Will the New Biology Lead to New Weapons?

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Biology is in the midst of what can only be described as a revolution. It began in the mid-1970s with the development of recombinant DNA technology. Slowly at first but with increasing speed, related technologies have been developed that have dramatically expanded the experimental capabilities of modern research biologists and that are rapidly being adopted in such areas of applied biology as drug development.

These new technologies include genomics, proteomics, microarray technology, high-throughput screening techniques, combinatorial methods in both chemistry and biology, site-specific mutagenesis, knock-out mice, and many others. Collectively, these technologies are referred to as genomic sciences, or the “new biology.”

This technology will have great power both for peaceful and hostile uses. Peaceful applications will include a wide range of new therapeutic agents of much greater specificity and safety than are currently available; hostile applications could include a wide range of new biochemical weapons that could transform the nature of combat in unprecedented ways.

Yet, policymakers have paid little attention to the new biology and its potential hostile applications, even though human physiology might be altered in ways that will raise a broad range of ethical, legal, political, and military issues. Policymakers need to consider these issues now before undesirable applications develop a momentum that will narrow the options for control.

The New Biology

Until recently, attempts to manipulate natural processes were largely unsuccessful as scientists were stumped by the fiendish complexity of physiological systems. The newly detailed understanding of the physiology of living organisms, however, is paving the way for breakthroughs in biology and biotechnology. By any measure—number of professional scientists, number of publications, new journals, funding level, etc.—the growth of this field is extremely rapid, with no sign of leveling off.

There has been a related growth in relevant computer and instrumentation technologies. For example, an entirely new discipline, bioinformatics, has evolved to manage the collection and analysis of massive amounts of new data. Likewise, a major instrumentation industry has developed to provide the sophisticated technology on which the new biology depends. Instrumentation technology has matured quickly: slow, crude prototypes requiring skilled operators have given way to highly sophisticated equipment that can be operated with minimal technical expertise. Additionally, experiments that needed milliliters or milligrams of material a few years ago now require only microliters or micrograms.

The result has been the swift production of new knowledge. This knowledge and related technologies have spread quickly around the globe as these commercially-available tools have become easier to use, more reliable, and increasingly affordable to individual laboratories.

Soon, scientists around the world will be able to tailor pharmaceutical agents to enhance or block specific physiological pathways. This will be a great boon for medicine but will also allow the development of a wide range of novel biochemical agents for hostile purposes.

Two aspects of the new biology have particular potential for military application: our new...
understanding of the nervous system and our greater comprehension of the mechanisms by which disease-causing microbes interact with humans, animals, and plants.

**Manipulating the Nervous System—for Good and Ill**

The nervous system is of great interest to biologists, for intrinsic reasons and because there is a huge economic market for the development of new pharmaceutical compounds for the treatment of mental illness, pain, and other medically important nervous system disorders. As we come to understand the detailed mechanisms that underlie such phenomena as pain, depression, panic attacks, post-traumatic stress, anxiety disorder, schizophrenia, and sleep disorders, we will be able to design new medications that will offer much greater effectiveness and specificity than current ones and that will have greatly reduced side effects. A combination of humanitarian and economic incentives ensures that progress will be very rapid.

Of course, the capabilities that emerge, like all advanced technologies, will be capable of hostile as well as peaceful exploitation.[2] Hostile applications include the manipulation of humans to increase their effectiveness as soldiers; the creation of novel weapons for combat use, including a range of nonlethal, incapacitating biochemicals; and new agents for interrogation.

**Designer Soldiers**

For at least half a century, militaries have used amphetamines as stimulants for pilots or soldiers on long missions. In the future, we can anticipate that at least some countries would use forced medication to produce troops who are not only alert and energetic for days at a time, but who have heightened sensory awareness, enhanced aggressiveness, decreased fear, decreased sensitivity to pain, and a dulled moral sense. The beginnings of the understanding of the chemical bases of all of these attributes is already emerging, and to anticipate the development of drugs that can provide such capabilities is not much of an extrapolation. Further into the future, it might be possible to make soldiers stronger and quicker than normal; the “superhuman” strength conferred by some street drugs is a common experience among law enforcement personnel and suggests that a biochemical basis for enhancement of physical capabilities might emerge. Selective memory erasure may also be possible, once we understand the molecular basis of repression. Briefing and debriefing sensitive missions could include erasure of selected memories.

