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SPECIAL ISSUE: THE BIOLOGICAL THREAT - PART TWO

FEATURE ARTICLE

Implications of COVID-19 for Bioterrorism

Gary A. Ackerman, Zachary Kallenborn, and Philipp C. Bleek

A VIEW FROM THE CT FOXHOLE

Shmuel Shapira

Former Director General, Israel Institute for Biological Research

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FROM THE EDITOR

With more than a million Americans dead from COVID-19 and the pandemic associated directly or indirectly with around 15 million deaths globally by the end of 2021 according to World Health Organization estimates, it is essential to reassess the global biological threat landscape, including the possibility that bioterrorists or other bad actors might seek to exploit advances in biotechnology to engineer a future pandemic.

In a joint effort, the Combating Terrorism Center and the Department of Chemistry and Life Science at West Point have assembled some of the best and brightest thinkers in the counterterrorism, policy, and scientific communities around the world for their perspectives and analysis on the evolution of the biological threat picture. The result is a two-volume set of special issues, with the second volume being published this month.

In the feature article, Gary Ackerman, Zachary Kallenborn, and Philipp Bleek present a bioterrorism classification schema to evaluate the pandemic's impact on bioterrorism. They assess that "when it comes to bioterrorism, the pandemic probably has not moved the needle much. Although COVID-19 might encourage apocalyptic cults, some radical environmentalists, some extreme right-wing groups, and some Islamist extremist groups toward biological weapons, most other terrorist groups are more likely to be discouraged. The pandemic has bolstered some terrorists' bio-related capabilities but in at most modest ways. At the same time, lessons from the COVID-19 experience may both help reduce the consequences of a future attack and heighten perceptions of bioterrorism risk."

Our interview is with Shmuel Shapira, who served as Director General of the Israel Institute for Biological Research between 2013 and 2021.

Audrey Kurth Cronin argues that "the most significant new risks of [biological] attacks come largely from insider threats by knowledgeable scientists with questionable motives, proxy actors backed by adversarial states, or even those experimenting with new biotechnologies irresponsibly." She writes that "the old threats of bioterrorism remain, but they are joined by new ones that are falling between the seams of biology and other disciplines, especially engineering, data science, and computer science, and especially at the intersection between molecular biology and artificial intelligence."

Jaime Yassif argues it is vital to "take action to safeguard the life sciences to prevent biotechnology catastrophe, in addition to bolstering law enforcement and intelligence capabilities to more effectively anticipate and prevent bioterrorism and other biological threats." She writes: "In biosecurity, there is no single solution or intervention that can eliminate all risk. That is why a layered defense is needed, in which multiple interventions in aggregate add up to substantial risk reduction."

Paul Cruickshank, *Editor in Chief*

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Cover: Anthrax bacteria, computer illustration (Kateryna Kon/Science Photo Library via Getty Images)

Going Viral? Implications of COVID-19 for Bioterrorism

By Gary A. Ackerman, Zachary Kallenborn, and Philipp C. Bleek

COVID-19 has drawn greater attention to the prospect of biological weapons use. But when it comes to bioterrorism, the pandemic probably has not moved the needle much. Although COVID-19 might encourage apocalyptic cults, some radical environmentalists, some extreme right-wing groups, and some Islamist extremist groups toward biological weapons, most other terrorist groups are more likely to be discouraged. The pandemic has bolstered some terrorists' bio-related capabilities but in at most modest ways. At the same time, lessons from the COVID-19 experience may both help reduce the consequences of a future attack and heighten perceptions of bioterrorism risk. Fundamentally, bioterrorism has to date been rare, and even after COVID-19, it is likely to remain so. Even if the threat of bioterrorism might increase due to technological and other dynamics, this trajectory appears unlikely to be appreciably affected by the COVID-19 pandemic.

The COVID-19 pandemic provided a stark reminder of the potential damage that biological agents can wreak on society. Over a million people have died from the disease in the United States alone. The International Monetary Fund estimated COVID-19 "will cost the global economy $12.5 trillion through 2024."[1] The pandemic even emphasized that the world's militaries are vulnerable to disease as well, for example when the USS Theodore Roosevelt evacuated most of its crew because of a severe COVID outbreak.[2]

COVID-19 has also raised larger fears about the future of biological warfare: If a naturally occurring pandemic can cause so much harm, what about a human-engineered one? After all, adversaries, both state and non-state, have been using biological organisms or their products to harm one another for thousands of years.[3] Given the inordinate global harm, bad actors might be expected to scramble to acquire such weapons in hopes of visiting this level of destruction on their adversaries. And at the forefront of this group would presumably be terrorist groups and individuals who, as consummate asymmetric actors, would surely not be able to resist the clarion call of the microbe. While pursuit of large-scale, sophisticated biological weapons only took off in the 20th century, concerns about bioterrorism really only began to arise in the 1990s.

The implications of COVID-19 for bioterrorism appear complex and contingent. For example, terrorist ideology acts as a critical mediating factor. While the COVID-19 experience might encourage certain groups with apocalyptic goals to pursue biological weapons, it might equally discourage groups with narrower goals that recognize widespread harm might result in significant blowback both upon and from their own supporters. Indeed, it probably does little to energize actors who were already oriented toward bioterrorism, besides educating them on some key nuances, including the difficulty of controlling the outcomes when using contagious bioagents. In general, the authors assess COVID-19 will have a limited overall effect on bioterrorism risks, though it may have greater effects on *perceptions* of those risks.

For government agencies concerned with bioterrorism, this therefore suggests that fundamental changes in their risk assessments or countermeasures are likely not needed. Counterterrorism efforts should largely continue to focus on the same set of pre-COVID-19 actors and threats (including the impact of emerging technologies). Two possible, additional recommendations are: a heightened focus on groups holding ideologies of an apocalyptic-millenarian character, and to direct specific intelligence collection and analysis efforts toward regions where extremists might exploit new vaccine development capacity to develop capabilities related to handling pathogenic agents. Agencies should also support broader efforts for resilience against

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disease generally as responding to man-made pandemics is not likely to be drastically different than responding to natural ones.

To unpack this argument, the authors first construct a schema for bioterrorism, which identifies the main categories of threat actors and threat vectors. This provides a baseline of pre-COVID assessments of the bioterrorism threat and how bioterror risks vary considerably between actors and vectors. Then the authors use this schema as a basis for considering the changes wrought by COVID-19 and situating the pandemic's effects on different areas of bioterrorism risk. The article concludes with several policy recommendations.

What's What: Creating a Taxonomy of Bioterrorism

By bioterrorism, the authors are referring to terrorist acts[a] involving pathogenic microorganisms or biological toxins (complex, toxic molecules produced by living organisms). Although the scope of this article precludes a comprehensive survey of bioterrorism,[4] the authors will note some key features of the topic that are pertinent to the creation of a practical taxonomy, which can then be used to explore changes in the threat over time, specifically from before to after the COVID-19 pandemic.

First, bioterrorism is extremely rare within the annals of terrorism. Of the more than 200,000 terrorist events between 1970 and 2019 contained in the Global Terrorism Database, only 38 (0.02 percent) are listed as involving biological weapons.[5] This (fortunate) infrequency means that the empirical basis for constructing a taxonomy is limited. In addition, the current effort is intended to be more than merely a record of the past, but to enable forward-looking analyses of a highly dynamic context where technologies are advancing rapidly and adversaries are constantly adapting. For these reasons, a strict taxonomic approach is insufficient here and must be accompanied by typological elements.[b] The resulting classification schema is informed wherever possible by the (relatively meager) empirical record of bioterrorism, primarily drawn from the Profiles of Incidents involving CBRN and Non-state Actors (POICN) Database, which as of its latest update in 2017 contains 107 bioterrorist incidents.[6][c] It is supplemented where necessary with conceptually determined categories that encompass potential future threats. The authors label the resulting classification as the Bioterrorism Classification Schema.

The Bioterrorism Classification Schema (BTCS) is based on a standard risk construction of viewing threat as a combination of an adversary's intent and capability. It also takes into account both the *threat actor* (the individual or group seeking to perpetrate the bioterrorist attack) and the *threat vector* (the means by which the attack is perpetrated using a biological agent). With respect to the number of categories needed, the authors attempt to capture most of the historically and theoretically relevant categories, while at the same time seeking to prevent the framework from becoming too unwieldy for practical analytical usage. As a result, where two potential categories are determined to be more reasonably similar, then those categories are merged into one, unless there is a compelling conceptual reason not to do so.

Threat actor was defined mostly in accordance with the POICN database, with some minor modifications to better match the needs of the study. The intent to engage in bioterrorism varies more according to the threat actor's underlying motivation (ideology or cause),[d] while levels of capability vary more according to the organizational structure of the threat actor.[e] Of course, in practice, motivation and capability are not empirically or theoretically independent: Ideological groups may have different distributions of group capabilities, while ideology may support or detract from acquiring specific or general capabilities.

The authors chose motivation categories based on those of the known perpetrators listed in the POICN database. After placing animal rights and other environmental extremists into a single category for simplicity,[f] this yields seven categories: Islamist extremist, apocalyptic/millenarian cults, ethno-nationalist, extreme far-right, extreme far-left, animal rights/environmentalism, and idiosyncratic objective.[g] The last category is not incorporated directly into the schema, but needs to be assessed separately in each case (see Box 1).

a This article uses the same definition of terrorism as the Global Terrorism Database: "the threatened or actual use of illegal force and violence by a non-state actor to attain a political, economic, religious, or social goal through fear, coercion, or intimidation." Gary LaFree and Laura Dugan, "Introducing the Global Terrorism Database," *Terrorism and Political Violence* 19:2 (2007): pp. 181-204.

b While they are both involved in the classification of phenomena, the key differentiating factor is that taxonomies are empirical and inductive (i.e., constructed based on observations of the world), whereas typologies are conceptual and deductive, with a structure imposed by the designer. The effort here therefore includes elements of both classification approaches. See Kevin B. Smith, "Typologies, taxonomies, and the benefits of policy classification," *Policy Studies Journal* 30:3 (2002); Susan Lambert, "Do We Need a 'Real' Taxonomy of e-Business Models?" *School of Commerce Research Paper Series* 6:6 (2005).

c It should be noted that the Global Terrorism Database only covers actual terrorist attacks and attempted attacks, whereas the POICN database includes other activities as well, such as plots, attempts to acquire biological agents, weaponization of agents, and so forth.

d For example, Thomas Guarrieri and Collin Meisel found that individuals oriented around a single issue were more likely to pursue chemical and biological weapons than those who were extreme far-left or extreme far-right in orientation, while McCann found that religiously motivated (especially Islamist) terrorist groups were significantly more likely to pursue biological weapons. Thomas R. Guarrieri and Collin J. Meisel, "Extremists and Unconventional Weapons: Examining the Pursuit of Chemical and Biological Agents," *Behavioral Sciences of Terrorism and Political Aggression* (2019); Wesley S. McCann, "Outbreak: A Comprehensive Analysis of Biological Terrorism," *Studies in Conflict & Terrorism* (2022).

e For example, Jean Pascal Zanders maintains that a higher-end bioagent production capability is far easier for a "vertically organized, highly integrated and ideologically uniform" group than one that is amorphous or based on small cells. Jean Pascal Zanders, "Assessing the Risk of Chemical and Biological Weapons Proliferation to Terrorists," *Nonproliferation Review* 6:4 (1999): p. 30.

f There are extensive ideological and operational links between the extremist animal rights and environmentalist communities. See Zachary Kallenborn and Philipp C. Bleek, "Avatars of the Earth: Radical Environmentalism and Chemical, Biological, Radiological, and Nuclear (CBRN) Weapons," *Studies in Conflict & Terrorism* 43:5 (2020) and Gary Ackerman, "Beyond Arson? A Threat Assessment of the Earth Liberation Front," *Terrorism and Political Violence* 15:4 (2004).

g This does not prevent new categories from being added if it becomes necessary based on new empirical evidence.

Box 1: Idiosyncratic Perpetrators

Certain perpetrators (primarily lone actors) can have a variety of idiosyncratic motives for engaging in violence, arising from nurturing a personal or professional grudge and/or suffering from delusional mental illness. These are not an insignificant proportion of perpetrators, with such idiosyncratic motives being present in roughly 17 percent of recorded bioterrorism incidents in POICN[7] and among 23 percent of past non-state biological perpetrators in a related actor-level database.[8] However, owing to the wide variation in possible causes and forms such motives can take, it is far more difficult to apply even moderately consistent values to the motivation portions of the schema across the various agents. The authors therefore cannot include actors with idiosyncratic motivations in the BTCS in the same way as other motivational types. Nonetheless, some guidance regarding these actors' bioterrorism decision-making is available. For example, in a study of the psychology of chemical and biological perpetrators, it was found that those with an idiosyncratic motive are most likely to attack individuals and to use food or product contamination (27 of 51 cases).[9] Overall, when evaluating the motivational component of the schema for idiosyncratic actors, therefore, the specific psychological circumstances of the individual and the nature of the idiosyncratic belief system should be taken into account in assessing likely agent and delivery system selection.

When considering capability, the POICN database uses three categories of organizational structure: lone actor, small cell, and formal terrorist organization. Given recent geostrategic developments that suggest cash-strapped states could sell arms to terrorists[10] and considering that states have access to resources and capabilities that even the most advanced terrorist groups do not, the authors added another category at the high end of the capability spectrum for state-sponsored terrorist groups (though the economic pressures of COVID-19 may decrease the general financial support state sponsors provide to terrorist groups). In addition, the authors add a lone actor "rogue scientist"/insider category to capture the possibility of a highly knowledgeable individual with a minimal support network. Such a knowledgeable individual may also be a part of a small cell, formal terrorist group, or state-sponsored group, but this is not typical.[h]

With respect to *threat vector*, a weapon system consists of a harm agent together with the means to deliver said agent to the target(s), the delivery mechanism being especially relevant in the case of non-contagious biological weapons.[i] Therefore, the authors consider two separate components of the threat vector: 1) the acquisition, culturing, and preparation of the bioagent (pathogen or toxin), as well as 2) the dissemination mechanism. The authors distinguish between three categories of agent acquisition/production: a) crude agents requiring little to no formal biological training and no specialized equipment to acquire or produce, b) agents requiring moderate levels of training and some specialized equipment, and c) sophisticated agents requiring extensive expertise and high-end equipment. Examples of bioagents that fall into each of these categories are given in Table 1. Given the objective of assessing changes wrought by COVID-19, a highly contagious agent, the authors further subdivide the bioagent category into contagious versus non-contagious agents. This differs somewhat from typical military or CDC categorizations.

In traditional military contexts, bioagents are usually categorized according to the biological family of the agent (bacterium, virus, protozoa, toxin, etc.). This makes sense when the adversaries concerned are all states with a sizable resource base that would not normally intentionally seek to produce crude agents of low quality. Terrorists, however, often have a wider range of operational objectives and greater resource constraints, so the nuances of viral as opposed to bacterial agent production are less informative than the overall sophistication required for preparation of the agent and the quality (in terms of survivability,[j] infectiousness, dispersibility, etc.) of the resulting product. Similarly, while the CDC has published a list of Category A, Category B, and Category C agents,[11] these categories are at least partially based on the characteristics of the disease the agent causes (such as its morbidity, mortality, and infectious dose), and were designed to guide the levels of security and safety required for legitimate work with each agent. While incorporating the ease of dissemination and production of agents, the CDC categories are not designed to cover the entire range of agent preparations that terrorists might pursue, which have historically often been rather low-level, often involving agents (like abrin or HIV) that do not even appear on the CDC lists.[12] At the same time, much of the concern with respect to bioterrorism lies in the potential dangers posed by high-end emerging technologies,[13] especially the burgeoning fields of synthetic biology[k] (encompassing such advances as the CRISPR-Cas9 method of targeted genome editing, rapid DNA synthesis and genome transplantation technologies) and new delivery technologies (such as microencapsulation and bacteriophages[14]), which are not covered in these existing categorizations.

For delivery mechanism categories, the authors draw on the empirical record in POICN, as well as delivery mechanisms used in the history of biological warfare; the authors combine several POICN categories for simplification while preserving the essential features of each delivery method. The categories are also intentionally cast sufficiently broadly so as to allow for the inclusion

h In the event that it is known that a terrorist group (either small homegrown cell, formal, or state-sponsored) possesses such an insider, then for practical risk assessment purposes, an analyst would utilize the maximum of the insider capability score and the capability score for the type of terrorist group for each agent and delivery method. See Illustrative Example 2 in the appendix.

