

SELECTED TOPICS

Students' learning outcomes

After studying this chapter, students will be able to:

1. [B-12-V-01] Explain the role of biological warfare with examples.
2. [B-12-V-02] Describe how biodefense could work to protect from biological warfare with examples.
3. [B-12-V-03] Examine the hype behind the omics “genomics, transcriptomics, proteomics, metabolomics”. To what extent is it valid or overblown?
4. [B-12-V-04] Explain synthetic biology with examples.

14.1 BIOLOGICAL WARFARE

Man has a long history of engaging in wars or conflicts to weaken or defeat his enemies. Wars occur in different ways and use different strategies and tools, such as traditional warfare by means of armies, guerrilla warfare using unconventional methods, and modern types like cyber warfare and biological warfare.

Biological warfare is the use of harmful biological agents like bacteria, viruses, or toxins to intentionally cause disease and death in humans, animals, or plants. These agents are used as weapons to attack and weaken enemies during conflicts or wars. The goal is to spread illness and fear, create disturbance in societies, and damage economies. Understanding the role of biological warfare is crucial for developing effective biodefense strategies and for recognizing its impact on society.

Historical Overview of Biological Warfare

The use of biological warfare goes back to ancient times when early civilizations used biological methods to spread disease among their enemies. For example, in 590 BC, the Assyrians, an ancient civilization in the region of Mesopotamia, which is present-day Iraq, used biological weapons in war. They were believed to have poisoned enemy water supplies with bread infected with Ergot, a fungus that caused hallucinations and paralysis. Another example was in 1347 when the Mongol army threw plague-infected bodies over the walls of Caffa, a city in Ethiopia. This act resulted in spread of the Black Death in Europe, killing millions and causing widespread social and economic chaos.

During the Spanish attempts to settle and take control of the Americas in the 16th Century, European colonizers purposely spread smallpox to indigenous people. The disease caused many deaths and weakened these communities, making it harder for them to resist control on their land and resources. In 1763, British forces deliberately gave blankets contaminated with smallpox to Native American tribes during the French and Indian War. This act of biological warfare led to severe outbreaks of the disease, causing significant suffering and loss of life.

In the 20th century, advancements in science and technology enabled more sophisticated forms of biological warfare. During World War I, Germany experimented with using anthrax and glanders to infect livestock and horses used by the Allied forces. Although these efforts had limited success, but they marked the beginning of the modern biological warfare. In World War II, Japan conducted horrific experiments, spreading diseases like plague, cholera, and anthrax in China. These experiments caused the deaths of thousands of people and highlighted the deadly potential of biological weapons. The Cold War period of geopolitical tension between the United States and the Soviet Union and their allies, witnessed development of huge biological weapon programs, including pathogens like smallpox and tularemia. In the Soviet Union, an accidental release of anthrax spores from a military facility led to an outbreak that killed many people. This incident underscored the dangers of biological weapons research and the potential for accidental release. In 2001, letters containing anthrax spores were mailed to several media outlets and government offices in the United States. The attacks killed five people and infected many, causing widespread fear and prompting a significant response from public health and law enforcement agencies.

Current State of Biological Warfare

Biological warfare remains a significant threat in today's world due to advancements in technology and biotechnology. Modern biotechnology allows for the genetic modification of pathogens to increase their virulence, resistance to treatments, and ability to spread.

A modern concern regarding biological warfare arose when researchers created a synthetic version of the polio virus in 2002, sparking worries about the possibility of developing synthetic pathogens that could be utilized as bioweapons. Another such example relates to controversial experiments that modified the H5N1 avian influenza virus to increase its transmission among mammals, thus initiating discussions on the dangers associated with dual-use research.

Governments around the world continue to research and develop measures to defend against biological attacks. International agreements, such as the Biological Weapons Convention (BWC), aim to prevent the development and use of biological weapons. However, the risk persists due to the dual-use nature of biological research, where scientific advancements can be used for both peaceful and military purposes.

Impacts of Biological Warfare

Biological warfare has profound and far-reaching impacts on society, causing severe health crisis, economic losses, social unrest, and political instability. The planned release of pathogens can lead to widespread illness and death, destroying healthcare systems and causing long-term public health challenges. Economically, biological attacks can damage industries, effect trade, and lead to significant financial losses, particularly in agriculture and livestock sectors. Socially, the fear and panic induced by biological warfare can lead to widespread anxiety, chaos and breakdowns in community trust. Politically, the use of biological weapons can cause tension in international relations, lead to conflicts, and demand increased security measures and regulatory responses. The societal impact of biological warfare requires urgent need for global cooperation in biosecurity and public health preparedness to prevent and mitigate these undesirable consequences.