**Designer Biochemical Weapons**

The new knowledge about the nervous system will also make new biochemical weapons possible. It is worth remembering that the most potent, existing chemical weapons—the nerve agents—are analogs of acetylcholine, a neurotransmitter used in a number of different neural and neuromuscular circuits. As we learn the details of neural circuitry, there is every reason to believe that even more toxic agents will become available. Of even greater significance, it will likely be possible to develop a completely new range of disabling biochemical weapons (see below).

**Biochemicals for Interrogation**

New pharmaceuticals could also be of great interest to interrogators who are willing to ignore legal restrictions on interrogation methods. Although a genuine “truth serum” may not be possible, many pharmaceuticals would substantially reduce the ability of a captive to resist providing information. Chemical agents that cause submissiveness and eagerness to please are on the horizon and would be effective on many captives. Pharmaceutical forms of torture could also be highly effective in reducing the ability of captives to retain secrets—techniques in which depression, delirium, panic, and submissiveness are manipulated and perhaps alternated with euphoria and pleasure—would likely prove irresistible.

**New Vaccines or New and Deadly Viruses and Bacteria**

The mechanisms by which pathogenic (disease-causing) bacteria or viruses cause disease are complex. Yet, very rapid progress is being made in understanding these processes, known as pathogenesis, promising greatly enhanced public health and agricultural benefits.
The tools are rapidly becoming available that will produce improved vaccines (more efficient, longer lasting, and safer), produce new antibiotics and antivirals, enhance defenses against diseases, and protect against damage from overreaction of defensive systems. The same benefits may be realized in veterinary medicine, and better understanding of plant diseases can be expected to provide increased yields and improve nutritional quality.

However, as with our greater understanding of the nervous system, greater understanding of pathogenesis also opens the door to potential military applications. Within the next decade, some possible military uses include:

- genetically engineered pathogens that evade diagnosis and treatment
- pathogens that are exceptionally lethal
- pathogens intended to disable permanently
- pathogens with enhanced contagiousness
- pathogens with enhanced environmental stability

**Evading Diagnosis and Treatment**

The first of these is not new. The ability to create antibiotic-resistant pathogens has existed for decades, and the idea of using mutant forms of a virus or bacterium to confuse diagnosis is also not new. The new technologies, however, make the construction of such altered pathogens easier and faster and provide a range of new options. Until now, the development of such pathogens has been limited by the interconnectedness of virulence with other traits, such that, if scientists changed one property in a pathogen, such as surface proteins to defeat vaccines or diagnostics, they would commonly reduce virulence. Soon, their new understanding will allow them to manipulate agent properties while avoiding such undesirable secondary effects.

**Increasing Lethality or Causing Disability**

In nature, the virulence of pathogens is the result of a complex selective process that often limits virulence in favor of transmissibility: a pathogen that kills its host so quickly that it has little chance to transfer to a new host will quickly die out.[3] Microbes perpetuated in the laboratory, however, are free of such selection, and thus genetically engineered organisms might reach a level of lethality that is exceptionally high and rapid compared to existing pathogens. This is not speculation; it has already been achieved inadvertently: a benign mousepox virus with very low lethality became highly lethal when a mouse gene related to the immune system was incorporated into its DNA. The development of such potentially highly lethal bioweapons agents poses a significant risk of a renewed biological arms race and also raises serious biosafety concerns, as an accident in a military laboratory could lead to the inadvertent release of extraordinarily dangerous pathogens.

Researchers will not be limited to transforming benign viruses into lethal agents. Perhaps more disturbing, they could also engineer viruses to produce pharmaceutically active compounds, causing a wide range of disabling effects, from mild disorientation to severe psychosis. Such viruses could be contagious and could persist for years in the body (like herpes viruses and retroviruses), causing permanent, contagious, mental or physical disability.

