

The Challenge of Global Preparedness For Outpacing Infectious and Parasitic Diseases

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**Presentation at RVC Symposium:
Who Owns Disease?
18 September 2009**

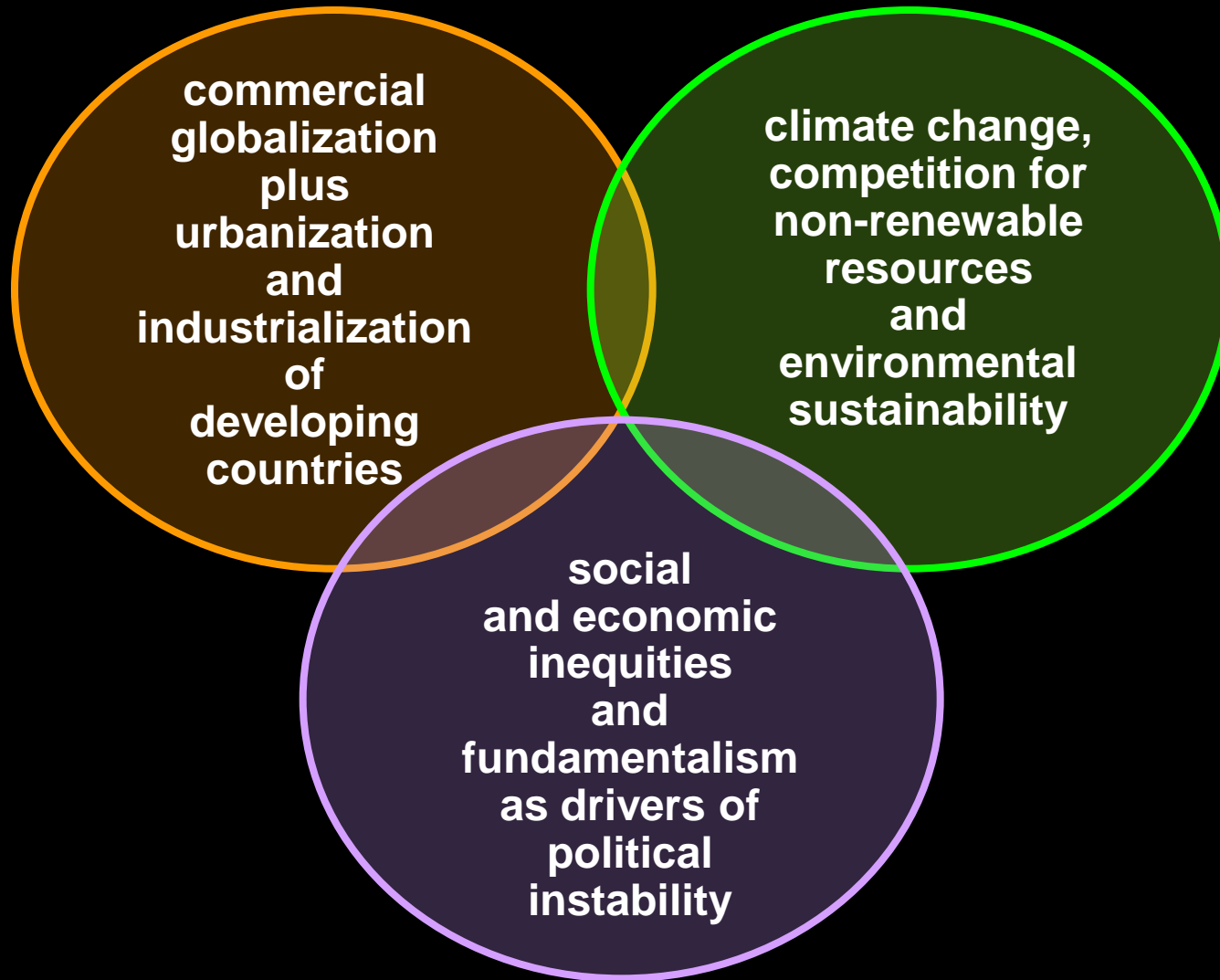
Communicable Disease: An Unchanging Dimension in the Human Condition



“There is no torture that a human being has inflicted on his worst enemy that nature does not inflict on thousands of diseased human beings every day.”

J.S. Mill, ‘On Nature’

The Macro-Forces Shaping Global Events the Early 21st Century



Outpacing Infectious and Parasitic Diseases: Adapting to Relentless Change and Pervasive Uncertainties

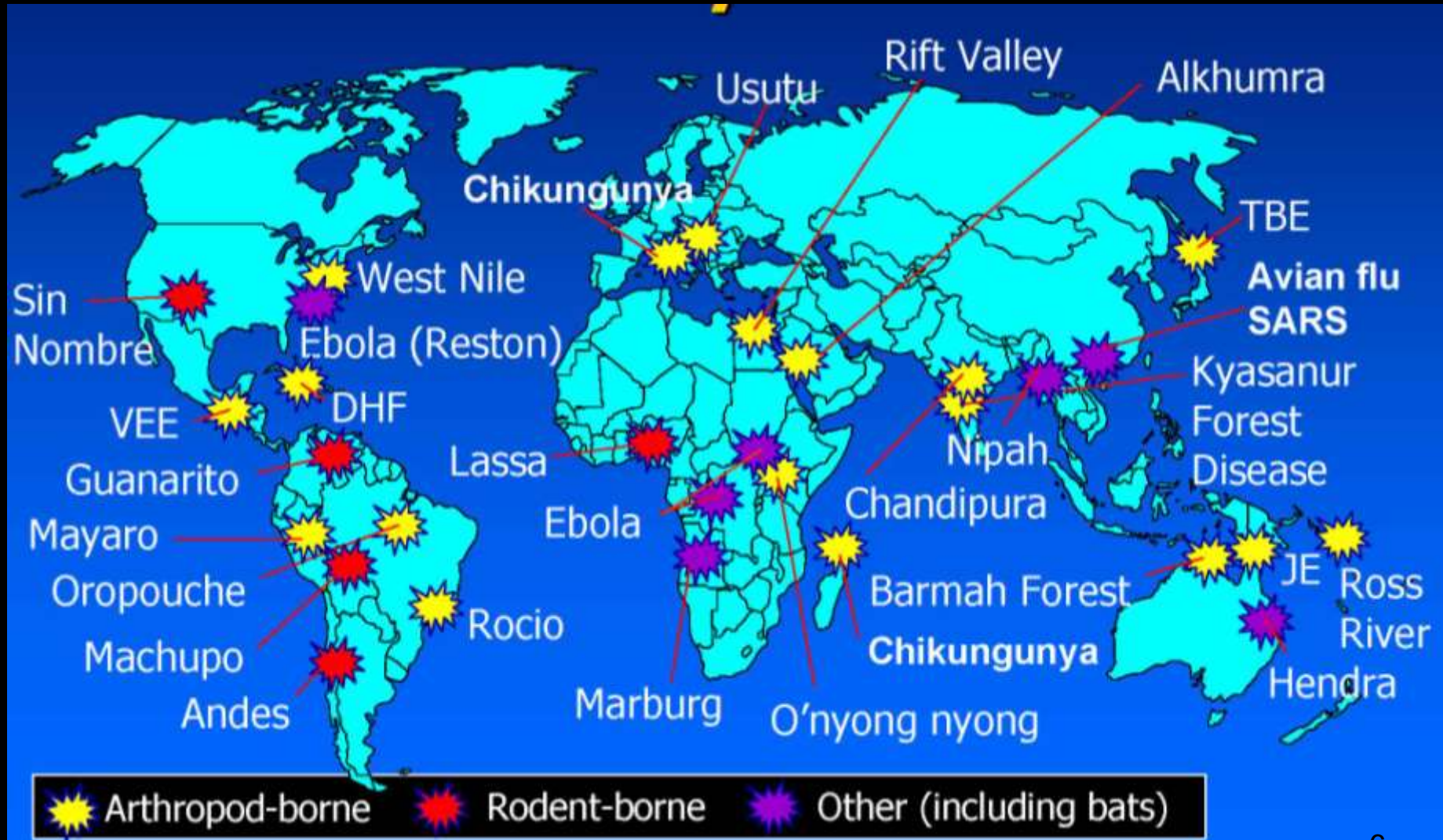
- **systems-based approach**
 - **recognition of the complex, multi-dimensional and constantly shifting determinants of pathogen-host interactions and adaptive control measures**
- **success is measured by things that “don’t happen”**
- **political populism and the retreat from complexity**
 - **spin and quick fixes**
 - **delusional value of ‘doing something’ versus the demanding realities of pursuit of meaningful solutions**
- **fragile economic and political commitment to long term, trans-generational strategies**

Ranking of Communicable Diseases by DALYs

Disease	Burden
HIV-AIDS	84.5 million
Neglected Tropical Diseases	56.6 million
Malaria	46.5 million
Tuberculosis	34.7 million

Hotez PJ, Molyneux DH, Fenwick A, Ottesen E, Ehrlich Sachs S, Sachs JD
PLoS Medicine 2006; 3: e102

Emerging Infections:



The Evolving Nature of Human Infectious and Parasitic Diseases

Mark Woolhouse Univ. Edinburgh

- **Trends Ecol. Evol. (2005) 20, 238**
- **Emerg. Infec. Dis. (2005) 11, 1842**

1407 species of human pathogens

- **538 bacteria ● 208 viruses ● 317 fungi**
- **57 protozoa ● 287 helminths**
- **60% are zoonoses**
- **over 70% zoonoses arise from interactions with wildlife**
- **90% IUCN listed wild mammals threatened by disease share these diseases with domestic species**
- **EIDs**
 - **39 in last 25 years (now 46)**
 - **viruses are significantly over-represented**
 - **helminths are under-represented**