Pathogens as Weapons of Biological Warfare

Biological agents used in warfare include bacteria, viruses, fungi, and toxins. These agents can be spread in various ways to infect large populations.

1. **Bacteria:** *Bacillus anthracis*, which causes anthrax, is a notable example. There are three forms of anthrax infection i.e., cutaneous (skin), inhalation (lungs) and gastrointestinal (stomach and intestine) that can cause severe illness and death. Anthrax can be easily spread through inhaling the spores, eating contaminated meat, or having the spores come in contact with the skin.

2. **Viruses:** The smallpox virus, which causes a highly spreadable and deadly disease, has been considered for use as a biological weapon due to its potential to cause widespread panic and mortality.



Fig. 14.1: Human skin infected with anthrax causing bacteria

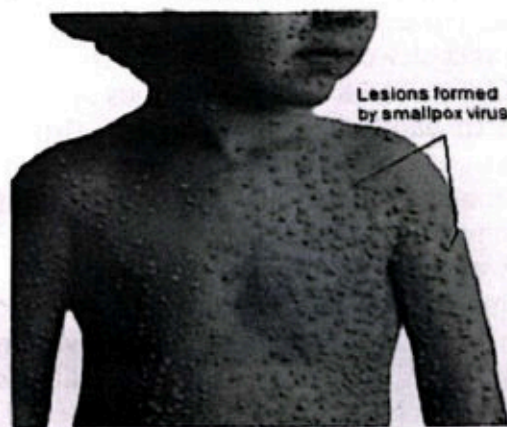


Fig. 14.2: Child effected with the smallpox virus

Delivery Methods

Biological agents can be delivered through various means, including aerosols, contaminated food or water, and infected vectors like insects. Some common methods are discussed below:

1. **Aerosols:** Aerosols can be used to infect large groups of people quickly. Aerosolization is a method where pathogens are dispersed in the air in tiny droplets. This allows them to be inhaled by people, leading to respiratory infections. The delivery vehicle in deliberate aerosolization could range from a cluster of small bombs to a simple leaf blower or nebulizer. A notable example is the accidental release of anthrax spores in Soviet Union in 1979, causing numerous deaths.
2. **Food and Water Contamination:** Deliberately contaminating food or water supplies can cause outbreaks of diseases like cholera or typhoid fever. This method spreads the infection when people consume the contaminated items. One example is *Salmonella* bacteria, which can be purposely introduced into food supplies, causing widespread illness among those who eat contaminated food.
3. **Infected Vectors:** Insects such as mosquitoes or fleas can be deliberately infected with disease-causing organisms like malaria parasites or plague bacteria which are then used to spread these diseases.
4. **Direct Contact:** Direct contact with infected individuals or contaminated surfaces can also be used to spread pathogens. For instance, during the 2014 *Ebola* outbreak in West Africa, the virus rapidly spread as people came into physical contact with infected patients or handled the bodies of those who had died from the disease without proper protective measures.

Types of Biological Weapons

Biotoxins

Biotoxins are toxic substances produced by living organisms. Examples include botulinum toxin, produced by the bacterium *Clostridium botulinum*, which is extremely potent and can cause paralysis and death.

Bioregulators

Bioregulators are chemicals that change how the body works. They can be used to mess up important processes in the body, making people very sick or even causing death. Some bioregulators can affect the nervous system, leading to paralysis or severe pain. Others might change the way the immune system works, making it hard for the body to fight off infections. These types of chemicals could be used as weapons to harm or disable people. An example of a bioregulator is ricin, a toxic protein from the castor bean plant. Even in small amounts, ricin can cause severe illness or death if inhaled, ingested, or injected, making it a potential bioweapon.



Fig. 9.3: Gram positive bacterium *Clostridium botulinum* that produces botulinum toxin



Fig. 9.4: Ricin is a highly toxic compound found in the castor bean seeds

Biovectors

Biovectors are living organisms, like insects or rodents, that can carry and spread diseases. For example, fleas can be used as bio vectors. If these fleas are infected with some pathogen e.g. plague causing bacteria *Yersinia pestis*, they can spread the disease to humans. This method has been used in biological warfare to intentionally make people sick by releasing these infected fleas into populations.

