JSTO in the News

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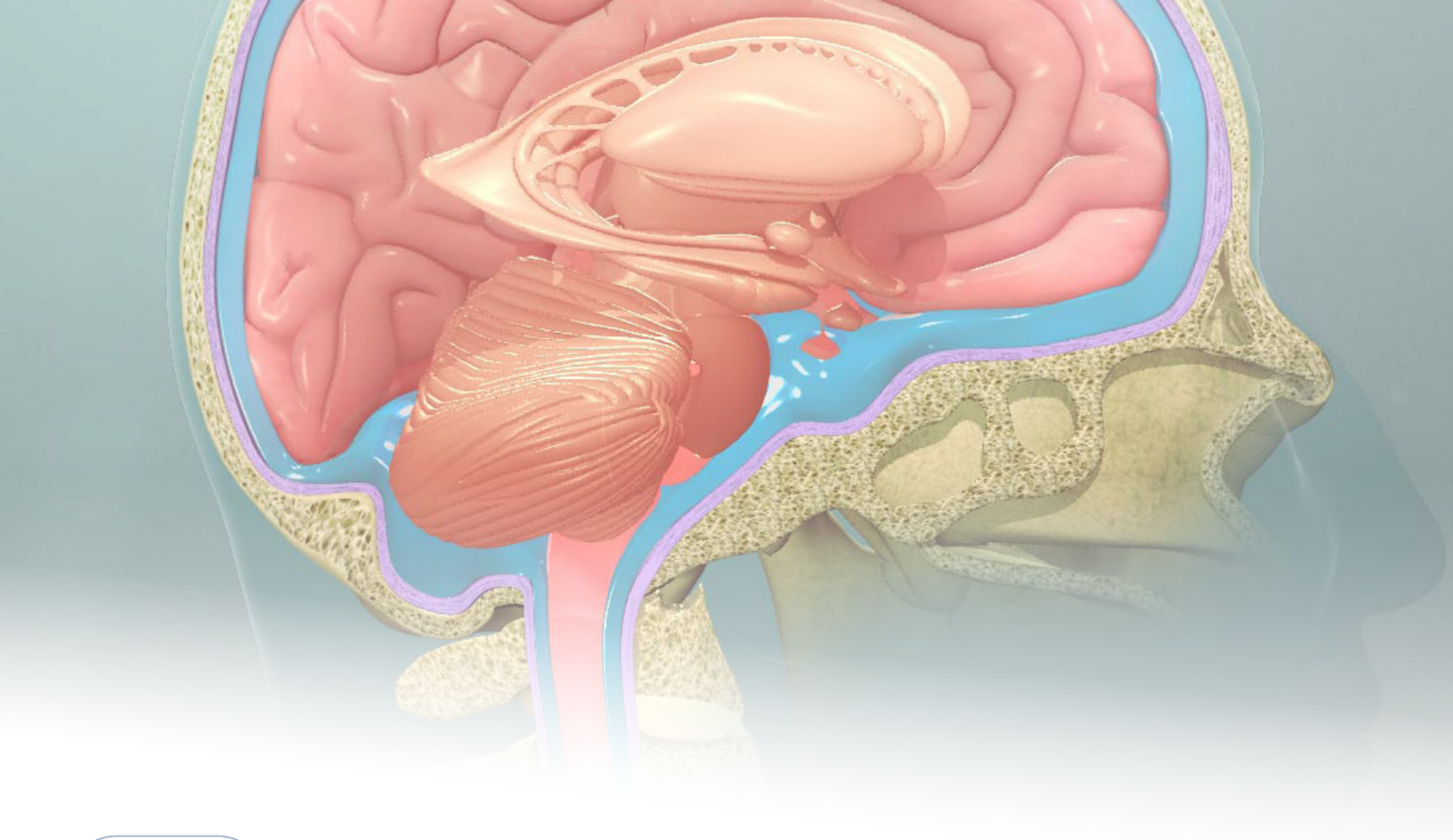
Release the Helpful Viruses