**Making Diseases Spread Faster and Live Longer**

Currently, many pathogens only have a limited capacity to spread from host to host. That could change with the new technology. It should thus be possible, at least for some pathogens, to create variants with increased (or decreased) contagiousness. Of course, this property could be combined with increased lethality. For instance, the monkeypox virus could be engineered to be contagious among humans and also feature increased lethality, creating a fearsome weapon, perhaps worse than smallpox.

One of the obstacles to transforming naturally occurring microbes into military weapons has always been the limited persistence of many when released, a persistence that was sometimes measured in
minutes. Plague, for instance, has a fearsome lethality in the pneumonic form but is transmissible only over very short distances (a few feet), in part because it is short lived in aerosol form. For this reason, it was not successfully weaponized by the United States during its offensive biological weapons program, although the Soviet Union was able to do so. Better understanding of the reasons that some bacteria persist for long periods while others do not will very likely allow the modification of pathogens to persist longer and thus become candidates for weaponization.

**Long-Term Dangers**

In the longer term—20 years or more—we can expect not only the further development of the aforementioned technologies, but additional technologies as well. Likely capabilities will include:

- synthetic viruses and prions
- synthetic cellular pathogens of exceptional virulence
- synthetic, nonreplicating cell-like entities as vectors for biochemical agents
- stealth pathogens
- genotype-specific pathogens of crop plants and domestic animals
- ethnic-specific human pathogens
- pathogens that cause ethnic-specific autoimmune diseases with effects such as sterility

**Synthetic Life**

One of the most dramatic developments of the new biology is the impending capability to create synthetic living systems—living in terms of being able to replicate themselves using known life processes involving nucleic acids and proteins. Synthetic replicas of existing viruses already have been created chemically, and scientists are actively working on the synthetic creation of cellular life. It will not be long before completely novel synthetic viruses are produced. The capability to produce effective, synthetic, new viral pathogens will surely follow. Such agents could have significant utility in biocontrol of pests such as weeds, rodents, or insects, so their development is likely to be pursued vigorously. Yet, the lessons could easily be transferable to the construction of weapons. Synthetic viruses could be designed to be contagious or noncontagious, lethal or disabling, acute or persistent, and so on; and they could be invisible to the immune system and resistant to existing forms of antiviral therapy. They would be very hard to diagnose on first use. Similarly, as understanding deepens of the biology of self-perpetuating prions, which are infectious protein agents, it will be possible to develop novel, synthetic forms of these agents.

Living synthetic cells will likely be made in the next decade; synthetic pathogens more effective than wild or genetically engineered natural pathogens will be possible sometime thereafter. Like synthetic viruses, such synthetic cellular pathogens could be designed to be contagious or noncontagious, lethal or disabling, acute or persistent, etc. They could lack the usual targets of antibiotic therapy, be invisible to the immune system, and be very hard to diagnose on first use.

It will also be possible to create novel, cell-like entities that could be used to target biochemical agents to specific tissues. They would have great utility in medicine by allowing pharmaceuticals to be targeted to specific tissues, but they would have equal potential for facilitating the delivery of weapons agents.

**Stealth Pathogens**

It might also be possible to engineer stealth pathogens, the microbial equivalent of sleeper cells. These would be pathogens, either natural or synthetic, that are engineered to become latent after a period of mild or asymptomatic replication, to be reactivated later for symptomatic replication in response to a particular stimulus. Such a pathogen would spread unnoticed through a susceptible population, and all those infected could at a later time be induced to display symptoms in response to, for instance, an otherwise benign chemical compound added to such things as water supplies and imported food materials. The resulting symptoms could be lethal or disabling.

**Ethnic Weapons**
There has been much talk of ethnic-specific or genotype-specific biological weapons, and they are likely to become technically feasible. Their development will be easiest for agricultural targets because cultivated plants and domestic animals tend to have very little genetic variability. Such genotype-specific weapons could, for instance, specifically target a cultivar of corn widely planted in the United States but not in other countries. The rapidly increasing use of genetically engineered crop plants in the developed world provides genetic targets for such designed pathogens, or natural genetic sequences unique to specific types of crops or breeds of animal could be targeted.