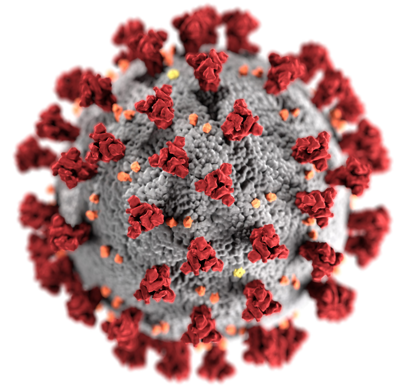
i The main steps involved in developing a bioweapon consist of: a) acquiring a seed stock of the agent; b) culturing the agent to increase the amount; c) refining and preparing the agent to make it suitable for storage, transportation, and delivery (e.g., drying, milling); and d) mating it with a mechanism for dissemination. Gary A. Ackerman and Kevin S. Moran, "Bioterrorism and Threat Assessment," Paper #22 commissioned by the Weapons of Mass Destruction Commission (The "Blix" Commission), 2004. In this *CTC Sentinel* article, the authors treat all of the steps that require biological expertise (a through d) in a single component.

j Survivability usually refers to the ability of a bioweapons agent to persist in the environment without being rendered harmless by such factors as sunlight, oxidation, and atmospheric forces.

k The field of synthetic biology is concerned with designing and building new biological materials (e.g., enzymes, proteins, lipids not already found in nature), devices, systems, and/or functions, especially by (re)programming DNA circuits to manipulate cellular behavior. Gary A. Ackerman and Lauren E. Pinson, "An Army of One: Assessing CBRN Pursuit and Use by Lone Wolves and Autonomous Cells," *Terrorism and Political Violence* 26:1 (2014): footnote 3.

of emerging technologies. For example, drone swarms as delivery platforms[15] could be included as a subcategory of Aerosol/Spray[l] delivery mechanisms, and a wide range of munitions ranging from mortars to cluster bombs can be included under the Explosive category. This leads to seven possible categories: Aerosol/Spray, Direct Contact/Latent,[m] Food/Product Contamination, Explosive, Animal Vector, Mail, and Water Supply.

Table 1 depicts the completed Bioterrorism Classification Schema matrix. Individual cells have been populated with a simple five-scaled measure of "Very Low," "Low," "Medium," "High," or "Very High" to denote the relative likelihood of the particular threat actor having the intention or capability to successfully pursue a given threat vector (agent or delivery mechanism). These values reflect the threat just prior to the outbreak of the COVID-19 pandemic at the end of 2019. The metrics used, however, are not integral to the structure of the Bioterrorism Classification Schema, and future efforts can replace the current measure with a more complex construction. It should also be noted that to thoroughly determine the value for each cell of the Bioterrorism Classification Schema would require a degree of analysis (both empirical and deductive) that is beyond the scope of this paper.[n] However, it is not strictly necessary to do so for the authors' current purpose, since the structure of the matrix itself allows for systematic consideration of which elements are likely to be affected by the COVID-19 pandemic and whether they are likely to increase or decrease. Nonetheless, preliminary values for each cell have been estimated, based on the authors' expertise studying bioterrorism and its perpetrators, descriptive empirical information obtained directly from the POICN database, and other results drawn from the literature. Furthermore, while a rigorous threat assessment is not the focus of this article, some illustrative worked examples of how the Bioterrorism Classification Schema can be utilized to estimate the threat of particular bioterrorism scenarios are provided in the appendix.[o]



COVID-19 Coronavirus molecule, March 24, 2020 (CDC/API/Gamma-Rapho via Getty Images)

Although the authors are not seeking to provide rigorous justifications for each of the individual likelihood values in the Bioterrorism Classification Schema, they offer several observations to demonstrate that the Bioterrorism Classification Schema largely concurs with the pre-COVID-19 expert consensus with respect to bioterrorism:

- The matrix shows not all terrorists will seek to utilize bioterrorism to cause mass death, or even mass casualties.[16] The motive for the case of the Rajneeshee cult in Oregon in 1984 was merely to prevent people from voting in a local election,[17] while at least part of the objective for sending the 2001 "anthrax letters" in the United States was to leverage the natural human fear of disease and doubt regarding exposure to inflict psychological harm and social disruption. Therefore, several threat actors in the Bioterrorism Classification Schema are estimated to have a fairly high likelihood of pursuing the use of rather crude agents.
- The Bioterrorism Classification Schema overall reflects the widely proffered dynamic that the more sophisticated the bioagent and/or delivery system is, the less likely any given actor will possess or be able to acquire the capability to effectively deploy it.[18]
- Both older and more recent studies suggest that religiously motivated terrorists in general, and Islamist terrorists in particular, have the highest overall motivation to engage in bioterrorism,[19 p] while apocalyptic millenarian cults (like the erstwhile Aum Shinrikyo) probably have the highest interest in high-end biological weapons specifically.[20 q]
- The moderate interest shown by ethno-nationalist groups in low-moderate level bioterrorist attacks and the lower overall interest of extreme far-left organizations reflect the empirical record in POICN, while the atypical, somewhat elevated interest of the animal rights/environmentalist milieu in specific

l The Aerosol/Spray category involves dissemination that after initial release allows natural air currents and gravity to disperse the particles or droplets, whereas the Explosive category involves mechanisms that use the kinetic energy of a detonation to disperse particles that are also technically aerosols.

m In this context, "Latent" follows the description of the POICN Database as a delivery system where an agent "is left out without forcing direct contact. For instance, leaving breakable vials of an agent on the floor intending for the target to step on the vials and release the agent." "POICN Database Codebook V8.71," December 2017.

n This would require, for instance, robust analyses of databases like POICN and the Chemical and Biological Non-state Adversaries Database (CABNSAD), while taking into account the current strategic orientation and capabilities of prominent adversaries in each category, as well as recent technological developments that might affect these. This can be done, but would take considerable resources, as demonstrated in other bioterrorism-related risk assessments, such as the Bioterrorism Risk Assessment, National Research Council, 2008, and U.S. Department of Homeland Security, *Bioterrorism Risk Assessment: A Call for Change* (Washington, D.C.: National Academies Press, 2008).

o The matrix as presented does not capture possible interaction effects between its components, which would need to be considered if the BTCS were to be utilized as a basis for assessing threat. For example, in some cases, motivation can drive capability, or vice versa, while there might be dependencies between certain agents and delivery mechanisms that are difficult to represent in a simple two-dimensional matrix. The authors leave such enhancements to future research.

p Islamist extremist groups also tend to be particularly good fits for the criteria for pursuing CBRN terrorism (being embedded in alliance structures, being based in an authoritarian state with relatively strong connections to a globalized world, being relatively large, and having more experience with terrorism in general) derived in Victor H. Asal, Gary A. Ackerman, and R. Karl Rethemeyer, "Connections Can Be Toxic: Terrorist Organizational Factors and the Pursuit of CBRN Weapons," *Studies in Conflict & Terrorism* 35:3 (2012).

q This assertion does not include the "idiosyncratic" category, which is discussed in Box 1.

agents and delivery systems is drawn from various theoretical analyses.[21]

- The relatively greater values across threat actors for crude non-contagious and moderate non-contagious agents (which include ricin and botulinum toxin, respectively) reflect the high frequency of use for these agents.[r]
- The estimates of delivery mechanism selection likelihoods are mostly drawn from POICN; for example, the observation that the contamination of food and consumer products has traditionally been among the more commonly attempted and successful delivery methods, while only Islamist extremist and ethno-nationalist groups have attempted to utilize explosives to disseminate bioagents. This is supplemented with theoretical arguments and broader tactical records where these are relevant, such as when extreme far-right groups were assigned a higher likelihood of attacking the water supply.[s]
- Capability likelihoods were similarly derived from POICN and shaped by the results of prior analyses. For example, they reflect the findings that lone actors are particularly adept at using biological agents (albeit at the less sophisticated end of the spectrum)[t] and that existing published manuals indicate a continued low-level competency to enact sophisticated or large-scale bioterrorist attacks.[22] The absence of any evidence of a successful mass-casualty bioterrorist attack using contagious agents and only 11 small-scale incidents occurring since 2012 demonstrate the difficulty of acquiring a viable capability for all but the crudest bioweapons and smaller-scale attacks.[23] Concerns regarding the provision of bioweapons from state-run programs,[24] the singular capabilities of technically proficient insiders,[25] and the facilitating effects of emerging technologies such as CRISPR-Cas9 and biotechnology "kits,"[26] are also reflected in the matrix.

The Effects of COVID-19 on Bioterrorism

The effects of COVID-19 on bioterrorism risk can be considered across three general aspects: (a) terrorist interest in bioterrorism; (b) capabilities of terrorist groups to carry out bioterrorism; and (c) impacts on the consequences of bioterrorism. There is also a fourth, more abstract but still meaningful impact on how policy makers and the policy intelligentsia think about bioterrorism risk, with it being possible that (d) COVID-19 impacts threat assessment more than it impacts the threat itself. The changes relating to (a) and (b) are summarized in Table 2.

a) COVID-19 will probably boost interest in biological weapons among terrorist groups with maximalist ideologies, but decrease it for others.

The COVID-19 pandemic clearly illustrates the significant, global harm a contagious biological weapon could cause. A typical terror attack using guns or even bombs might kill a handful of people; a complex, sophisticated attack like the 9/11 attacks can kill thousands; but a COVID-like biological weapon might kill millions. Given the extreme way COVID-19 has spread throughout the world, disrupted most aspects of society, and captured global attention, COVID-19 undoubtedly encouraged many terrorist groups to at least consider biological weapons. The question remains, though: Do terrorists perceive such extreme harm as a good thing? And how does the prospect of indiscriminate, potentially uncontrollable, mass harm fit into their broader ideology, strategies, and goals?

Groups with maximalist ideologies aiming for drastic, global, or even cosmic change such as apocalyptic cults, some extreme environmental groups,[u] or accelerationist extreme right-wing groups[27] necessarily require extreme means to achieve their goals. While a handful of attacks aimed at garnering public attention and perhaps support may help, drastic ends require drastic means, especially for more misanthropic ideologies. Biological weapons are one of the few avenues available to cause globally catastrophic, and especially existential, harm. For example, the green anarchist group RISE in 1970s Chicago sought biological weapons as a way to kill off most of humanity to repopulate the Earth with enlightened environmentalists.[28] COVID-19's impacts on the motivations of such groups might also not manifest in the short-term. After all, groups with such apocalyptic ideologies are relatively rare, and even rarer still are those with meaningful capabilities. Decades from now, however, some future apocalyptic extremist group may look back at the COVID-19 pandemic as evidence of the potential utility of biological weapons.

However, groups with narrower objectives or even ambitious, but not global, goals may see the harm as a strong reason not to pursue biological weapons, or at least not contagious biological weapons whose effects are difficult to either gauge or control. COVID-19 killed millions, but it was relatively indiscriminate in doing so. COVID-19 spread throughout the world, with major outbreaks in virtually every country. People, especially those in big cities, were infected, regardless of race, class, gender, religion, and political ideology (though exact infection and mortality rates do differ across these demographics). A group using a contagious biological weapon would have to accept significant potential risk of

r Markus Binder and one of the authors (Gary Ackerman) analyzing the POICN database observe that toxins were the primary agent in most of the cases in the database (which, as noted earlier, include failed, aborted, and thwarted plots). Out of the 86 bio-incidents where the nature of the agent could be identified, 53 of these (61.6 percent) were toxins, with the dominant (67.9 percent) toxin being ricin, which featured in 36 events. Markus K. Binder and Gary A. Ackerman, "Pick Your POICN: Introducing the Profiles of Incidents involving CBRN and Non-state Actors (POICN) Database," *Studies in Conflict and Terrorism* 44:9 (2021). Frida Ekren provides a more recent example where, in 2019, a cell of the Islamic State-linked Indonesian group Jamaah Ansharut Daulah plotted to disperse the toxin abrin by explosive as part of a suicide bombing. Frida Ekren, "Understanding the Current Threat of Bioterrorism: A study of Violent Non-State Actors' Online Instruction Manuals," master's thesis, Charles University, July 2021.

s Among others, in the 1980s the extreme far-right apocalyptic group the Covenant, Sword and the Arm of the Lord in the United States plotted to attack the water supplies of major cities with the chemical agent cyanide, which provides some indication of possible proclivities for disseminating bioagents through this mechanism. See Kerry Noble, *Tabernacle of Hate: Seduction into Right-Wing Extremism, 2nd ed.* (Syracuse, NY: Syracuse University Press, 2010).

t Thirty-one percent of events in the POICN database where a lone actor pursued a biological weapon resulted in actual attacks with agent dispersal, while only 19 percent of similar events involving formal organizations reached this level. Ackerman and Pinson.

u As an example of such thinking among this milieu, there is the following appeal by an environmentalist writing under the pseudonym of "Gula": "Contributions are urgently solicited for scientific research on a species-specific virus that will eliminate Homo shiticus from the planet." Gula, "Eco-Kamikazes Wanted," *Earth First! Journal* (1989): p. 21.

infecting, and killing, their own real and potential supporters.[v] Even for contagious diseases that spread less readily than the SARS-CoV-2 virus has, a would-be bioterrorist cannot comfortably predict which communities the disease will spread to, and which it will not.

So, the pandemic is unlikely to cause a disinterested ideological group to strongly favor bioterrorism post-pandemic (e.g., a change from low to high motivation for carrying out a bioterrorism attack), or similar dramatic changes in motivations for bioterrorism overall. A subset of the already-small subset of groups with maximalist aims that were not already interested in biological weapons might view the effects of the pandemic and be more attracted to the ability of bioagents to spread indefinitely and sicken millions. For the remainder of terrorist groups, the pandemic seems likely to disincentivize the use of contagious bioagents at the very least. As for non-contagious bioagents, the pandemic should have minimal impact: Those already interested in non-contagious agents pre-COVID-19 will likely remain interested, while the contagious nature of the pandemic means that it does not present other terrorists with any advantageous lessons that might make them more interested in non-contagious agents.

b) COVID-19's effects on terrorist bioterrorism capability are likely modest at most.

The COVID-19 pandemic is likely to have at most modest impacts on terrorists' capabilities to conduct bioterrorism. Terrorists generally have been affected by the pandemic, too, so some of them will have been "calling in sick," or even dying, thus reducing the operational capabilities of those groups, at least temporarily (the exception is groups in conflict zones where there appears to be no reduction in terrorist activity).[29] On the other hand, the downtime from lockdowns and the inability to continue normal operations might provide time and space to focus on building organizational and operational capabilities that could manifest in attacks down the road.[30] The same dynamics potentially apply to bioterrorism.

Terrorists and other actors might seek, and in some cases already have sought, to weaponize the coronavirus that causes COVID-19.[31] These appear often to be small-scale, opportunistic attempts to spread the disease through casual or personal contact, which may support the general spread of disease but not create a major unique effect. As such, terrorist efforts have to date and are likely in the future to have at most modest consequences on the course of the disease, especially given the increasing availability of vaccines and treatments. Potential attacks utilizing COVID-19 are only likely to have noticeable effects in areas with low prior exposure to the disease, lower vaccination rates, or if a new strain emerges that is not susceptible to current vaccines, although all of these circumstances provide terrorists with only a limited window for action.[32]

The massive increase in medical and public health resources as a result of the pandemic might also create new opportunities for terrorists to exploit in the medium- to long-term. For example, new laboratories built in response to the pandemic might provide new opportunities for stealing pathogens or for radicalized insiders to build technical skills.[33] Likewise, even though the pandemic likely curtailed academic teaching and research laboratories in the short-term, the spread of vaccination efforts and efforts to achieve rapid up-skilling in related medical expertise, particularly in the global South,[34] may support the proliferation of knowledge necessary to create and disseminate biological weapons agents. That is, gaining comfort and expertise with handling and manipulating contagious pathogens in general can be applied to handling and manipulating contagious pathogens intended for bioterrorism. However, the magnitude of this knowledge transfer should not be overstated, because even if a would-be bioterrorist were provided with this knowledge and skill, they are unlikely to cover the full biological weapons acquisitions cycle. That is, a rapidly trained virologist or vaccine production technician has no need to learn the technical details of weaponizing and disseminating a biological weapons agent *en masse*, even if they had access to the technical resources to do so.