One World



**Human
Health**

One Health

**Ecosystem
Health**

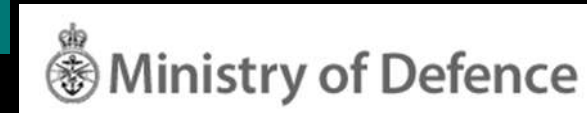
**Animal
Health**

One Objective

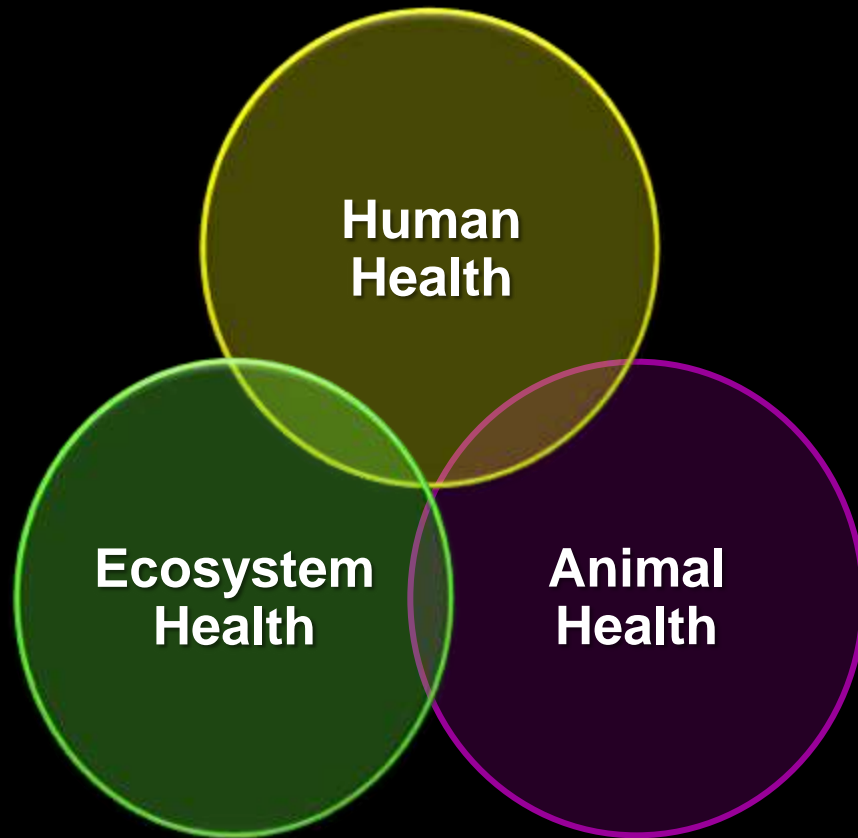
An Integrated Approach to Infectious Diseases in the UK

RS Policy Document 2/09

- establish an interdepartmental Advisory Committee on Infectious and Zoonotic Diseases
- establish a National Institute for Infectious Diseases



The Imperative for Integration of Historically Separate Domains and Responsibilities



- **most effective control route for zoonotic threats to humans is via the relevant animal population(s)**
- **knowledge of the potential impact of ecosystem perturbations on emergence of novel zoonoses must be accorded higher priority**
- **disparity in animal and human public health capacity undermines global disease control**
- **failure to optimize disease control in food production wastes limited resources and increases global food production footprint**

Factors Shaping The Dynamics of Global Communicable Diseases

Global Transport and Trade: New Interactions of People, Animals and Product Supply Chains

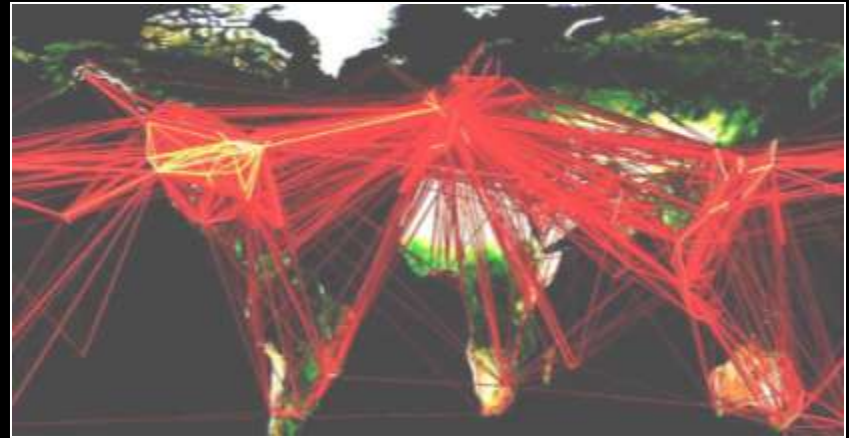
The Super Vector



**World Container
Traffic Doubled
Since 1997**



Billion Cross-Border Travelers



Global Food Networks



The Global Public Health Challenge Posed by Rapid Urbanization in Developing Countries

High Disease Transmission



Lack of Safe Water



Toxic Waste

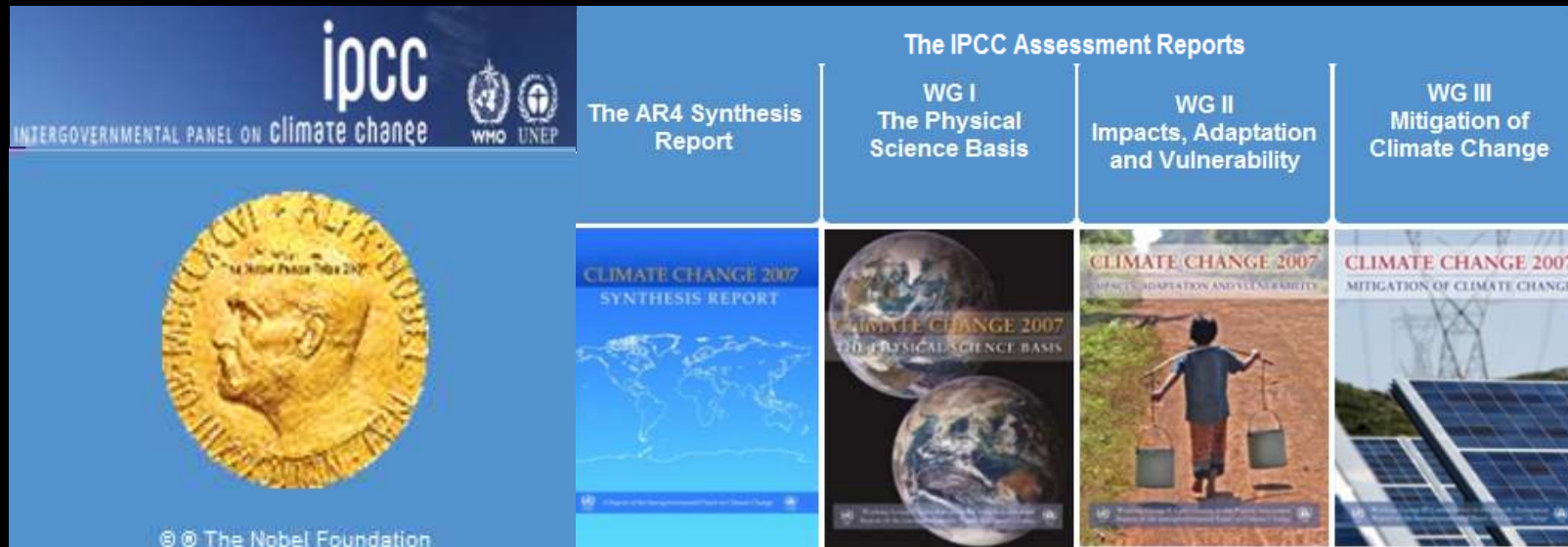


Major Deficits in Health Infrastructure



Expanded Eco-niches and Increased Zoonotic Risks

The Challenge of Modeling Global Climate Change



“Climate Change is the most severe problem that we are facing today ...more serious even than the threat of terrorism”

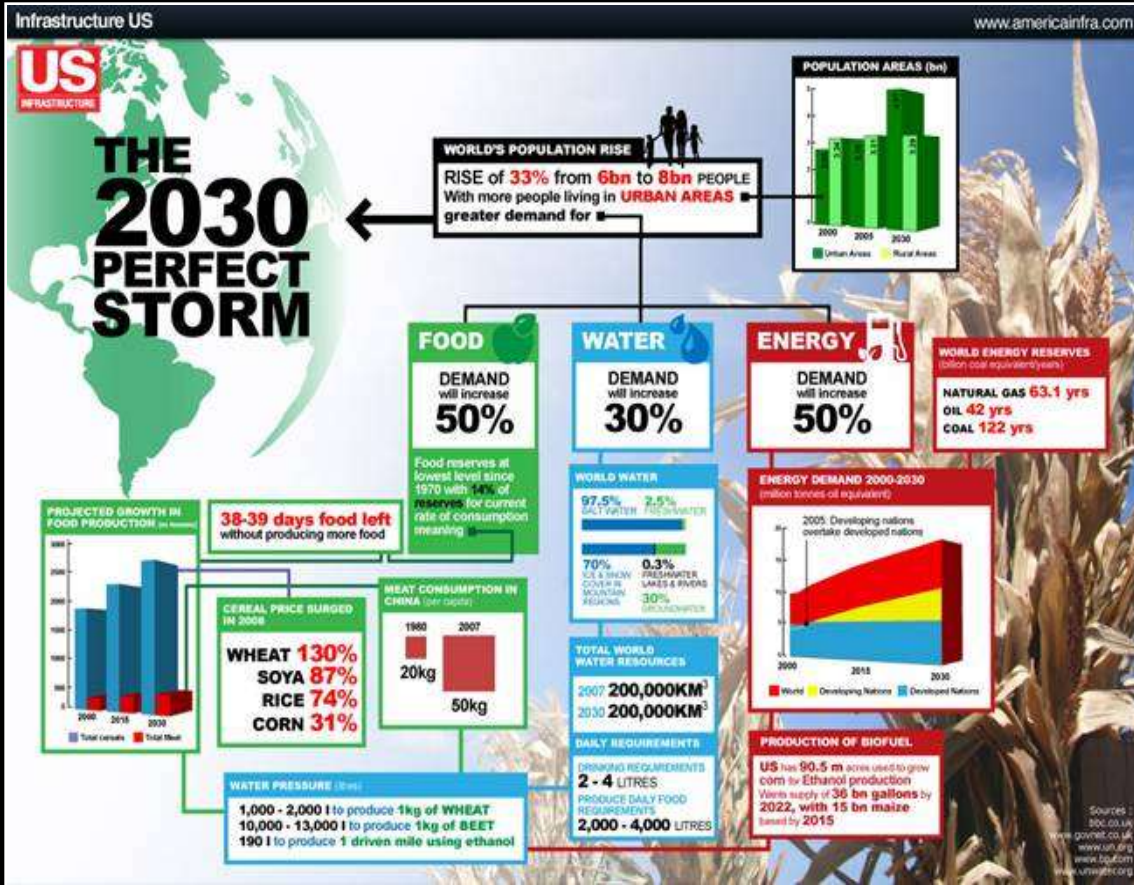
**Sir. David King
Science**

9 January 2004, p 176

“The potential range and magnitude of health risks should be central to the rationale for actions to mitigate the occurrence of climate change.”

