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

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Guest Lecture:
Stanford University Biosecurity Course
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Declared Interests:

- Board of Directors: Monsanto, Exelixis, Caris Life Sciences
- Scientific Advisory Board: Burrill and Co., Synthetic Genomics, Univ. Michigan, Haplogen GmbH
- IOM Forum on Global Infectious Diseases
- USG Activities: DoD, DHS
Biosecurity and Global Health: Understanding the Implications of Major Economic Disparities and Environmental Dislocations
Seeking Security in an Unsecure World: The Military and National Security Calculus

Expanding Conflict Zones, Political Instabilities and Terrorism

- WMD Proliferation
- New Power Centers
- US Retrenchment: Geopolitical/Fiscal
The VUCA World

- Volatility
- Uncertainty
- Complexity
- Ambiguity
The Biosecurity Triad

Infectious Diseases of Natural Origin

Urbanization, Environmental and Ecological Impacts on Disease Emergence

Bioterrorism
Biosecurity

**Today**

- **bioterrorism**: likely low probability, but high consequence
- **natural infections**: high probability, high consequence
  - old foes, resurgent foes and new EIDs

**2020 and beyond**

- new patterns of natural infections and therapeutic challenges
- **bioterrorism**
  - an expanded risk due to access to new technologies?
- **synthetic biology**
  - promise and peril: the ultimate dual-use technology
Infectious Disease: A Powerful Force in Human Evolution
Terrorism and The New Calculus of National Security and Foreign Affairs
"I will show you fear in a handful of dust"
T.S. Elliot
Preparedness:
The “All Hazards” Challenge and Building Resilient Systems
Outpacing Infectious Diseases

- Growing resistance to existing Rx and vaccines
- Urbanization, climate change and new patterns of exposure and disease spread
- Emerging infectious diseases (EIDs)
The Global Public Health Challenge Posed by Rapid Urbanization in Developing Countries

- High Disease Transmission
- Lack of Safe Water
- Bush Meat Food Chain
- Major Deficits in Health Infrastructure
- Expanded Eco-niches and Increased Zoonotic Risks
Emerging Infectious Diseases (EIDs)
Human Coronaviruses

Emergence of SARS-CoV (PRC 2003)

Emergence of MERS-CoV (KSA 2012)
Understanding Animal to Human Transmission
Evolution of Coronaviruses from Ancestors in Bat and Avian Hosts

From: P. C. Y. Woo et al. (2014) EID 20, 560
Maintaining Global Preparedness for a High Virulence Pandemic

- H1N1: high transmissibility - low virulence/mortality
- H5N1: low transmissibility – high virulence/mortality
- H5N1 x (H1N1) or (X): potential for devastating pandemic
“The future of humanity and microbes will likely evolve as episodes of our wits versus their genes”

Dr. Joshua Lederberg, Nobel Laureate
Science (2000) 6, 427-30
The Evolving Nature of Human Infectious and Parasitic Diseases

1407 species of human pathogens

- 538 bacteria
- 57 protozoa
- 60% are zoonoses
- over 70% zoonoses arise from interactions with wildlife

Emerging Infectious Diseases (EIDs)
- 58 in last 25 years
- viruses significantly over-represented
- RNA viruses most variable and rapidly changing
- helminths under-represented
One Health

The Need for a Holistic View of Host-Pathogen Ecology
“One Health”: The Rationale for Integration of Historically Separate Domains and Responsibilities

- Urbanization of DCs and emergence of new zoonotic threats
- Food chain as increasing source of disease risks
- Enhanced agricultural productivity for food security to support global population growth
- Economic impact of agricultural disease on trade, development and resources/production footprints
Preparedness: Building Resilient Systems

- are the risks known and analyzed?
- are there actions for meaningful intervention?
  - tractable, measurable
- if not, how can these be developed and implemented (resources, infrastructure, logistics, cost)?
- what are the principal risks and obstacles to success? (technical, economic, political, social, legal)
- how are these barriers being addressed and, if not, what is needed to reduce/eliminate them? (vulnerability assessment and mitigation)
Global Disease Surveillance

EMERGEncy ID NET

World Health Organization

Public Health Department’s Surveillance

Infectious Diseases Society of America

BioPortal

Quarantine Activity Reporting System (QARS).

U.S. Influenza Sentinel Provider Surveillance Network

DoD-GEISWeb

Global Emerging Infections System

TropNet Europ

GIDEON

Quarantine Activity Reporting System (QARS).

