A Primer on Pathogen Research and Biological Weapons

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Introduction

When participants gathered at Asilomar in 1975 to discuss the safety of recombinant DNA technology, biological weapons were largely absent from the agenda. With the Biological Weapons Convention (BWC) entering into force just after the conference, perhaps bioweapons seemed soon to be an issue of the past. The conference instead focused on biosafety – preventing accidental harm through safe working practices – rather than preventing intentional misuse of biotechnology. Today, as we mark the 50th anniversary of that meeting, the landscape has fundamentally changed. The revealing of biological weapon capabilities by both state and non-state actors amidst rapidly advancing biotechnology tools have renewed concerns about biological threats.

The evolving threat landscape

Numerous states have pursued biological weapons capabilities throughout history and into the present day. The U.S. began researching biological weapons during World War II and maintained an offensive program until 1969, when President Nixon unilaterally terminated it and supported an international ban that culminated in the BWC. It became public later that the Soviet Union, despite signing the BWC, secretly expanded the world's largest bioweapons program – employing over 60,000 people at its 1980s peak – until the USSR's collapse in 1992 [1]. This included work on weaponizing smallpox, plague, and Marburg virus. Today, the U.S. State Department assesses that North Korea and Russia maintain offensive biological weapons programs while others pursue dual-use research that could cross into offensive weapons development [2].

Beyond state actors, history reveals that some groups and individuals have had both the intent and capability to cause harm through biological means. The apocalyptic Aum Shinrikyo cult, which possessed over $1 billion in assets and employed numerous graduate-trained scientists, injured thousands in Tokyo with chemical weapons in 1995, and attempted to develop and test biological weapons including anthrax [3]. Other examples include the Rajneesh cult's use of *Salmonella* in the U.S. in 1984, the 2001 U.S. anthrax attacks, Al Qaeda's attempted bioweapons development, and reports from the United Nations and others that Islamic State branches pursued biological as well as chemical weapons [4–6].

The rapid advancement of biological knowledge and tools has enabled many beneficial capabilities in areas ranging from human health to biodiversity, but it has also lowered technical barriers for malicious actors [7]. For example, DNA synthesis costs have plummeted while methods for assembling DNA pieces into longer fragments, including constructing viruses, have drastically improved [6]. Current safeguards around DNA synthesis not only remain inadequate at detecting threats but will become easier to circumvent with emerging benchtop synthesizers [8]. Meanwhile, AI systems are emerging as expert-level tutors in biology, potentially helping enable non-experts in creating pandemic pathogens [9], and are poised to vastly improve biodesign and automation capabilities [10,11]. As technical barriers fall, the risk grows that actors with extremist ideologies could obtain the necessary knowledge and materials to conduct catastrophic bioattacks.

Pandemic-potential pathogen research under scrutiny

The proliferation of powerful biotechnology tools has coincided with increased scrutiny of research regarding pathogens that could pose pandemic-scale or mass-casualty risks, particularly following the COVID-19 pandemic. While the origins of SARS-CoV-2 remain contested between natural spillover and laboratory-related scenarios, the debate has spotlighted longstanding concerns about biosafety and biosecurity in pathogen research. From the 1977 re-emergence of H1N1 influenza likely due to a lab release [12] to the 2004 SARS laboratory accidents in Beijing [13], history provides sobering examples that even well-intended research can pose serious risks.

Particularly contentious is “gain of function” research that could potentially make pandemic-potential pathogens more dangerous whether through enhanced transmissibility, virulence, or ability to evade immunity. The controversy gained prominence in 2011 when two laboratories, led by Ron Fouchier and Yoshihiro Kawaoka, conducted experiments making H5N1 avian influenza transmissible between ferrets [14]; a growing number of countries have since tightened oversight for this type of research given concerns over the risks. Furthermore, virus hunting – expeditions to sample and characterize potentially dangerous viruses from wild animals – has also faced similar debates as to whether the benefits of identifying and potentially developing countermeasures for future pandemic threats outweigh the biosafety and biosecurity risks of coming into contact with and publicizing novel pathogen genomes [15].

Global change mechanisms

International frameworks exist to help navigate these emerging challenges, but struggle with their own limitations. The Biological Weapons Convention (BWC), a widely adopted treaty and the first to effectively ban a class of weapons, is currently undergoing efforts to strengthen its applications; as an example, a recently proposed Science and Technology Advisory Mechanism works to incorporate independent scientists to provide expert guidance [16]. However, past efforts to strengthen the BWC have faced significant obstacles. A 2001 attempt to establish verification protocols, which the treaty has lacked since its inception, collapsed due to disputes over site visits and intellectual property protection – challenges that remain relevant today given difficulties in distinguishing legitimate research from weapons development. More recently, Russia has used the BWC to spread unsupported claims that U.S.-supported Ukrainian labs are advancing biological weapons, and blocked development of the S&T Advisory mechanism [17].

Beyond the BWC, other international bodies are grappling with dual-use concerns in biotechnology. The Convention on Biological Diversity's expert group on synthetic biology has identified several emerging technologies that warrant careful oversight; gene drives, for example, can have harmful effects on populations, increasing the risk of ecosystem fragmentation, the spread of new diseases, and decimation of agricultural services, thereby opening the door for their possible use as bioweapons [18]. These technologies highlight how advances intended to benefit human health and biodiversity could potentially be misused.

More broadly, these debates reflect fundamental tensions in governing biological research. Biology is a massive global enterprise that has yielded tremendous benefits for human health and scientific understanding. Yet it is also capable of causing catastrophic harm – potentially exceeding even nuclear weapons in destructive potential. The field's distributed nature, dual-use potential, and rapid technological progress make it particularly challenging to govern. Growing distrust in scientific institutions further threatens responsible research progress and global biosecurity [19]. Going forward, the scientific community must grapple with how to preserve and advance biology's benefits while implementing appropriate safeguards against catastrophic risks.

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