14.2 BIODEFENSE

Biodefense encompasses measures taken to protect people against the threat of biological warfare and bioterrorism. The principles of biodefense are guidelines and strategies designed to protect against biological threats, whether from natural outbreaks or intentional attacks. These principles ensure preparedness, prevention and effective response to biological warfare incidents. The main principles include:

Surveillance and Detection

Surveillance and detection are critical for early identification of biological threats. Effective surveillance systems help monitor and track the spread of infectious diseases. Monitoring disease outbreaks and unusual patterns can help detect a potential biological attack. For example, during the 2001 anthrax attacks in the United States, rapid identification of anthrax spores in mailrooms helped controlling the spread.

The detection technologies can be used to identify specific pathogens. Advanced biosensors can detect the presence of biological agents in the environment. For instance, tiny biosensors carried by soldiers on potential battlefields could reveal presence of threat molecules.

Prevention

Preventive measures aim to reduce the risk of biological attacks and limit their impact. Vaccines are a primary defense against biological agents. For example, the smallpox vaccine has been used to protect against potential smallpox outbreaks, and there are ongoing efforts to develop vaccines for other high-threat pathogens like anthrax and Ebola. Measures such as quarantine, travel restrictions, and sanitation can prevent the spread of infectious diseases. During the COVID-19 pandemic, these strategies were essential in controlling the spread of virus.

Preparedness

Preparedness involves setting up plans to respond to biological incidents with established protocols. Regular training for healthcare professionals and emergency responders is essential to effectively manage biological threats and ensure readiness during emergencies.

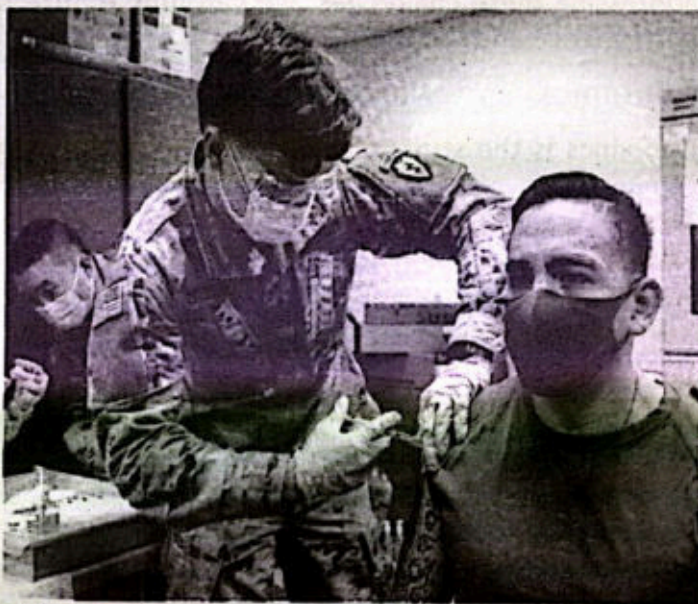


Fig. 9.5: Vaccination campaigns can help prevent the spread of infectious diseases among soldiers.

Research and Development

Research and development in biodefense focuses on creating medical countermeasures such as drugs, vaccines, and diagnostic tools to combat biological agents effectively. Innovations in biotechnology play a crucial role in enhancing detection, prevention, and treatment of biological threats, ensuring advancements in public health preparedness and response capabilities. Advances in synthetic biology enable the creation of new treatments and rapid vaccine development. For example, synthetic biology helped in developing mRNA vaccines for COVID-19.

Biosafety and Biosecurity

Biosafety and biosecurity are important for handling dangerous pathogens safely. Laboratories must follow strict safety rules to prevent accidents or the accidental release of pathogens. Also, oversight of research that could be used for both good and bad purposes help ensure safe and responsible practices.

14.3 OMICS

In recent years, the scientific fields of 'omics' including genomics, transcriptomics, proteomics, and metabolomics have generated significant interest in the scientific community and beyond. These fields promise to revolutionize our understanding of biology and medicine by providing comprehensive insights into the structure, function, and dynamics of biological systems. However, it's important to critically assess whether the claims about these technologies are valid or exaggerated. Although each field has advanced significantly with practical applications, it's important to keep a balanced perspective. The hype about these technologies should be balanced with a realistic view of their current abilities and challenges. Through ongoing research and addressing these challenges, we can fully realize the potential of the 'omics' fields, benefiting both science and society.

Genomics

Genomics is the study of the complete set of DNA of an organism, including all of its genes. Genomics involves sequencing, mapping, and analyzing genomes to understand genetic variations and their effects on health and disease. The most significant example and application of genomics is the Human Genome Project that was completed in 2003. This project mapped the complete human genome, identifying all the genes present in human DNA. It has paved the way for personalized medicine, where treatments can be tailored based on genetic makeup of an individual. Another example is genetic testing that provides information about ancestry, traits, and potential health risks based on genetic profile of an individual.