Engineering an ethnic-specific weapon targeting humans is much more difficult, as human genetic variability is very high both within and between ethnic groups. Nevertheless, it is possible to find combinations of traits, no one of which alone correlates highly with ethnicity, that together do. Using such combinations as a basis for pathogen specificity makes for a formidable problem in genetic engineering, but there is no reason to believe that it will not eventually be possible. If so, pathogens could be designed that are essentially restricted to one race or ethnic group; however, they would only infect a limited proportion of that group (perhaps on the order of 10 percent or so of the targeted group).

If such weapons are ever contemplated, it is likely that the sought-after effects would include sterility, mental illness, or other disabilities that are not obviously the result of biological attack. Mental illness could be produced by designing the pathogen to produce bioregulators, as described above. Sterility could be induced by causing autoimmune reactions to sperm or egg proteins, an approach that is already being actively pursued for biocontrol of pest animals. Such infectious sterility, if coupled with ethnic-specific targeting, could go undetected for a long time, as fertility rates in the target group gradually fall.

As a final long-term prospect, the likely merger of the new biology with nanotechnology, artificial intelligence, and microrobotics will lead to a hybrid technology of enormous power, for good and ill.

Policy Reponses to the Prospects of the New Biology

The preceding analysis has outlined some possible hostile applications of the revolution in the biological sciences. It is far from exhaustive; many other applications can be imagined, and others that we cannot yet imagine may soon emerge. These are all logical applications of knowledge that will be acquired as the inevitable result of peaceful medical, veterinary, and agricultural efforts. There is no way to avoid the knowledge that will make new hostile applications possible while still enjoying the benefits of the peaceful applications. Thus, if we wish to enjoy the benefits and avoid the perils offered by new biological knowledge, we need a coherent policy to control the applications.

Clearly it will be desirable to prevent many, perhaps all, of the hostile applications of the new biology. Even a country such as the United States, whose technological capabilities will likely keep it in the lead in the development of such new weapons, would eventually conclude that these weapons reduce, rather than enhance, its security. Without effective restrictions on development and proliferation, terrorists and states that do not respect international humanitarian laws will gain access to this technology, constituting a serious threat to more scrupulous states.

Many of the international legal tools to prevent the development of these weapons are already in place, notably the Biological Weapons Convention (BWC) and the Chemical Weapons Convention (CWC), which together ban military use of all of the weapons imagined here. Nevertheless, these may prove insufficient to prevent proliferation, and we should not shy away from new international treaties as necessary. Foremost among the new treaties that should be considered, or reconsidered, are those that would:

- add a compliance regime to the 1972 BWC;
- make development, possession, or use of chemical or biological weapons a crime over which nations may claim universal jurisdiction (like piracy, airline hijacking, and torture) [4]; and
- impose a single control regime over the possession and transfer of dangerous pathogens and toxins.[5]
Consideration should also be given to a new convention that would prohibit the nonconsensual manipulation of human physiology, to support and extend the provisions of the CWC, BWC, and international humanitarian law.

Even with sustained political commitment to ensuring compliance, treaties by themselves will be insufficient to prevent determined nations from secretly developing prohibited weapons. A variety of other means must supplement the international legal regime. Many of these are already in place, such as export controls. Others will be needed. Perhaps foremost would be a system of review and prior approval for potentially dangerous experiments, whose results might be readily applied to weapons development.[6] Such a system would usefully begin as national programs in the United States and other countries with strong biomedical research communities. Ultimately, they would have to become international, or at least be widely implemented in a harmonized fashion, to truly address the problem. The United States has taken the first step by establishing the National Science Advisory Board for Biosecurity to advise federal agencies and departments that conduct and support research in biology and to develop guidelines for oversight of research. However, there is a long way to go, and substantial political commitment required, to transform these first steps into an effective system.

