards placing the threat in the context of the public health measures needed to combat disease. If non-proliferation efforts were inherently more difficult in the biological than in the nuclear case, and if deterrence by the threat of punishment was of questionable utility against certain terrorist groups, then it made sense to place greater reliance on defence, in the form of improvements in disease surveillance and response. Many (although not all) of the required measures would have the significant advantage of being intrinsically dual-use, bolstering defences against naturally occurring epidemics as well as intentional attacks.[17] Because most dangerous contagious pathogens (smallpox, plague, SARS) have incubation periods longer than international flight travel times, it is crucial that international disease surveillance and response be improved along with its domestic counterpart.[18]

An emphasis on disease surveillance and response does not mean that the realm of prevention should be neglected. Aum Shinrikyo's failed anthrax attacks in Tokyo in 1993 are a reminder that even a group with substantial financial resources and some scientific training did not find it

easy to carry out an effective biological attack. Aum Shinrikyo obtained both the wrong strain (a generally non-lethal vaccine strain) of the anthrax bacterium, and it did not master aerosolisation technology.[19] It is clear that efforts to restrict the availability of the worst pathogens and key weaponisation technologies should not be abandoned. We must resist the 'silver bullet fallacy' – the notion that if a particular step does not magically solve a problem in its entirety, it is not worth pursuing. Rather, we must construct a web of measures to make biological terrorism more difficult. Therefore, even as we improve disease surveillance and response, we should work to stem proliferation where possible by, for example, maintaining and extending Australia Group suppliers' export standards that impede state and non-state weapons programmes. We should also improve the international security of the most dangerous pathogen stocks, to deprive would-be terrorists of the surest and easiest path to just the right disease organism.[20] But such steps will have only limited impact, and if not pursued wisely could unduly constrain legitimate biodefence research.[21]

In addition to broad improvements in prevention, surveillance and response, specific defensive measures against the most likely threat scenarios are also necessary. There is a large array of viruses and bacteria that can cause disease in humans, animals and crops. Even greater are the number of scenarios, from the subtle to the apocalyptic, that analysts can spin about possible terrorist attacks. An effective defence requires setting priorities; these should include identifying the most likely near-term threats and implementing research, detection and response agendas designed to take these off the table in the near future.[22]

The decision to stockpile enough smallpox vaccine for every American is an example of a step in this direction. To remove known strains of smallpox as a potential threat, however, this step must be supplemented either by research to develop a vaccine that is sufficiently safe so that widespread pre-attack vaccination is possible, or by the capability to vaccinate vast numbers of citizens rapidly after the earliest signs of an outbreak. (And here, too, a safer vaccine would be valuable.) Similarly, an effective and easily administered vaccine against anthrax, coupled with existing antibiotic stockpiles and a realistic and tested plan to distribute these rapidly and widely after an attack, would help to remove another of the most serious near-term threats. The biomedical research needed to achieve these and other high-priority objectives is being funded by a $1.5bn expansion in the National Institutes of Health annual biodefence research budget, and Bush's ten-year $5.6bn Bioshield initiative.[23]

But these near-term steps, while necessary, will not by themselves cope with the longer-term threats we face. For example, developing a

strain of anthrax that is resistant to a particular antibiotic requires only standard microbiological techniques. And experiments published in the open scientific literature in 2001 suggest a way to modify the smallpox virus so that it could overwhelm the immune systems of even those who have been vaccinated against it. Steps taken today to prepare for the greatest biological threats risk committing the 'fallacy of the last move' – the failure to realise that a defensive measure taken to counter a particular offensive threat might in turn be circumvented by a competent adversary.[24] In fact, one lesson of experiments published in the open scientific literature over the past few years is that the capabilities for overcoming biodefence measures are becoming more widespread and available to groups of the technically competent. Each defensive move may be placed at risk by an offensive counter-move. The short- and medium-term steps we take now are still needed to protect us against the most immediate and severe threats, but they may be insufficient to meet the longer-term challenge.

