SCUSA 72 Table Paper: Public Health and the Biomedical Revolution

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COVID-19 has brought public health and epidemics to the forefront of the national debate. COVID-19 wreaked havoc on the world economy, travel, and tourism, and strained international political relationships. How might America use disruptive technologies to combat against other epidemics and issues pertaining to global health? To what extent should the U.S. cooperate, if at all, with other countries concerning global health issues? Will any such cooperation depend to some extent on the quality of beneficial disruptive technologies? For example, the response to the COVID epidemic underscored the capacity of science to develop technologies in the form of vaccines that manage the threat of global infection. How can the United States use vaccine technology to advance its global interests and values? To what extent do US-based multinational corporations that control vaccine development and other technologies have influence over U.S. foreign policy, and does such influence hurt or help U.S. interests? What does the future of U.S. foreign health policy look like?

I. The COVID-19 pandemic and vaccine technologies

The global human and economic costs of COVID-19 cannot be accurately calculated in part because the pandemic is far from over. Much of the global population has yet to receive an effective vaccine, leaving large numbers of individuals vulnerable to infection. Another complication in knowing the approximate number of human casualties at any given time is that under-reporting is a chronic problem due to several factors, particularly inadequate administration for tracking vital health statistics in many countries. Cultural disincentives also play a role in under-reporting. While 98% of deaths from all causes are officially registered by health information systems in Europe, that percentage plummets to 10% in Africa.[1] Despite these barriers to accurate assessment, the World Health Organization estimates that the pandemic was responsible for approximately 3,000,000 deaths in 2020 alone.[2] That number rose to over 4,800,000 deaths as of early October 2021.[3] The United States registered a total of over 44 million cases of COVID-19 by early October 2021, with more than 713,000 deaths.

COVID-19, inequality, and vaccine diplomacy

While the enormous loss of life is the greatest cost of the current pandemic, COVID-19 also exacts an immense toll on socio-economic well-being and human security in general. The pandemic has particularly exacerbated inequality within and between countries. By October 2021, only 36% of the global population was fully vaccinated. In Nigeria, the most populous country in Africa, 1.1% of the population was fully vaccinated. In the United States, the percentage was 56%.[4]

Perhaps inevitably, the rush to develop vaccines to counter COVID-19 has taken on elements of

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[1] Ruth Maclean, "A Continent Where the Dead Are Not Counted," New York Times, January 2, 2021, at https://www.nytimes.com/2021/01/02/world/africa/africa-coronavirus-deaths-underreporting.html
[2] World Health Organization, "The True Death Toll of COVID-19," at https://www.who.int/data/stories/the-true-death-toll-of-covid-19-estimating-global-excess-mortality
[3] World Health Organization, Coronavirus Dashboard, at https://covid19.who.int/
[4] https://www.nytimes.com/interactive/2021/world/covid-vaccinations-tracker.html

great power competition among the United States, China, and Russia. Russia has fared the worst in its vaccine diplomacy and the quest for soft power. Despite a noisy propaganda campaign attending the roll-out of Sputnik V, and its attendant disparagement of rival Western vaccines, Russia has consistently overpromised and underdelivered in terms of quality and distribution. The Kremlin has done little to burnish the image of Russian science or that of the Russian state given the frequent failure to fulfill deliveries, a problem often traced to production inefficiencies and corrupt deal-making.[5]

Unlike Russia, China was off to a strong start in distributing its vaccines to the world, particularly to less developed countries in East Asia and Southeast Asia. In mid-2020, Beijing launched a determined effort to mobilize its domestic pharmaceutical industry.[6] Nevertheless, there have been shortfalls with Chinese deliveries and Chinese vaccines often have to compete with Russian and American counterparts. By September 2021, sufficient doubts were raised about the efficacy of Chinese vaccines that much of the population in Asia and beyond began to look elsewhere for inoculations.[7]

This shift has provided an opening for the United States as Washington began its pursuit of soft power through vaccine diplomacy. Yet American efforts have been hampered by the slow start under President Trump who was relatively uninterested in the international political dimensions of the pandemic. The effects of Trump's vaccine nationalism still linger under President Biden, often prompting domestic and international accusations of vaccine stockpiling for domestic populations despite Washington's vocal promises to increase the shipments of US vaccines abroad.[8] A central question is whether China, Russia, or the United States will demonstrate the industrial capacity and political will to net the greatest yield in soft power due to their global distribution of COVID-19 vaccines.