To the extent that state sponsors provide witting aid to terrorists, COVID-19 might influence states' motivations to aid terrorists and what they have to offer them. The pandemic could both increase and decrease states' motivations to aid bioterrorists. On the one hand, the impact of the pandemic might motivate some states to use terrorist proxies in the service of biological plots, especially small-scale attacks where states want to avoid attribution or at least maintain plausible deniability. On the other hand, to the extent that COVID-19 is perceived as illustrating that a contagious agent cannot be easily contained, even when states adopt robust public health measures, it may reinforce hesitancy about launching biological attacks, especially with transmissible agents. A state sponsor of terrorism would likely recognize that providing a contagious biological weapon to a terrorist could literally or figuratively blow back and cause infections in the sponsoring state.

c) COVID-19-related public health and epidemiological measures may help reduce consequences from bioterrorism.

Public health capabilities built up in response to the pandemic might provide better defenses against bioterrorism. COVID-19 responses involved the rapid development, implementation, and refinement of public health measures aimed at containing the spread of the disease. This included requirements for mandatory stay-at-home orders, mask mandates, and rapid vaccination development and dispersal, such as the United States' Operation Warp Speed. Such measures would also likely be useful in combating the spread of a contagious agent spread in a bioterrorist attack, and reduce the overall consequences of such an attack.

The effectiveness and applicability of public health measures will depend in large part on the contagiousness, rarity, and transmission routes of the agent chosen and the method of dissemination. If there is early warning, efforts like masking can be effective against aerosols, even of non-contagious agents like *bacillus anthracis* spores. However, in the absence of such warning, which is unlikely in most cases of bioterrorism, masking is generally only effective against contagious agents spread through aerosols and, to a lesser extent, against contact-mediated disease.

Likewise, viral agents that have already been well-characterized

v There is a subsection of the Islamist extremist milieu that has a more pronounced apocalyptic orientation, as well as those who have justified extensive "collateral damage" among Muslims in the service of their jihad. For example, there is the widely referenced *fatwa* of Nasir al-Fahd's that permitted the killing of millions with unconventional weapons as well as the targeting of areas including many Muslim residents. Nasir bin Hamad al-Fahd, "A Treatise on the Legal Status of Using Weapons of Mass Destruction Against Infidels," *Rabi` I* 1424 (May 2003). Al-Qa`ida ideologue Anwar al-Awlaki also permitted the use of poisons and other WMD in densely populated areas. Anwar al-Awlaki, "Targeting the Populations of Countries that are at War with the Muslims," *Inspire* 8 (2011).

and studied may lead to rapid vaccine production and the development of treatments. Some of the breakthroughs associated with combating the coronavirus, such as mRNA-based vaccines and rapidly produced antibody treatments, will have broader application against future outbreaks of a variety of diseases. However, not all of the successes against COVID-19 are necessarily transferable to other bioagents, especially more exotic ones. The spread of uncommon or rare biological agents, viral or bacterial, in an area may delay the adoption of response measures. Public health officials may not give due consideration to a spreading disease that they are not familiar with, and so may not take measures (or may take inappropriate measures) to contain it. This dynamic is particularly acute with sophisticated biological agents—for example, more common pathogens that have been genetically modified so as to not exhibit typical behaviors.[35]

COVID-19 also demonstrated the existence of upper bounds on public health measure effectiveness. March 2022 Morning Consult polls show over 20 percent of Americans remain unwilling to get a COVID-19 vaccine.[36] This is probably due to some combination of uncertainty about efficacy, concern over vaccine safety, distrust of public health officials, disinformation, and other factors.[37] Likewise, support for policies like mask mandates and stay-at-home orders have been mixed, and states have been hesitant to reinstate those policies once dropped, even with new COVID-19 variants on the rise. While the who and why of policy opposition can be expected to shift based on normal policy fluctuations, the core concept seems applicable: Some proportion of the population will probably resist consequence-reduction measures, which does not bode well for limiting the harm of future possible bioterrorism events.

d) COVID-19 may impact threat assessment more than it impacts the threat itself.

In addition to directly affecting the threat of bioterrorism, the COVID-19 pandemic is and will impact various analysts' *assessments* of bioterrorism threats, obviously including the content presented in this article. These include individuals serving in governments, whose assessments drive responses. Since to date government activity to respond to perceived bioterrorism threats vastly outweighs incidents of actual bioterrorism, it will almost certainly be the case that the pandemic affects responses to potential bioterrorism far more significantly than actual bioterrorism.[w] That is, heightened sensitivity to bioterrorism and related trends unconnected to COVID-19 might have a greater impact on bioterrorism risks than the COVID-19 related impacts discussed above.

Much of this depends on perceptions of how well authorities and the public have responded to the pandemic. Policymakers who believe that the response to the pandemic was adequate and effective might be lulled into a false sense of complacency regarding future biological threats, including bioterrorism, while those who perceive widespread failure on the part of governments and communities might emphasize the population's vulnerability to disease and invest more resources in preventing the intentional spread of disease.

If the pandemic bolsters and/or undermines government responses to bioterrorism, that has implications for potential subsequent attacks as well. As Richard Danzig and his co-authors, including one of the authors of this article, noted, "Responses to a catastrophic bioterror attack are likely to greatly amplify or substantially mitigate the attack's consequences. No less significant, if our post-attack responses fail, we are likely to encourage future attacks by demonstrating their efficacy in spreading terror."[38]

The pandemic is heightening awareness of biological threats generally, of contagious pathogens more specifically, and of viral threats even more specifically. The pandemic is also sharpening knowledge about biological threats and providing a mental framework to make sense of such threats. That is, analysts and policymakers now have a far better sense of how a contagious viral pandemic might manifest and what its impacts might be, having lived through this one. In addition to being helpful, by enabling individuals to better comprehend various biological threats, it might also be counterproductive, because this particular pandemic might be a poor analogue for understanding rather different biological threats.[39] COVID-19 may also create or exacerbate mirror-imaging biases in which analysts or policymakers see the harm of COVID-19, but fail to consider the ideological nuances that make such harm a demotivating factor for some bad actors.

As long as the pandemic continues—and it may continue well into the foreseeable future—it also has the potential to be a distraction from and to siphon resources away from addressing other threats, possibly to include bioterrorism threats.[40] These effects might cast a long shadow into the future because lessened counterterrorism efforts now may manifest in plots at a later time. Of course, such distractions and siphoning can only occur insofar as bioterrorism response and general bio-preparedness are distinct. And whether such a trade-off is justified necessarily depends on comparing actual harm (COVID-19) versus the theoretical harm of a hypothetical bioterrorism attack.

Conclusion

The massive economic and human toll of COVID-19 illustrates the potential consequences of a major, contagious bioterrorism attack. But the reality is that COVID-19 probably has not changed the bioterrorism threat landscape all that much. Table 2 indicates the portions of the Bioterrorism Classification Schema that are likely to be affected by COVID-19. Most changes are moderate, with at most an increase or decrease by one quantity from pre-COVID values. Moreover, with respect to the Agents portion of the Schema, only contagious agents are affected. Terrorist ideology and related motivations concerning biological weapons are a key discriminating factor. Overall, the types of terrorists most likely to pursue biological weapons have not changed appreciably from before the COVID-19 pandemic. The only increases were seen in the case of apocalyptic/millenarian groups, environmental extremists, and extreme right-wing groups with maximalist (e.g., accelerationist) ideologies. Several of the other types of terrorist ideologies either decreased or remained the same (since they were already at the lowest level). Islamist extremists in general are estimated to have decreased their interest in contagious agents across the board, except for the subset that is less concerned with inflicting damage on their co-religionists.

Moving from motivation to capability, the more widespread research activity and laboratories dealing with sophisticated viral

w There is a lively debate among analysts about the severity of the bioterrorism threat and the responses it warrants. For a particularly skeptical perspective on the threat, see Milton Leitenberg, "The Self-Fulfilling Prophecy of Bioterrorism," *Nonproliferation Review* 16:1 (2009): pp. 95-109.

pathogens might provide increased opportunities for scientist insiders to access these agents or to prepare agents for aerosol dispersal. It might also provide more opportunities for small terrorist cells to steal such agents. In addition, the diffusion across the globe of many sophisticated biotechnologies relevant to working with viruses might provide state sponsors of terrorism with capabilities to produce sophisticated bioagents that they can bequeath to their terrorist proxies. Although arrived at via a somewhat different analytical approach, the results here accord closely with those reached by Gregory Koblentz and Stevie Kiesel in a recent study.[41]

When looking beyond the threat to efforts to counter it, the authors' analysis indicates that the public health efforts created to reduce COVID-19 harm may be applicable to bioterrorism, but only if either warning systems provide reliable early alerts or the agent used is contagious. On a meta-level, COVID-19 may influence analyst risk assessment more than the threat actually changes, through greater awareness of biological threats, personal assessments of COVID-19 response, and mirror-imaging biases.

What should governments do about all this? First, government agencies interested in countering bioterrorism should prioritize groups holding apocalyptic ideologies, whether these take the form of standalone cults or the fringes of other extremist movements like Islamist extremists or radical environmentalists. These are the groups for whom COVID-19 has likely bolstered interest in bioterrorism most. Domestic intelligence agencies should identify and monitor these groups and look for indicators of interest in biological terrorism.[42] Particularly noteworthy is whether these groups seek to acquire specialized biological laboratory equipment, find employment for their members in biotechnology-related facilities, or recruit individuals with expertise in the biological sciences.

Second, intelligence collection and analysis efforts should focus on areas of new vaccine and other biotechnological development, including drug delivery technologies. Those are areas where extremists may seek to acquire capability or individuals who become radicalized can do particular harm. Of particular interest should be known terrorist groups showing an interest in vaccine-related activities to potentially use that knowledge in support of bioterrorism or state sponsors of terrorism whose biological weapons capabilities show signs of growing. State-sponsored groups that control territory and support civilian populations may create false positives, however, because some of those groups who control territory may have a legitimate interest in vaccine related activities as part of their provision of social services. Of course, such behavior may also be a mask for biological weapons-related activities, but this is far less likely for groups whose ideologies display lower interest in bioterrorism in the Bioterrorism Classification Schema, such as ethno-nationalist and extreme far-left groups.

Third, at the level of national strategy, emphasis should be placed on early warning, preparedness, and response to biological agents writ large, as opposed to a particular focus on bioterrorism. Response to a terrorist-induced outbreak of a contagious disease is likely to be much the same as any other disease, requiring an emphasis on managing hospital and healthcare resources, acquiring and distributing protective gear, and minimizing person-to-person interaction. Nonetheless, some specific differences that apply to both biological warfare and bioterrorism warrant attention. Potential bioterrorists (or covert state operatives) may utilize biological agents that are uncommon to a particular locality or nation. In that scenario, health officials will be less if not entirely unprepared to recognize the symptoms, adopt appropriate risk reduction policies, and engage in general response. While unlikely due to the sophistication required, bioterrorists may also genetically modify biological agents to increase survivability, lethality, or transmissibility. This would complicate public health response, potentially causing the agent to spread in unexpected ways.

COVID-19 might have reinforced fears of catastrophic bioterrorism, but the complex motivational and capability-related dynamics surrounding the phenomenon reveal that the strategic nature of the threat has not appreciably changed since before the pandemic. This is not to say, however, that bioterrorism is not or will not be a substantial threat; the preliminary assignment of values to the Bioterrorism Classification Schema suggests there are several areas where the threat might be high or growing. What the authors are arguing is that despite superficial expectations that COVID-19 would impact bioterrorism as much as it has impacted many other areas of society, upon closer examination the pandemic appears unlikely to affect the bioterrorist threat emanating from the vast majority of terrorist groups. CTC

Table 1: Bioterrorism Classification Schema: Estimated Values Pre-COVID-19

	Threat Actors (non-exhaustive)										
	Motivation						Capability				
Threat Vectors	Islamist Extremist (mostly Sunni)	Apocalyptic/ Millenarian Cult	Ethno-National	Extreme Far-Right	Extreme Far-Left	Animal Rights/ Environ.	Lone Actor	Lone Scientist/ Insider	Small Homegrown Cell	Formal Terrorist Organization	State-Sponsored Terrorist Organization
Agents (including Acquisition, Culturing, Formulation)											
Contagious											
Crude (e.g., common cold viruses; naturally occurring influenza)	Medium	Low	Medium	Medium	Low	Medium	Medium	Very High	High	Very High	Very High
Moderate (e.g., *Y. Pestis*; Highly Pathogenic Avian Influenza; MERS)	High	High	Very Low	Medium	Very Low	Medium	Low	High	Low	Medium	High
Sophisticated (e.g., smallpox; synthesized coronavirus)	Medium	Very High	Very Low	Low	Very Low	Medium	Very Low	Medium	Very Low	Low	Medium
Non-Contagious											
Crude (e.g., raw sewage; ricin; foot and mouth disease virus)	High	Low	Medium	Very High	Low	Medium	Medium	Very High	High	Very High	Very High
Moderate (e.g., *F. tularensis*; *B. anthracis*; botulinum toxin)	High	High	Medium	High	Very Low	Medium	Low	High	Low	Medium	High
Sophisticated (e.g., bio-engineered antibiotic-resistant *B. anthracis*; encapsulated toxins)	Medium	High	Very Low	Low	Very Low	Medium	Very Low	Medium	Very Low	Very Low	Medium
Delivery Mechanism											
Aerosol/Spray (includes ventilation system dispersal)	Medium	Very High	Medium	High	Low	Low	Very Low	Medium	Low	Medium	High
Direct Contact/Latent*	Medium	High	Low	High	Medium	Medium	Medium	High	Medium	Very High	Very High
Food/Product Contamination	Medium	Medium	Medium	High	Medium	Medium	Medium	Very High	Medium	High	Very High
Explosive (including munitions like rockets, bombs, etc.)	High	Low	High	Medium	Medium	Very Low	Very Low	Low	Low	Medium	High
Animal Vectors	Low	Medium	Very Low	Low	Very Low	High	Very Low	Medium	Very Low	Low	High
Mail	Medium	Low	Low	Low	Low	Medium	Medium	Very High	Medium	High	Very High
Water Supply	Medium	Medium	Medium	High	Medium	Medium	Very Low	Medium	Low	Medium	High

** mainly relevant for contagious agents*

Table 2: Bioterrorism Classification Schema: Estimated Values Post-COVID-19, with changes highlighted (reductions with blue border, increases with red border)

	Threat Actors (non-exhaustive)										
	Motivation						Capability				
Threat Vectors	Islamist Extremist (mostly Sunni)	Apocalyptic/ Millenarian Cult	Ethno-National	Extreme Far-Right	Extreme Far-Left	Animal Rights/ Environ.	Lone Actor	Lone Scientist/ Insider	Small Homegrown Cell	Formal Terrorist Organization	State-Sponsored Terrorist Organization
Agents (including Acquisition, Culturing, Formulation)											
Contagious											
Crude (e.g., common cold viruses; naturally occurring influenza)	Low/ Medium	Medium	Low	Low	Very Low	Medium/ High	Medium	Very High	High	Very High	Very High
Moderate (e.g., *Y. Pestis*; Highly Pathogenic Avian Influenza; MERS)	Medium/ High**	Very High	Very Low	Low	Very Low	High	Low	High	Medium	Medium	High
Sophisticated (e.g., smallpox; synthesized coronavirus)	Low/ Medium	Very High	Very Low	Medium	Very Low	High	Very Low	High	Low	Low	High
Non-Contagious											
Crude (e.g., raw sewage; ricin; foot and mouth disease virus)	High	Low	Medium	Very High	Low	Medium	Medium	Very High	High	Very High	Very High
Moderate (e.g., *F. tularensis*; *B. anthracis*; botulinum toxin)	High	High	Medium	High	Very Low	Medium	Low	High	Low	Medium	High
Sophisticated (e.g., bio-engineered antibiotic-resistant *B. anthracis*; encapsulated toxins)	Medium	High	Very Low	Low	Very Low	Medium	Very Low	Medium	Very Low	Very Low	High
Delivery Mechanism											
Aerosol/Spray (includes ventilation system dispersal)	Medium	Very High	Medium	High	Low	Low	Very Low	High	Low	Medium	High
Direct Contact/Latent*	Medium	High	Low	High	Medium	Medium	Medium	High	Medium	Very High	Very High
Food/Product Contamination	Medium	Medium	Medium	High	Medium	Medium	Medium	Very High	Medium	High	Very High
Explosive (including munitions like rockets, bombs, etc.)	High	Low	High	Medium	Medium	Very Low	Very Low	Low	Low	Medium	High
Animal Vectors	Low	Medium	Very Low	Low	Very Low	High	Very Low	Medium	Very Low	Low	High
Mail	Medium	Low	Low	Low	Low	Medium	Medium	Very High	Medium	High	Very High
Water Supply	Medium	Medium	Medium	High	Medium	Medium	Very Low	Medium	Low	Medium	High

* *mainly relevant for contagious agents*

** *The lowering of motivation only applies to the less apocalyptically focused elements of the Islamist extremist milieu.*

Appendix

This article does not utilize the taxonomy the authors have developed (the Bioterrorism Classification Schema) directly to perform a threat assessment of bioterrorism, since the purpose of this article is to identify changes in the threat as a result of COVID-19. However, particularly once robust values for each cell have been determined, it is possible to employ the taxonomy to provide an initial indication of threat level. Below, the authors provide two illustrative examples of how this process might work in hopes that this might be of use to scholars and analysts. The current Bioterrorism Classification Scheme is just the beginning. Further development is needed, for instance regarding how to incorporate more complex interdependencies. These examples use the pre-COVID-19 values from Table 1.