Shots across the bow

Experiments performed and published over the last decade already demonstrate that biological power for constructing dangerous pathogens is becoming widespread. New examples now appear frequently in the open scientific literature. Describing a few of the experiments of concern illustrates what is to come.

In 2001 the *Journal of Virology* published a paper describing experiments conducted at the Australian National University with the mousepox virus, a smallpox-analogue virus that infects rodents.[25] Seeking to find a contagious contraceptive to suppress the wild mouse population, researchers spliced into the mousepox genome the gene for a mouse protein called interleukin-4 (IL-4), a signalling protein that is used by the mouse's immune system to regulate its response to infection. IL-4 suppresses the antiviral immune response, so the effect was to give the mousepox virus the ability to shut down the relevant part of the mouse's immune system. The modified virus proved far deadlier, killing mice that were naturally immune or that had been vaccinated against mousepox.

Since mousepox is the rodent analogue to smallpox, and since mouse IL-4 is analogous to the IL-4 used by the human immune system, there is reason to suspect that a similar experiment carried out with the human smallpox virus could lead to a virus that would circumvent the existing smallpox vaccine. The techniques used by the Australian researchers are not sophisticated; a recent report by the National Research Council of the US National Academies of Science, Engineering and Medicine describes them as 'standard and quite simple procedures'.[26] Of course, any terrorist

group wishing to modify smallpox in this way would face the hurdle that, at least officially, the smallpox virus exists in only two well monitored and protected locations in the United States and Russia. Nevertheless, this experiment, and previously published related research, points the way to modifying a variety of viruses to subvert the human immune system. At the same time, these results also give researchers the knowledge needed to pursue countermeasures to such engineered – and some naturally occurring – pathogens.

Smallpox is the first, and so far only, virus to be eliminated from the natural world; the World Health Organization and other health agencies are working to ensure that polio soon follows it into oblivion. However, a recent experiment dramatised the fact that extinction is not necessarily forever in the case of the polio virus. A group of scientists working at the State University of New York (SUNY) published a paper in 2002 that showed they could synthesise an infectious polio virus from scratch using chemicals purchased on the open market.[27] Therefore, even if the polio virus is eliminated from the natural world, it could be reconstructed in the private laboratory. The SUNY team took three years to synthesise the virus; research by a group at the Institute for Biological Energy Alternatives in Rockville, Maryland in 2003, armed with the most sophisticated techniques available, reduced the time to manufacture a virus of comparable genomic size to two weeks.[28] The smallpox virus has a genome 25 times as large as that of the polio virus, and cannot reconstitute itself from its DNA alone, so it constitutes a fundamentally greater challenge. But many other viruses could now be synthesised in the laboratory.

One of the great killers of the twentieth century is the influenza virus, with a genome about twice the size of polio. The 1918–19 strain was especially virulent, killing at least 20–40m people worldwide. Research based in part on samples preserved from 1918 is now revealing the reasons why the strain was especially lethal.[29] This research may prove vital to protecting humanity against new strains of deadly influenza, but will also suggest modifications needed to convert the genome of contemporary influenza viruses to ones that could be especially deadly, were modern antiviral drugs to prove ineffective or be insufficiently available.

Nor are viruses the only disease agents that can be manipulated for greater lethality. Using classical microbiological techniques, the Soviet state bioweapons programme reportedly developed multiple-antibiotic-resistant strains of the bacteria responsible for anthrax and pneumonic plague.[30] Modern engineering techniques will confer more subtle capabilities. A US–Japanese academic team published in the *Proceedings of the National Academy of Sciences* in 2003 their creation of a 'hypervirulent

mutant' of the bacterium responsible for tuberculosis; genetic manipulation yielded a deadlier strain that side-stepped the mouse's immune system.[31] The research is important for understanding why natural tuberculosis remains latent and asymptomatic in some of its infected victims; once again the capacity for harm is a by-product of the attempt to understand, and hence combat, a major human disease. Enhanced virulence had earlier been produced by other research groups, including the 2001 creation of a 'hypervirulent' version of the protozoan parasite responsible for the disease leishmaniasis.[32]