Brain Games



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Joint Science and Technology Office for the
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Front cover: Soldiers test their knowledge of chemical, biological, radiological and nuclear (CBRN) threats at the CBRN lane during the 25th Infantry Division Non-Commissioned Officer/Soldier of the Year 5-day competition. Soldiers have to react to chemical attacks, perform first aid for nerve agent injuries, identify chemical agents using an M256A1 Chemical Agent Detector kit, and submit a CBRN 1 Report. (U.S. Army photo by Sgt. Sarah D. Williams)

Inside cover: The central nervous system organs – brain and spinal cord – are physically protected by meninges, skull bones, and spinal vertebrae, while chemically shielded by the blood-brain barrier. (Scientific Animations image)

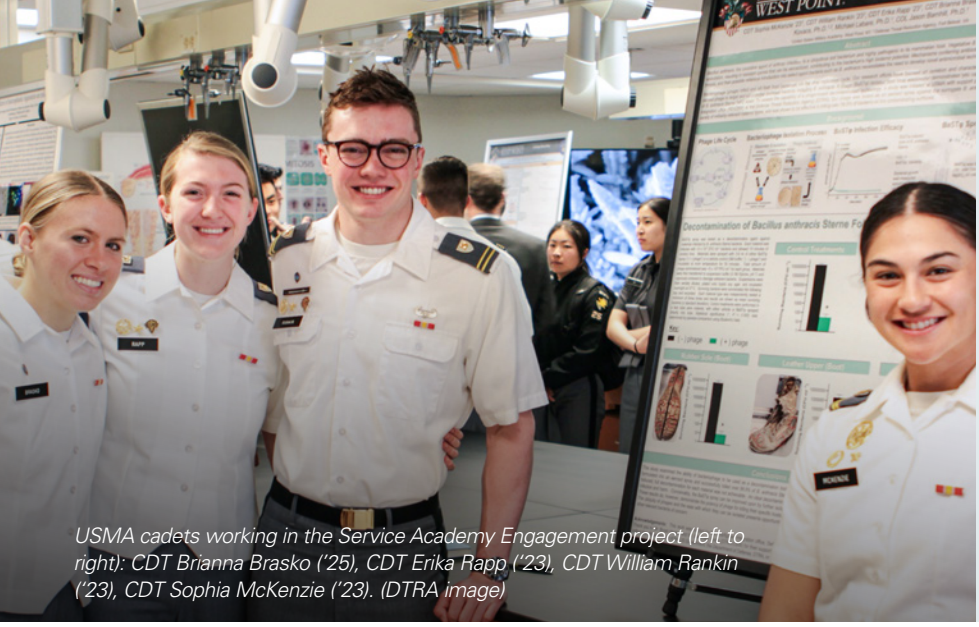
Back cover: Bacteriophages are viruses that infect bacteria. They do this by injecting genetic material into the bacteria, which then takes the DNA and incorporates it into its own genome for replication. (Flickr image by ZEISS Microscopy)

Release the (HELPFUL) Viruses

Exploiting the natural ability of viruses to act as an equipment decontamination method for bioweapons

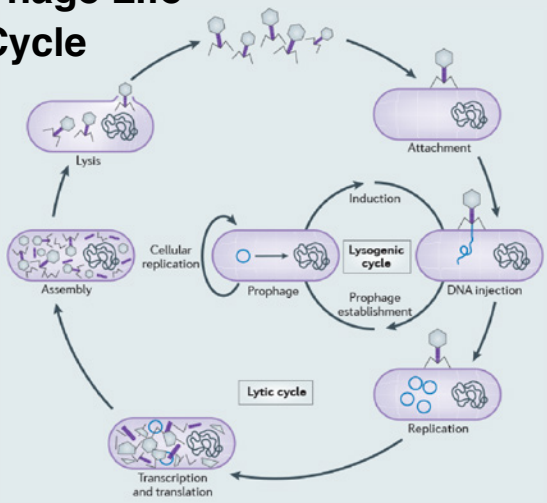
At the U.S. Military Academy (USMA) at West Point, New York, cadet researchers are working to demonstrate the natural bacteria-killing ability of bacteriophages ("phages") to create a potential new biothreat decontamination tool for Joint Force equipment. Phages are viruses that infect bacteria and use their host's internal cellular machinery to replicate, which then leads to the bacteria's death. Phage therapy has been used to successfully treat drug-resistant bacterial infections where traditional antibiotic therapy had failed.