One of the most significant factors usually spurring interest in new weapons is the suspicion that other nations may be developing them. The development and production of chemical and biological weapons has an increasingly small footprint and may become nearly invisible to national technical means of intelligence. It is thus increasingly difficult to have confidence in the compliance of many countries with the BWC and the CWC. This problem will worsen as the technology becomes more sophisticated; production facilities decentralized, miniaturized, and robotically controlled; and the potential weapons more potent. For this and other reasons, serious consideration should be given to making transparency in biodefense and chemical defense a central component of U.S. efforts in counterproliferation. This would allow the United States to take a leadership role in encouraging others to be transparent, to offer incentives to those that do, and to impose sanctions on those that do not. A world in which biology and chemistry are transparent to the maximum degree without betraying important vulnerabilities or clues to offensive technology is much more likely to deter proliferation of biological and chemical weapons and to allow detection of cheaters than one in which military biology and chemistry are shrouded in secrecy.

Making transparency a central pillar of biological weapons disarmament policy will clearly require a major transformation of current U.S. attitudes and policy. In reality, however, this would be less a radical departure and more of a return to a prior philosophy. After President Richard Nixon renounced offensive biological and toxin weapons programs in 1969 and 1970, the U.S. biodefense system was for 20 years nearly completely unclassified, with vulnerability assessments the only significant exception. There is no evidence that this openness caused adverse security consequences. However, the United States now has the world’s most aggressive biodefense program and is moving rapidly in the direction of increased classification. For instance, the recently announced Biothreat Characterization Center at Fort Detrick, Maryland, part of the National Biodefense Analysis and Countermeasures Center of the Department of Homeland Security, is expected to engage in a wide range of exploratory activities, including developing new pathogens by genetic engineering; developing new methods of packaging and delivering agents; developing techniques for enhancing environmental stability of pathogens; and assessing the suitability of bioregulators as weapons. Although this research will be carried out in the interest of better understanding the hypothetical threat to the United States, it constitutes a de facto program for the development of a sophisticated offensive bioweapons capability. As such, it will by necessity be classified. Such activities are clearly incompatible with transparency, as well as quite provocative. An independent review is urgently needed to assess the relative benefits and disadvantages of transparency versus such aggressive threat analysis and the consistency of the latter with U.S. treaty commitments under the BWC and the CWC.

**Conclusion**

The revolution in the biological sciences is making it possible for biology, especially medical and pharmaceutical sciences, to become a full-fledged military technology. This raises the specter of a new generation of biological and chemical weapons, as well as a sophisticated capability to
manipulate the physiology of human beings for military purposes. Designing and weaponizing these agents would require a substantial investment of time, expertise, and money; it is not a feasible activity for terrorists, although with time some terrorist groups might be able to develop some of the simpler alternatives. However, these new weapons will lie well within the capabilities of any country with a biomedical research community—an increasingly large number of states that includes most that are suspected of current or past interest in biological and chemical weapons. The implications for weapons proliferation are thus grave.

Clearly, such a prospect deserves careful analysis and wide-ranging debate. National and international security are not well served by ignoring the issues and allowing the world to creep toward new biochemical and biological weapons, as departments of defense and justice in the developed world continue to explore their utility for short-term tactical goals. We owe it to our children and grandchildren to consider our choices carefully, rather than thoughtlessly allowing momentum to carry us forward, irreversibly, down one fork in the road ahead.

ENDNOTES

1. For a brief discussion of some of these technologies and their application to drug and weapon development, see Mark Wheelis, “Biotechnology and Biochemical Weapons,” Nonproliferation Review, Spring 2002, pp. 48-53.


3. An exception is pathogens that have alternative hosts. Ebola virus, for instance, with a very high human lethality and low human-to-human transmissibility, could not persist in nature without an alternative host (still not identified) in which its lethality is lower and its transmissibility higher.

4. For a draft of such a treaty, see “A Draft Convention to Prohibit Chemical and Biological Weapons Under International Law,” Chemical and Biological Weapons Conventions Bulletin no. 42, December 1998, pp. 1-5.