Evaluating the US Response to the Pandemic

Preparing for the next pandemic first requires an assessment of what was done right and what was done wrong in terms of America's response to COVID-19. One common evaluation is that "more than anything else, the COVID-19 crisis has been a failure of governance" across the globe.[9] Nevertheless, the dramatic roll-out of vaccines in response to COVIOD-19 should be viewed as the result of an enormous effort on the part of governments worldwide to confront the crisis.

In the case of the United States, much could be written about the mistakes of the political leadership as well as the scientific institutions of the US government in understanding why over 700,000 Americans have died from COVID-19 as of October 2021. At the same time, other observers find the American response to be, on balance, a successful example of public-private

[5] Grace Kier and Paul Stronski, "Russia's Vaccine Diplomacy is Mostly Smoke and Mirrors," Carnegie Endowment for International Peace, August 3, 2021, at https://carnegieendowment.org/2021/08/03/russia-s-vaccine-diplomacy-is-mostly-smoke-and-mirrors-pub-85074
[6] Yanzhong Huang, "Vaccine Diplomacy is Paying Off for China," *Foreign Affairs*, March 2021, at https://www.foreignaffairs.com/articles/china/2021-03-11/vaccine-diplomacy-paying-china
[7] https://www.nytimes.com/2021/08/20/business/economy/china-vaccine-us-covid-diplomacy.html
[8] https://www.nytimes.com/2021/08/20/business/economy/china-vaccine-us-covid-diplomacy.html
[9] Editorial, "Preparing for the Next Pandemic," *Nature Medicine*, March 2021, at https://www.nature.com/articles/s41591-021-01291-z

partnership rising to a challenge of enormous proportions. The US government played the dominant role in this estimation. The appearance and success of new US vaccines to fight COVID-19 was partly the product of decades of previous investments by the federal government in developing platforms to meet the earlier threats of HIV and pandemic flu. For example, it is estimated that between 2000 and 2019 over $15 billion was spent on HIV vaccine research. 80% of these funds were provided by the federal government.[10]

The response to COVID-19 benefited significantly from this existing infrastructure. More billions were then devoted to developing novel vaccines to meet the new pandemic. As of mid-2021, it is estimated that the Biomedical Research and Development Authority (BARDA), under the US Department of Health and Human Services, alone invested $19 billion in COVID-19 vaccine research and development.

As the experience with COVID-19 has demonstrated, commercial solutions were inadequate by themselves to meet the threat. Here the government played a crucial role in bolstering the market responses of the pharmaceutical industry, including the expenditure of billions of dollars to support research and clinical trials at companies such as Moderna, Johnson and Johnson, and AstraZeneca. Further, the government dramatically reduced market risk by offering contracts for advance purchases. Even Pfizer, which claims to have received little government support in its vaccine rollouts, benefited from advance purchase contracts from the US government that approached $6 billion. In its support for the development of multiple vaccines, Washington increased the likelihood that at least one effective vaccine would be available for use.[11]

II: The Threat of Synthetic Biology[12]

Whether or not the COVID-19 pandemic originated in pathogens found in the natural environment, man-made biological weapons have long been a very real and deadly threat. Synthetic biology (SynBio) is the scientific discipline that encompasses all aspects of the engineering of biological systems. Beginning with the discovery of the chemical structure of DNA in the 1950s, SynBio tools such as recombinant DNA technology and genome editing tools have developed at a fast pace as the fundamental molecular mechanisms underlying biology are discovered. These SynBio tools are lowering the education, training, cost, time, and equipment threshold required to modify and employ pathogenic organisms as biological weapons.

The asymmetric threat posed by biological weapons will continue to increase as new tools and techniques are developed and as terrorist organizations become aware of and inspired by the society-wide economic, emotional, and government-destabilizing impacts caused by the COVID-19 pandemic. Indeed, it can be argued that the total cost of this pandemic—including the loss of

[10] Richard Frank, et al., "It Was the Government that Produced COVID-19 Vaccine Success," May 14, 2021, at https://www.healthaffairs.org/do/10.1377/hblog20210512.191448/full/
[11] Richard Frank, et al., "It Was the Government that Produced COVID-19 Vaccine Success," May 14, 2021, at https://www.healthaffairs.org/do/10.1377/hblog20210512.191448/full/
[12] This section reproduces, with the permission of the authors and publisher, segments of the following article: J. Kenneth Wickiser, Kevin J. O'Donovan, Michael Washington, Stephen Hummel, and F. John Burpo. "The Future Threat of Synthetic Biology," *CTC Sentinel*, August 2020, volume 13, issue 8, pp. 1-7 at https://ctc.usma.edu/engineered-pathogens-and-unnatural-biological-weapons-the-future-threat-of-synthetic-biology/
Please refer to the original article for the complete list of endnotes.

life and the stress to the economy—could be rivaled only by the deployment of an atomic bomb. Therefore, developments in SynBio should be continually monitored and reassessed within the context of technological change and its capacity to shift the geopolitical paradigm.