STRUCTURE OF BACTERIOPHAGE



USMA cadets working in the Service Academy Engagement project (left to right): CDT Brianna Brasko ('25), CDT Erika Rapp ('23), CDT William Rankin ('23), CDT Sophia McKenzie ('23). (DTRA image)

Phage Life Cycle



Salmond & Fineran, 2015. Nature Reviews, Microbiology. *(DTRA image)*

The Defense Threat Reduction Agency's (DTRA) Chemical and Biological Technologies Department in its role as the Joint Science and Technology Office (JSTO) for the Chemical and Biological Defense Program is investing in this Service Academy Engagement project at the USMA to determine if phages can act as an equipment-specific decontamination method for bioweapons. This endeavor is part of DTRA JSTO's role to anticipate emerging threats the Joint Force may face in the future and prepare to counter them.

For this project, the phage's bacteria-killing effect was assessed for its ability to treat contaminated surfaces. The cadets used a solution containing phage to destroy the anthrax-causing *Bacillus anthracis* applied to military-relevant surfaces, such as boots, uniform fabric, and stainless steel. It is important to develop a method to decontaminate surfaces coated with *B. anthracis* because it is a natural bioweapon. It's a human pathogen, its spore stage is highly resistant to heat and most cleaning methods, and it can be become antibiotic resistant.

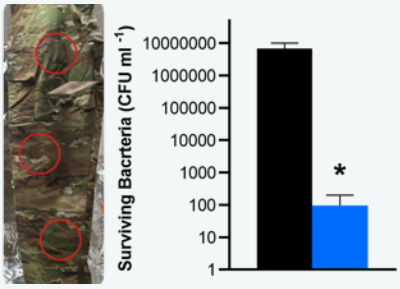
The phage used in the study was isolated from a sewage plant near the USMA. The cadet researchers chose this phage because of its demonstrated lytic capability (disintegrating a cell by rupturing its cell wall or membrane) and complete kill of *B. anthracis* Sterne strain bacteria, and the inhibited outgrowth of *B. anthracis* Sterne from spores by 75% in different tests. The West Point cadets video recorded portions of their project and received a favorable response when they presented the results of their study during the USMA Project Day event.

This phage decontamination study may lead to additional research on using phages as a reliable treatment tool for the Joint Force to combat bio threats where traditional antibiotics can fail. ●

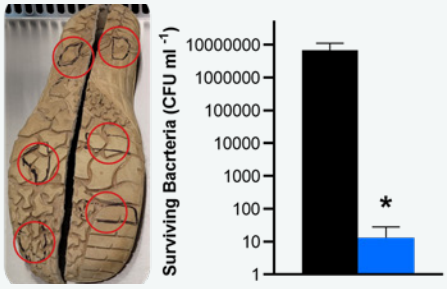
Decontamination of *Bacillus anthracis* Sterne Following BaSTϕ Spray Treatment

Key: (-) phage (+) phage

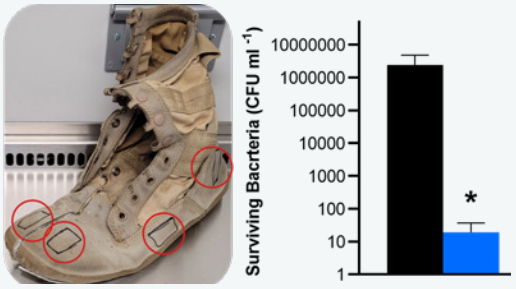
Pants



Rubber Sole (Boot)



Leather Upper (Boot)



POC: Bryan Horner, bryan.j.horner.civ@mail.mil

BRAIN GAMES

Researchers are investigating methods to deliver life-saving pharmaceuticals through the brain's selective barrier

Chemical defense researchers are working on a way to deliver effective pharmaceuticals across the blood-brain barrier (BBB) that protects the brain and spinal cord of the central nervous system (CNS) to combat the serious threat that chemical warfare agents (CWAs) pose to the Joint Force. The BBB is a selective gate-keeper to the brain and spinal cord that allows useful small molecules like glucose to cross into the CNS while protecting it from some harmful toxins, bacteria, and viruses that can circulate through the rest of the body.