The Danger of "Nonlethal" Weapons

When Russian forces used a derivative of the anesthetic fentanyl to knock out 50 Chechen hostage-takers in a Moscow theater in October 2002, they provided a glimpse of what may happen with the development of a new class of “nonlethal” pharmaceutical weapons. These calmatives, or “knockout gases,” are intended to cause rapid sedation or unconsciousness and are viewed by many militaries as a less-than-lethal means to limit civilian casualties. The Moscow incident, however, also showed the downside of these new pharmacological weapons and the need for countries to pause and reflect before racing to embrace this new technology.
In the Moscow confrontation, the hostage-takers were holding 800-900 hostages and were threatening to blow them up if their demands for a Russian withdrawal from Chechnya were not met. After a standoff of several tense days, Russian authorities tunneled into the basement and fed the fentanyl derivative into air conditioning ducts. The male hostage-takers, armed with automatic weapons, immediately left the theater for surrounding hallways in order to defend against the impending attack. The female hostage-takers were left inside and were soon overcome by the anesthetic, still holding the bombs they had threatened to detonate to kill the hostages.

Half an hour later, Russian special forces stormed the theater, killing the male Chechens in a firefight and executing the comatose female ones. The unconscious hostages were removed from the theater and taken to local hospitals. Unfortunately, nearly 130 died of overdoses, and an undisclosed number were left with permanent disabilities.

Whether it was necessary for the Russian military to use fentanyl remains unclear. The hostage-takers had sufficient time to detonate their bombs before the anesthetic took effect, but for some reason did not.

Still, this event is seen by advocates of such weapons as a model. They regret the loss of more than a hundred innocent hostages, but they point to the saving of more than 600. Additionally, they look to advances in pharmaceutical sciences to provide safer agents that might truly deserve the term “nonlethal.”

On the other hand, opponents of these weapons say that the theater episode points to a number of disturbing implications of these weapons.[1]

The first is safety. It may indeed be possible to develop an anesthetic agent that would technically be as safe as tear gas (which does cause occasional deaths).[2] Yet, when used under realistic conditions, such an anesthetic weapon would likely cause significantly more fatalities because there is always a risk of death from airway obstruction or of accident when people are rapidly made unconscious without medical supervision.

Second, critics point to the erosion of the Chemical Weapons Convention. That pact prohibits the development, production, stockpiling, and use of all chemical weapons, defined as weapons that depend on direct chemical toxicity for their effects. This ban explicitly applies to nonlethal as well as lethal chemicals. It has a significant loophole, however: it permits the use of these weapons for law enforcement. For this reason, most analysts consider the Russian use of a fentanyl derivative to have been legal. Yet, it would be clearly illegal for such an agent to have been developed, produced, stockpiled, or used for military combat. The fact that the Russian special forces appear to have had a stockpile of this agent suggests a military as well as law enforcement interest. It is also clear that the U.S. military has been interested in calmatives for some time.[3] Whether the United States has gone beyond permitted research into prohibited development remains an open question. Unfortunately, recent U.S. work appears to be classified, and it is not possible to determine how far the U.S. military has progressed.

Military interest in such knockout gases is understandable in a time in which military forces are commonly deployed for nontraditional roles, such as peacekeeping, counterterrorism, and others in which combatants and noncombatants are intermixed and in which minimizing civilian casualties is politically important. An unfortunate side effect may be the development of considerable pressure to relax the ban on chemical weapons, which is rightly seen as an important milestone in arms control. Because calmatives in combat will inevitably cause casualties, it may be very difficult to maintain a distinction between them and traditional lethal chemical weapons when the ranges of lethality overlap. For instance, mustard gas, the most heavily used and most effective chemical weapon in World War I, was lethal only in a few percent of casualties.

It will also be impossible to confine pharmaceutical weapons to responsible states that will use them with due respect for human rights and humanitarian law. Despotic regimes, terrorists, and criminals will be sure to find unpleasant uses for nonlethal chemical weapons, perhaps more so than responsible states: They will be less constrained to use them in a way that would minimize
fatalities or respect human rights. This is especially likely because it is so easy for a prepared terrorist, soldier, or criminal (with gas masks or with chemical antidotes) to defend against the effect of such weapons while it is virtually impossible for an unsuspecting civilian population to do so.

ENDNOTES


3. Voluminous documentation of U.S. military interest in calmatives has been developed by use of Freedom of Information Act requests by the Sunshine Project and is available at http://www.sunshine-project.org.

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