Human and Animal Rabies

Empres Watch

GeoSentinel

The Global Surveillance Network of the ISTM and CDC

a worldwide communications & data collection network of travel/tropical medicine clinics
Geodemographic Information Systems (GIS): Real-Time, Front Line, Ground Zero Data from Field Sampling and Sentinels
## Geodemographic Information Systems: Mapping Disease Patterns and Modeling Trends

<table>
<thead>
<tr>
<th>Anomaly Detection and Early Alert</th>
<th>Disease Progression</th>
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</thead>
<tbody>
<tr>
<td><img src="image1" alt="Map of disease patterns" /></td>
<td><img src="image2" alt="Map of disease progression" /></td>
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<tr>
<td><img src="image3" alt="Satellite surveillance" /></td>
<td><img src="image4" alt="Predictive modeling" /></td>
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</table>

**Satellite Surveillance and Predictive Modeling of Disease Trends**
Global Transport and Trade: New Interactions of People, Animals and Product Supply Chains

The Super Vector

World Container Traffic Doubled Since 1997

Billion Cross-Border Travelers

Global Food Networks
Coming to an Airport Near You:

Modeling Airport Connectivities, Traffic and Distance Relationships and Implications for Epidemic Spread via the Global Aviation Network

“Insufficient data, Captain”

“Insufficient data is not sufficient, Mr. Spock. You’re the Science Officer. You’re supposed to have sufficient data all the time”

Star Trek
The Immunity Syndrome
398 WHO-verified outbreaks 1996-2009

- 23 days for event detection
- 32 days for public communication
- 35 days for official laboratory confirmation
- 48 days for inclusion in WHO Disease Outbreak News
Real-time Remote Health Status Monitoring: The Value of Mobile Devices and Sensors

- geolocation data (where)
- temporal information (when)
- contextual information (what)
- improved decision support (action)
The Public Health, Economic and Political Challenges of a Major Bioincident

Preparedness for Managing Substantial Societal Dislocations

Silos Subvert Solution
Detection of a Major Bioincident

Not A Hazmat or Wide Area Sensor Network Solution

Emergency Rooms and Farms Will be the Front Line
Education and Training

Diagnostic Accuracy

Overload and Triage

Infection Control

Availability of Therapy
Earlier Diagnosis and Intervention Saves Lives

Improved speed, breadth and accuracy of clinical diagnosis

- faster Rx
- accurate Rx
- prophylactic Rx for incident personnel

- robust triage
  - rationing
  - reassurance of “worried well”
  - quarantine decisions

- real time disease surveillance data
- faster ID of incident evolution
- faster incident containment and exposure controls

The Single Most Important Leverage Point
For Rapid Mobilization of Resilient Responses to Epi-/Pandemics, Epizootics and WMD Bioterrorism
Genome Sequencing, Microbial Identification and Epidemiology
E. Coli Strain STEC 0104: H4 (Germany 2011)
US States Poorly Prepared to Manage Infectious Disease Threats:
Trust for America’s Health and Robert Wood Johnson Foundation*

- 33 states scored 5 or lower on scale of 10
- failure to ID select agent pathogens
- lack of common data reporting formats and/or obligations
- one-third do not have mandatory reporting of HAI
- failure to meet vaccination herd immunity levels (>90%)
- impact of fiscal austerity (State, Federal)
- 40,000 jobs lost in last 5 years

The Outbreaks 2013 Report
The Lag Phase in Bioincident Detection

Primary Care Physicians and Pharmacists

Social Media and m.Health

Unusual illness patterns

Hospitals

BIOINCIDENT CONFIRMATION

ER Walk-ins
The Three Core Components of Bioincident Management

- Command and Decision Authorities
- Healthcare System and Public Health Capabilities
- Maintenance of Civil Order and Public Trust

- robust inter-operable communication networks for real-time situational awareness and rapid actions
- managing the media and the ‘worried well’
- transparency, credibility and public trust
Consequence and Crisis Control in a Bioincident: Compartmentalization and Calming

**COMMAND CENTER**
- public health
- logistics
- communications
- medical
- law enforcement
- coordination
- local
- national
- regional
- national
- international

**Primary Care Physicians and Pharmacists**

**Social Media and m.Health**

**Neighborhood Emergency Help Centers**
- patient registration
- Dx triage
- transport logistics
- mass Rx/vaccination

**Hospitals**
- acute care
- triage
- mortuary

**Media**

**Community Outreach and Citizen Mobilization**
- police, EMS
- volunteers
- military

“The Worried Well”