**World Health Organization
January 2009**

A 30 Year Countdown to Catastrophe?



Sir John Beddington
UK Government's
Chief Scientific Adviser
GovNet SDUK09

“The ‘perfect storm’ of population, food, water and energy demands.”

The Global Food Supply and Food Borne Pathogens

- **food chain increasingly complex, international and inter-dependent**
- **food production over next 25 years Ξ total for 10,000 years**
- **expanding middle class (1-2 billion) in NICs and some DCs and increased demand for grain and meat projected to increase by 160% by 2020**
- **famines, shortages and food riots in DCs**
- **least expensive sourcing also least safe**
- **the impact of climate change**

Mitigating Food Borne Pathogens



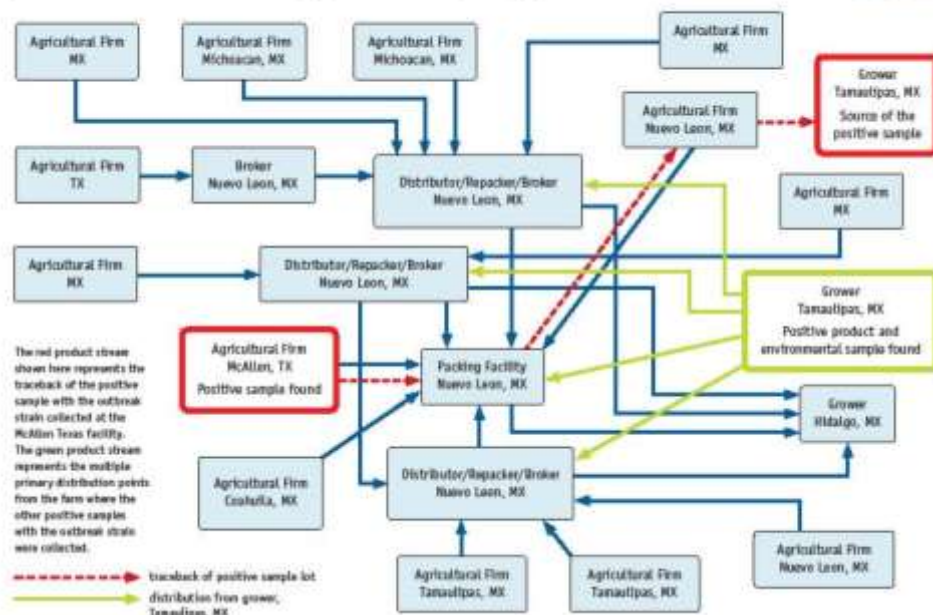
- most effective control at source
- reduce carriage of pathogens into processing facility on live animal/plant
- new anti-microbial processing technologies
- US domestic product inspection
 - 8.2 billion lbs poultry
 - 3.2 billion lbs egg products
 - 140 million lbs livestock
 - over 250,000 different product categories
 - 7,600 inspectors and 1100 veterinarians

Traceability

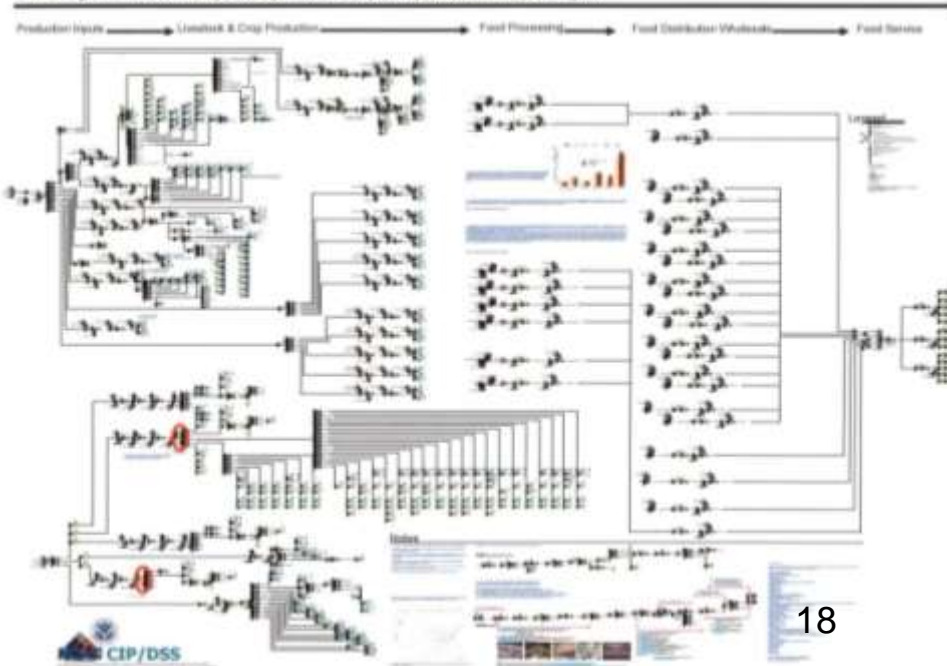


Salmonella Saintpaul Outbreak Traceback & Distribution

Partial view of the traceback & distribution of peppers from Mexico: July 16 - July 22, 2008



Food & Agriculture Commodity Flow System Labor Inputs Input/Process/Output Diagram



New Animal Production Technologies



Ensuring The Safety of Food Imports

- 15% US food imported from over 150 countries
- 300 ports and over 200,000 registered importers
- China 3rd largest food exporter to the U.S.
- China is in the top five in imported Fish/Crustaceans (#2), Vegetables (#3), Meat/Fish Preps (#3), Cereal/Starch (#4) & Vegetable/Fruit Preps (#2)
- full extent of imports from China unknown due to ingredients & trans-shipments

EUROSURVEILLANCE Vol . 14 · Issue 27 · 9 July 2009 · www.eurosurveillance.org

**FORESIGHT INFECTIOUS DISEASES CHINA PROJECT - A
NOVEL APPROACH TO ANTICIPATING FUTURE TRENDS IN RISK
OF INFECTIOUS DISEASES IN CHINA: METHODOLOGY AND
RESULTS FROM AN INITIAL APPLICATION**

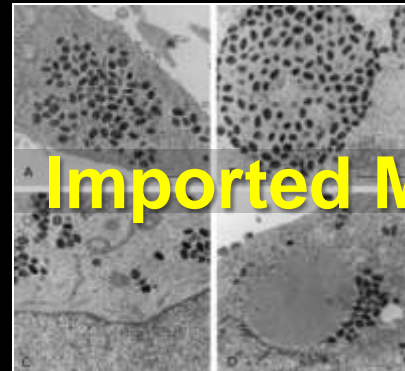
A Nicoll (Angus.Nicoll@ecdc.europa.eu)^{1,2,3}, J Huang⁴, Z Xie⁴, the Foresight China Project Group⁵

Annual Global Trade in Exotic Animals

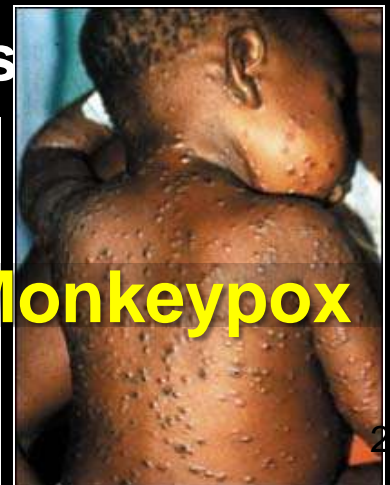


US Importations (2006) LEMIS Data

- 136,216 mammals 129 species rodents
- 243,000 birds
- 1.3 million reptiles
- 4.6 million amphibians
- 222 million fish



Imported Monkeypox



Non-Traditional Food Chains and Zoonotic Diseases

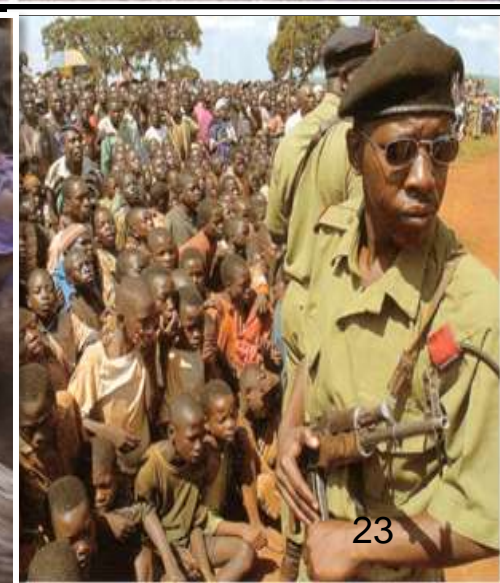
SARS



Rapid Expansion of Bushmeat Trade



Armed Conflict and Political Instability: New Humanitarian Crises and Refugee Migration