The recent outbreak of SARS was a reminder that the natural world continues to challenge the human population with novel and deadly diseases, independent of whatever human beings may engineer. Over 11m people die annually from infectious and parasitic diseases, suggesting that the benefits of fundamental research on disease organisms currently likely far outweigh the dangers.[33]

The good news is that SARS was contained

The good news is that SARS was contained, even though no vaccine or cure for it exists. Traditional methods of contact-tracing and quarantine proved sufficient, albeit after more than 800 deaths and major economic consequences.[34] However, success in containing the SARS outbreak should not be misinterpreted to mean that concerns over designer contagious pathogens for which no cures or vaccines exist are overblown. Engineered pathogens could have worse characteristics than SARS, for example, much longer incubation periods or greater communicability. In fact, in a recent review paper in the journal *Science*, influenza researchers warned that 'because epidemiological modelling has suggested that it is much more infectious than SARS, influenza is unlikely to be controllable by SARS-like quarantine measures'.[35]

The dangers posed by advances in biotechnological research do not derive merely from experiments with pathogenic micro-organisms. The mousepox experimenters relied on research on the nature of the immune system to show them how to create a virus to subvert the mouse's immune response. Similarly, basic medical research into the human immune system or the human genome itself will inevitably point the way towards increasingly powerful and possibly quite subtle methods to cause human disease. Essentially all of this knowledge will be in the public domain.

The increasing ease with which micro-organisms may be given deadly modifications emphasises how even more misleading the moniker 'weapons of mass destruction' (WMD) will become in the future. The term already misleads by glossing over profound differences in the applicability of non-proliferation, deterrence, and defence to nuclear,

chemical, or biological weapons, as well as in the consequences of their use.[36] But because it also fails to capture the disparate future trajectories of the technologies underlying these weapons, it will become ever more misleading over time.

It is important to distinguish between diseases that are contagious – capable of spreading from person to person, like smallpox, influenza or pneumonic plague – and those that are not (such as anthrax). To cause mass casualties, non-contagious biological agents will still require aerosolisation – the processing of the agent into an extremely fine powder or mist, and its effective dissemination. Aum Shinrikyo's failure with this technology is a reminder that, without specialised knowledge or a research and development programme, mastering these techniques is not easily done. However, contagious agents could be used by terrorists to cause widespread outbreaks on the basis of person-to-person transmission, possibly skipping the aerosolisation step. Given this fact, the kinds of experiments just surveyed suggest that, in future, in the realm of biology, we could face a 'banalisation' of WMD capacity. Many laboratories may have the capability to modify or synthesise deadly contagious pathogens, albeit with substantial risk to the researchers in the absence of proper containment facilities. This is altogether different from the hurdles facing those who would make nuclear weapons-usable material. It will be important, in a world where WMD capabilities may be the cause of war, to distinguish clearly between biological, chemical and nuclear weapons or 'WMD programme-related activities'.[37] Chemical and biological weapons, and 'programme-related activities' pertaining to these weapons, while of great concern, will often pose far lesser threats than nuclear weapons, so any call for war on the basis of 'WMD' should distinguish clearly between these possibilities, rather than conflating them.

Of course, it will remain of the highest importance to prevent proliferation of nuclear weapons capabilities. We do not want our nuclear future to begin to resemble our biological future.

Global review

It is unclear how we should cope with the ongoing proliferation of biotechnology, and the prospects for non- or sub-state terrorism that will result. One suggested approach is oversight of potentially high-consequence biological research. A recent report by the National Research Council recommends several measures, including:[38]

Review of plans for experiments. The Department of Health and Human Services should establish a review system for seven classes of

experiments with microbiological agents that raise concern. Precedent exists in three-decades-old measures taken to review the safety of potentially hazardous recombinant DNA experiments. However, the recommended review would be binding only for those funded by federal research grants; private companies not supported by the National Institutes of Health would subscribe on a voluntary basis.