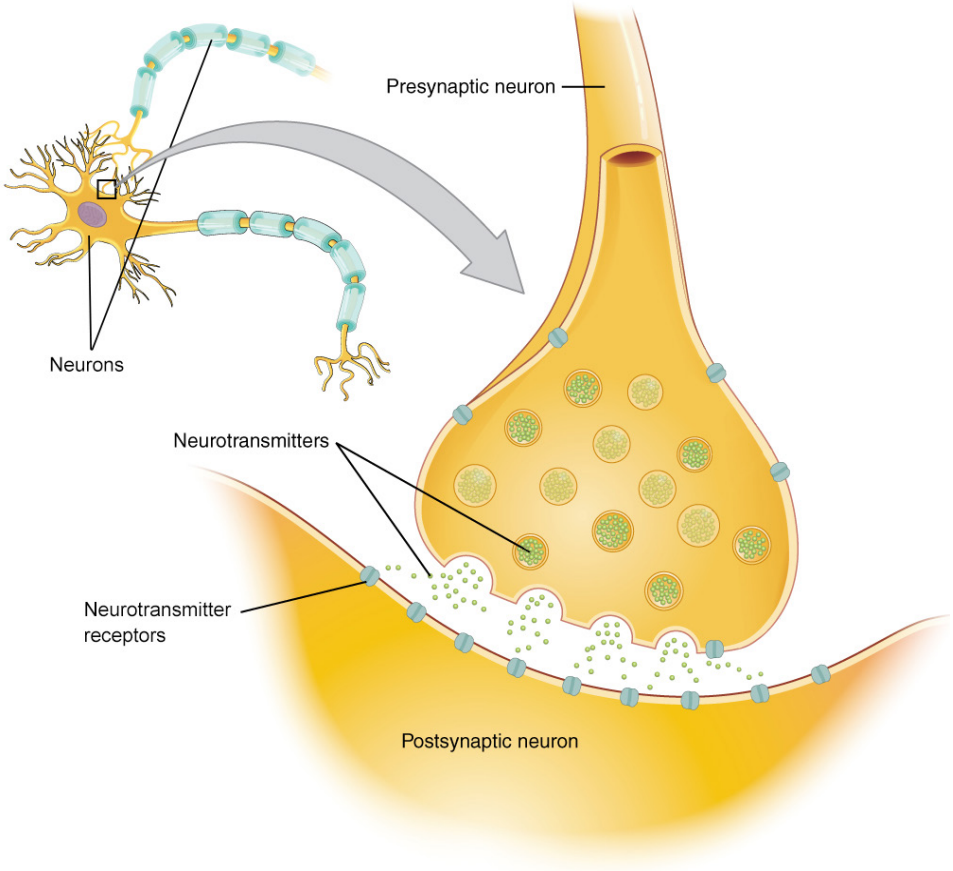


Illustration of the synapse between two neurons (nerve cells), and the release of neurotransmitters from one neuron to another. Neurotransmitters, such as acetylcholine, are chemicals released by nerve cells to transmit signals. (OpenStax image)

Organophosphate nerve agents (OPNAs), such as soman and sarin, and organophosphate (OP) pesticide poisoning cause severe symptoms throughout the human body, including those represented by the acronym SLUDGE: salivation, lacrimation (tears), urination, defecation, gastrointestinal upset, and emesis (vomiting). Many of the most serious symptoms are a result of OPNAs and OP pesticides blocking the function of acetylcholinesterase (AChE), which is a critical enzyme that is responsible for recycling and breaking down the neurotransmitter acetylcholine.

A neurotransmitter is a chemical released by nerve cells to transmit signals to other nerve cells. When OPNAs or OP pesticides render AChE dysfunctional, acetylcholine builds up to dangerously high levels and results in cholinergic crisis exhibiting the SLUDGE symptoms. The overstimulation in the synapses between neurons in the brain and CNS disrupts other neurotransmitters and ultimately causes severe seizures and even death if left untreated.

