Biosecurity: A Multi-Dimensional Challenge of Escalating Complexity and Urgency

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Biological Warfare and Bioterrorism
Biological Warfare and Bioterrorism

- **biowarfare**
  - nation states: conflict superiority and conquest

- **bioterrorism**
  - substate actors and terrorist groups (with potential sponsorship by nation states)
  - create chaos and widespread fear
  - erode distrust in leaders and institutions
  - progressive societal collapse
Biological Warfare and Bioterrorism

- civilian and military targets
- tactical and operational differences
  - scale of pathogen production and size of attack zone(s) (warfare = large; terrorism = small)
  - complexity and logistics of payload delivery systems
  - level of ‘pathogen engineering’ to circumvent opponent’s detection and control defenses
  - desire to avoid attribution and retribution risk
Strategic and Operational Objectives of Purposeful Bioattacks

- evade or confuse early detection and diagnosis
- overcome resistance to existing Rx and VacX
- overload healthcare systems and other biopreparedness response capacities
- economic disruption and societal collapse
- sever supply chains of essential goods
- multi-focal strikes with different biological agents and/or combinations of agents
- combine with cyber warfare to crash essential biodefense networks and command structure
Biological Warfare and Bioterrorism

- targets not limited to human populations
- vulnerability of agricultural livestock and crops
  - potential for major economic impact
  - endanger food security
  - enhance famine risk
  - lower threshold for retribution versus widespread attack on humans?
Biological Warfare: A Long Military History

Catapult Delivery of Infected Corpses
Deliberate Infection / Dissection to Study Disease Progression
The PRC and Unrestricted Warfare: PLA Doctrine
“Armies of the future will need weapons based on new physical principles, including genetic and psychophysical science.”

President Vladimir Putin essay, Rossiyskaya Gazeta, 2012
The Appeal of CBW for Asymmetric Warfare and Terrorism

North Korea’s Biological Weapons Program
The Known and Unknown
Hyun-Kyung Kim
Elizabeth Philipp
Hattie Chung
Biological Warfare

- Strategic perspectives differ among military planners in different nations on tactical value of offensive biothreats.
- Illegal if used by signatory States to the BWC, but overt violation of stockpiling already known.
- Attacker’s objectives for control of post-attack society and cost of rebuilding/decontamination.
- Uncertain ability to ‘fight through’ heavily contaminated zones unless mass prophylaxis and PE available exclusively to attackers.
- Risk of ‘bounce-back’ onto attackers own civilian population from highly contagious agent(s) absent availability of large-scale countermeasure capacity.
“Amerithrax” October 2001

“I will show you fear in a handful of dust”
-T. S. Elliot

US Select Agent List of Potential Biowarfare/Bioterrorism Agents
### HHS Select Agents and Toxins

- Abrin
- *Bacillus cereus* Biovar *anthracis*
- Botulinum neurotoxins*
- Botulinum neurotoxin producing species of *Clostridium**
- Conotoxins
- C. burnetii
- Crimean-Congo hemorrhagic fever virus
- Diocotyloscirpenol
- Eastern Equine Encephalitis virus
- Ebola virus*
- Francisella tularensis*
- Lassa fever virus
- Lujo virus
- Marburg virus*
- Monkeypox virus
- Reconstructed 1918 Influenza virus
- Ricin
- Rickettsia prowazekii
- SARS-associated coronavirus
- Saxitoxin
- Chapare
- Guaranito
- Junin
- Machupo
- Sebia
- Staphylococcal enterotoxins
- T-2 toxin
- Tetrodotoxin
- Tick-borne encephalitis complex (flavi) viruses
  - Far Eastern subtype
  - Siberian subtype
- Kyasanur Forest disease virus
- Omsk hemorrhagic fever virus
- Variola major virus*
- Variola minor virus*
- Yersinia pestis*

### USDA Select Agents

- African horse sickness virus
- African swine fever virus
- Avian influenza virus
- Classical swine fever virus
- Coniothyrium glycines (formerly *Phoma glycicola* and *Pyrenochaeta glycines*)
- Foot-and-mouth disease virus*
- Goat pox virus
- Lumpy skin disease virus
- Mycobacteria capricolum
- Mycoplasma mycoides
- Newcastle disease virus
- *Peronosclerospora philippinensis* (Peronosclerospora sacchari)
- Peste des petits ruminants virus
- Ralstonia solanacearum
- Rathayibacter toxicus
- Rinderpest virus*
- Sclerotinia solani
- Sheep pox virus
- Swine vesicular disease virus
- Synchytium endobioticum
- Xanthomonas oryzae

### Overlap Select Agents

- *Bacillus anthracis*
- *Bacillus anthracis* Pasteur strain
- *Brucella abortus*
- *Brucella melitensis*
- *Brucella suis*
- *Burkholderia mallei**
- *Burkholderia pseudomallei**
- Hendra virus
- Nipah virus
- Rift Valley fever virus
- Venezuelan equine encephalitis virus

*These are regulated by both HHS and USDA due to their potential to pose a severe threat to both public health and safety and to animal health or products.*

List last updated on September 24, 2018
The Appeal but Unrealized Use of CBW for Asymmetric Warfare and Terrorism

Aum Shinrikyo (1995)

ISIS Caliphate (2014-2019)
Drones as Delivery Systems for CBW Agents

A dramatic increase in the number of threats, incidents, and incursions by drones at NFL stadiums. We are all very fortunate that the drone over Levi’s Stadium dropped only leaflets.