Publication review. Scientists and the editors of science journals would review their own publications for potential national security risks. In some cases, certain information might be withheld from publication.

Harmonised international oversight. The United States would pursue harmonised national, regional and international measures to provide a counterpart to its own review system.

The most important aspect of these recommendations may be the recognition by the scientific community that biotechnology requires greater attention to the ways in which their research could be misused. Nevertheless, even the full implementation of the system recommended by the National Research Council would leave tremendous gaps: domestically, in those private laboratories that were not federally funded and chose to remain outside the system of review; internationally due to a 'crazy-quilt' pattern of oversight that would likely vary from country to country, and could be nonexistent in practice in countries of greatest concern. John Steinbruner and his colleagues at the University of Maryland's Center for International and Security Studies have instead elaborated a truly global system of internationally agreed rules for the oversight of high-consequence biological research.[39] But any such system would face at least three challenges:

Global implementation. How would such a system be effectively and widely implemented? Admittedly, such a system may come to seem less utopian after a first major engineered pandemic killed vast numbers of people. After that kind of horror, implementing such a system could move from the realm of the incredible to the realm of the mandatory. But we are in a far better position now to engage in careful thinking about how such a system should balance conflicting interests than we would be in that post-attack world.

Capturing bad actors. In the absence of remarkably invasive oversight, the envisioned regime could fail to capture those bad actors of greatest concern. Legitimate research might be hamstrung while illicit research

would proceed covertly without constraints. But to some extent this objection misapprehends the problem. Most non-state terrorist groups are unlikely to conduct sophisticated biotechnology research and development programmes. Rather, most will, at best, follow in the scientific literature those discoveries made by legitimate scientists, then attempt to implement those techniques. Therefore, by overseeing certain high-consequence work in the legitimate scientific community, we might hope to diminish the threat of misuse by bad actors.

Defining high-consequence research. A great deal of high-consequence work has nothing to do with pathogen manipulation, but rather lies in the realm of fundamental understanding of the human organism. In this sense, a vast amount of biomedical research is potentially of high consequence. Yet again we must resist the silver-bullet fallacy, if restrictions on the manipulation of pathogens would prove valuable. Even in this case, it may prove difficult to give a detailed account of those experiments that are of the greatest concern without in effect providing hints to less competent groups about the directions they should go in to achieve deadly results. A balance will need to be struck.

Despite these difficulties, we should not conclude that it is best simply to do nothing. Oversight regimes should continue to be explored, so that a detailed understanding of their promise and drawbacks is gained. Meanwhile, the production of biological agents for terrorism should be criminalised worldwide, and so-called 'societal verification' – the encouragement of scientists and other citizens to blow the whistle on illicit biological weapons activity – should be fostered. Finally, biotechnologically competent intelligence gathering and analysis must keep pace with the latest research.

An eternal arms race?

In the absence of a comprehensive and effective system of global review of potential high-consequence research, we are instead trapped in a kind of offence–defence arms race. Even as legitimate biomedical researchers develop defences against biological pathogens, bad actors could in turn engineer countermeasures in a kind of directed version of the way natural pathogens evolve resistance to anti-microbial drugs. The mousepox case provides a harbinger of what is to come: just as the United States was stockpiling 300m doses of smallpox vaccine as a defence against a terrorist smallpox attack, experimental modification of the mousepox virus showed how the vaccine could possibly be circumvented. The United States is now funding research on antiviral drugs and other ways of combating smallpox that might be effective

against the engineered organism. Yet there are indications that smallpox can be made resistant to one of the few known antiviral drugs. The future has the appearance of an eternal arms race of measures and countermeasures.

The 'arms race' metaphor should be used with caution; it too is in danger of calling up misleading analogies to the nuclear arms race of the Cold War. First, the biological arms race is an offence–defence race, rather than a competition between offensive means. Under the BWC, only defensive research is legitimate. But more fundamentally, the driver of de facto offensive capabilities in this arms race is not primarily a particular adversary, but rather the ongoing global advance of microbiological and biomedical research. Defensive measures are in a race with nefarious applications of basic research, much of which is itself undertaken for protection against natural disease. In a sense, we are in an arms race with ourselves.