Social Media and m.Health
Consequence Management of a Major Bioincident

- modular emergency services
  - expansion options and ‘surge’ resources
- non-healthcare sites for massive casualty management
- isolation and quarantine locations
- housing and welfare of staff (+ families)
- transfer of hospitalized patients to intermediate care facilities
- sites for distribution of medicines, food, water to public
- control of transport routes and supply chain logistics
Preparedness: Building Resilient Systems

- Are the necessary resources available: financial, personnel, skills, infrastructure?
- Have all elements been tested under simulated emergency situations?
- Are organizational structures and processes sufficiently agile for rapid response?
- Are roles, responsibilities and accountabilities defined and understood for every constituency involved?
  - From local to global
Seamless Communication Networks: A Key Success Factor in Bioincident Management
Use of GIS for Management of Population Movement, Healthcare Facilities and Supply Chains for Optimum Bioincident Control
Distribution of Medical Emergency Supplies for a Major Epidemic/Pandemic

- pre-positioning for known threats: The Strategic National Stockpile (select agents only)
- rapid movement by commercial carriers
- managing political/public/media responses for bioincidents with limited or no Rx/vaccine options
Potential Disruption of Access to Conventional Rx in a Major Epidemic/Pandemic
Vulnerability of Global, National and Local Supply Chains in a Major Epidemic/Pandemic

Medicines

- “just-in-time” supply networks
  - major hospitals 2 or 3 deliveries per day
- out-patient prescription drugs
  - insurance company limits on prescription volume (USA)
- majority of drug intermediates, excipients and final products sourced off-shore
- 95% generic drugs used in US (64% of total Rx) are made off-shore, primarily in PRC and India
- no national stockpile for routine prescriptions
**Medical Countermeasures (MCMs) for Special Populations: Emergency Use Authorization**

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<tr>
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<td>Immunosuppressed</td>
<td>Impaired Major Organ Function</td>
<td>ICU-Critical Care</td>
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</table>
The Likely Real Picture!

“FOG”

“FUBAR”

Ill-Defined Responsibilities and Accountabilities

Lack of Well-Rehearsed Master Plans: Federal, State and Local
The first question President Obama received during his press conference on April 29, 2009 was: “Why aren’t you closing the Mexico-US border to prevent the entry of swine flu (SO-H1N1)?”
Informing the Public: A Critical and Unenviable Challenge

- media sensationalism and public panic
- pressure on governments to make illogical but politically expedient decisions
- in a severe outbreak the shock factor from any major level of fatalities will be unprecedented in modern peace times with unpredictable consequences for public responses
- unpredictable unilateral decisions by other governments, restricting trade, travel and shipment of goods
- extended supply chains might break down completely
The ‘Fog of Disaster’: Crisis Standards of Care and Proliferation of Unanticipated Events and Consequences
FIVE DAYS AT MEMORIAL

LIFE AND DEATH IN A STORM-RAVAGED HOSPITAL

SHERI FINK
Mass Casualty Care: Transition from Individuals to Populations
The Fragmented Silos of USG: A Dangerous Vulnerability
Legal Aspects of Public Health and Counter-Terrorism Actions to Contain Bioincidents

- suspension of civil liberties
- imposition of quarantine
- triage decisions and rationing
- mandatory medical examination and treatment
- mandatory treatment with unapproved drugs and vaccines
  - informed consent
  - indemnification
  - special populations
Changing Clinical in a Bioincident: From Standard of Care to Sufficient Care

- provide the most good for greatest number of people under adverse conditions and constrained resources
- clinical triage
- rationing of health resources/pharmaceutical
- omnipresent vulnerabilities and risks from public panic and civil disorder
Who’s In Charge?
“I’m In Charge”

“DHS will manage and direct the Federal Response to a pandemic of avian flu.”

Secretary Chertoff 23 August 2005

- DHHS and many in the public health community objected to this declaration
- asserted that DHS was “incapable of understanding the complexity of a medical disaster”
- DHHS subsequently directed to be lead agency

DOES DHHS OR THE PUBLIC HEALTH AND CLINICAL COMMUNITIES REALLY “UNDERSTAND THE COMPLEXITY OF A LARGE SCALE DISASTER?”
Who Is In Charge?