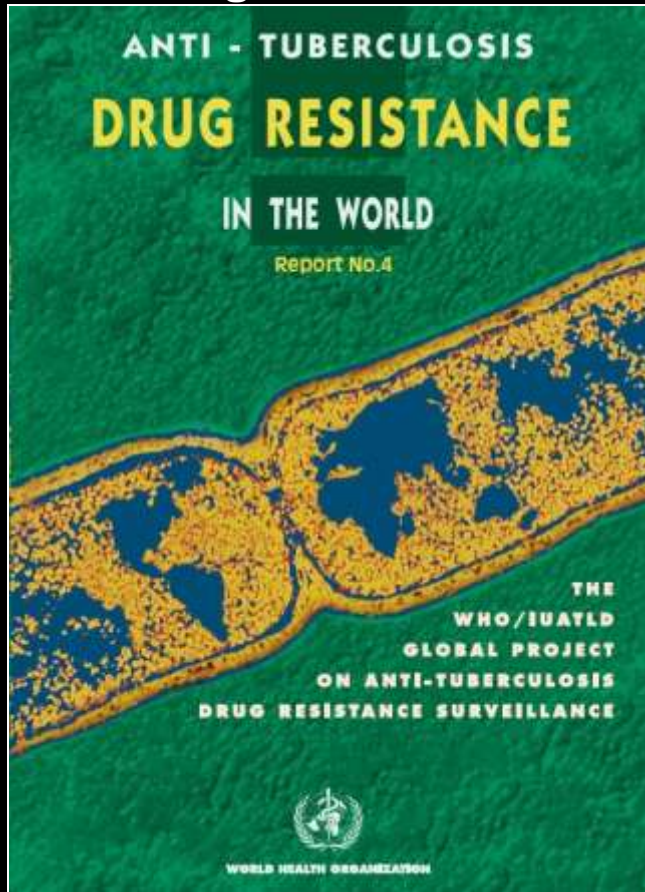


Pathogen Adaption to New Selection Pressures: The Most Powerful Force in the Challenge of Outpacing Infectious and Parasitic Diseases

- **ecoshifts**
 - changes in host distribution and/or demographics
 - environmental degradation
 - new pathogen ranges, new hosts, new vectors
- **rapid evolution of 'escape' variants**
 - drug resistance
 - immune evasion
- **impact of new technologies**
 - global mobility
 - industrial scale agriculture
 - implanted devices and microbial biofilms

The Alarming Rise of Resistant TB

WHO Report on Anti-TB Drug Resistance



- 490,000 new cases of MDR-TB each year, with >110,000 deaths¹
- accounts for 5% of 9 million new cases of TB²
- MDR-TB rates higher than ever (up to 22.3%), particularly in former Soviet Union countries
- XDR-TB reported by as many as 49 countries (by June 2008)³
- recent WHO/IUATLD Global Surveillance report indicated 7.5% (301/4012) of MDR TB to be XDR⁴
- around 40,000 XDR-TB cases emerge every year¹

1Tuberculosis: MDR-TB & XDR-TB—The 2008 Report. The Stop TB Department, WHO.

2Hargreaves S. <http://infection.thelancet.com>, Vol 8, April 2008, p.220

3Raviglione MC. NEJM 2008;359:636-8.

4Anti-TB Drug Resistance in the World: Report No. 4. The WHO/IUATLD Global Project on Anti-Tuberculosis Drug Resistance Surveillance 2002-2007. World Health Organization, 2008 (WHO/HTM/TB2008.394).



Copyright of Sidney Harris 2003, <http://www.ScienceCartoonsPlus.c>

“WOULD YOU LIKE THAT TO BE A STEAK WITH A BROAD-SPECTRUM ANTIBIOTIC, OR ONE WITH A VARIETY OF THERAPEUTIC PROTEINS?”