It is hard to see how this arms race is stable

It is hard to see how this arms race is stable – an offence granted comparable resources would seem to be necessarily favoured. As with ballistic missile defence, particular defensive measures may be defeated by offensive countermeasures. In the biological case, implementing defensive measures will require not only research but drug development and distribution plans. Offensive measures need not exercise this care, although fortunately they will likely face comparative resource constraints (especially if not associated with a state programme), and may find that some approaches (for example, to confer antibiotic resistance) have the simultaneous effect of inadvertently reducing a pathogen's virulence. The defence must always guard against committing the fallacy of the last move, whereas the offence may embrace the view of the Irish Republican Army after it failed to assassinate the British cabinet in the 1984 Brighton bombing: 'Today we were unlucky, but remember we have only to be lucky once – you will have to be lucky always'.[40] At the very least, the defence will have to be vigilant and collectively smarter than the offence.

The only way for the defence to win convincingly in the biological arms race would seem to be to succeed in discovering and implementing certain de facto last-move defences, at least on an organism-by-organism basis. Perhaps there are defences, or a web of defences, that will prove too difficult for any plausible non-state actor to engineer around. Whether such defences exist is unclear at this time, but their exploration should be a long-term research goal of US biodefence efforts. Progress might also have an important impact on international public health. One

of the 'Grand Challenges' identified by the Bill and Melinda Gates Foundation in its $200m initiative to improve global health calls for the discovery of drugs that minimise the emergence of drug resistance – a kind of 'last move' defence against the evolutionary countermeasures of natural microbes.[41] Should a collection of such defensive moves prove possible, bioterrorism might ultimately succumb to a kind of globalised dissuasion by denial:[42] non-state groups would calculate that they could not hope to achieve dramatic results through biological programmes and would choose to direct their efforts elsewhere.

Bioterrorism might succumb to a kind of globalised dissuasion by denial

The objection might be raised that the vision of an eternal arms race smacks too much of technological determinism; after all, Kennedy and Wohlstetter foresaw a world replete with nuclear weapons, yet this world has so far been averted – and would not have been averted had we given in to claims of its inevitability. But biotechnology is fundamentally different from nuclear-weapons technology in its broad availability, and once again, the analogy to the nuclear case fails.

Given the proliferation of capabilities described here, greater weight must necessarily be placed on addressing the possible motivations of terrorist groups. After all, remarkably few non-state groups have ever attempted biological attacks. Understanding why this is so, to what extent it has been due to motivations as opposed to means, and working to preserve whatever inhibitions have been at play, should receive high priority.

Racing against ourselves

Short of de facto last-move defences, another way for the defence to try to maintain an advantage is for it to classify its most important countermoves. These might still be described publicly in broad terms so that some dissuasive benefit could be gained. Such an approach may seem natural, almost automatic, to the national security community – although it is not the approach that has been taken for smallpox biodefence research, which is overseen by the World Health Organization (WHO). But in fact, classified defence research carries dangers in the biological case that should not be overlooked.

First, from an ethical point of view, it would simply be unacceptable to keep secret certain potentially effective defensive measures. For example, in an era when certain strains of bacteria are already resistant to all known antibiotics, and with antibiotic resistance spreading rapidly, keeping a

newly developed effective antibiotic in reserve for the event of a biological attack would lead immediately to avoidable deaths due to naturally occurring diseases. Only in a future where there were a huge variety of effective antibiotics available for infectious disease would such a biodefence strategy be acceptable. (And even then, one would worry whether such a stockpile could be kept secure against the small theft needed to permit biological countermeasures to be explored.) Our insufficient effort against naturally occurring disease and increasing antibiotic resistance currently limits our strategies for bioweapons defences.