- delusional to believe that optimum disaster response is a physician/health system-centric process

- crucial medical component but multi-disciplinary, multi-sector ‘bigger picture’ complexities require sophisticated integration and operational expertise in large scale logistics and disaster exercises
Cascading Effects:

The Consequence of Inter-Connectivities In Complex Systems
Control of Population Movement and Supply Chain Networks
Compromising Critical Systems
Vulnerability of Global, National and Local Supply Chains in a Major Epidemic/Pandemic

Energy

Net Power Generation in the US by Fuel Source, 2007

- Coal: 48.70%
- Natural Gas: 21.50%
- Nuclear: 19.40%
- Hydroelectric: 6%
- Other Renewables: 2.50%
- Petroleum: 1.60%
- Other Gas: 0.40%
- Other: 0.30%
Key Success Factors

- tested disaster management plan
- responder training and education
- command structure
  - demarcated roles, responsibilities, authority
  - robust communication channels
- single source POC for key interfaces
  - ground zero staff (multiple ground zeros in CBW)
  - emergency services and first responders
  - medical/public health
  - politicians and inter-agency coordination
  - conventional media and social media
The Growing Threat from Infectious Agents

Asleep at the Switch!

Bad Bugs and Few New Drugs
Comfort and Complacency: The Enemies of Vigilance and Preparedness
increasing resistance in G+ and G- pathogens in hospital and community settings

the **ESKAPE** pathogens

- *Enterococcus faecium*
- *Staphylococcus aureus*
- *Klebsiella pneumoniae*
- *Acinetobacter baumanii*
- *Pseudomonas aeruginosa*
- *Enterobacter species*
The Valley of Dea(r)th: The Consequence of Declining R&D Investment in Antibiotic Discovery

- 75% decrease in antibacterials approved from 1983 to 2011
- only 16 agents currently in Phase II / III clinical trials
  - only 3 as new ‘classes’ with novel mechanisms of action
  - major gap in new agents for therapy of G- bacilli
  - lack of systemic agents in advanced development for organisms resistant to all current antibacterials
“Millions demand it, millions refuse it, and millions don’t know what to think”

John Carroll
Editor, Fierce Biotech (23 Oct. 2009)
Who Pays for Preparedness?

The Obligate Role of Private-Public Partnerships in Biosecurity Policy
Biosecurity

- who pays for preparedness? (public policy, market dynamics)
- who is responsible/accountable for biosecurity? (public policy, organization, politics, media responses)
- what is the balance between public and private sector responsibilities?
- myriad ethical and legal issues (surveillance, civil liberties, rationing, counter-terrorism targets, publication of dual-use knowledge)
Hollywood Doesn’t Live in the Real World (Really?)

... and then a technical miracle cure occurs with dramatic rapidity
... and always created by an individual scientific genius
Drug Discovery and Development: One of the Most Complex Intellectual and Logistical Exercises Undertaken by Modern Industry

- $750 million to $2 billion R&D cost/drug
- 9-15 year R&D cycle

“Fewer countries have discovered, developed and registered drugs to an international standard, than have developed atomic bombs”

Chris Hentshel
New Incentives for Industry R&D Investment in Novel Anti-Infectives and Vaccines

- ‘orphan-drug’-type incentives for ‘prioritized’ diseases
- R&D tax credit
- Extension of patent life or market exclusivity
- Transferable priority review vouchers for expedited review of another product
- Advanced purchase commitments
- ‘non-use’ market compensation for next-generation agents held ‘in reserve’ to combat pan-resistant infections
Future Trajectory Trends and Threat Expansion

New ‘Dual-Use’ Technologies
Dual-Use Technologies

Expanding the Biothreat Spectrum

Synthetic Biology: A Powerful Dual-Use Technology
Synthetic Biology: New Dual-Use Dilemmas

The Expanded Dimension of the ‘Bio’ Challenge

- thinking beyond ‘bio’ as just infectious agents

- systems biology
  - targeted disruption of ANY body function
  - novel C and B threats

- synthetic biology
  - exploring biospace: designing new life forms
  - designer organisms to attack materials/infrastructure
Nature (2012) 482, 153

**Dual-Use Research of Concern (DURC)**

**COMMENT**

Adaptations of avian flu virus are a cause for concern

Members of the US National Science Advisory Board for Biosecurity explain its recommendations on the communication of experimental work on H5N1 influenza.
Dual-Use Research of Concern (DURC)

Proposed Policy Targets Dual Use Research of Concern

Science Safety Security
Finding the Balance Together

Framework for Guiding Funding Decisions about Research Proposals with the Potential for Generating Highly Pathogenic Avian Influenza H5N1 Viruses that are Transmissible among Mammals by Respiratory Droplets

Posted February 21, 2013
“Security is always deemed excessive .....until it’s not enough”
Silos subvert solutions

Multi-dimensional challenges demand cogent, holistic solutions

Current US capabilities are dangerously fragmented and under-resourced

Bugs don’t respect borders: Biosecurity cannot be addressed solely from a narrow national perspective
Biosecurity: A Classic Complex Systems Challenge