Factors Driving the Evolution of Microbial Drug Resistance

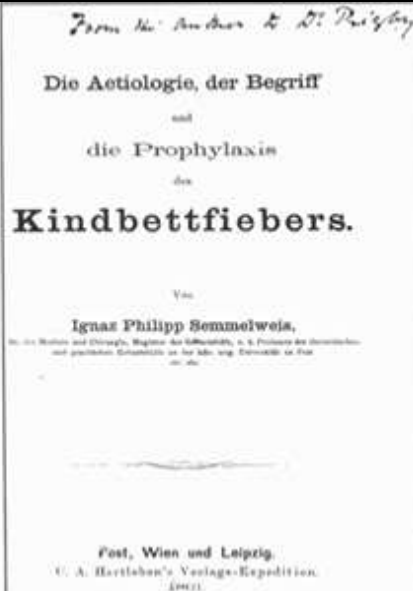
Intensive Agriculture



Aquaculture



Empirical Rx

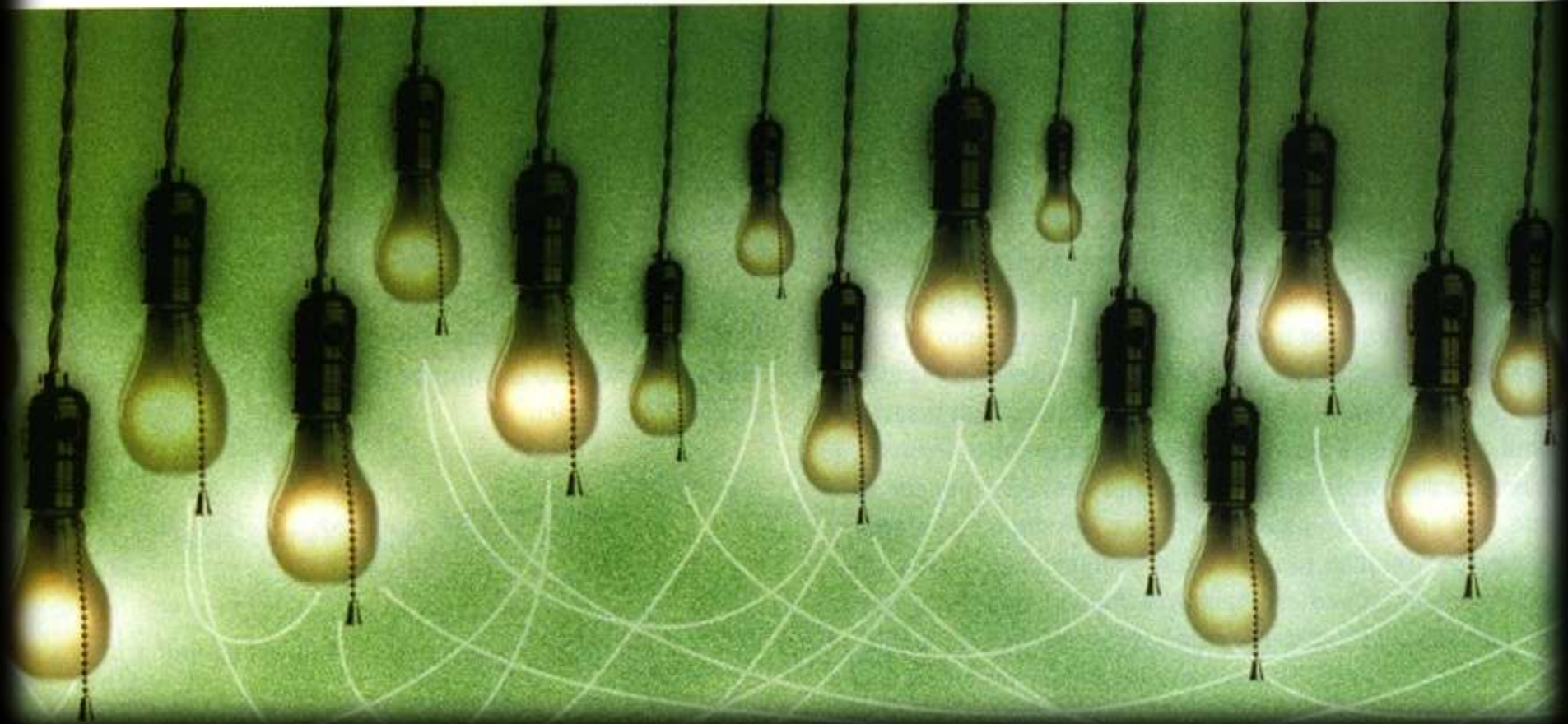


Poor Infection Control in Healthcare Facilities

Preparedness: Building Resilient Systems



HELL IS THE PLACE WHERE NOTHING CONNECTS — T.S. ELIOT



CHARTE
der
Geographische Ausbreitung der
KRANKHEITEN

NÖRDLICHER OCEAN
SÜDLICHER OCEAN
AFRIKA
ASIA
EUROPA
AMERIKA

30



HealthMap

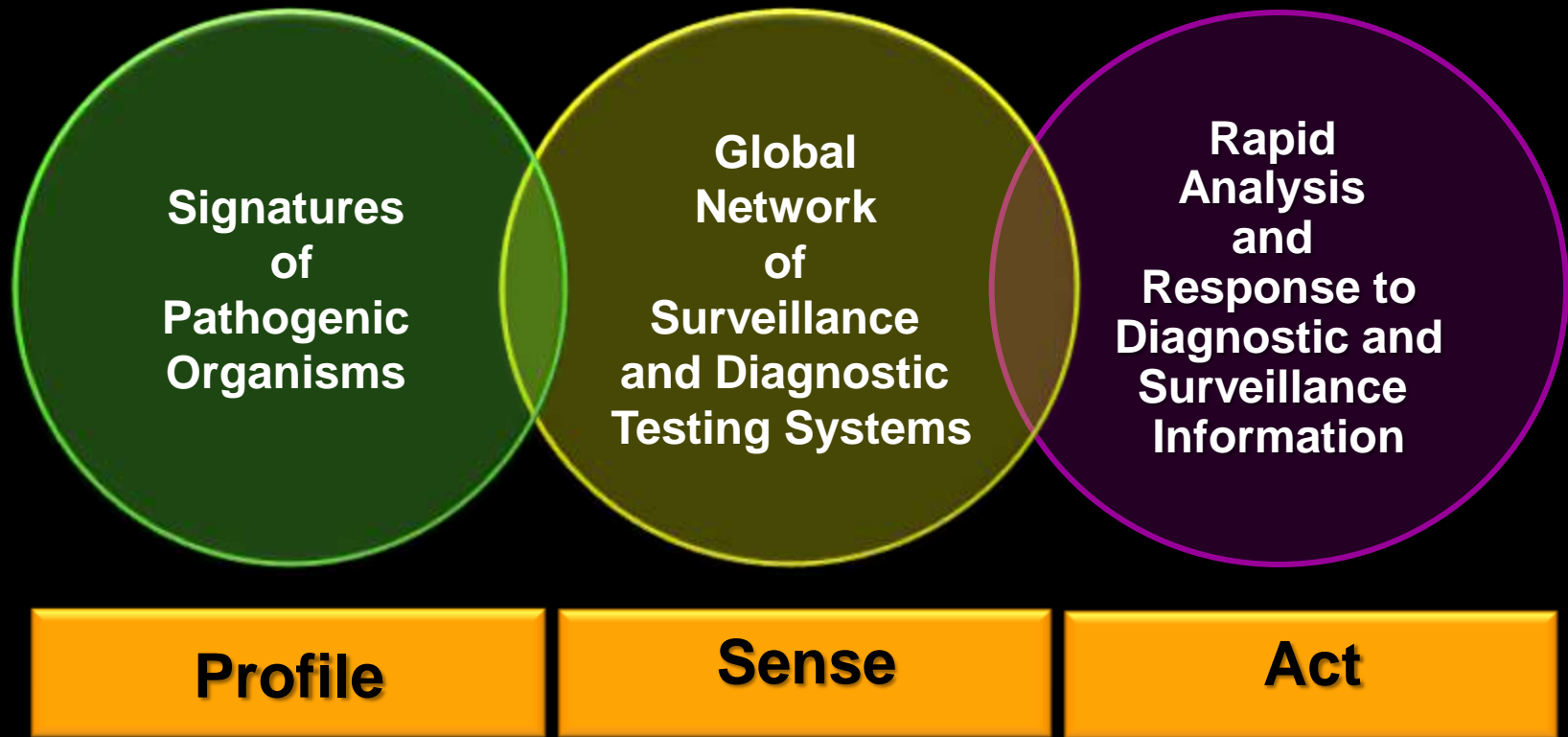
Global Disease Alert Map

English | Español | Français | Português | Русский | 中文 | العربية

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Surveillance Systems for the Rapid Detection and Control of Infectious and Parasitic Diseases





EMERGENCY ID NET



Public Health Department's Surveillance



U.S. Influenza Sentinel Provider Surveillance Network

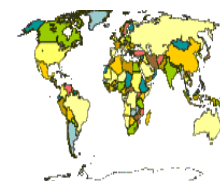
biocaster



GIDEON

Quarantine Activity Reporting System (QARS).

google.org

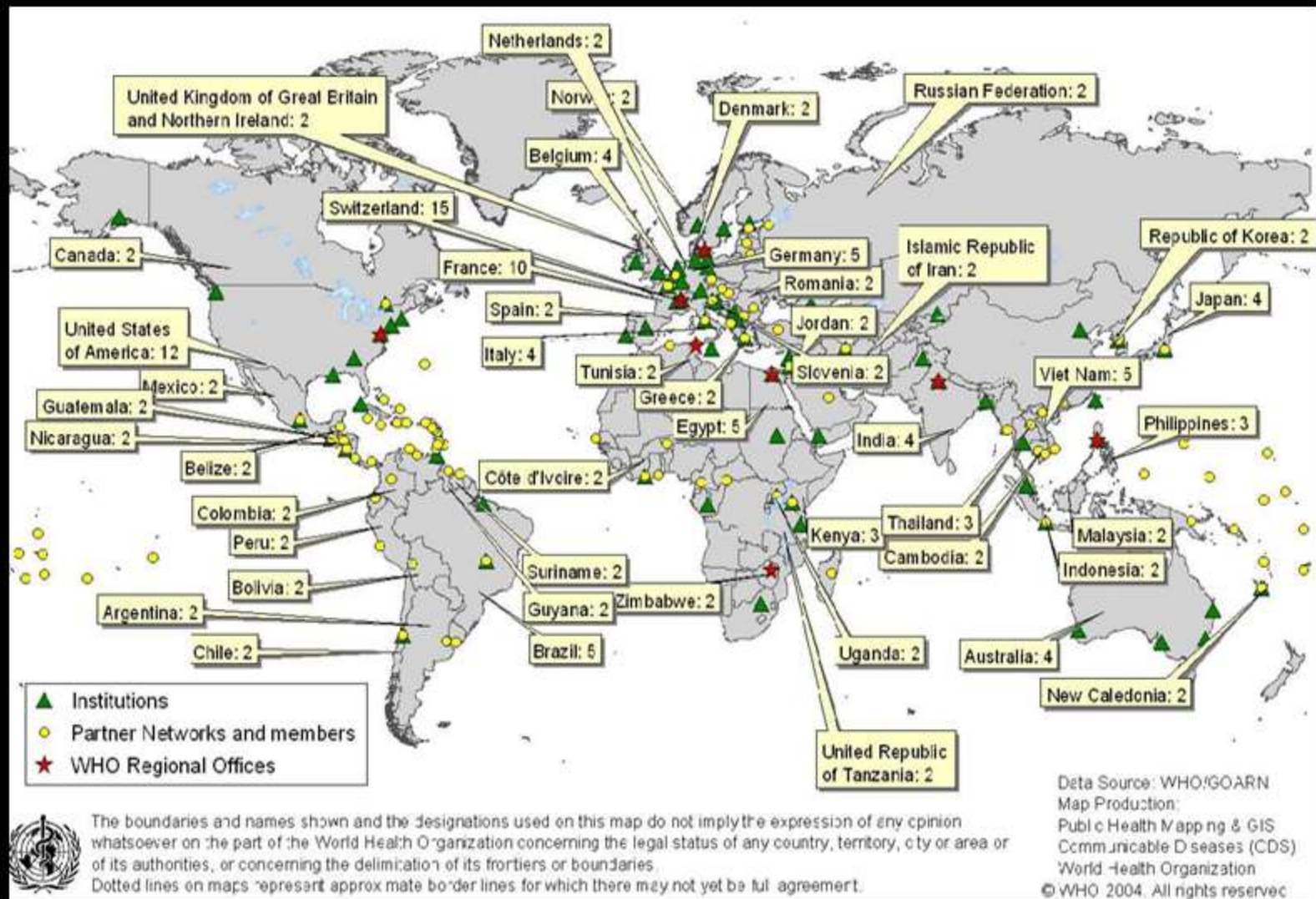


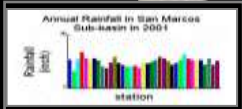
GeoSentinel

The Global Surveillance Network of the ISTM and CDC
a worldwide communications & data collection network of travel/tropical medicine clinics



GOARN: Institutions and Partner Network



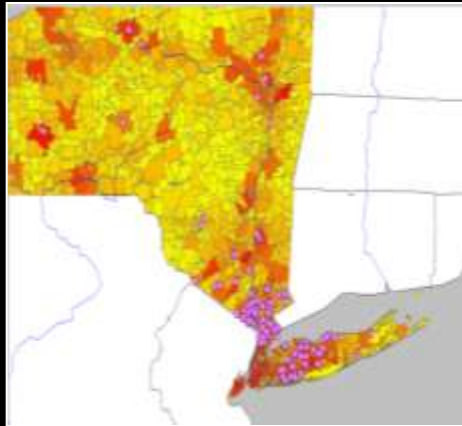


Geodemographic Information Systems (GIS): Real-Time, Front Line, Ground Zero Data from Field Sampling and Sentinels

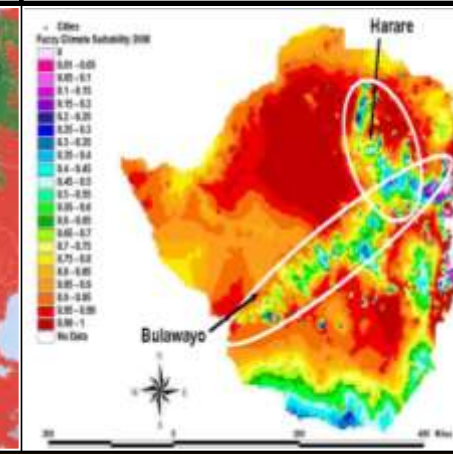
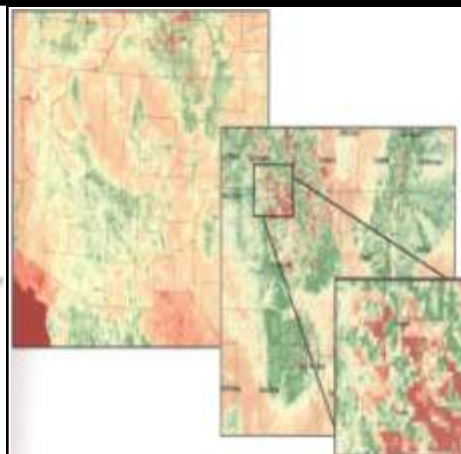
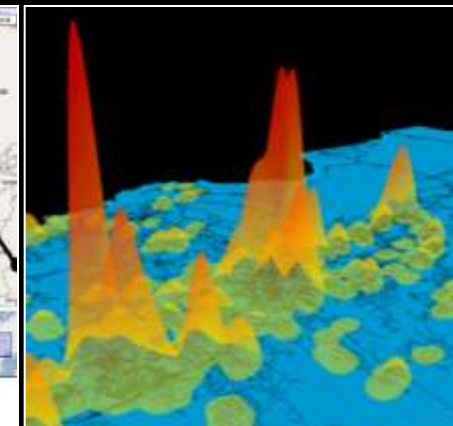
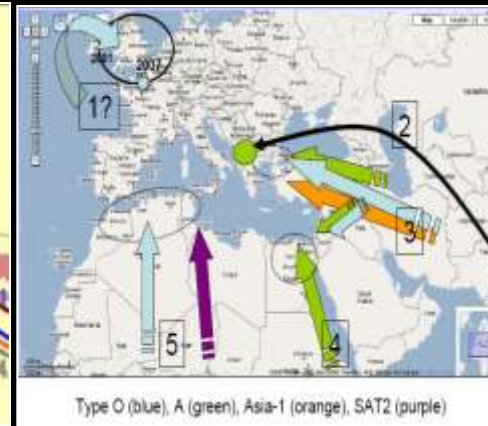
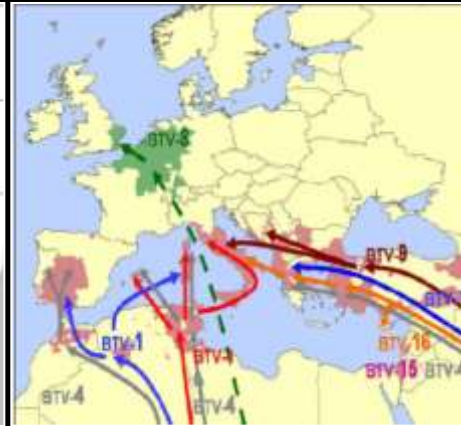