Second, it will be vital from a strategic perspective to consider carefully what types of biodefence work should be classified, and whether some international transparency will be needed even in these cases. According to the *New York Times*, some classified research in the United States has involved genetically engineering pathogens in order to replicate steps believed to have been taken in the Soviet biowarfare programme.[43] Such work would be legally permitted under the BWC as legitimate biodefence research; however, if it were conducted in secret and news of it leaked, other nations might wonder whether the US had an offensive programme involving genetic modifications underway.

A more difficult question is whether it would be legal and wise to have classified biodefence research produce genetically modified pathogens that, to our knowledge, no adversary has yet created. On the one hand, we should know how to defend ourselves against such potential threats that we can already anticipate. On the other, such research risks making the US government a primary driver of the very biological arms race we hope to avoid, and risks convincing other nations of our offensive intent. Strategic decisions must be made about what biological weapons research the US or any other government will conduct in the name of biodefence, how much of this research will be classified and how that programme will be publicly described.

A congressional or presidential commission should be created to advise on these issues, while defusing international concern that the US is secretly pursuing an offensive weapons programme. A 'trigger list' of research that government agencies may only perform with White House approval and congressional oversight should ultimately be promulgated, to ensure that classified biological weapons research of potential high consequence anywhere within the US government is not conducted without its strategic and legal ramifications being weighed. A permanent body, with access to classified biodefence information government-wide, and responsibility to both the executive and legislative branches, should be created to ensure that this vigilance is in fact exercised. This body would go beyond intra-agency legal reviews such as those now

conducted by the Department of Defense Compliance Review Group;[44] it would be both government-wide and have the mandate to make recommendations to the president regarding the strategic wisdom of lines of research. The body would combine the independence and access of the president's Foreign Intelligence Advisory Board with accountability to both the executive and legislative branches. The scientific community would have to play a central role for such steps to be realistic, current and viewed as legitimate.

The United States should carefully consider what classified biodefence research will be performed and do so in as transparent a way as possible consistent with national security, to reassure the world of its commitment to the BWC. In this way the US would seek to minimise incentives for other states to pursue or accelerate illegal offensive programmes. Rather, broad-based and publicly acknowledged biodefence research would aim to globalise dissuasion, convincing non-state terrorist groups that they cannot hope to counter the entire array of defences that the world's legitimate biodefence research community has arrayed against them. With research on de facto 'last-move' defences, the biodefence community should thereby endeavour to circumvent, or at least mitigate, an otherwise endless biological arms race.

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Notes

1 President John F. Kennedy, News Conference Number 52, 21 March 1963, John F. Kennedy Library and Museum, Washington DC, http://www.jfklibrary.org/jfk_press_conference_630321.html. While this authorisation legislation has had some success in the United States Senate, it has faced more difficulty in the US House of Representatives.

2 Albert Wohlstetter, *Moving Toward Life in a Nuclear Armed Crowd?* ACDA/PAB-263, prepared by Pan Heuristics Division of Science Applications Inc., Los Angeles, December 1975, revised April 1976. A subsequent version may be found as Chapter 6, 'Life in a Nuclear Armed Crowd', in Albert Wohlstetter, Thomas A. Brown, Gregory S. Jones, Henry Rowen, Vince Taylor and Roberta Wohlstetter, *Swords from Plowshares* (Chicago: University of Chicago Press, 1979), pp. 126–150.

3 Much of this history is reviewed in Christopher F. Chyba, 'Biological Terrorism and Public Health', *Survival*, vol. 43, no. 1, spring 2001, pp. 93–106. For statistics on disease emergence over the past two decades, see Jonathan R. Davis and Joshua Lederberg (eds), *Emerging Infectious Diseases from the Global to the Local Perspective: A Summary of a Workshop of the Forum on Emerging Infections* (Washington DC: National Academy Press, 2001).

4 Global Pathogens Surveillance Act of 2003, S. 871, 108th Congress, 1st Session, http://www.theorator.com/bills108/s871.html.

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