- Global impact
- Biological, social, economic, technical, political and military

Science and Technology

Public Health and Healthcare Delivery

Intelligence, Foreign Policy and Military Strategies

- Societal priorities and cost of biosecurity
- Political and military conflict: ideologies, intents and capabilities
The Multi-Dimensional Complexity of Biosecurity

- **one health:** humans, animals, ecosystems
- **urbanization,** environmental sustainability and depletion of non-renewable resources
- **economic and political instabilities** and “health spillover”
- **conflict,** civil war, terrorism and international security

International Engagement, Commitment and Political Resolve
Fighting Polio in Regions of Political Instability

Syria's Polio Outbreak*

*Laboratory-confirmed wild polio cases reported by government of Syria

*WHO data as of 12 March

[Image of a map showing locations of polio outbreaks in Syria, Turkey, Iraq, Lebanon, and Jordan.]

[Image of a group of people handling large white bags, presumably as part of a vaccination campaign or related activity.]
Africa: A Zone of Escalating National Security Challenges With ‘Spill Over’ Health Effects

- widespread proliferation of defense spend
- civil wars and instabilities
- jihadic fundamentalism: Al-Qaeda, Al-Shabaab, Abu Lyad al-Tunisi, Boko Haram
Conclusions:

Biosecurity

Understanding the Global Impact of Increasingly Inter-connected Biological Systems

Medicine, Agriculture, Environmental Sustainability and National Security
Building Robust Defenses for Biosecurity

- naturally occurring infectious diseases pose an equal, and likely greater, current threat to society than bioterrorism
- governments must accord higher priority to ‘biosecurity’ as a integral component of national security and foreign policy
- (re)building a national and international infrastructure for the surveillance, diagnosis and containment of infectious diseases is fundamental to future protection against major instabilities triggered by infectious agents, whether of natural or malevolent origins
Meeting the Challenge(s) Posed by Global Infectious Diseases

- growing threat awareness as catalyst for action
- availability of powerful new genetic and biotechnology capabilities for discovery of diagnostics (Dx), drugs (Rx) and vaccines (Vax)
- building global surveillance networks using advances in sensor technologies, mobile devices, computing and telecommunications
- strengthening national public health and epidemic/pandemic management capabilities
- new financial incentives for R&D on Dx, Rx and vaccines
- global political engagement and commitment
The VUCA World

- Volatility
- Uncertainty
- Complexity
- Ambiguity

WHAT TO EXPECT, WHEN NO ONE’S EXPECTING
The Need for Greater Urgency and Adoption of Systems-Based Approaches to Biosecurity

- current USG institutions and academia are ill-suited to address current and projected R&D challenges
- ‘rapid’ and ‘translation’ are countercultural to much of the academic and USG communities
- the cosmetic salve of seeming to ‘do something’ is meaningless absent of results
- extravagant resources are/will be wasted until a forceful integrated, ‘systemic’ approach is adopted
- the engagement of corporate and international agencies is a critical success factor in addressing global biosecurity challenges
Building Robust CB Defenses

- major vulnerabilities exist across the full spectrum of biosecurity
  - pre-emptive detection and interdiction
  - rapid diagnosis
  - healthcare resources for mass casualty management
  - drug and vaccine coverage (quantitative and qualitative)
  - outdated public health laws
  - emergency control of media/commerce
The Curse of Contemporary Governance: ‘Quick Fixes’ and the Retreat from Complexity

- society increasingly “cocooned” from complexity and risk
- pervasive and dangerous scientific illiteracy among legislative and policy makers about biosecurity
- “quick fixes”: uni-dimensional, short term policies that do not address long term, multidimensional complexity
- public policy defined increasingly by length of legislative terms
- influence of media in shaping public policy and operational constraints
Ignoring Systems Complexity: Void in Global Public Health and National Security

- Pernicious constraints on USG analysis and decision-making frameworks
- Growing expertise gap in USG agencies
  - Threat diversification, new technologies
  - Open-source analysis
- Under-leveraged engagement with private sector
  - Novel technology trajectories
  - Broadening international scope
  - Expertise pool

Must catastrophe be the only vehicle to provoke radical reform?
“History is the sum total of the things that could have been avoided.”

Chancellor Konrad Adenauer
“Politics is the art of the possible, the calculated science of survival”

Prince Otto von Bismarck

“Survival owes little to the art of politics, but everything to the calculated application of science”.

Professor Rudolph Virchow (in reply)