Geodemographic Information Systems: Mapping Disease Patterns and Modeling Trends

Anomaly Detection and Early Alert



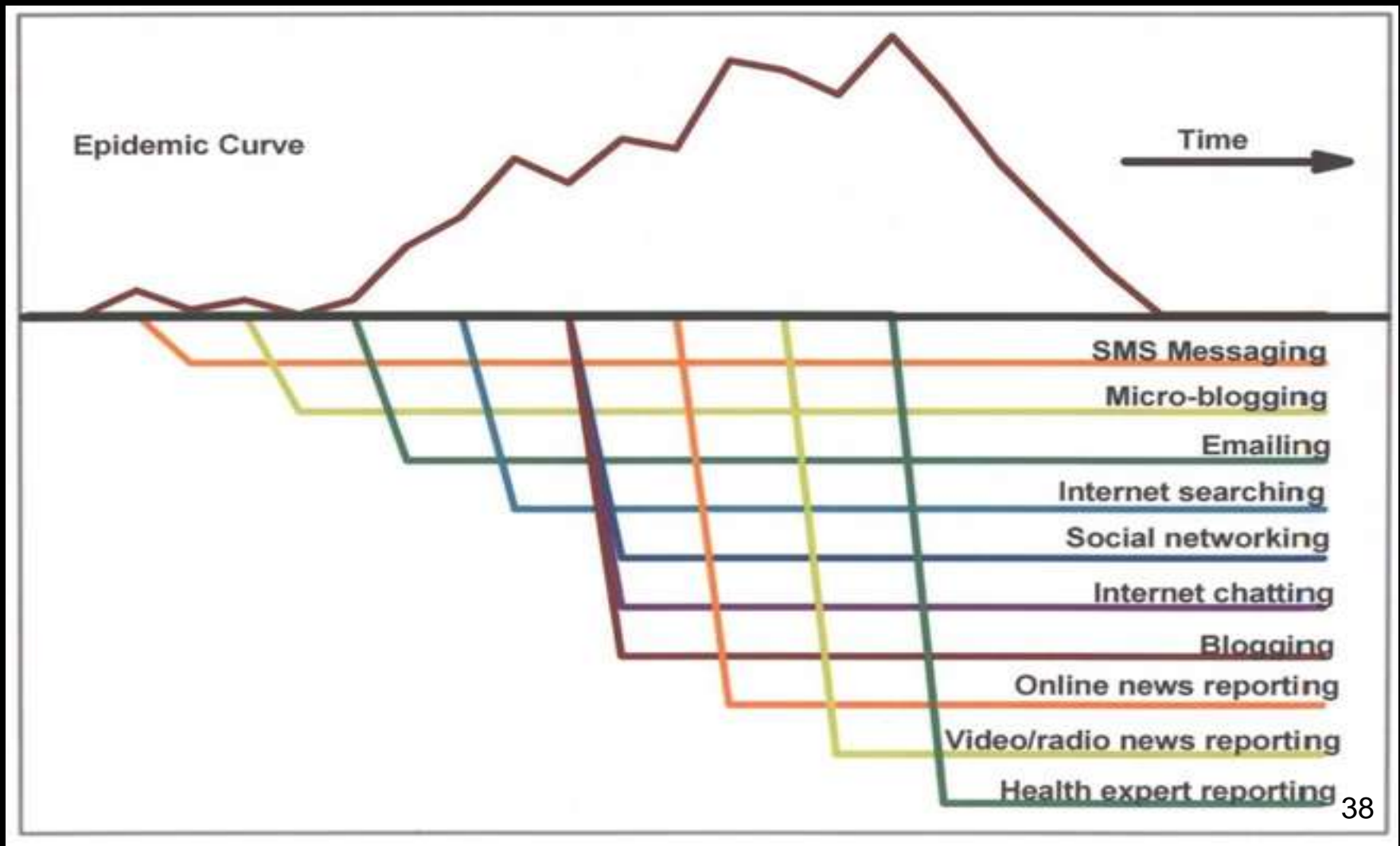
Disease Progression

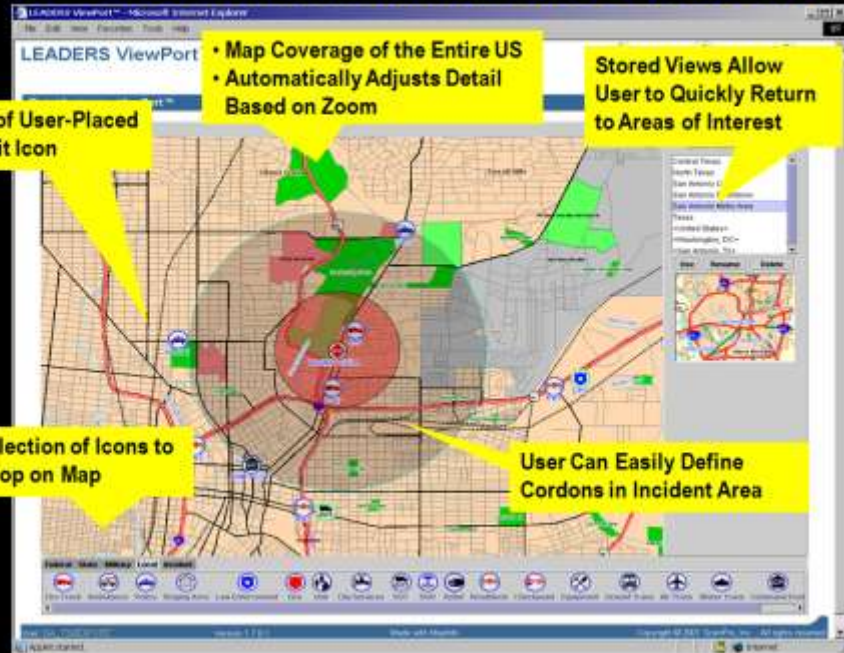


Satellite Surveillance and Predictive Modeling of Disease Trends

Geodemographic Information Systems (GIS): Real-Time, Front Line, Ground Zero Data from Field Sentinels

Leveraging Social Networks for Early Reporting and Alerting





Shepherding the 'FLOCK': Fast Local Clustering of Critical Knowledge

- **sentinels, sensors, diagnostics and continuous monitoring**
- **hybrid combinations of fixed and mobile detection**
- **intelligent systems that deploy and reconfigure**
 - **instructed reporting vs. autonomous actions**
- **wireless communication networks**
- **multi-layer hierarchical data integration and automated customized extraction for optimum end-user decision-support**
- **complex legal and ethical issues related to privacy and trans-national information exchange**