Illustrative Example 1: Small cell of Islamist extremists seeks to deploy *F. tularensis* (the causative agent of tularemia) delivered through contaminating candy bars.

Motivation = minimum[aa] of the likelihood for Islamist extremist(s) to have the motivation to employ a moderate non-contagious agent AND food/product contamination
= minimum of (High AND Medium)
= Medium

Capability = minimum[ab] of the likelihood for a small cell to have the capability to employ a moderate non-contagious agent AND food/product contamination
= minimum of (Low AND Medium)
= Low

Overall preliminary threat ranking = **Low-Moderate**

Illustrative Example 2: Extreme far-right formal terrorist organization with access to a scientist insider seeks to use a bioengineered novel coronavirus via aerosol dispersal to cause widespread disease.

Motivation = minimum of the likelihood for far-right extremist(s) to have the motivation to employ a sophisticated contagious agent AND doing so via aerosol delivery.
= minimum of (Low AND High)
= Low

Capability = minimum of the likelihood for an extreme far-right formal terrorist organization (with scientific insider) to employ a sophisticated contagious agent AND aerosol

[*Extra step for group with insider*: For a group with a scientific insider, the respective capabilities for the agent and delivery mechanism components are drawn from the maximum of the group (in this case, a formal terrorist organization) and the insider value for each component. For a sophisticated contagious agent, this is maximum of (Medium AND Low) = Medium
For aerosol dispersal, this is maximum of (Medium AND Medium) = Medium]

Capability = minimum of (Medium and Medium)
= Medium

Overall preliminary threat ranking = **Low-Moderate** (Note: Repeating the above calculations for an extreme far-right formal terrorist organization post-COVID (i.e., using Table 2), the overall preliminary threat ranking changes to Moderate-High.)

aa The authors assess the minimum value across the agent and delivery components, because if an adversary lacks the motivation to proceed in either one, it will not conduct the attack; therefore, whichever likelihood is lower dominates.

ab The authors assess the minimum value across the agent and delivery components, because if an adversary lacks the capacity to succeed in either one, it cannot conduct the attack; therefore, whichever likelihood is lower dominates.

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40 Ackerman and Peterson.
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A View from the CT Foxhole: Shmuel Shapira, Former Director General, Israel Institute for Biological Research

By Paul Cruickshank

Professor Shmuel Shapira, M.D., MPH, served as the Director General of the Israel Institute for Biological Research (IIBR), Israel between 2013 and 2021. He is the founder and head of the Department of Military Medicine of the Hebrew University Faculty of Medicine and IDF Medical Corps. He is also a Senior Research Fellow at the International Institute for Counter-Terrorism (ICT) at Reichman University in Israel.

Professor Shapira previously served as Deputy Director General of the Hadassah Medical Organization and as the Director of the Hebrew University Hadassah School of Public Health. He is a Full Colonel (Res.) in the Israel Defense Forces (IDF) and served as the IDF Head of Trauma Branch. He is an authority on terror, trauma, emergency medicine and military medicine, and instructs medical students, physicians, EMS, medical leaders, and rescue teams on terror medicine, management of mass casualty's events, military medicine, advanced trauma life support, and risk management. He has published more than 110 articles and is the editor of Essentials of Terror Medicine, Best Practice for Medical Management of Terror Incidents *and* Medical Response to Terror Threats. *He is the author of* The Pandemic Circus *(Yediot Books, Rishon LeZion 2021).*

CTC: Between 2013 and 2021, you served as the Director General of the Israel Institute for Biological Research (IIBR), a unit affiliated with the government of Israel that researches all areas of defense against chemical and biological threats, including the operation of national laboratories for detection and identification of such threats. Could you explain the purpose and work of IIBR, and the degree to which the pandemic has changed mindsets about biological threats?

Shapira: Like you said, last year, I finished my term as the head of this very important and unique institute. It's an R&D institute focusing on preparedness for chemical threats and biological threats. It's very unique because it's an academic institute but with very practical objectives. So, you have always to find the right balance.

Obviously, the pandemic was the challenge of a lifetime, and if it had happened after my term, I would have deeply regretted it, though it was very tense, a lot of pressure. It certainly didn't add much to my health and well-being, but it was fascinating. I felt like it was everything that I had been preparing for all my life, because I studied medicine, I had a military career, I was in the Navy. I had a lot of exposure to mass-casualty events and disasters. I've been in delegations abroad. I was in a delegation in Rwanda, which was a real biological disaster. It started with tribal conflict, but then you see how the cover of civilization is thin and will break up if there is disaster. There were really big, bad epidemics of cholera, pneumonia, and meningitis.

And so everything in my career had prepared me for this challenge. Very soon after the start of my term [in 2013], I decided that one of our main focuses should be preparedness for a potential future pandemic. We built generic capabilities to produce a vaccine and built up our diagnosis capabilities. We were prepared as much as we could be for such a surprising event.

CTC: Tell us a bit more about the IIBR specifically and how that organization responded to the pandemic.

Shapira: Like in any good organization, the strength of the IIBR is the people. A very big part of this is the exceptional percent of our people who are PhDs in four different main areas: biologists, chemists, physicists, and mathematicians. Therefore, we're doing really cutting-edge research in the fields that we are interested in. We have many publications in the open literature, in the best scientific literatures like *Science* and *Nature*. We give presentations—in the last two years, certainly because of COVID, less often—but we have been giving presentations at international conferences. We very often have guests and good collaborations with peers from the United States; peers from France, from the Louis Pasteur Institute; peers from Germany, from the Robert Koch Institute and the Paul-Ehrlich Institute.

So we have a lot of collaborations, including of course with universities in Israel, and the main thing we do is we develop modes of medical response. First, you study the pathogen, or you study the agent; then you develop preventive measures, you create a protocol for response, a protocol for self-defense, for public defense; and then therapy and vaccination if it's feasible.

CTC: You have this extraordinary concentration of scientific knowledge at IIBR, and you and your colleagues have dedicated your lives to protecting against biological threats. Do you feel there was a big change in mindset—more widely within Israel at the policy-making level, at the government level, at the population level—about biological threats as a result of the pandemic?

Shapira: I think that the pandemic certainly will make a change, but sometimes we in Israel are short-distance runners. We see something, we respond, we panic, we take very extreme measures, but then after a while, especially given the perception the pandemic is subsiding (which I hope will be true), we focus on other obligations, budget obligations, and things like this. I wrote a book whose title, if you translate it to English *The Pandemic Circus* (2021, Hebrew),"[1] makes clear it is critical of the overall response of Israel to the pandemic. I think there were many good attempts to respond, but there was a failure to mount a consistent joined-up response.

The book draws on the lessons learned from terror medicine, a new field of medicine I helped develop at the international level. More than a decade ago, I jointly edited "Essentials of Terror Medicine" with two American co-authors.[2] Terror medicine is coping with terror in two ways: in the clinical way, but also in an organizational way. If there is another pandemic, I hope people can open the book and try not to reinvent the wheel.

As a matter of fact, I think that the risk of a pandemic is going up. I think that with globalization, with the chopping down of huge forests and everything like this, the intermixing of people and wild animals, the chances of pandemic are increasing. With bacteria that are antibiotic-resistant, with all this, I think it's probable that we will see the next big pandemic before a century will pass.

CTC: What in your view have been the strengths and weaknesses of the Israeli response to the pandemic? And then what for you are the key lessons that should be learned from the pandemic in protecting Israel and other countries against biological threats moving forward?

Shapira: One of the strengths of Israel is that there is a very strong culture of preparedness for emergencies because of its experience with military conflicts and terror attacks. So, there is something in the Israeli culture that lends itself to this, but I don't think that we used this strength enough. I think that we could have done better than we did.

One source of strength when it came to the pandemic is that the management of the hospital and medical system in Israel is top-down. There is an emergency division in the Ministry of Health, and everything goes down from there, and almost all the hospitals in Israel are public hospitals; there are very few private hospitals. And therefore you can enforce the hospital policy, where you can come in and give the hospitals their accreditation. One of the things that is checked is the emergency preparedness and equipment. Among the organizations in Israel that really deserve medals are the sick funds (HMOs), which provide primary and some of the secondary care. In Israel, there is obligatory medical insurance, and it's run by the sick funds, which are a bit like Kaiser Permanente. And all the citizens in Israel are insured by them, and they responded very well during the pandemic to protect the health of the community. So I think that we have a good system here to cope with this kind of challenge. But one of the things that I regret and one of the things that I am critical about in my book is that we didn't use our strength enough. We could have done better with what we have; we have a good basic system.

Another point about Israel—and this is something in the Israeli culture, and I've referred to this already—is that we are short-distance runners. We sprint very well. We run, but then after a while, we lose our interest and focus. In situations like the Six-Day War in Israel, we're the best in the world. We respond in an emergency when we must, and we do it well. But if something lasts longer, it's harder. We are not that persistent.

If we talk about the lessons—and part of the lessons are not unique to COVID; some of the lessons are very generic to other disasters, to floods like with Katrina or to big wars or to an earthquake or stuff like this—I'll stress the most important one three times: preparedness, preparedness, and preparedness. The most important thing is to prepare. And this also involves being prepared mentally, because that makes it much easier to react in an emergency situation. We at IIBR and I myself personally were able to switch our focus very quickly when the pandemic occurred because we were mentally prepared.

"I think that the risk of a pandemic is going up. I think that with globalization ... the intermixing of people and wild animals, the chances of pandemic are increasing. With bacteria that are antibiotic-resistant, with all this, I think it's probable that we will see the next big pandemic before a century will pass."

And a very important part of preparedness is to write good SOPs, standard operating procedures. And I don't think SOPs should be that detailed because some of the challenges are generic. Sometimes you cannot cover everything in SOPs, but you have to have an SOP, for pandemics, for a big war, or maybe for an earthquake. For short events, but not so much for a long-haul pandemic situation, checklists are very important just like they are for airline pilots. Few in Israel have managed more mass-casualty events, mostly terror-related, than me. Even on the 30th or the 40th that I managed, I would always open my wallet, I had a small card with the initial checklist, and I operated by that checklist so that I wouldn't forget anything important.

Another important part of preparation is drills and exercises. They are very efficient uses of resources. A tabletop drill is not very expensive. Sometimes you try to do a full-scale drill, but one of the things that you should be very cautious about is the lessons that you learn from them. You have to remember that it was a drill, and you can never simulate reality well enough. Let me give you one example. Usually in the drills, there are dummies that simulate the casualties. In reality, the casualty would weigh at least 170, 180 pounds, but the dummy will weigh maybe 20, 30 pounds. Or if the simulation involves intubation use, in the drill you [go], "Ok, I did intubation. Check." But in real life, not everyone will know how to perform it properly. But still I think drills are very efficient.

Another thing that you should do very often after drills is to draw conclusions that SOPs should be updated from time to time. It wasn't rare that during an inspection of one of the hospitals in Israel, I would see some 20-year-old phone numbers with their five or six digits, and certainly they were not up-to-date digits. Phone numbers change. Medicine changes. Preparedness changes. You have to update.

Another important thing is to have certain stockpiles. You can never stockpile everything, but there should be some minimal generic stockpiles of antibiotics, vaccines if you have them, personal protective equipment, ventilators, just things to begin with. This is very relevant to the COVID pandemic because we all saw the interruptions in the supply chain. So you cannot always trust that things will come in via ship or airplane.

Another thing that is important—and this didn't work well in Israel because of fluctuations in which ministry was taking the lead—the chain of command should be very clear. Just like in a terror event, the chain of command should be very clear during a pandemic.

Perhaps the most important lesson specific to the pandemic—was the issue of media communication and transparency. Of course today, this also involves social media as well as TV and newspapers. What would have been massively helpful is for a skilled and popular official to have appeared on the 8:00 o'clock news in the morning, 8:00 PM at night, and for people to have known that this was the formal message of the government of Israel or the United States or any other country. Then in between, other people could have said whatever they wanted, but it would have been clear that this was the official message. And this was missing, and I think that not just in Israel but in many other countries, you saw declining trust during this period. There was a dynamic where one official appeared and then other officials appeared soon after to say much the same thing, and those in the media of course had to fill up the time in between. So they brought medical analysts on, and some people talked a lot about things that they didn't understand and didn't know. You'd find a cardiologist talking about immunology; you'd find rehabilitation people talk about an area outside their expertise, and sometimes political reporters started to compare vaccines. I don't think it was managed well.

Another thing that is crucial in any such event—and I think it should be done more than once, especially in a public health emergency that has lasted now more than two years—is the debriefing or what in the United States is called the 'after action review.' I think the debriefing is very important. So if it's a terror attack, you do the debriefing as soon as possible after the terror attack, and you should do it quickly because cognitive processes tend to change reality, not because you want to lie, but because you perceive the reality as you think it should have been and not like it really was. You say, "I put the chest drain in in two minutes," and if someone was recording, it turns out you did it in 10 minutes. So certainly with a terror attack, you did a debriefing very quickly, as soon as you possibly can with the most relevant participants.

In a case like this [the pandemic], I think there should be periodical debriefing. I don't think it should be scheduled by calendar or anything like this, but after a major decision, after the first lock-down, after the first round of vaccination, there should be debriefings. And I don't think there was a very organized effort to do debriefings. People learned lessons, but I feel not enough.

One vital lesson learned, which I refer to in my book, is that Israel—and this also applies for the United States—must create its own vaccine manufacture capabilities. I think that the capability to manufacture vaccines is a strategic capability. It's like the ability to bake bread, to manufacture ammunition, and things like this. I think this is strategic. You cannot depend on other people. I think that Israel has to have a formal capacity to plan and manufacture vaccines for future events. And then on a daily basis, it can manufacture routine vaccines like for flu or for hepatitis or things like this.

CTC: You played a central role in the original development of Israel's BriLife COVID-19 vaccine. Could you describe the efforts to develop this vaccine and the lessons learned for developing medical countermeasures for future pandemics? Can you explain the promise that this vaccine and the technology behind it holds, including as a booster, for inoculations in the developing world and for potential future pandemics?

Shmuel Shapira

Shapira: How it all started was very strange. It was Saturday night. I was watching a movie at the cinema, and then I saw that I had five phone calls from an unknown number. My phone was silent but still it was vibrating. On the fifth call, I thought, I don't know, maybe a war started or something like this. I went out to take the call, and they invited me the next day—February 2, 2020—to join the Prime Minister to present the option for manufacturing vaccines or therapeutic antibodies.

Before the meeting, I sat with a group of scientists to discuss the best approach. There are a few approaches for developing vaccines. There is one that today sounds very natural, but it's certainly not natural: the messenger RNA vaccine like by Pfizer or Moderna. This is one approach. Then there is the approach of a protein-based vaccine, and that's another good and relatively modern approach. And there is the traditional approach by attenuated or by dead viruses. So these were the options. We hesitated. We hesitated for a few hours, and we made a decision to pursue two main options. One of those was to pursue a protein-based vaccine. We thought the messenger RNA vaccine was too modern, and while we thought it might be the future, we thought it was too risky.