CATHY LANIER
Senior VP of Security, NFL
COVID-19 and Bioterrorism

- profound disruption of western economies not unnoticed by terrorist groups based on internet traffic
- ease of spread and deception against background of continued natural pandemic infection
- dissemination by asymptomatic purposely infected carriers
  - a less onerous demand to “the cause” than martyrdom by suicide bombing?
- potential adverse impact on DOD operational readiness
High Contagion Infections as a Threat to DOD Operational Readiness?

rapid and extensive infection of COVID-19 on USS Theodore Roosevelt (4/20)
Laboratory Synthesis of New Coronavirus Variants

Rapid reconstruction of SARS-CoV-2 using a synthetic genomics platform

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Thinking Beyond Select Agents:
New Technologies and the Expanded Threat Spectrum

AGENT X

• exotic natural EID/zoonose?
• deliberately engineered bioterror agent?
• bioerror (inadvertent release from biocontainment facilities/biohacking)?
Engineering Microbial Pathogens: Shifting the Impact from Acute to Chronic Effects

- agents causing delayed mortality (4-12 weeks) to overwhelm preparedness resources and paralyze healthcare delivery systems
- agents with high survival but cause chronic illnesses and resulting in long term clinical burden (human) or economic loss (agriculture and disrupted critical supply chains)
- pervasive and protracted damaging psychological effects on exposed societies
Biological Warfare and Bioterrorism
New ‘Dual-Use’ Knowledge

- rapid pace of advances in molecular genetics, biotechnology and advanced computing
- intellectual foundation for mapping the causes of disease at the molecular level to improve healthcare
  - “precision medicine”
  - identify new molecular targets for diagnostics (Dx), therapeutics (Rx) and vaccines (VacX-note not Vx)
- but same knowledge of perturbations in the molecular pathways (circuit diagrams) causing disease can be used to design new biological/chemical weapons that cause the same circuit disruptions
Mapping Genetic Control Circuits in Human Organs and Cells

- Cortex (205) / Frontal cortex (BA9) (175)
- Anterior cingulate cortex (BA24) (147)
- Caudate (basal ganglia) (194)
- Nucleus accumbens (basal ganglia) (202)
- Putamen (basal ganglia) (170)
- Hypothalamus (170)
- Amygdala (129)
- Hippocampus (165)
- Substantia nigra (114)
- Cerebellum (209) / Cerebellar hemisphere (175)
- Spinal cord (cervical c-1) (126)
- Pituitary (237)

Cell type composition in tissues
Gene expression and splicing

Expression quantitative trait loci (eQTLs)
Splicing quantitative trait loci (sQTLs)

cis-eQTLs
cis-sQTLs
trans-eQTLs
trans-sQTLs

GTex Consortium
- precision medicine: mapping the molecular networks - (circuit diagrams) of every cell type in the body and the circuit disruptions that cause disease
- roadmap for next-generation CBW agents to target specific molecular circuits (✱, ✡, ✢)
Biological Warfare and Bioterrorism
New ‘Dual-Use’ Knowledge

- Malevolent design of biological circuit modulators (BCMs) to disrupt biological signaling processes
  - Theoretically an organ, any cell type, any organism
- Enemy likely to target biological circuits with maximum adverse health impacts
  - Chronic disease: direct cost of care; indirect psychological impacts on population mental health
  - Immune system (suppression, hyper-activation)
  - Cognition (fear induction, hallucinations, memory erasure, addiction)
  - Systemic fatigue/malaise (impact on workforce productivity and national economy)
New Dual-Use Technologies

- further review
- week 6 (Nov 16 - Nov 22)
  - Pressing Threats II: New and Emerging Bioweapons
- week 7 (Nov 23 - Dec 4)
  - Planning for Future
Biological Warfare and Bioterrorism: Development of Medical Countermeasures (MCMs)

- theoretically large (almost unlimited) spectrum of attack pathogens with widely differing properties and risk scenarios
  - natural pathogens
  - engineered pathogens
- plan for ‘all hazards’ response capabilities
- further discussion in weeks 5 (Nov 9 -15) & 6 (Nov 16 - 22)