This section of the SCUSA paper describes how biological systems' modular nature makes them amenable to engineering, the recent advances in synthetic biology, the impact of synthetic biology on the threat landscape, and the potential policy responses to the maturation of biotechnology in general, and synthetic biology in particular. This article has been developed using both primary and secondary literature sources recently published in peer-reviewed scientific papers.

The extent and impact of SynBio on future state-on-state conflicts and terrorist violence will increase as the tools and techniques of this discipline continue to mature and diffuse throughout the scientific community, as well as among the novice citizen-scientists in the do-it-yourself biology labs that have emerged around the world in recent years. The ability to produce custom-designed bacterial and viral pathogens will enhance the ability of hostile state and non-state actors to develop and deploy relatively inexpensive and efficient biological weapons. Additionally, some of these weapons will likely be engineered with increased pathogenicity, environmental stability, and the ability to withstand the shock of the rapid changes in temperature and pressure that may accompany delivery by an explosive warhead. Below are several notable 21st-century examples where scientists employed emergent SynBio techniques to rediscover or recreate pathogenic microorganisms.

In 2002, scientists from the State University of New York at Stony Brook chemically synthesized the complete poliovirus genome, highlighting the transformative potential of SynBio. While this effort was accomplished by experienced professional scientists over the course of years in well-equipped laboratories, the playbook is now freely available and the tremendous advances in molecular engineering techniques since then have only reduced the complexity of this once-monumental effort. This achievement was followed by the first chemical synthesis of a much larger bacterial genome in 2008 and the development of an entirely synthetic cell in 2010.

The use of SynBio tools has endowed scientists with the ability to purposefully dissect the inherently complex series of coupled chemical reactions that compose fundamental cellular metabolism. These networks of reactions can be engineered using modular genes and molecular tools to enhance synthetically-produced organisms with desired biochemical properties. Significantly, by combining standard molecular and cellular laboratory techniques with cellular selection (or evolution) strategies, which are accomplished daily by high school and college students in biology classes and research competitions across the world, detailed knowledge of the nature of each chemical reaction is not required to achieve the desired outcome for the engineered biological agent.

In 2005, a group of researchers from the U.S. Centers for Disease Control (CDC), the Mount Sinai School of Medicine, the Armed Forces Institute of Pathology, and the Southeast Poultry Research Laboratory reconstructed the 1918 pandemic influenza virus. This was a particularly striking example of how the modular nature of a viral genome could be used to manufacture a pathogen. The reconstruction was performed by first determining the genomic coding sequences of the virus from lung tissue specimens obtained from pandemic victims who were preserved in permafrost. The relevant DNA sequences were then inserted into a set of circular DNA strands known as plasmids, which were subsequently used to infect host human kidney cells. As predicted, fully functional and replicative viral particles emerged from the kidney cells.

The pathogenicity of the reconstructed virus was evaluated in mice, ferrets, and non-human primates, and it was found that the 1918 influenza strain was significantly more lethal than modern strains. It produced severe damage to the lungs, stimulated an aberrant immune response, and led to the development of high viral titers (levels of virus) in both the upper and lower respiratory tracts. The reconstruction procedure was conducted in a standard molecular biology laboratory setting, and all the materials needed for the construction of this viral particle are present in many university biology laboratories. The methods that were employed are not beyond the means of the talented amateur and therefore not beyond the means of a dedicated, well-resourced terrorist organization.

More recently in 2018, a small Canadian research group was successful in constructing infectious horsepox virus directly from genetic information obtained solely from a public database for the relatively modest sum of $100,000 in U.S. currency. Horsepox is a genetically distinct relative of the now extremely rare smallpox virus. Smallpox was once a highly feared pandemic disease that either permanently disfigured or ended the lives of millions of people worldwide. The same techniques used to construct horsepox can easily be adapted to construct smallpox with a minimal investment of time and money. SynBio has therefore placed the ability to recreate some of the deadliest infectious diseases known well within the grasp of the state-sponsored terrorist and the talented non-state actor.