Improved Diagnostic Tests for Infectious and Parasitic Diseases

 The Academy of
Medical Sciences



Global health diagnostics: research, development
and regulation

Workshop report

April 2009

**The Single Most Important
Leverage Point
for Short Term Gains in
Global Public Health**

Earlier Diagnosis and Intervention Saves Lives

**Improved speed, breadth and accuracy
of clinical diagnosis of biothreat exposure**

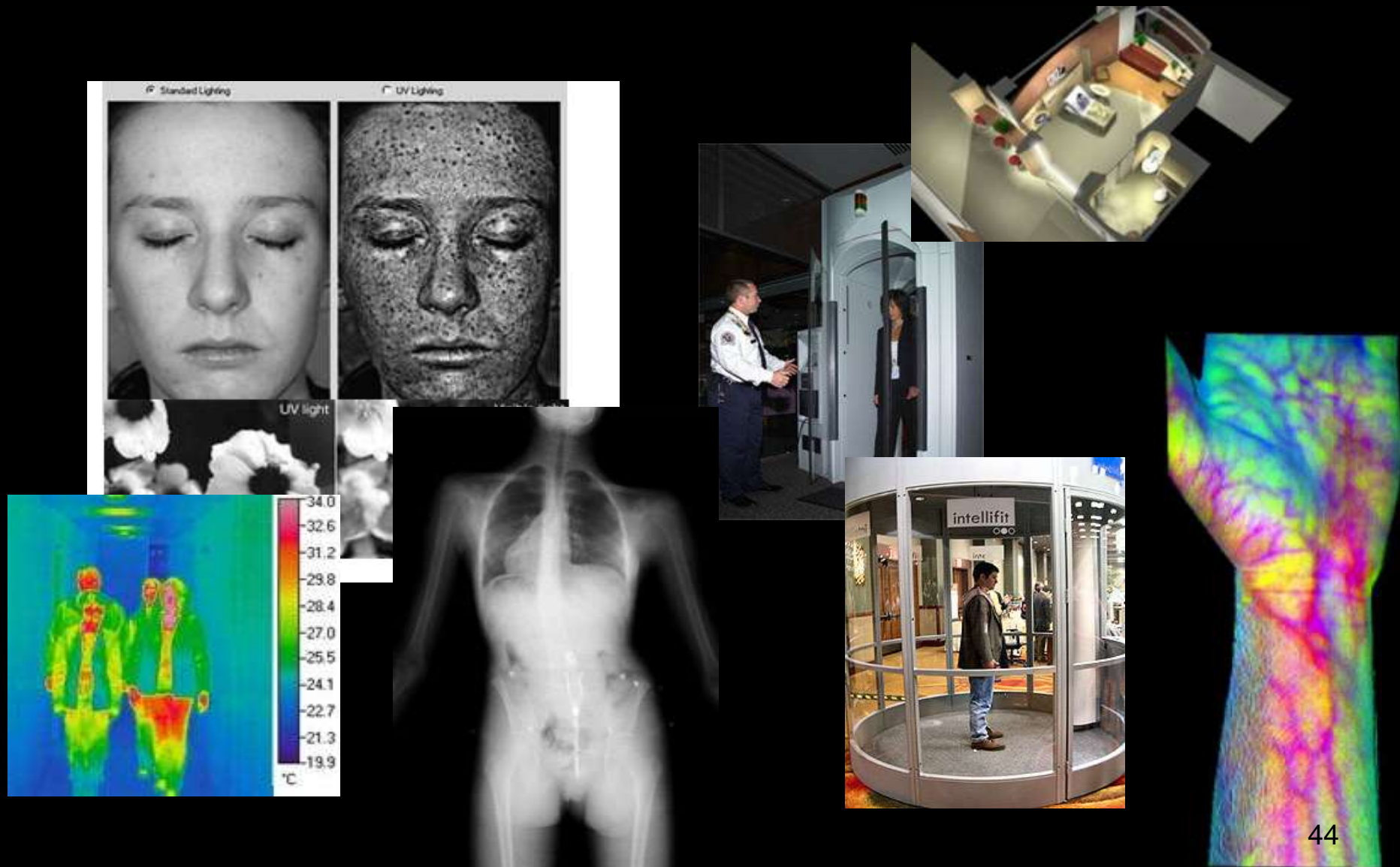


- faster Rx
- accurate Rx
- prophylactic Rx for incident personnel
- robust triage
 - rationing
 - reassurance of “worried well”
 - quarantine decisions
- real time disease surveillance data
- faster ID of incident evolution
- faster incident containment and exposure controls

Inadequate Investment in Multiplex Diagnostics for Infectious and Parasitic Diseases

- **worldwide IVD market is \$34 billion (ct. Rx)**
 - **developing world c. 5%**
- **dominated by oncology, cardiology and diabetes**
- **infectious disease Dx investment focused primarily on HIV/AIDS and blood supply safety**
- **unmet needs**
 - **low cost, automated POC on tests for resource-constrained settings in DC's**
 - **dip-stick type simplicity with rapid read out**

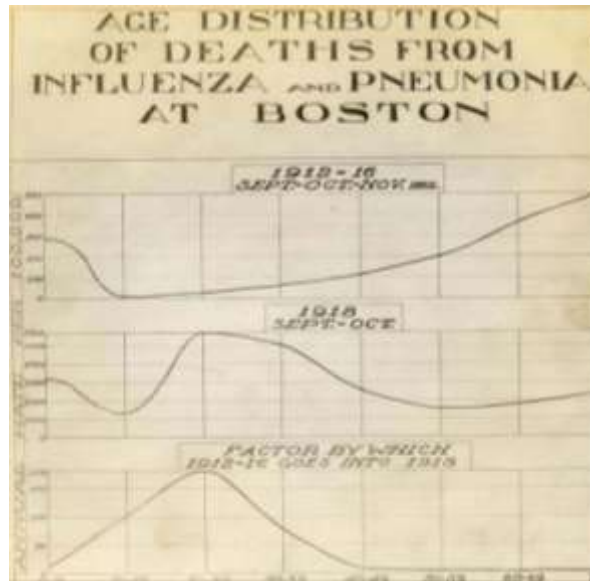
Stand-Off Diagnostics



SOI H1N1 Influenza (“Hamageddon?”)



Modeling the Likely Evolution of Pandemic Influenza



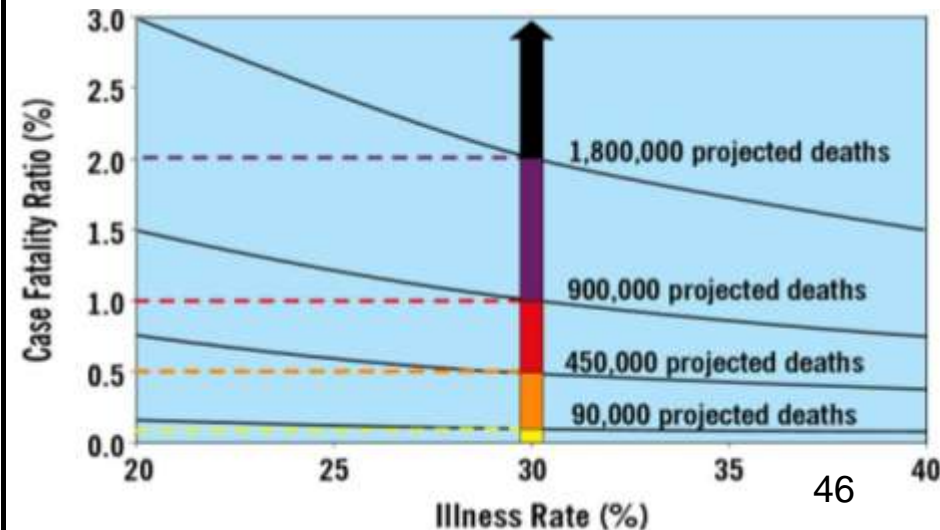
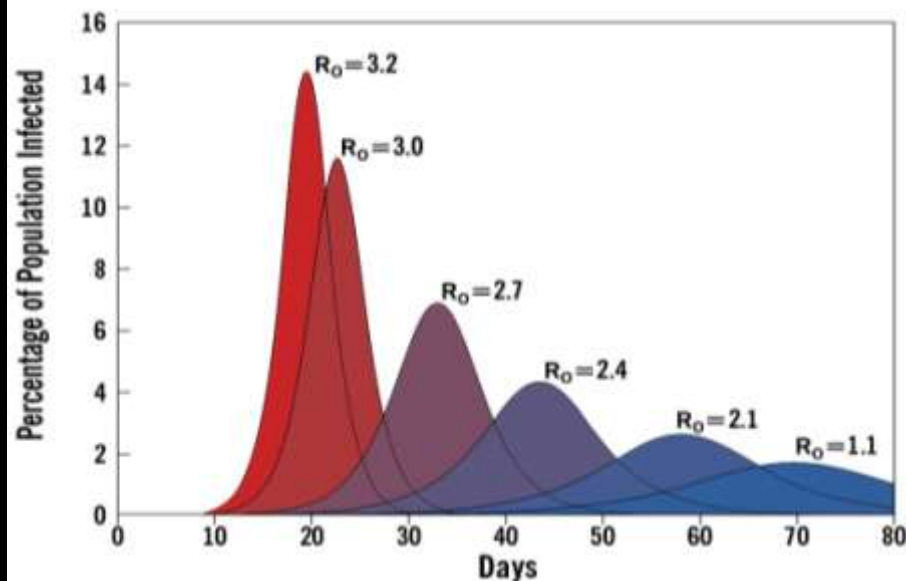
$$\frac{dX(t)}{dt} = \mu - X(t) \left[\sum_{i=1}^4 \beta_i \left(Y_i(t) + \phi_i \sum_{j \neq i} Y_j(t) \right) \right] - \mu X(t)$$

$$\frac{dY_i(t)}{dt} = X(t) \left[\beta_i \left(Y_i(t) + \phi_i \sum_{j \neq i} Y_j(t) \right) \right] - \sigma Y_i(t) - \mu Y_i(t)$$

$$\frac{dZ_i(t)}{dt} = \sigma Y_i(t) - Z_i(t) \sum_{j=1, j \neq i}^4 \left[\beta_j \left(Y_j(t) + \phi_j \sum_{k \neq j, k=1}^4 Y_k(t) \right) \right] - \mu Z_i(t)$$

$$\frac{dY_{ij}(t)}{dt} = Z_i(t) \left[\beta_j \left(Y_j(t) + \phi_j \sum_{k \neq j, k=1}^4 Y_k(t) \right) \right] - \sigma Y_{ij}(t) - \mu Y_{ij}(t)$$

$$1 = X(t) + \sum_{i=1}^4 Y_i(t) + \sum_{i=1}^4 Z_i(t) + \sum_{i,j=1, j \neq i}^4 Y_{ij}(t) + Z_{-i}(t)$$



Key Planning Assumptions for Pandemic Influenza

- cumulative clinical attack rate of 25-30%
- 'worst' case of single wave with 25% attack rate
- case fatality rate of 0.35-0.4%
- greater burden on people under 25 years
- hospitalization rate 4-7%
- 50% admissions may require ICU for up to 10 days
- 70% deaths will occur in hospitals