The second option we decided to pursue would later become known as the BriLife vaccine. It's a vaccine based on a virus platform that affects only animals, the VSV [vesicular stomatitis virus]. This method was used to develop a vaccine against Ebola.[a] We chose this way because when we started, there had been a history of about 300,000 people vaccinated against Ebola with this vaccine in the preceding three years —so we thought it held promise. And what we did is that we took the VSV virus, which is the animal virus, and with some genetic engineering, we shaped it. The VSV has its own spike, and on this virus, we transplanted the spikes of the SARS-CoV-2, which is the virus that causes COVID-19. And this is the vaccine. We tested it on four animal models. It was also a challenge to get hamsters, and we thought that hamsters would be a good model. We evaluated it on mice, and also on what is called transgenic mice, that is mice with the relevant genes of people, and you can see the real disease in [such] mice, because otherwise mice are not affected that much by COVID. Then we tested it on rabbits and bigger animals. We did it on swine.

So we evaluated it. We saw that it's effective. We saw that it's safe. And we were ready by the beginning of July 2020. The scientists were very rapid. The bureaucracy was slow. And we were affected a lot by bureaucracy, and this really delayed us. We have only started phase three trials. We could have been ready much earlier. And I think it's a shame. I think it's a very good vaccine. We evaluated on all variants, including Omicron, and we saw that it's more effective than the others against the variants. It's less effective against the original virus, but it's more effective for the variants than the competitors. At the very least, I think that it should be a perfect candidate for boosters because I think mixing and matching different types of vaccines is a wise idea when it comes to boosting.

I should emphasize that our budget was [small], if you compare it to the mega pharmaceutical companies in terms of budget and number of people, with our core relevant team comprising about 80 scientists. And our budget was a little less than $60 million. And if you look at the mega companies, there were 3,000 people working on the vaccines and the budget was about $3 trillion. So it's a huge difference. So I still feel that it's a huge scientific and R&D achievement, which I'm very proud of. I perceive myself as the father of this vaccine, and I think it's very important capability. First of all, I think it will be used. And even if it will never be used, it's very important that we went through the whole process so it will be easier and faster next time. I don't think it was a waste of resources.

CTC: There's this attribute with this particular BriLife vaccine "in which the spike protein of the vaccine appears to evolve in a manner consistent with the evolution of the SARS-CoV-2 virus in nature."[3] Can you explain that further?

Shapira: The messenger RNA vaccines are like a still picture of what happened in January 2020. They were based on a sequence—for example, with Pfizer—it was based on the sequence from January 12, 2020. Because our vaccine is based on a live virus, it is more dynamic. So the live virus can change, it can mutate itself, and it can make the approach to receptors in the body better than just a synthetic reprint of an old-fashioned virus. Therefore, I think that our vaccine is more effective to the virus than the original one, the messenger RNA one. The messenger RNA vaccines are less effective against variants like Omicron in which there are so many mutations from the wild form that it's almost a different virus. Because ours is live, and it adapts better.

CTC: The BriLife [COVID-19] vaccine was originally licensed to NRx Pharmaceuticals and as you have noted was in clinical trials.[4] After NRx made a commercial decision to no longer pursue the project, in April 2022, the Israeli defense ministry stated that IIBR was examining other alternatives to develop and commercialize the vaccine.[5] What is your perspective on what the pathway forward for this vaccine should and could be?

Shapira: I finished my contract at the IIBR in June 2021, so I am not updated with the commercial decisions, but I know that it will be a great waste not to make this scientific achievement available for human care.

I'd like to mention one aspect of our efforts, which was very frustrating to me. We were the first in the world to produce the best therapeutic antibodies for the virus—monoclonal antibodies. To explain the concept, I always give a military comparison. Polyclonal is like a bomb, and there is a lot of collateral damage. If it's monoclonal, it's like a targeted missile.

Here is the frustrating bit: While in Israel we are capable of producing 15 million units of the vaccine for the citizens of Israel and the Palestinian Authority, there are no capabilities in Israel to manufacture antibodies under GMP, good manufacturing practice. And there are very few places in the world we can do it. We were negotiating with two places; then we were pressed to choose one of them, and then it didn't advance and it remained just an academic achievement.

Besides these efforts, we worked on evaluating mask protections, we created models for the spread of the virus, we were among the earliest places that could do proper PCR for this [virus] in Israel, and we evaluated antigen kits.

CTC: In *CTC Sentinel*, we think about threats and all the manifestations of those—via state actors, non-state actors. To that end, this question is about synthetic biology, which has increasingly come to the fore in national security conversations. For our readers, can you briefly describe what synthetic biology is, and outline the benefits and risks associated with its use? How has, if at all, COVID altered your perspective on the application of synthetic biology? Secondly, how would you describe the risk of a non-state actor using synthetic biology or other advanced scientific tools for malintent, and how likely or unlikely is that kind of a scenario?

Shapira: I think that synthetic biology provides mostly promises and opportunities. The definition of synthetic biology is a little bit vague because there is genetic engineering and there is synthetic biology and there is overlap between the two. Usually they say that 'genetic engineering is doing more of the same and synthetic biology is doing new things.'

So I will talk first of all about the promises. I think that synthetic biology holds promises for medicine: better tailor-made medicine, manufacturing organs for transplant, enhancing genetic therapy, and we see things today in agriculture—for example, substitutes

a Editor's Note: "The rVSV-ZEBOV vaccine uses a genetically engineered version of vesicular stomatitis virus (VSV), an animal virus that primarily affects cattle, to carry an Ebola virus gene insert. Experts at the Public Health Agency of Canada originally developed the vaccine, which is now licensed to Merck." "Ebola Vaccines," National Institute of Allergy and Infectious Diseases, last reviewed January 9, 2020.

"Rather than developing vaccines against specific viruses, the target should be to have some more generic protection: a vaccine that will enhance your immune system to cope against viruses—not to let them go into the cell, not to let them replicate, or even not to let them penetrate through the mucosa of the upper airways or the bronchi ... I think this should be the direction."

for meat, many of them are based on methods of synthetic biology. There are promises in manufacturing: less persistent types of polymers, plastics, all these kind of things. You can manufacture substitutes for fuels. There are uses in computers, the memory of computers. Because DNA is a type of code, it's a four-letter code, it holds promise for storing an enormous amount of information. They say that in one spoonful of DNA, you can store all the knowledge acquired in the world in one year. And it's much more long-lasting than CDs and flash drives. You can still find the DNA of very ancient creatures. So it's mostly promises. But like with every other promise, there are also dangers. It's a double-edged sword. And for each good utility, you can describe others. It's something that you have to keep in mind. You have to try to do the good and try to avoid the bad.

I'm really not aware of the source of COVID; I really don't know what it is, but I think that one of the lessons dealing with such a dangerous microorganism is the need for responsible science. And with responsible science, I'm talking about two things: first of all, to have safe facilities, safe laboratories; to have a very well-trained staff, to do periodical obligatory training for your staff and to evaluate them. And the second thing is responsible publication. This is very hard because with all the sciences, it's 'publish or perish.' You want to publish and want to publish in good journals, but some of the publications and some of the experimentations are dangerous. There was a famous case a few years ago about how someone was able to create an old pox from the past that he purchased through the internet.[b] This is one example. Another example is that people played with the avian flu. Avian flu is a very frightening disease, but one of the good things about avian flu is that it's not that contagious between people. There were two articles by researchers outlining how they made this flu contagious in two ways: one through genetic engineering and one through another form.[c] So one of the things that is important is responsible science.

Another issue of concern is do-it-yourself biology or backyard biology, also known as bio hacking: Things that could only have been done 10-12 years ago in the leading academic centers, you can now do in your garage; the equipment got much cheaper, much more efficient. The disposables and reagents, et cetera are very easy to get. It does not require huge knowledge. You don't have to be a super scientist.

All these things are very difficult to regulate in a democratic society. And I know that some of the leading journals create some review committees, but they very rarely stop publication. They might postpone the publication two to three months, but then at the end, they almost always publish.

CTC: When we're thinking about preparedness for the next pandemic, having the ability to quickly develop vaccines is going to be a huge part of it. It took about a year from the COVID-19 outbreak for vaccines against the virus to be approved and deployed. And although a vaccine has never been rolled out at such speed, many died around the world before they could get a shot. In March 2022, Moderna announced it was planning to begin human trials for vaccines against 15 threatening viruses and other pathogens by 2025, to speed up vaccination timelines in case of future pandemics. It was reported that "the new effort aims to complete preliminary dose and safety testing for vaccines against numerous threatening viruses preemptively. That way, if [any] of these viruses or a close relative causes a major epidemic, Moderna will have a prototype vaccine on hand and might be able to begin large human efficacy trials very quickly."[6] Given the need to prepare for the next pandemic, which could be natural, accidental, or deliberate in origin, how important are efforts to speed up vaccine deployment, and what role should governments play in encouraging them?

Shapira: First of all, I think that you should remember the quote 'the biggest bio terrorist is Mother Nature.' So this is something that we have to be ready for. There are millions of viruses, though not all of them are dangerous to people.

All I know about the Moderna vaccine initiative [to develop vaccines to protect against potential future pandemics] is the same information in the press that you just quoted. I think that it will be very difficult to focus on all viruses. One thing that is needed is international collaboration to try to make progress on this front. Even for a superpower like the United States, it will be difficult to do it by yourself. But I think that rather than developing vaccines against specific viruses, the target should be to have some more generic protection: a vaccine that will enhance your immune system to cope against viruses—not to let them go into the cell, not to let them replicate, or even not to let them penetrate through the mucosa of the upper airways or the bronchi or things like this. I think this should be the direction.

Another thing that people tend to forget—and I think it's very important, and it's related to the need to develop vaccines that offer more generic protection—we are advancing very quickly to a world without antibiotics. I'm named after my grandfather who I didn't know who died in around his 40s from pneumonia. And I think that we are in danger of getting back to this period again, that people will go to hospital for some minor surgery and they will die of these types of infections.

b Editor's Note: "In 2018, scientists announced they had created horsepox, a close cousin of smallpox, from chemically synthesized DNA fragments. This research highlighted some of the dangers of synthetic biology." Filippa Lentzos, Gregory D. Koblentz, and Joseph Rodgers, "The Urgent Need for an Overhaul of Global Biorisk Management," *CTC Sentinel* 15:4 (2022).

c Editor's Note: "In 2011, scientists manipulated the bird flu virus to enable it to transmit between mammals, including humans. Before then, the virus had only been transmitted from birds to humans, with a fatality rate of 30-60 percent." Ibid.

So, I think to try to chase every bacterium and every virus is futile. You cannot chase them, so we should find more generic protection, something that will enhance the immune system, something that will block the penetration of bacteria. I'm not talking about basic, obvious things like washing your hands and things like this, that goes without saying. But if I had more resources and was younger, I would aim to develop some generic protection against viruses such as SARS-CoV-2 and H1N1.

The agility of response is going to be crucial moving forward. I think that COVID-19 taught us that things can be done quickly. U.S. and British regulators switched quickly to a mode of emergency and made shortcuts when they felt that the shortcuts weren't endangering. So I think this is one of the things that should be done: You should understand where you can have a shortcut and cut the bureaucracy. But we need to be more ambitious than that. My vision for the future is a laboratory like an IIBR, NIH, or CDC that will confirm that a new vaccine works against a virus, and then will email the information to physicians, who'll have a printer with the bases, print it, and give it to their patients, and that's it.

To return to a previous point, I'm really concerned about where we are with antibiotics; we are very close to a very dangerous situation. There are very many bacterial-resistant infections in hospitals. And it's a major problem, certainly in the Western world. Diseases that we thought that we would never see again—for example, tuberculosis—we see them again and they are much more resistant. And so I think we need to develop more general protection than antibiotics and vaccines currently offer. The need is to develop what in essence is biological protection gear for the body against biological threats.

CTC: Can you talk a little bit more about the concerns about antibiotic-resistant bacteria?

Shapira: So far, we have talked mostly about a pandemic by viruses, but the Black Death plague was much more disastrous and was caused by bacteria. So pandemics can also be caused by bacteria.

One big problem is that the development of antibiotics is very minimal because it's not economical, even for the big pharmaceuticals. If you develop another fourth or fifth generation of cephalosporin, for example, which is one type of antibiotic, it'll be a very short-term achievement because the bacteria are much faster at adapting and in one year, two years, most of the relevant bacteria will be resistant to it.

The other thing is let's say that you develop at great expense and difficulty some 'super gun' antibiotic that is very, very strong. In that situation, physicians, if they act correctly, will put it on the shelf and use it only rarely when they have no other choice. But that creates no revenue stream to offset the expense for pharmaceutical companies. So it's not economical for the companies. So we're in some vicious circle that is very hard to break.

That's why I think that we have to think outside the box. One of the ways, and it's very developed especially in the country of Georgia, is phage therapy. Phages are viruses that destroy bacteria. Their capabilities are very, very high. There have been two cases in which they treat very resistant infections. So I think that we should really think outside of the box because we have almost consumed everything that is in the box. We have to think out of the box to find solutions that will last for 50 years, and not for [just] two years. Meanwhile, we shouldn't neglect all the regular things: developing, improving and using antibiotics, vaccinations, and so on. But we should try to be more creative, too.

CTC: On the antibiotic-resistant bacteria front, what you're saying is that the stakes for the planet are as high as for pandemics caused by viruses. That if things go wrong, this could create as disastrous a situation as a COVID-19 pandemic, unless the global community can get ahead of the game when it comes to this problem of antibiotic-resistant bacteria, correct?

Shapira: I think so. And it should be a non-political issue because all our interests are the same. You saw with COVID that it crossed borders like a fire. It started in China, and it very quickly was all over [the world]. Nobody managed to block it. All the attempts to do so failed, including even in New Zealand where they managed well for a while. Israel managed to delay the virus for two months, but afterwards, it flourished all over.

So I think there needs to be international cooperation in protecting against the full spectrum of biological threats, and I'm talking first of all about an intelligence attempt. I'm not talking about military intelligence. I'm talking about scientific intelligence to try to follow up on viruses, to see how they develop, how they mutate, to see where some viruses start to cross the borders between animals and human beings. It's not a coincidence that all the Ebola outbreaks started in places in the middle of the jungle, when you cut trees, people are interfering with the animals, interfering with their environments. And this is the thing with globalization. Globalization is good, but it's also a curse. You go in the airplane, and that's it. You're exposed. One hour, you're in the New York and then 10-11 hours later, you're in Tel Aviv Airport and you bring the infection.

The other thing to stress is that the costs created by the current pandemic are enormous,[d] with one economist likening it to the cost of buying everything in Manhattan 10 times over.

CTC: So, the message is that the world needs to invest big time in protecting against biological threats. And that investment will pale in comparison to what the costs might be of things going wrong.

Shapira: I think it would be a very cheap insurance policy compared to what we spent in the last two years.

CTC: You are a leading authority on terror medicine, the management of mass-casualty events, military medicine, advanced trauma life support, and risk management. In the case of treating victims of a potential future biological terrorist attack, what precepts need to guide authorities' emergency response? How well prepared is Israel to provide this treatment in the case of such attacks, and what can other countries learn from Israeli capacity-building in this area? It has long been feared that chemical and biological attacks could produce an even greater psychological impact than the immediate loss of

d Editor's Note: The International Monetary Fund (IMF) expects the COVID-19 pandemic will cost the global economy more than $12.5 trillion through 2024. "IMF sees cost of COVID pandemic rising beyond $12.5 trillion estimate," Reuters, January 20, 2022.

life. To avert panic, what needs to guide the communication strategy by authorities?

Shapira: I think that the main issue in any extreme event is as soon as possible to figure out how to best meet your needs given your available resources. This is the most important thing, and this is the way that prime ministers, chiefs of staff, people should think, 'what are the needs?' And the needs are mostly dictated by the number of casualties in an event. But there are also other details: economic considerations, the need to continue children's education, the well-being of the population. The other thing is what resources you have. Certainly in certain extreme cases, you have to be ready to do triage. Not everyone can get the optimal treatment. You have to, yourself as a manager or as a leader, be ready to cope with such imbedded ethical issues.

Fortunately during this pandemic, as far as I know, it was only in Italy and for a short period that there was a real need for triage to decide who will be ventilated or will not be ventilated. But I think that the better you are prepared for it, the less extreme ethical conflicts you will live through when you experience the event and the shorter the chaotic phase will be.