The current standard of care for OPNA/OP poisoning includes a pharmaceutical called pralidoxime or 2-PAM, which is effective peripherally in the body—meaning it acts everywhere except in the CNS. As an AChE reactivator, 2-PAM reverses the chemical damage of the AChE enzyme caused by the OPNA/OP pesticide poisoning and brings the acetylcholine down to its proper level.

The Defense Threat Reduction Agency's (DTRA) Chemical and Biological Technologies Department in its role as the Joint Science and Technology Office (JSTO) for the Chemical and Biological Defense Program is investing in research at industry, academia, and government laboratories to apply a variety of approaches to deliver medical countermeasures (MCMs) across the BBB and into the CNS. One such effort is to possibly attach 2-PAM to a molecule known to be able to cross the barrier, such as glucose, as an effective treatment for OPNA/OP pesticide poisoning. There are MCMs that can cross the BBB, but they largely treat just the symptoms and do not eliminate or fully reverse the effects of the OPNA/OP pesticide poisoning as 2-PAM does.

DTRA JSTO is transforming CB science and technology to prepare for current chemical and biological threats and anticipate the emerging threats the Joint Force may face in the future. Recent advances in materials science and nanotechnology offer many opportunities to expand the ways that pharmaceuticals are delivered. New and advanced materials like nanomaterials and

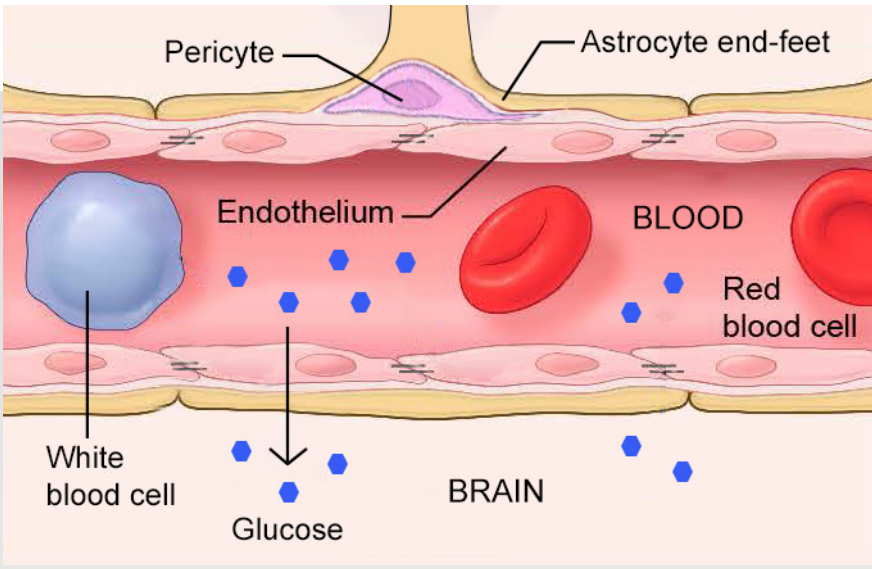


Illustration of the blood-brain barrier (BBB). The BBB is highly selective and allows certain large molecules, such as insulin, and small molecules, such as glucose, to pass through; but it may also inadvertently allow undesirable heavy metals into the brain's environment, which at high enough concentrations can cause damage to the nervous system. (National Institutes of Health Medical Arts image)

biomaterials can be used to stabilize drugs and vaccine formulations, as well as target them to different areas of the body. A relevant example: both of the messenger RNA (mRNA) vaccines approved for use in humans against COVID-19 would not have been successful without the nanoparticle formulation to encapsulate and protect the mRNA. (To read this article, see the link in the sidebar.)

DTRA-JSTO researchers across academic, industry, and government laboratories are working to apply a variety of different scientific nanotechnology and formulation approaches to deliver 2-PAM across the BBB and into the CNS:

- Nanoparticle encapsulation approaches like those in the mRNA vaccine
- Encapsulation techniques that specifically target and traffic the MCM across the BBB
- Fusing 2-PAM to other small molecules known to cross the BBB, such as glucose

Preliminary studies have shown the delivery of 2-PAM into the CNS protects against OPNA intoxication.