SynBio also facilitates the development of binary biological weapons. Although the design and production of binary biological weapons may have been difficult in the past, the ability to engineer and 'boot-up' entire genomes has revolutionized the process. With modern synthetic biology tools, an undergraduate student could conceivably engineer and produce two related, non-lethal viruses that are individually harmless. However, following host infection with the two viruses, mixing of the two strains allows for a full restoration and production of highly infectious, pathogenic viruses. Importantly, such genetic mixing has also been documented in nature wherein two or more non-pathogenic poliovirus vaccine strains can recombine to form pathogenic recombinants. Thus, it is not difficult to imagine a non-state actor developing binary weapons consisting of components stored separately for safety in transport and then brought together in a biological munition before delivery. The advances in SynBio have not occurred in isolation.

The increase in the understanding of biological systems and the development of the tools of molecular biology that occurred in the late 20th and early 21st centuries were paralleled by commensurate developments in automation, engineering, computer science, and information technology. In particular, the ease of scaling up the production of bacteria and viruses has increased exponentially in recent decades due to the availability of inexpensive instrumentation for the growth, or culture, of biological material, and the development of standardized reagents such as bacterial growth media by commercial laboratories. Once the purview of scientists with doctorates in microbiology, genetic engineering is practiced every day in high schools and colleges across the world. The instruction or protocols, for these processes, are freely available on the internet and in undergraduate microbiology and cell biology textbooks

Policy Responses to the Potential Threats Posed by Synthetic Biology

An effective response to the threats posed by those using synthetic biology for nefarious purposes will require vigilance on the part of military planners, the development of effective medical counter-measures by the research community, and the development of diagnostic and characterization technologies capable of discriminating between natural and engineered pathogens. A 2002 biological warfare counterproliferation study identified six key basic biological research areas that should be emphasized to protect against the threat: human genomics; immunology and the development of methods for boosting the immune response; bacterial and viral genomics; bacterial and viral assay development; vaccine development; and the development of novel antiviral agents and antibiotics. A continued research and education effort within the Department of Defense will be required to develop and maintain expertise in each of these areas.

The rapid availability of experienced civilian and military personnel is a prerequisite for effective incident response. Therefore, training and education in SynBio, biological engineering, and related disciplines should be emphasized and funded. Many organizations already exist to meet the threat of natural, man-made and weaponized biological material. These organizations include the Defense Threat Reduction Agency (DTRA); the Chemical and Biological Center (CBC) at Edgewood, Maryland; the Defense Advanced Research Projects Agency (DARPA); the Biomedical Advanced Research and Development Authority (BARDA); the National Institutes of Health (NIH); the Centers for Disease Control (CDC); and United States Department of Agriculture-Agricultural Research Service within the United States Research Service (USDA-ARS). The World Health Organization (WHO), a specialized organization within the United Nations, and several research and response organizations in other countries have historically served similar purposes.

Each of these entities deals with systems rooted in the natural world, and while some organizations restrict their focus to naturally occurring threats, they all deal—in one way or another— with the extraordinary pace of technology development unique to the biomedical community. Every advancement in biomedicine is dual-use, and so it is incumbent upon those who work in the scientific field to predict the ways that these technologies might be used for a harmful purpose and to develop the technologies and systems necessary to undermine the efforts of those who might use these unique biological entities as weapons.

Conclusion

SynBio is a rapidly developing and diffusing technology. The wide availability of the protocols, procedures, and techniques necessary to produce and modify living organisms combined with an exponential increase in the availability of genetic data is leading to a revolution in science affecting the threat landscape that can be rivaled only by the development of the atomic bomb. As 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. The economic and social impact of COVID-19 has highlighted the broad and lasting effects that can result from the spread of a novel biological agent. This collective experience has increased the chance that terrorist organizations will attempt to use biological agents to asymmetrically attack the United States and its allies. This possibility should be anticipated and planned for at all levels of government.

Questions for Discussion

COVID-19 has brought public health and epidemics to the center of national concern. The health crisis of the past 20 months has killed millions, wreaked havoc on the world economy, and strained international relations. Future responses to the rise of new pathogens or to old diseases that have become resistant to standard treatments will require government support for expensive research and development programs. But what other lessons should we take from the public-private partnership that marks the US response to COVID-19? And what reforms of US scientific institutions should be considered to speed and streamline the government's response to the next pandemic? Further, should the US join efforts to bolster institutions like the World Health Organization to better equip them to forge a united global response?[13] Do international agreements require better enforcement mechanisms? How can the United States use vaccine technology to advance its global interests and values? And what can be done to alleviate the enormous inequalities that exist globally in terms of vaccination rates?

While advanced technology has been mobilized to fight the COVID-19 pandemic, we should keep in mind that science can also be used by humans in malign ways, including the development of biological weapons. How serious is this threat to the United States on the part of our adversaries, at both state and non-state levels? What are US defense mechanisms and how effective would they be against this threat? How might these defensive measures be enhanced?

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