In each major disaster or major event, there is a sense of fear, and this has also been the case with the pandemic because you cannot see the virus. You sit in the plane and someone next to you takes off their mask, and he could give you the virus. You don't see the threat. You don't know if you touch the elevator button, if you're getting contaminated. So I think the most important lesson is transparency to the public, and in future pandemics to tell them as soon as possible and as clearly as possible things like whether or not surfaces are contagious and different types of mask are effective, even if it is not pleasant to hear. You need to feel like people are talking to you in a way you can understand. And while experts may differ, there needs to be a clear official line from the likes of a Dr. Anthony Fauci. We saw with the first Gulf War when Israel was attacked from missiles from Iraq, the military spokesperson was talking once, twice, three times a day, and everybody really remembers it was a good model.

So, there is a need to educate the public about the threat. Knowledge is important. But so too is providing the public with active things they can do: get vaccinated, putting on masks, wash hands. I think these things decrease the fears.

CTC: Our aim in publishing this two-part series of special issues on the biological threat is to underline that biosecurity is a major national security concern. What is the big picture message that you want to get across to leaders and policymakers reading this?

Shapira: First of all, I think that as a leader—a civilian leader, a military leader—you have a responsibility to know about certain things, even if you're not a biologist. You have to understand the main concept. I doubt that our major leaders are able to write a short chapter on what a pandemic is: What do you do in the first few days, first two or three weeks of a pandemic? Our leaders and politicians are expected to have knowledge about other subjects, for example the economy. Biological threats should be one of those things.

To wrap up the conversation, I would offer some initials: PPRR. The first P is prevention. The most important thing is prevention. Prevention is periodic vaccination, prevention is responsible science, prevention is knowledge, prevention is washing your hands, prevention is not giving antibiotics when they are not necessary. If you take antibiotics, finish the course of the antibiotics. This is prevention. The second P is preparedness. Be prepared.

Then the first R is response. If you are prepared and you have the knowledge, respond in the best way that you can. You can never be perfect. There will be always a short period of chaos but try to shorten this chaos; try to communicate. And the other part that I hope will be happening very soon is recovery. The world really underwent a major trauma. I've seen a few wars in Israel and many terror attacks, but this is a very traumatic incident for everyone. And I think recovery is necessary now. And part of recovery is also, God forbid, think of the next incident. There is a saying in Hebrew—I cannot translate it, but I'll try to explain it—Shabbat is Saturday, so they say whoever works on the eve of Shabbat will rest on Shabbat. So if you prepare well, it will pay dividends. Preparedness is key. Don't think it won't happen. Look at it as if tomorrow, God forbid, an earthquake can happen and be ready for it. Don't think 'it won't happen in my term.' In your term, it's your responsibility. CTC

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Biology's Tectonic Shifts and Novel Risks

By Audrey Kurth Cronin

Driven by digital technologies and commercial processes, the field of biology has fundamentally evolved, with widespread implications for war and peace. Biology's trajectory resembles the advancement of computer software and hardware during the 20th century, making the tools to manipulate life open and accessible. Today, it is easy to read (DNA sequencing), write (DNA synthesizing), alter (gene editing), and share (via the internet) genetic code. Addressing biosecurity requires expertise in computer science, data analysis, and artificial intelligence. Bioterrorism with known agents remains a concern, but the greater threat will be novel risks from trained insiders, unethical tinkerers, and state-sponsored proxies.

Many people worldwide can now read, write, alter, and share the building blocks of life. This development is as significant as the invention of the printing press or the discovery of human genetics, and it is changing what biology is and why it matters. Biology has become engineering, using computer power to make or create anything with a genetic code. New tools and approaches emerge daily, especially at the intersections of biology, materials science, computing power, big databases, and artificial intelligence. So, assessing the security risks and opportunities of today's rapidly developing biotechnology demands a broad focus and agile thinking, or we will miss things.

The standard approach of using historical incident data or case studies of terrorist attacks or bioarms programs may not take account of radical developments in biotechnology. Life's software and the hardware to dissect it are evolving. Driven by a juggernaut of commercial profit-making, a biological revolution is unfolding that echoes the computer revolution of the last century, and it is directly or indirectly affecting *everything*, including war and peace, as well as the impact, likelihood, and provenance of bioweapons.

What follows first is a description of the broad global revolution underway in biology, especially its open patterns of technological innovation, which differ from those of the 20th century. Our thinking and frameworks must also change. Second, it explains how progress in biotechnology echoes the evolution of computer software, programming cells as if they were individual computers. Biological hardware is also evolving, the third section argues. It is getting smaller, cheaper, and more accessible—just as computers evolved from mainframes to laptops in the last century. But truly understanding bioweapons requires looking not only at biology but also at clusters of new digital technologies, and the fourth section explains why and what these are. Fifth, given all these new developments, we examine the implications for bioterrorism. The sixth section considers where the greatest future threats are emerging—notably insider threats, unethical tinkerers, and proxies clandestinely supported by states. Finally, the conclusion draws together the themes and suggests policy solutions.

The Open Biology Revolution

The field of biology has changed in the past five years, and commercial processes drive those changes. Reading (DNA sequencing), writing (DNA synthesizing), altering (gene editing), and sharing (via the internet) genetic code is now easily done. In assessing what this means for future threats, looking exclusively to states, conventions, and treaties will only get you so far. Without understanding the full scope of capabilities and techniques that private biotech companies are developing, you cannot see where we are headed in terms of both risks and opportunities.

States dominated technological innovation in the 20th century. Military or scientific elites limited the availability of new technologies—things like nuclear, chemical, or biological weapons. Biological agents such as smallpox or anthrax, or *Yersinia pestis* (which causes plague) were hidden away in secret biological weapons facilities. Those clandestine, well-equipped laboratories required high levels of expertise, were protected by security classifications, and were very difficult to find. We spoke of the 'proliferation' of known bioweapons and used phrases like 'dual use,' meaning they had two types of users: civilian and military.

Now, given the widespread ability to create new molecules or alter existing bacteria and viruses, the term 'proliferation' seems inadequate. Synthetic biology and gene editing mean we may not even know what new agents or living organisms to track.[1] 'Diffusion' better captures the concept.[2] Plus, there are many types of users: professionals in private companies or universities, government scientists, "prosumers"[3] (amateurs with professional equipment and interest), hobbyists (as in, the makers' movement), and even amateurs—all well beyond 'civilian' and 'military.' The phrase 'dual

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use' is an anachronism. As Kenneth Wickiser and his co-authors concluded in this publication in August 2020, "As the technology improves, the level of education and skills necessary to engineer biological agents decreases. Whereas only state actors historically had the resources to develop and employ biological weapons, SynBio is changing the threat paradigm."[4]

In the last century, we also built a robust international structure of treaties and conventions that curbed the worst state excesses, notably the 1975 Biological Weapons Convention.[5] According to NDU biological weapons expert Seth Carus, in the years between 1915 and 2015, the maximum number of state biological weapons programs operating simultaneously was eight, with some existing for very short periods.[6] It was not perfect: Western intelligence agencies failed to identify the Soviet Union's large covert biological weapons program, along with those of Iraq, South Africa, Chile, and what was then Rhodesia.[7] But overall, this state-centered approach stigmatized and reduced the military use of biological weapons.[8]

Now, patterns of innovation in biology are far more open.[9] Virtually all of today's technological advances were first initiated by publicly financed basic and applied government research during the Cold War, then commercialized in the 1990s, which vastly sped up technological progress. Genetic engineering started in 1973, when biologists Herbert Boyer and Stanley Cohen first cut a gene from one bacterium and implanted it into another.[10] The field developed very slowly at first. But with advances in computing power, data storage, and machine learning at the end of the century, a wider range of scientists in private companies and universities began working on things like gene editing, synthetic biology, and using open-source datasets and AI to discover new molecules. They are producing exciting new developments that could help feed the world's population, cure diseases, create new biofuels, and mitigate climate change.

But open technological innovation is also much harder to monitor.[11] For good or ill, innovation in the life sciences is driven by commercial processes that lie outside traditional state purview. In this respect, it echoes the development of digital computers, especially commercial software, hardware, and expanding computing power.

Biological Software

Progress in biotechnology is deeply entwined with the development of digital technologies, especially computers. Both the hardware and software of biotechnology are changing rapidly, and that magnifies the risks.

This relationship to computers is not accidental. One of the founding pioneers of synthetic biology was MIT-trained computer engineer Tom Knight, who was also co-engineer of ARPANET[a] and spent the late 1960s and 1970s designing hardware and software at the MIT Computer Science and Artificial Intelligence Laboratory. In the 1990s, Knight went back to school to learn about biology, and then he set up a molecular biology lab within MIT's computer science lab.[12] Progress in biotechnology and computer science has been deeply intertwined ever since.

It is easier to see how commercial biotechnology patterns are unfolding if we briefly reprise the recent evolution of computer software and hardware. At the beginning of the computer age, hardware was king—clunky, expensive, and rare. By contrast, software was built collaboratively and shared. Early pioneers thought that hardware was something you paid for, while software was something you copied and shared. Indeed, in the 1970s, part of the hacker's credo was "software wants to be free."

When Bill Gates was first getting his start, for example, Microsoft's BASIC spread freely among hobbyists. A crucial turning point was Gates' 1976 "Letter to Hobbyists," published in the Homebrew Computer Club newsletter, insisting that software should be paid for. This planted the seed of Microsoft's business model. Gates' software was good quality and designed to run on many types of machines, which enabled Microsoft's software to drive the market, ultimately displacing the dominance of hardware built by powerhouses like IBM.[13]

Still, the communitarian ethos of computer hackers building and sharing their code for free never went away. Today, the free and open-source software movements remain potent forces that make software accessible and alterable by everyone. Richard Stallman and Linus Torvalds created the GNU and Linux open-source operating system that has been ported to more hardware platforms than any other operating system.[14]

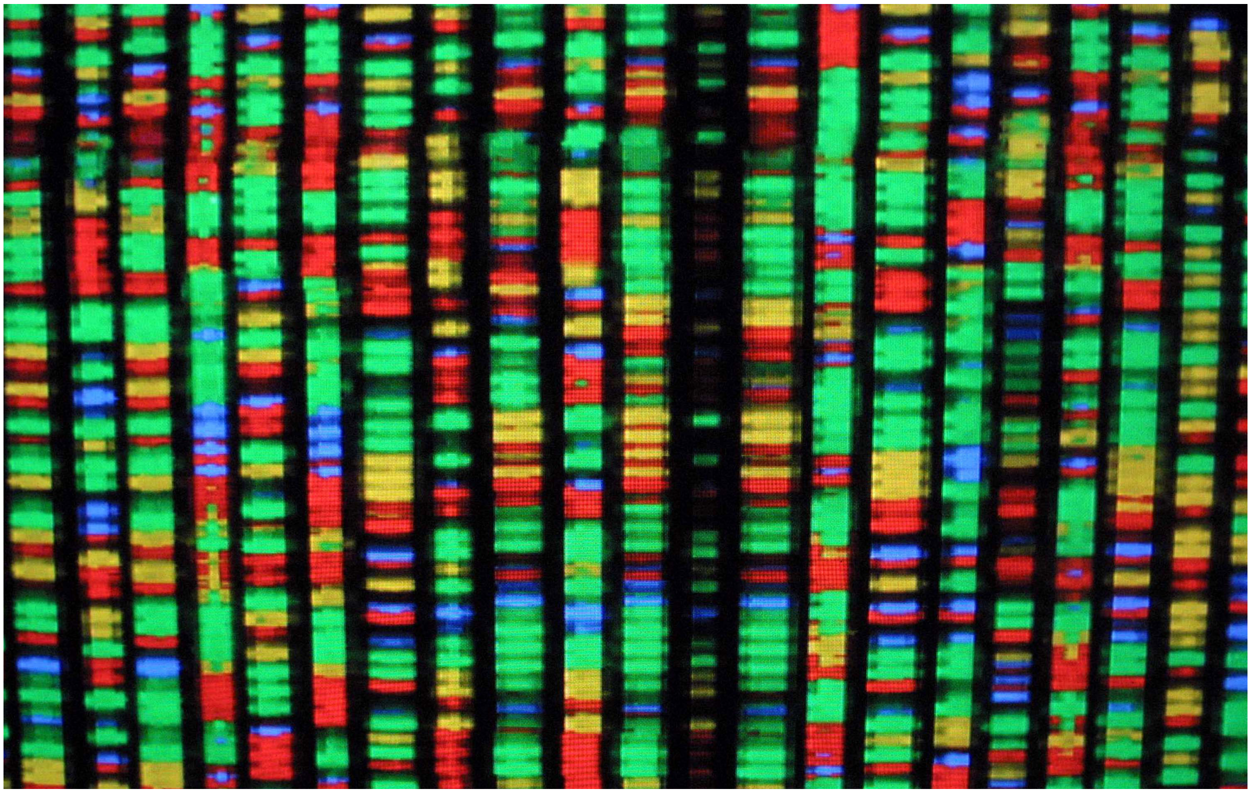
A similar dynamic is happening in the biotech industry. The goal of synthetic biology companies is to program cells as if you were programming individual computers. DNA is treated as if it were code for digital software, but instead of zeros and ones, it has ATGC (Adenine, Thymine, Guanine, and Cytosine), DNA's nitrogenous bases, as its code. The business model is predicated on building molecules essentially at cost, then licensing the right to use them, as Microsoft does its software. Now, synthetic biology companies like Gingko Bioworks own databases of new biological material at a vast scale. Like Microsoft, these biotech companies are by far the most important actors in the market, but they do not have a monopoly on the ability to create new organisms. With the right training and hardware, virtually anyone can do that.

Biological Hardware

Even in hardware, the biotech industry is following the same route the computer industry followed, decentralizing from mainframes to desktops, to laptops, to smartphones, making them more user-friendly and affordable. Makers movement and makerspace companies such as Genspace, BioCurious, and ChiTownBio have built user-friendly bio labs designed to help people experiment, especially with basic synthetic biology. The Open Source Hardware Association and related initiatives leverage 3D printing and other accessible forms of manufacturing to widen public access to science.[15] These initiatives are excellent ways to bring more ordinary people into science, which is vital, and makers labs will never compete with high-end microbiological laboratories; but they do widen access to the capacity to write, edit, copy, and create new or altered organisms.

Bioprinters are the next evolution in this process. These are

a ARPANET, or Advanced Research Projects Agency Network, was "a pioneering network for sharing digital resources among geographically separated computers. Its initial demonstration in 1969 led to the Internet." It was a product of the Advanced Research Projects Agency, funded by the U.S. Department of Defense. See "ARPANET," U.S. Defense Research Projects Agency (DARPA), n.d.



A digital representation of the human genome is pictured on August 15, 2001, at the American Museum of Natural History in New York City. Each color represents one the four chemical compenents of DNA. (Mario Tama/Getty Images)

various types of additive manufacturing[b] printers that create layered arrangements of cells and support structures that theoretically could facilitate the production and delivery of biological weapons.[16] Desktop bioprinters are becoming cheaper, smaller, and more accessible, and they will soon be as available as desktop printers are.

With biohacking and the makers movement, barriers to entry in gene editing are lower than they used to be. Kids can buy bacterial gene-engineering kits online for $169, and a whole genetic engineering home lab kit for less than $2,000.[17] High school students compete in gene editing. The annual International Genetically Engineered Machine (iGEM) competition encourages undergraduates to create novel products via synthetic biology.[18] This is mostly good, as we want people to learn to use new technology ethically, and proctored school competitions are the perfect place to teach ethical guidelines and behavior. But not everyone gets that ethical training, and experts do not even agree on what ethical oversight of biohacking should look like.[19]

These experiments are not advanced molecular biology, of course, and compared to that, their risk is minimal. Amateurs do not have the tacit knowledge to produce a serious threat. Certainly, this is not sophisticated biology, like editing the human genome or designing a new biological agent from scratch. But prosumers and hobbyists can do a lot more than they *used* to be able to do, and some of that capability is also more dangerous than it used to be. As has been well covered by other analysts,[20] it is a matter of lowering the threshold of access and use, to incorporate broader numbers of people.

Like digital computers, both the software and the hardware of biology are evolving. The field is also more widely accessible and more deeply intertwined with other disciplines than it used to be. That is driving surprising new developments—especially across the full range of new and emerging digital technologies.

Clusters of Digital Technologies Are Key

We can only fully understand the threat of bioweapons if we think in terms of clusters of new and emerging technologies. Existing pathogens such as those that cause anthrax, Ebola, smallpox, tularemia, and plague, covered under the biological weapons convention, are deadly enough. But advances in materials science, computer processing power, and autonomy have brought changes in delivery systems and threat vectors.