Preliminary studies have shown the delivery of 2-PAM into the CNS protects against OPNA poisoning. Current research invested in by DTRA-JSTO focuses on using the FDA-approved 2-PAM antidote as the cargo or payload for each of these drug-delivery techniques. If successful, these platform approaches may also be applied to the next generation of MCMs against OPNAs. The potential for a nanoparticle-based reformulation to increase the effectiveness and improve this OPNA antidote could have therapeutic benefits to both the Joint Force and others suffering from OP pesticide poisoning. ●

Chemical and Engineering News: "Without these lipid shells, there would be no mRNA vaccines for COVID-19"

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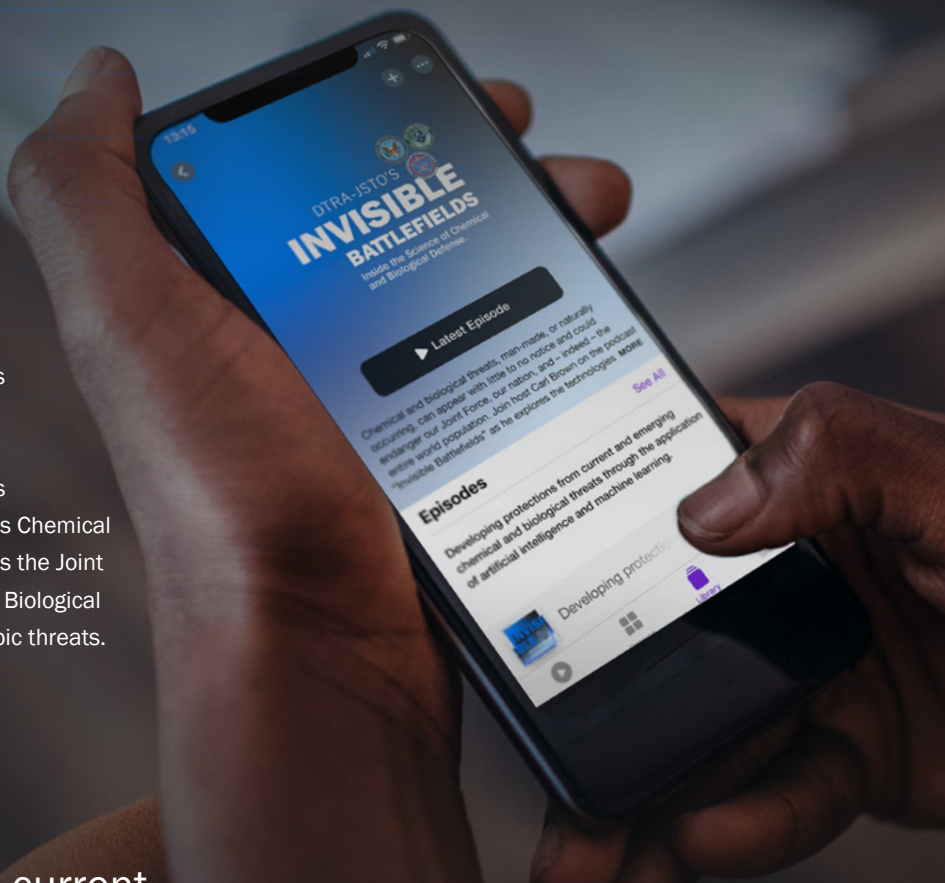
Invisible Battlefields: Inside the Science of Chemical and Biological Defense



Invisible Battlefields is a podcast meant to engage with the chemical and biological defense community and is another platform providing a voice highlighting the continuous collaborations that the DTRA-JSTO program explores with industry partners, academia, and other government agencies concerning chemical and biological threats and protecting our Joint Force against them.

Join host Carl Brown as he explores the technologies developed by the Defense Threat Reduction Agency's Chemical and Biological Technologies Department in its role as the Joint Science and Technology Office for the Chemical and Biological Defense Program to protect against these microscopic threats.

AVAILABLE NOW

EPISODE 01

Developing protections from current and emerging chemical and biological threats through the application of artificial intelligence and machine learning.