While genomics has certainly provided valuable insights and applications, some claims about its capabilities may be exaggerated. For instance, the promise of curing all genetic diseases solely through genomic information is still far from being realized. Ethical concerns, such as genetic privacy and discrimination, also need careful consideration.



Fig. 9.6: Commercially available genetic testing kits

Transcriptomics

Transcriptomics studies all RNA molecules in a cell or group of cells. It focuses on how these changes affect RNA, showing their effects. Transcriptomic analysis can reveal the expression levels of genes in cancer cells compared to normal cells, helping identify potential targets for treatment. In agriculture, transcriptomics can be used to study how plants respond to different environmental conditions or stresses, such as drought or disease. By analyzing which genes are activated or deactivated in response to these conditions, researchers can develop crops that are more resilient and productive in challenging environments. Transcriptomics provides a deeper understanding of gene function and regulation. However, it is important to recognize that gene expression is only one part of the complex regulatory networks within cells. The interpretation of transcriptomic data requires careful validation and integration with other 'omics' data.

Proteomics

Proteomics is the large-scale study of proteins, including their structures and functions. Since proteins are the main functional molecules in cells, proteomics provides insights into cellular processes and disease mechanisms. Proteomic studies have identified biomarkers for diseases such as Alzheimer's and cancer, which can aid in early diagnosis and monitoring. Understanding protein interactions and functions helps in the design of new drugs that can target specific proteins involved in diseases. Proteomics has made significant contributions to biomedical research. However, the complexity of the proteome, with its dynamic modifications and interactions, poses challenges. High costs and technical limitations also restrict the widespread application of proteomics in clinical settings.

Metabolomics

Metabolomics is the study of the complete set of small-molecule metabolites found within a biological sample. Metabolites are the end products of cellular processes, and their analysis can provide a picture of the physiological state of a cell or organism. Metabolomic studies can identify how different diets affect metabolism and health, leading to personalized nutrition plans. Metabolomics can be applied in disease diagnosis where metabolomic profiles can help diagnose metabolic disorders and monitor disease progression.

Metabolomics offers a comprehensive view of metabolism, but it also faces challenges such as the diversity of metabolites and the influence of external factors on metabolic profiles. While promising, the field requires further development to overcome these hurdles and fully realize its potential.

14.4 SYNTHETIC BIOLOGY

Synthetic biology is an interdisciplinary field that combines biology, engineering, and computer science to design and construct new biological parts, devices, and systems, or redesign existing biological systems for useful purposes. Synthetic biology involves the design and construction of new biological entities such as enzymes, genetic circuits, and cells. This rapidly advancing field holds the potential to revolutionize medicine, agriculture, and environmental management.

Synthetic biology operates on several key principles that guide the design and construction of new biological systems. One of the key principles of synthetic biology is the standardization of biological parts, known as BioBricks. These standardized genetic parts can be easily assembled in various combinations to create new biological systems. Other essential principles include modularity, orthogonality, abstraction and automation.

Applications of Synthetic Biology

Synthetic Microbes: Scientists have engineered microorganisms like bacteria and yeast to produce valuable chemicals, fuels, and pharmaceuticals. For instance, genetically modified bacteria can efficiently convert sugar into biofuels such as ethanol, offering a renewable alternative to fossil fuels. By inserting the human insulin gene into *E. coli*, bacteria can produce insulin that is harvested and purified for medical use. Similarly, engineered yeast strains are used to produce many important drugs more cost-effectively than traditional methods. Bioremediation is another application where engineered microorganisms can be used to clean up environmental pollutants. For example, bacteria can be modified to degrade oil spills or break down plastic waste.

Gene Editing: Gene editing involves precisely modifying DNA to correct genetic disorders in humans, enhance agricultural crops, improve livestock health, advance biomedical research, and aid conservation efforts for endangered species. Gene editing tools enable targeted changes to specific genes, offering potential treatments for diseases such as sickle cell anemia, enhancing crop resistance and nutrition, and creating disease-resistant livestock. For example, golden rice is engineered to produce beta-carotene which is essential for producing vitamin A, to combat vitamin A deficiency in developing countries. In biomedical research, gene editing helps study disease mechanisms and develop new therapies.

Bio-Sensing Devices: Synthetic biology has enabled the development of biological sensors that detect specific molecules or environmental conditions. These sensors often use genetically engineered cells that produce detectable signals in response to target substances. For example, biosensors are used to detect contaminants in water sources or to monitor glucose levels in diabetic patients, offering rapid and accurate diagnostic tools.