Analysts have warned for years that autonomous drone swarms could deliver known biological or chemical agents by dispersing them over military forces or civilian populations.[21] If an individual or group were able to gain access to a weaponizable pathogen, it would be feasible to use unmanned aerial vehicles to scatter it—although, as we also know from the experience of the Japanese group Aum Shinrikyo, weaponizing a pathogen (in Aum's case, *C.*

b "Additive manufacturing uses data computer-aided-design (CAD) software or 3D object scanners to direct hardware to deposit material, layer upon layer, in precise geometric shapes. As its name implies, additive manufacturing adds material to create an object. By contrast, when you create an object by traditional means, it is often necessary to remove material through milling, machining, carving, shaping or other means. Although the terms '3D printing' and 'rapid prototyping' are casually used to discuss additive manufacturing, each process is actually a subset of additive manufacturing." "What is additive manufacturing?" GE Additive website, n.d.

botulinum and *B. anthracis*) is a key challenge.[c] (To kill, maim, or intimidate civilian populations, groups are more likely to use small explosives, which are much easier to obtain.) Still, accessible, small drones are coming of age in Ukraine, where small-scale, off-the-shelf commercial drones are being used at an unprecedented scale, and extremists are presumably taking note.

But to fully understand where we are headed longer term, we must also dig deeper into the evolving nature of biotechnology itself. The field is converging with engineering, chemistry, mathematics, quantum mechanics, computer science, and information theory.[22] The intersections between these areas of study are reshaping the entire landscape of what biology actually *is*, which in turn changes our focus regarding what a biothreat in the 21st century could look like. The most dangerous threats are coming not just from biology, but from the intersections between disciplines.

For example, in early 2022, scientists from the company Collaborations Pharmaceuticals tweaked their machine learning model and came up with a scary result that shocked them. The Swiss Federal Institute for Nuclear, Biological and Chemical Protection (Spiez Laboratory) had convened its biennial conference to study how new technological developments might affect the chemical and biological weapons conventions. Collaborations Pharmaceuticals, based in Raleigh, North Carolina, uses computational machine learning to discover new drugs for rare diseases. As you might expect, the company's technique seeks out and jettisons anything predicted to be toxic (as it would kill the patient).

For the conference presentation, they decided to use the same technology but flip the parameters of their model to favor—rather than avoid—toxic molecules easily absorbed by humans. This was an experiment they expected to produce gibberish. To their surprise, in less than six hours, the AI designed not only a VX nerve agent but also novel, even *more*, toxic agents that were not even in the training datasets—a total of 40,000 new possible weapons.[23] According to the authors, "By inverting the use of our machine learning models, we had transformed our innocuous generative model from a helpful tool of medicine to a generator of likely deadly molecules. ... It was a thought exercise we had not considered before that ultimately evolved into a computational proof of concept for making biochemical weapons."[24] [d]

Using AI for developing new drugs is an example of new, cutting-edge research that the U.S. government has undertaken in its National Artificial Intelligence Initiative[25]—as have a wide range of commercial actors with access to the same capabilities, unmindful of national and international security risks. Of course, operators must still know about chemistry or toxicology to create extremely harmful new chemicals, toxic substances, or biological agents. And in the Collaborations Pharmaceuticals case, generating a list of chemicals did not mean the results could be synthesized or would prove stable and effective. Pharmaceutical companies use the same method to create drugs; yet out of millions of compounds, they find few viable enough to enter into production.[26]

"The field is converging with engineering, chemistry, mathematics, quantum mechanics, computer science, and information theory. The intersections between these areas of study are reshaping the entire landscape of what biology actually *is*, which in turn changes our focus regarding what a biothreat in the 21st century could look like. The most dangerous threats are coming not just from biology, but from the intersections between disciplines."

Still, the team's results came from open-source toxicity datasets using open-source software. They noted, "Without being overly alarmist, this should serve as a wake-up call for our colleagues in the 'AI in drug discovery' community ... All you need is the ability to code and to understand the output of the models themselves."[27] And they continued, "By going as close as we dared, we have still crossed a grey moral boundary, demonstrating that it is possible to design virtual potential toxic molecules without much in the way of effort, time or computational resources."[28]

Implications for Bioterrorism

Given fundamental changes in biology as opposed to chemical, nuclear, and radiological weapons (which have changed less—especially nuclear and radiological weapons), then, they should no longer be lumped together as "CBRN."[e] Unconventional armaments remain an essential subject to study, as terrorists and insurgent groups are still interested in pursuing them, especially for their psychological impact.[29] But CBRN framing misses the fundamental technological changes that have happened in biology and not in the other three fields. Biology is a much faster moving target.

The threat of traditional state bioweapons programs and terrorist groups using known agents has decreased in recent years. Al-Qa`ida is no longer in a position to attempt to build biological weapons like anthrax,[30] for example, although it is possible the Taliban could provide a safe haven for a bio lab in the future. The Islamic State experimented with chemical agents, particularly chlorine gas

c Aum Shinrikyo's efforts to weaponize *C. botulinum* and *B. anthracis* were failures. The group had more success with chemical weapons, especially VX nerve agent and sarin, which on March 20, 1995, it released in the Tokyo subway, killing 14 people and injured more than 1,000. Richard Danzig, Marc Sageman, Terrance Leighton, Lloyd Hough, Hidemi Yuki, Rui Kotani, and Zachary M. Hosford, *Aum Shinrikyo: Insights Into How Terrorist Develop Biological and Chemical Weapons* (Washington, D.C.: Center for a New American Security, 2011).

d Their article was published as a commentary, meaning the authors did not validate their concept, and no molecules were created and tested.

e The same ability to manipulate molecules affects chemical weapons. Biological weapons are changing fastest, however, because of the explosive growth in biotechnology and genetic engineering. Plus, their potential impact is greater. A highly engineered, particularly virulent pathogen could wipe out food supplies, devastate economies, kill millions of people, and then spread from there, posing an existential threat to all human beings. "Biosecurity," Future of Humanity Institute, University of Oxford, n.d.

and homemade sulfur mustard, out of Mosul University,[31] but it has lost that facility. Affiliates like Islamic State Khorasan could theoretically redevelop one in Afghanistan.

Islamists and domestic extremists have long experimented with ricin, given the ease of extracting ricin from castor beans and access to recipes on the internet explaining how to do so; however, ricin is most effective in assassinations or small-scale attacks. State actors have been more successful, as in the infamous London assassination of dissident Georgi Markov, pricked in the thigh by an umbrella tip spring-loaded with a ricin pellet, for example.[32] With state-sponsored terrorism on the rise, it is possible that such tactics will also increase.[33]

In any case, traditional biological weapons are difficult for individuals and small groups to deliver in large quantities. Even Aum Shinrikyo, whose members included highly trained scientists with laboratory facilities, had difficulty delivering biological weapons effectively, after years of effort.[f] Traditional biological weapons are now far more likely to be used in state-sponsored assassinations or small-scale targeted attacks than in mass-casualty events by non-state groups.[34]

Beware Insiders, Tinkerers, and State Sponsors

Biology is no longer a discrete field where biological risks come from a known staple of biological agents that are difficult to handle, acquire, and weaponize. Especially with the use of robust computing power and machine learning tools, the broad landscape of biotechnology is shifting in dramatic ways. It is becoming easy to gain access to DNA sequences from public databases, reproduce known pathogens, alter current viruses or bacteria, or dream up new ones that are neither covered in existing treaties nor even known about. In the same way, the key actors involved are no longer state-funded government laboratories or rogue non-state actors like terrorists. The most significant new risks of attacks come largely from insider threats by knowledgeable scientists with questionable motives, proxy actors backed by adversarial states, or even those experimenting with new biotechnologies irresponsibly.

Given where we are in the biological revolution, we are thinking of biothreats too narrowly. We should consider unprecedented challenges that affect security across new dimensions. The unethical use of bio data collected from unknowing individuals and used for economic or military advantage is one novel threat. For instance, Shenzhen-based BGI collects genetic data from prenatal testing kits that the firm developed with the Chinese military.[35] Some 8.4 million women have used the kits in at least 50 countries, including Australia, Canada, Denmark, Germany, India, and the United Kingdom.[36] Sensitive information on some mothers and their unborn babies is stored in China's government-funded gene database, one of the largest in the world.[37] Designed to screen for abnormalities such as Down syndrome, the samples yield valuable information on genetic traits across global populations, especially when analyzed with AI tools.[38] China could theoretically use that data to design pharmaceuticals or target genetic vulnerabilities with engineered pathogens.[39] This risk should not be overstated, of course, since biology also has a natural tendency to diversity. As Brad Ringeisen explained in the April 2022 issue of *CTC Sentinel*, even with the ability to rapidly scan data at scale, and regardless of how homogenous a population may appear, successful targeting is difficult. Small but important genetic variations affect the results.[40] Still, the Pentagon has reportedly warned its own personnel that unwittingly sharing genetic data opens individuals to risk.[41]

"We need more collaboration between hard scientists and human behavioral scientists. There is a troubling disconnect between those steeped in the study of biology and related digital technologies, on the one hand, and those focused on human behavior, motivations, and risk, on the other."

Self-scrutiny among international scientists has failed to hold off troubling developments in synthetic biology. Despite ethical guidelines, professional stigma, and peer pressure that forbids it, gene editing is already changing the human genome. Much to the horror of their peers, Chinese scientists have been the forerunners in genomic editing. In 2015, they tried to edit the genes of a human embryo in a petri dish; discovery triggered outrage and calls not to make a baby via genetic engineering.[42] Three years later, Chinese scientist He Jiankui altered the DNA of twins, Lulu and Nana, before their birth using the gene-editing tool CRISPR-Cas9. He eliminated a gene called CCR5 to make the twins immune to HIV, but evidence emerged that he may also have made them smarter by eliminating that gene. No one knows what other off-target effects might emerge—good or bad.[43] It also appeared that a third baby was born following similar gene editing.[44]

The Chinese case was heavily publicized, eliciting outcry among gene-editing scientists. Jiankui and two collaborators were found guilty of "illegal medical practices;" Jiankui was sentenced to three years in jail.[45] His two collaborators received lesser sentences of two years and 18 months, respectively.[46] Nonetheless, it put in question the wisdom of relying on the ethical codes of millions of scientists throughout the world—and especially in China.

Most scientists see the complexity of making inroads in altering genes, including the human genome, and the vast majority are upstanding and ethical. Yet partially trained graduate students or tinkerers may not foresee the full impact of their experimentation. In other words, with such powerful tools now available, we have to anticipate both malign actors and incompetent ones.

This said, some of the answers to the risks of biotechnology involve creating more and better biotechnology. For example, under a program called "Safe Genes," DARPA in 2017 began funding a $65 million program at five universities to search for treatments to switch off CRISPR and other gene-editing technologies.[47] This is a fast-moving field, with more than 50 anti-CRISPR (Acr) proteins reportedly discovered thus far that interfere with CRISPR tools and may reverse their effects.[48]

Conclusion

We have scratched the surface of how biotechnology is evolving and why it poses novel threats. Patterns of innovation are not like those we became familiar with decades ago, because the field of

f Unfortunately, Aum Shinrikyo had more success weaponizing chemical weapons. See footnote C.

biology itself is now fundamentally different, evolving via open processes. The old threats of bioterrorism remain, but they are joined by new ones that are falling between the seams of biology and other disciplines, especially engineering, data science, and computer science, and especially at the intersection between molecular biology and artificial intelligence. Biotechnology is already changing the balance of power between states, enriching private corporations at stunning speed, and opening new avenues of attack by terrorists and individuals. To preserve the promise of biotechnology, we must fully confront the risks before it is too late.

Biorisk management at the global level was well covered by Filippa Lentzos, Gregory Koblentz, and Joseph Rodgers in the April 2022 issue of *CTC Sentinel*.[49] The following policy recommendations focus primarily on the U.S. government.

First, to protect our national security, we need more collaboration between hard scientists and human behavioral scientists. There is a troubling disconnect between those steeped in the study of biology and related digital technologies, on the one hand, and those focused on human behavior, motivations, and risk, on the other. Disciplinary stovepipes hamper us as we face a future where traditional fields are merging and recombining. Workshops, seminars, inter-disciplinary brainstorming, and cooperation is vital. We must learn to think in more agile ways across boundaries, or we will fail to recognize both risks and opportunities.

Our leaders, by and large, do not understand biotechnology. We need significant retraining, including at senior levels of government and in the military, to stop relying on outdated ways of thinking. This includes focusing on the intersection between biotechnology and artificial intelligence. We should also establish short-term training courses for early career scientists on how to talk to policymakers, write policy-relevant articles, and explain research in accessible ways for general audience outlets.

Specifically in my own field, those who study terrorism and other non-state threats must update their skills and get smarter about new technologies. Relying on the same old frameworks, case studies, and incident databases we have used in the recent past will not prepare us to meet future risks. Biology has fundamentally changed. Patterns of terrorist innovation from the last 40 years of the 20th century do not tell us much about where bioterrorism is likely to evolve.

Finally, highly trained, well-respected scientists need to be more open in acknowledging the potential for misuse of biotechnology, and young scientists need dedicated ethical training that is as high a priority as their technical training currently is. Insisting that professional norms, stigmas, and self-policing are working well is simply unsupportable. But curiosity, innovation, and professional and commercial success are not at odds with mitigating risk. Ultimately, if there is a major incident, or accident, or even additional ethical lapses like those we have seen in gene editing, the future of humankind could be jeopardized. CTC

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Preventing Catastrophic Bioterrorism: Guarding Against Exploitation of the Life Sciences and Biotechnology

By Jaime Yassif

Bioscience and biotechnology advances offer extraordinary promise, but they are also accompanied by emerging biological risks—specifically the potential for catastrophic accidents or deliberate misuse by malicious actors seeking to cause harm. These risks include the possibility that non-state actors could exploit the legitimate global bioscience research and development enterprise to gain the knowledge and materials to develop and disseminate a biological weapon. We must take action to safeguard the life sciences to prevent biotechnology catastrophe, in addition to bolstering law enforcement and intelligence capabilities to more effectively anticipate and prevent bioterrorism and other biological threats.

The COVID-19 pandemic has revealed that countries around the world are woefully unprepared to prevent and respond to pandemics. The SARS-CoV-2 virus has infected more than 520 million people, killed more than six million, and caused trillions of dollars in economic damage.[1] The events of the past two and a half years have highlighted the world's vulnerability to future high-consequence biological events, which could cause damage as severe as the current pandemic or possibly much worse.

This article outlines the actions that governments, the private sector, and civil society can take to prevent a catastrophic act of bioterrorism and how to guard against exploitation of the life sciences and biotechnology. It first outlines the changing biorisk landscape and gaps in oversight, before discussing approaches for preventing biological attacks. Next, it provides a proposed threat reduction strategy and outlines initiatives by the Nuclear Threat Initiative (NTI) to develop a more comprehensive approach to biosecurity, which helps fill gaps in oversight. The article then examines how intelligence and law enforcement capacity to prevent bioterrorism can be bolstered, before offering final thoughts on the path forward.

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The Biorisk Landscape

In addition to the large loss of life from the COVID-19 pandemic—with more than a million deaths in the United States alone[2]—recent events in Ukraine have further highlighted biological risks. Russia's disinformation campaign alleging bioweapons development in Ukraine's legitimate bioscience laboratories has led to concerns that Russia may itself use chemical or biological weapons in Ukraine as part of a false-flag operation.[3]

Along with concerns about state bioweapons risks and global pandemics that could be caused by a naturally emerging infectious disease outbreak or an accidental laboratory release, the world also faces biological risks posed by non-state actors—specifically that they could attempt to develop or acquire a biological weapon and use it. The impact of a bioweapons attack by a terrorist group could range from local damage on a relatively small scale to a catastrophic biological event with global reach. Efforts to guard against high-consequence biological events must therefore include efforts to guard against bioterrorism. Unfortunately, these risks are only growing over time as rapid technological advances drive emerging biological risks.

Bioscience and biotechnology advances offer extraordinary promise; they are critical for advancing public health and pandemic preparedness, helping guard against climate change, and fostering economic development.[4] A classic example is rapid progress in developing capabilities to read, write, and edit DNA, which encodes the underlying designs for all life on earth. This is part of a wider revolution in the biosciences that is driving advances in fundamental capabilities to engineer biology—including accelerating cycles for developing, building, and testing new designs for biological systems. This includes new, more efficient tools for automating high-throughput bioscience experiments, coupled with ongoing advances in artificial intelligence-based approaches. Twenty-first century bioscience is often described as a revolution, with exciting potential future gains over the horizon,[5] and this enthusiasm is often warranted. However, these rapid developments can also pose important challenges—increasing risks of deliberate exploitation or accidental misuse of the tools of modern bioscience and biotechnology—with potentially catastrophic consequences.