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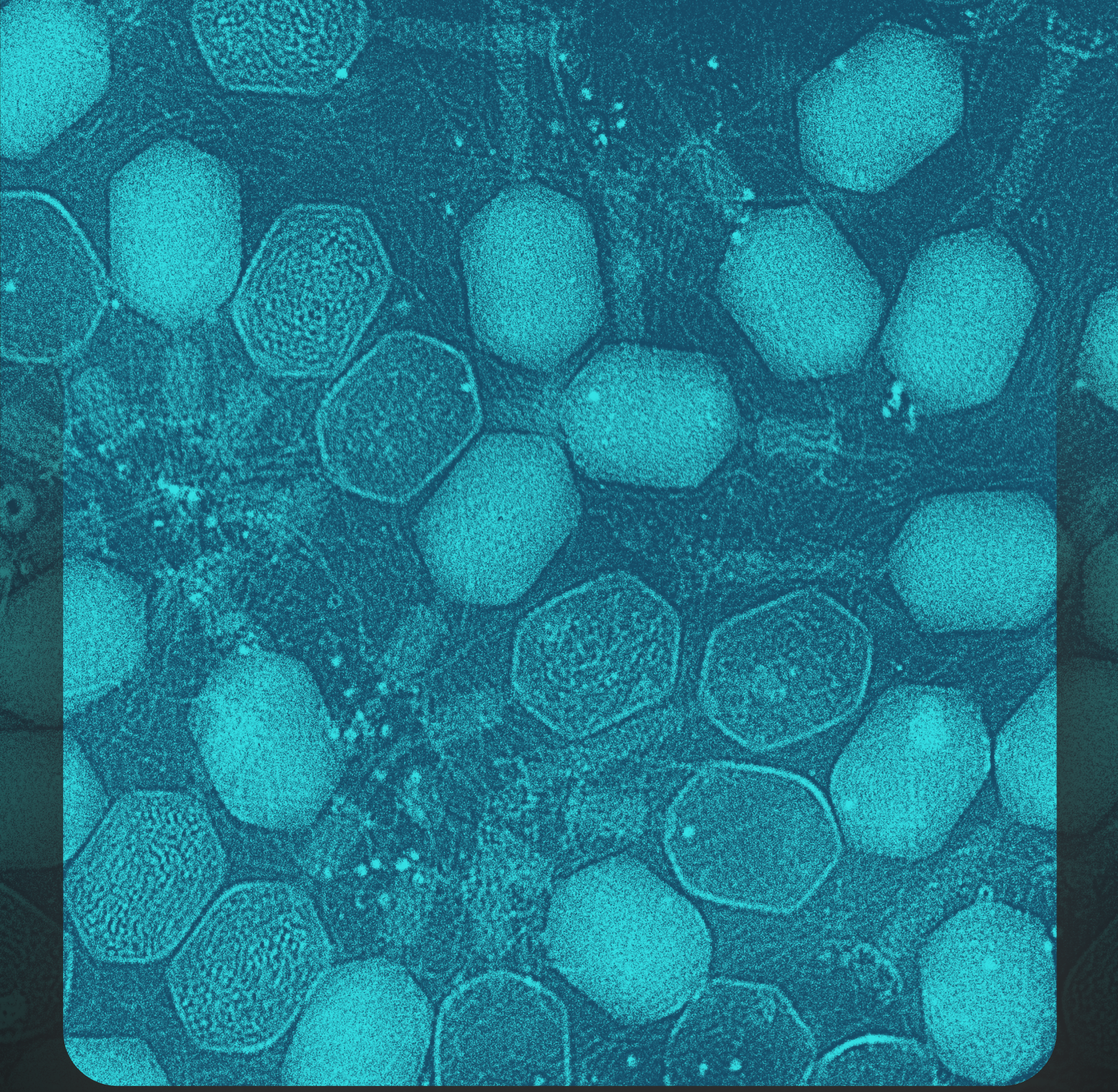

Within the Defense Threat Reduction Agency's Research and Development Directorate resides the Chemical and Biological Technologies Department performing the role of Joint Science and Technology Office for the Chemical and Biological Defense Program. This publication highlights the department's advancements in protecting the Joint Force and citizens from chemical and biological threats through the innovative application of science and technology.

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