Biological Computers: Biological computers are devices that use biological components, like cells and proteins, to perform computations instead of traditional electronic circuits. These computers can mimic processes found in living organisms, such as communication between cells or the processing of biological signals. Researchers are exploring their potential for tasks like medical diagnostics, environmental monitoring, and even enhancing our understanding of biological systems. Biological computers offer distinct advantages such as requiring significantly less energy and operating efficiently in conditions where conventional computers may face limitations. For instance, they can be designed to function within biological environments, such as the human body, where they could assist in detecting diseases at the cellular level which is something traditional computers can not do.

EXERCISE

Section I: Multiple Choice Questions

Select the correct answer:

1. Which international treaty aims to prevent the development and use of biological weapons?
A. Paris Agreement
B. Kyoto Protocol
C. Biological Weapons Convention
D. All of above

2. How has modern biotechnology impacted biological warfare?
 - A. It has facilitated the genetic modification of pathogens.
 - B. It has promoted international cooperation in biodefense.
 - C. It has decreased the lethality of biological agents.
 - D. It has restricted the development of new bioweapons.
3. Aerosolization is the delivery method for spread of biological agents through.
 - A. Dropping contaminated blankets
 - B. Use of infected insects as vectors
 - C. Dispersing pathogens in tiny droplets in the air
 - D. Contaminating food and water supplies
4. Surveillance and detection are critical in biodefense because.
 - A. They enable rapid identification and containment of biological threats.
 - B. They ensure complete eradication of all biological agents.
 - C. They eliminate the need for vaccination programs.
 - D. They guarantee 100% accuracy in identifying bioterrorists.
5. The dual-use nature of biological research can be explained as
 - A. It involves both peaceful and military applications
 - B. It focuses on natural outbreaks only
 - C. It is limited to genomic studies
 - D. It excludes ethical concerns
6. What was the result of the accidental release of anthrax spores from a Soviet military facility in 1979?

A. Outbreak of plague	B. Widespread cholera
C. Extensive smallpox cases	D. Numerous deaths
7. Which principle of biodefense involves setting up plans and protocols to respond to biological incidents

A. Surveillance and Detection	B. Prevention
C. Preparedness	D. Research and Development
8. What is the role of synthetic biology in bioremediation?
 - A. Producing biofuels from renewable sources
 - B. Cleaning up environmental pollutants
 - C. Enhancing crop resistance
 - D. Improving livestock health
9. What sets metabolomics apart from genomics and transcriptomics?
 - A. It studies the complete set of DNA of an organism
 - B. It focuses on all RNA molecules in a cell
 - C. It examines the complete set of small-molecule metabolites
 - D. It analyzes the structures and functions of proteins
10. Which scientific field studies the complete set of DNA of an organism, including all of its genes?

A. Proteomics	B. Transcriptomics
C. Genomics	D. Metabolomics

Section II: Short Answer Questions

1. What is biological warfare, and how does it utilize harmful biological agents?
2. Provide any two historical examples of biological warfare from ancient times to the 20th century.
3. Explain the impact of biological warfare on society, including health, economic, and political consequences.
4. Name three types of biological agents used in warfare and give examples of each.
5. How has modern biotechnology impacted biological warfare? Discuss with one example.
6. List the principles of biodefense. Why preparedness is considered a crucial principle of biodefense.
7. What are the main goals of international agreements like the Biological Weapons Convention?
8. Explain the concept of biosafety and biosecurity in the context of handling dangerous pathogens.
9. What is gene editing. How it contributes to both biodefense and potential biological threats?
10. What are genetic testing kits? Give any one application.

Section III: Extensive Answer Questions

1. Explain the concept of biological warfare and provide two historical examples where biological agents were used in conflicts.
2. Describe in detail different methods used to deliver biological agents during warfare. Give an example of each method.
3. Discuss the impact of biological warfare on societies, including its effects on health, economy, and politics. Provide examples to support your answer.
4. Critically analyze the ethical considerations surrounding the development and potential use of genetically modified pathogens as bioweapons, weighing the problem of dual-use of research and implications for global biosecurity.
5. What are bioregulators and biovectors in the context of biological weapons? Give examples of each and explain their role in warfare.
6. Explain how modern biotechnology has influenced the development and use of biological weapons. Provide two examples to illustrate your answer.
7. What are 'omics? Briefly describe genomics, proteomics, and metabolomics, and explain their potential applications in understanding biological warfare agents.
8. Examine the role of surveillance and detection in biodefense. Why are these aspects crucial, and what technologies are used for early identification of biological threats?