These are not new risks, but they have been compounded by the current pandemic, which has given rise to a surge of research into the SARS-CoV-2 virus and other pathogens with pandemic potential. This has been accompanied by the proliferation of new labs to house this work in countries around the world. Although such research can offer significant potential benefits for public health and pandemic preparedness, some experiments can also pose dual-use risks. Additionally, with the extraordinary disruption brought about by COVID-19, terrorist groups and other malicious actors may now understand the catastrophic damage that can be caused by highly transmissible pathogens and other biological agents, and to use them in an attempt to deliberately cause the next pandemic.[6] This threat becomes increasingly pressing as rapid, globally distributed technology advances continue to lower the barriers to the synthesis and engineering of pathogens and other biological agents, thereby enabling a wider range of actors to engage in this type of work—including non-state actors.

Governments should play a key role in safeguarding the life sciences against these growing risks, but they have been unable to keep up with rapid advances in technology. According to the 2021 Global Health Security Index, 94 percent of countries have no national-level oversight measures for dual-use research, no agency responsible for such oversight, and no evidence of national assessment of dual-use research.[7] At the same time—notwithstanding the important and valuable role of the World Health Organization (WHO)[8] and the Biological Weapons Convention[9]—no international entity has dedicated its primary mission to strengthening biosecurity and bioscience governance, which is critically important for guarding against bioterrorism risks.

NTI has highlighted these global governance gaps through a series of tabletop exercises focused on reducing high-consequence biological threats, which we have convened in partnership with the Munich Security Conference over the past four years.[10] Exercise participants have included senior leaders and experts from across Africa, the Americas, Asia, and Europe with extensive experience in public health, biotechnology, and international security. In our reports on these high-level discussions, NTI has shared key findings and offered a number of recommendations for concrete action to counter catastrophic biological threats—ranging from strengthening international capabilities for assessing pandemic origins and improving national-level pandemic preparedness, to developing catalytic financing tools to accelerate pandemic preparedness capacity building and improving bioscience governance globally to guard against emerging biological risks. For example, our 2021 exercise report found that "the international system for governing dual-use biological research is neither prepared to meet today's security requirements, nor is it ready for significantly expanded challenges in the future. There are risk reduction needs throughout the bioscience research and development life cycle." To address this gap, NTI recommended establishing an "international entity dedicated to reducing emerging biological risks associated with rapid technology advances," specifically focused on "reducing the risk of catastrophic events due to accidental misuse or deliberate abuse of bioscience and biotechnology."[11]

Preventing Bioweapons Attacks: Constraining Capabilities and Shaping Intent

The full range of work to reduce biological risks posed by non-state actors includes prevention of bioweapons development and use, as well as early detection and effective response, so that biological events can be contained before they grow and spread out of control. Activities across this spectrum can all effectively reduce non-state actor biorisks, but this paper will focus on *prevention* in particular.

At a basic level, there are two types of approaches to preventing deliberate biological threats: shaping the intent of malicious state or non-state actors and constraining their capabilities. The strategy for combating biological risks posed by non-state actors is different than the approach that is likely to be most effective for preventing development and use of bioweapons by states. One key reason for this is that it is very difficult to shape intent of non-state actors and to deter them from pursuing bioweapons development or use. This is because many non-state actor groups are not motivated by the same rational political, military, and economic goals that motivate most states. As a result, it is unlikely that those responsible for guarding against bioterrorism threats could ever get to a point of high confidence that there are no groups anywhere around the world with the intention of causing large-scale catastrophic damage and who would use biology to do so given the opportunity.

"Twenty-first century bioscience is often described as a revolution, with exciting potential future gains over the horizon, and this enthusiasm is often warranted. However, these rapid developments can also pose important challenges—increasing risks of deliberate exploitation or accidental misuse of the tools of modern bioscience and biotechnology—with potentially catastrophic consequences."

We have to assume that such groups exist now and that they will continue to exist for the foreseeable future. In fact, there is publicly available evidence that such groups have existed in the not-distant past. For example, the Aum Shinrikyo cult, which is widely viewed as an apocalyptic group, pursued the development of chemical and biological weapons in the 1990s and made multiple failed attempts at launching large-scale chemical and biological attacks in Japan.[12] We should assume that there are other extremist groups in existence at the moment with similar intentions.

However, while it may be difficult to deter non-state actors, it is more tractable to constrain their capabilities to develop and use bioweapons. That is because non-state actors do not typically have access to the same resources that states do—particularly in terms of trained personnel and financial resources. Therefore, erecting barriers to non-state actor acquisition or development of dangerous pathogens—and increasing their odds of being caught by law enforcement if they do make an attempt—is likely to be one of the most effective ways to counter bioterrorism risks.

To effectively constrain the capabilities of non-state actors, bioscience and biotechnology stakeholders will need to work closely with the biosecurity community to make it more difficult to obtain the know-how, materials, and services needed to acquire or develop dangerous biological agents. This will require more effective safeguards on the global bioscience and biotechnology enterprise to help prevent exploitation.

It is also feasible to increase the chances that a non-state actor group will be detected and get caught by law enforcement in the act of trying to acquire or produce biological agents. As will be discussed later in this article, part of this involves strengthening biothreat intelligence to improve capabilities to detect these types of activities before a bioweapons attack occurs.

Guarding Against Exploitation of Modern Bioscience and Biotechnology

The tools of modern bioscience and biotechnology are increasingly democratized, and access is globally distributed. Importantly, this allows a wide range of communities to access and benefit from these tools. However, this also poses a challenge: how to constrain access of malicious actors to these tools so they cannot be exploited for bioweapons development or use.

The threat reduction strategy should have two key elements:

1. Constraining access to goods and services needed to conduct life science research and development, such as DNA synthesis services, key laboratory reagents, pathogen strains, and some types of equipment.
2. Preventing publication of information that could provide a roadmap that would make it easier for non-state actor groups to engineer or synthesize a dangerous biological agent—for example, by preventing publication of papers that share domain-specific, expert knowledge about how to engineer a pathogen to make it more virulent or transmissible among humans or about how to synthesize dangerous pathogens from scratch.

To help achieve the goals outlined above, there are intervention points throughout the bioscience and biotechnology research and development life-cycle: from project conceptualization and funding, to research execution, and on to publication or commercialization (Figure 1).[a]

However, with governments unable to keep pace with rapid advances in the life sciences and provide adequate oversight, and without an international organization dedicated to reducing emerging biological risks associated with rapid technology advances, these strategies have not been sufficiently explored or implemented. The world therefore remains vulnerable to exploitation of the legitimate global bioscience and biotechnology enterprise—with potentially catastrophic global consequences.

To address this gap, NTI is working with the World Economic Forum and international partners to develop and launch the International Biosecurity and Biosafety Initiative for Science (IBBIS), an independent organization that will have the mission of working collaboratively with global partners "to strengthen biosecurity norms and develop innovative tools to uphold them. IBBIS will undertake this work to safeguard science and reduce the risk of catastrophic events that could result from deliberate abuse or accidental misuse of bioscience and biotechnology."[13]

A biohazard sign is pictured on a restricted area door at a virology institute on March 3, 2020. (Oliver Bunic/Bloomberg via Getty Images)

IBBIS' initial activities will focus on DNA synthesis screening,[b] in order to prevent the building blocks of dangerous pathogens from falling into the hands of malicious actors.[c] However, IBBIS' scope of activities will expand over time to encompass multiple intervention points throughout the bioscience and biotechnology research and development life-cycle, such as:

- Strengthening and supporting the development of standards for pre-funding biosecurity review by public and private funders of bioscience research and biotechnology development. Funders have significant leverage, and they are well positioned to incentivize incorporation of biosecurity measures into grant or investment proposals.
- Guiding universities and industry in developing effective approaches for strengthening oversight of dual-use bioscience

a A key goal of engaging publishers to conduct more effective pre-publication biosecurity review is to shift incentives within the scientific community toward adherence to biosecurity best practices. While such an approach may not prevent the sharing of information in other open fora, it could still significantly reduce risks by shifting incentive structures. Many scientists are motivated by the opportunity for a prestigious publication, which can advance their reputation and standing. An open posting that is not followed by a prestigious publication is likely to be less appealing. There are other complementary approaches that could deter scientists from publishing potentially dangerous information in open fora. For example, if there were strong norms against doing so in the community, this could damage their reputation. NTI is exploring the possibility of shaping incentive structures within the scientific community through a "seal of approval" project. See Indira Nath and Jaime Yassif, "Paper 5: Establishing a Seal of Approval to Incentivize Adherence to Biosecurity Norms," NTI Biosecurity Innovation and Risk Reduction Initiative, October 29, 2018.

b "DNA synthesis is a service that is widely used in bioscience research in laboratories around the world," and it "is critically important for a wide range of biotechnology advances. However, safeguards for DNA synthesis technology … have not kept pace with growing global demand for this service and declining costs." Most but not all DNA providers screen DNA synthesis orders on a voluntary basis, as it is not legally required by any national government. "To preserve safe and secure global access to DNA synthesis services, NTI is working with the World Economic Forum" and a Technical Consortium of experts "to develop an international Common Mechanism for DNA synthesis screening. This mechanism will be a tool that DNA providers can use to screen DNA synthesis orders" to help ensure that they do not inadvertently sell the building blocks of dangerous pathogens to malicious actors. Jaime M. Yassif, Sarah Carter, and Nicole Wheeler, "Preventing the Misuse of DNA Synthesis Technology," NTI, n.d.; "NTI and World Economic Forum Release New Report on DNA Synthesis Technologies," NTI, January 9, 2020.

c NTI's current efforts to bolster DNA synthesis screening are focused on traditional DNA providers, as well as the application of these approaches to benchtop DNA synthesis devices. Next-generation benchtop devices are coming online, which will make it easier to print DNA within one's own laboratory as opposed to ordering it online from a centralized provider. These newer devices are easier to use than older versions of this technology and, in the coming years, will likely have much better capabilities to produce longer DNA fragments at higher sequence accuracy. It will be important to manage access to these devices—both by screening customers and their orders. This is being actively discussed within the U.S. government and through our work at NTI, and we plan to publish a report on benchtop devices in the coming months.

research conducted within their laboratories.

- Partnering with industry to develop biosecurity and biosafety requirements for customers who want access to materials and services to support bioscience research.
- Working with publishers to update their guidelines regarding publication of manuscripts and pre-prints containing information that might be misused.
- Developing proposals for governments to incentivize or require biosecurity practices through funding conditions, regulation, and guidance.

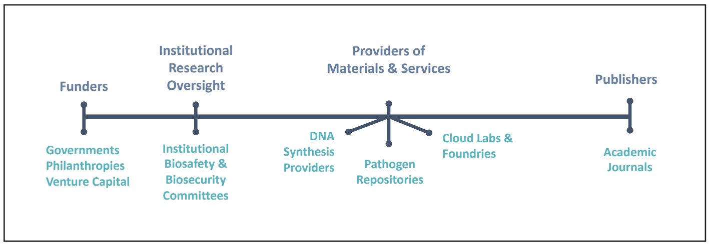

Figure 1: Proposed bioscience governance solution set—intervention points throughout the research and development life-cycle. To comprehensively reduce biological risks, it will be important to have a layered defense comprised of multiple risk reduction interventions, including at the project conceptualization and funding stage, through research execution, and on to publication or commercialization.

In biosecurity, there is no single solution or intervention that can eliminate all risk. That is why a layered defense is needed, in which multiple interventions in aggregate add up to substantial risk reduction. Furthermore, even if these interventions cannot eliminate all risk, reducing the number of individuals and organizations that have both the capabilities and the intention to carry out a bioweapons attack constitutes a successful risk reduction effort.

Intelligence and Law Enforcement

Catching non-state actors in the act of trying to exploit the legitimate global bioscience and biotechnology enterprise is another way to make risk reduction efforts effective. To achieve this, governments and international organizations need to foster better linkages between law enforcement and efforts by the scientific community to safeguard the life sciences against exploitation.

For example, the United States takes such an approach with DNA synthesis providers, who are asked to report suspicious activity to law enforcement.[14] While the bar for such reporting is set quite high and such reports are extremely rare, the underlying idea is that malicious actors should not be able to extensively explore DNA provider systems to see what they can and cannot get away with, without eventually facing negative consequences. If enough red flags add up, the activity should in principle draw the attention of law enforcement. Even if screening is not perfect, if there is a risk of being caught accompanied by unacceptable consequences, that could serve as a powerful deterrent for malicious actors seeking to exploit infrastructure of the legitimate bioscience and biotechnology enterprise.

As noted above, another opportunity for meaningful bioterrorism risk reduction is strengthening biosecurity intelligence capabilities to more effectively detect non-state actors who are seeking to exploit biology to cause harm, so that biological attacks can be prevented before they are attempted. Such an approach would be complementary to the bioscience governance approaches described above, as it would focus on the groups and organizations that may be looking to develop or acquire bioweapons.

"In biosecurity, there is no single solution or intervention that can eliminate all risk. That is why a layered defense is needed, in which multiple interventions in aggregate add up to substantial risk reduction."

Efforts to bolster biothreat intelligence should include investments in both traditional and more modern approaches. First, it would make sense to invest in human intelligence resources that are focused on identifying malicious actors who express interest in exploring bioweapons development and use. This could include dedicating more existing human intelligence resources to this specific issue set, as well as training a cadre of experts with bioscience and biotechnology specific expertise and skills. Second, analysis of publicly available information, including with machine learning-based tools, could be a powerful resource in early identification of emerging biothreats. NTI has demonstrated the efficacy of this approach for preventing nuclear proliferation,[15] and similar approaches may be helpful in detecting signals of activity related to bioweapons development or acquisition.

Biosecurity has not been prioritized by the intelligence community in recent years, both in the United States and internationally, and it is an area that needs significantly more investment.

The Path Forward

As bioscience and biotechnology advances continue to progress, within the next 10-20 years radically new possibilities will likely emerge for engineering and synthesizing biological organisms, and these technologies are likely to become very widely distributed.

If the scientific community does not begin to put more effective safeguards in place now, the capability to synthesize or engineer deadly pathogens or other dangerous biological agents could become increasingly widespread, and it could become very difficult to prevent exploitation by terrorist groups seeking to cause harm with biology.

To get ahead of these emerging risks, it will be important to make a more concerted international effort to strengthen global biosecurity norms and to develop practical, effective governance approaches for putting those norms into practice. The WHO has invested significant resources in developing stronger global norms for safeguarding bioscience research,[16] and states parties to the Biological Weapons Convention are contemplating adding a Science and Technology Review Mechanism to address emerging biological risks.[17] NTI's work to develop and launch the International Biosecurity and Biosafety Initiative for Science is designed to develop practical tools and governance approaches to put stronger biosecurity norms into practice in countries around the world, which will complement and reinforce existing efforts. Support and engagement with IBBIS when it is launched as a new organization—including by governments, international organizations, the bioscience research community, biotechnology industry, and the philanthropic sector—will be critically important for its success.

As part of international efforts to bolster biosecurity, national governments will need to take steps to strengthen bioscience governance and biosecurity within their respective borders, and NTI's aspiration is for IBBIS to serve as a resource to support such efforts. As noted above, much of this work will need to focus on more effective safeguards for dual-use bioscience. However, these efforts will also require more effective biosafety and biosecurity measures for high-containment laboratories, as noted by Filippa Lentzos, Gregory Koblentz, and Joseph Rodgers in the first of this two-part series of *CTC Sentinel* special issues focused on biological threats.[18]

And as Lawrence Kerr noted in the same issue, "at one point in time, there were 3,000 named apocalyptic groups around the world," including terrorists "solely interested in annihilation of humans."[19] A comprehensive strategy for preventing such groups from using biology to cause catastrophic harm on a global scale will require investment of significantly more resources in biothreat intelligence and law enforcement capabilities—both in the United States and internationally. These tools will be critically important for early detection of groups looking to carry out a bioweapons attack, so they can be apprehended before they make an attempt.

We must take action now to safeguard the life sciences so society can reap all of their benefits, while guarding against the risks of exploitation and the potential for biotechnology catastrophe caused by terrorist groups or other powerful actors. CTC

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