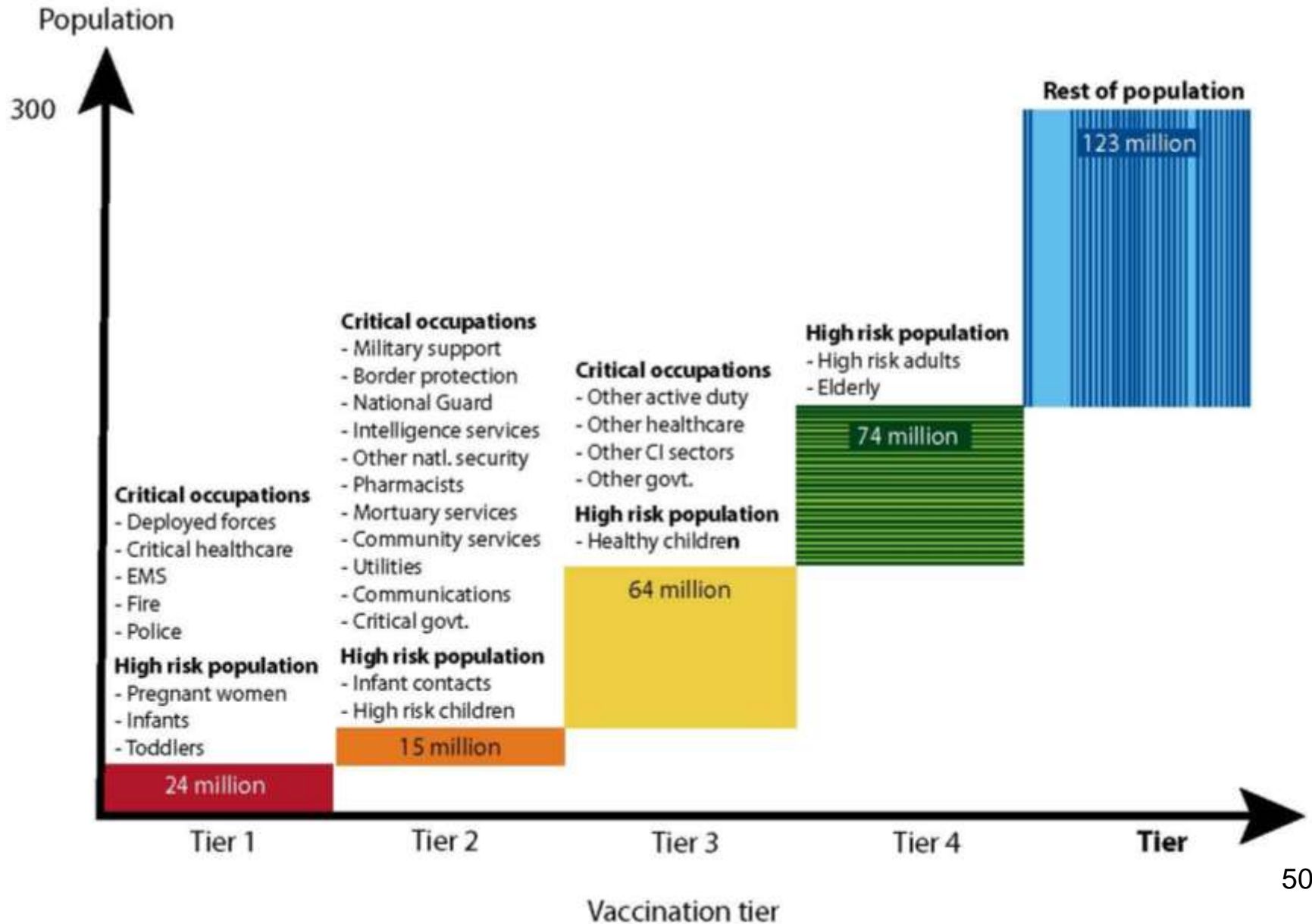
**The first question President Obama received during his press conference on April 29, 2009 was:
“Why aren’t you closing the Mexico-US border to prevent the entry of swine flu?”**





- major (90%) restriction of international travel would delay pandemic by few weeks at most
- closing schools/educational facilities would reduce impact on students in these locations but not in the broader population
- cancelling large public events would have no significant impact

US Government H1N1 Influenza Vaccine Priorities



Healthcare Delivery in a Major Epidemic/Pandemic

Defining Surge and Resiliency Capacities

Key:	
ICU-level Care	
Med/Surg Inpatient Care	
Ambulatory Care	
Decedent Services	

Site of Care	Level of Care								
	Inpatient		Ambulatory						Decedent
	ICU	Med/Surg	Diag/Treat	Mental Health	Urgent	Obstetrics	Emergent	Chronic	
Acute care hospitals									
Rehab hospitals									
Mobile field hospitals									
Nursing homes									
Urgent care centers									
Community health centers									
Home health agencies									
Community medical practices									
Emergency medical services									
School-based health centers									
University health services									
Occupational medicine services									
Tribal health services									
Households									
Other non-traditional sites									

The top image shows a FedEx Express MD-11 cargo aircraft on a tarmac. The aircraft is white with a purple and orange livery. The FedEx logo is prominently displayed on the side of the fuselage and on the vertical stabilizer. The bottom image shows a UPS 747-400 cargo aircraft in flight against a sunset sky. The aircraft is white with a brown and gold livery. The UPS logo is on the vertical stabilizer. The text "Worldwide Services" and "Synchronizing the world of commerce" is visible on the side of the fuselage.

- **pre-positioning for known threats**
- **rapid national deployment plus local practice/individual packaging for validated incident**
- **vendor managed inventory for rapid resupply and refreshment of outdated stocks**
- **rapid movement by commercial carriers**
- **managing political/public/media responses for bioincidents with no Rx/vaccine options**

Medical Supply Chain Risks in a Major Epidemic/Pandemic: People and Products



Vulnerability of Global, National and Local Supply Chains in a Major Epidemic/Pandemic

Medicines

- **“just-in-time” supply networks**
 - **major hospitals 2/3 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 Supply Chain Risks in a Major Epidemic/Pandemic: Respiratory Protection for Aerosol-Mediated Agents

- **mask and respirator production for US largely off-shore or key materials originate in Asia**
- **predicted rapid exhaustion of critical supplies.**
- **CIDRAP (Minnesota) Ventilator Study**
 - **39 models with little standardization**
 - **12 models with proprietary (non-interchangeable) circuits**
 - **disposal elements sourced in PRC with no secondary supplier**
 - **14 circuits/ventilator to sustain single 8 week event but average hospital inventory is 3 to 9 circuits**

Medical Consequence Management of a Major Epidemic/Pandemic

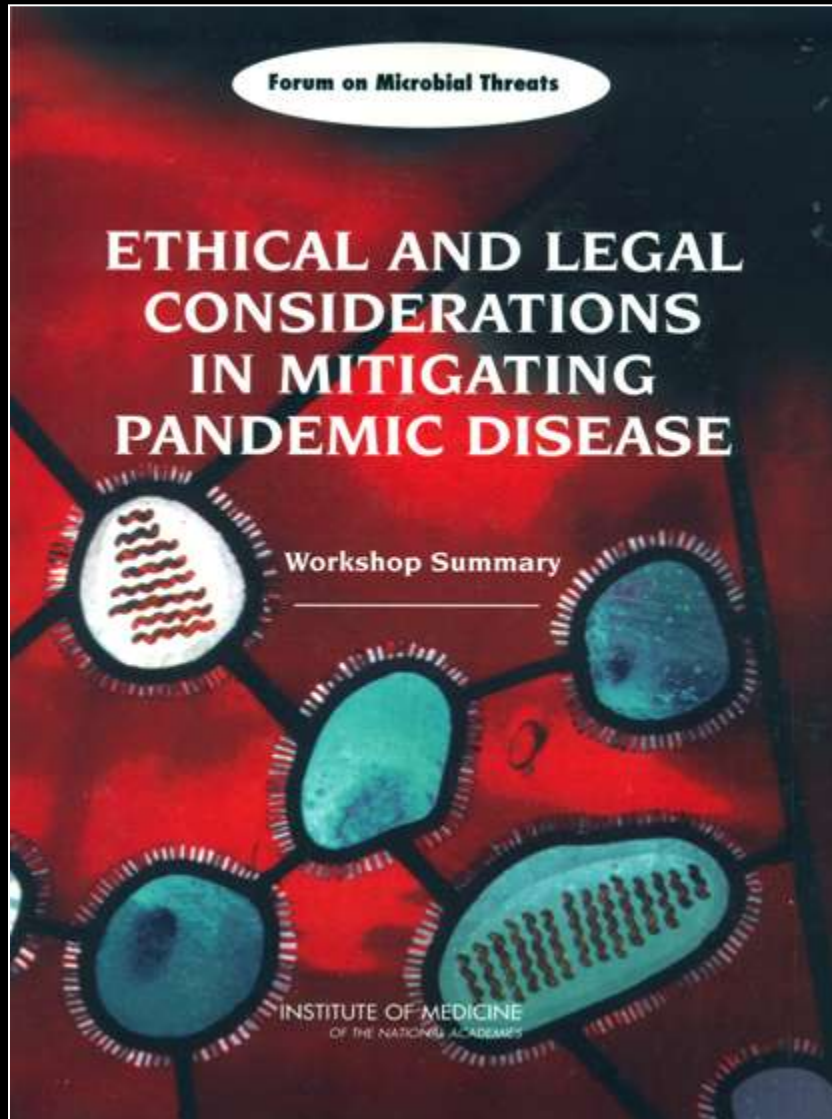
Key Success Factors

- 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
 - emergency services and front line personnel
 - medical/public health
 - politicians and inter-agency coordination
 - media

Quarantine



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

Vulnerability of Global, National and Local Supply Chains in a Major Epidemic/Pandemic

Transportation



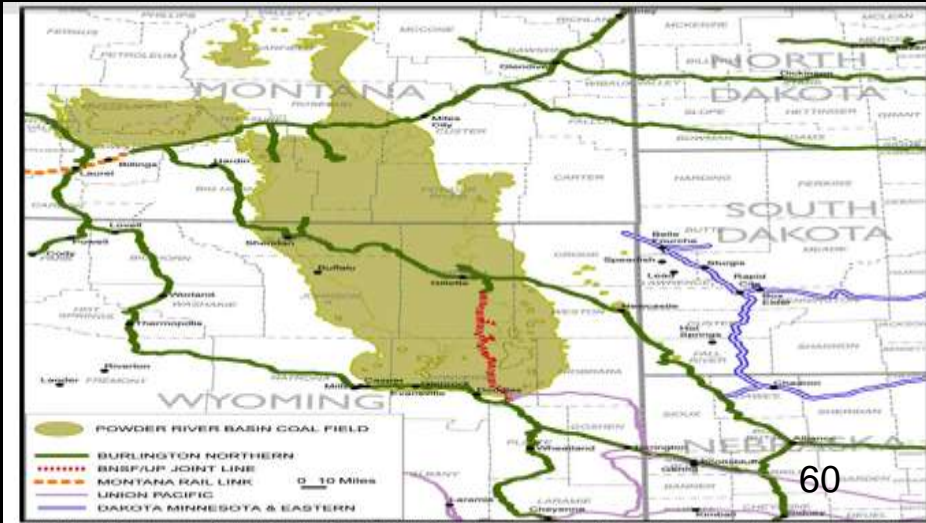
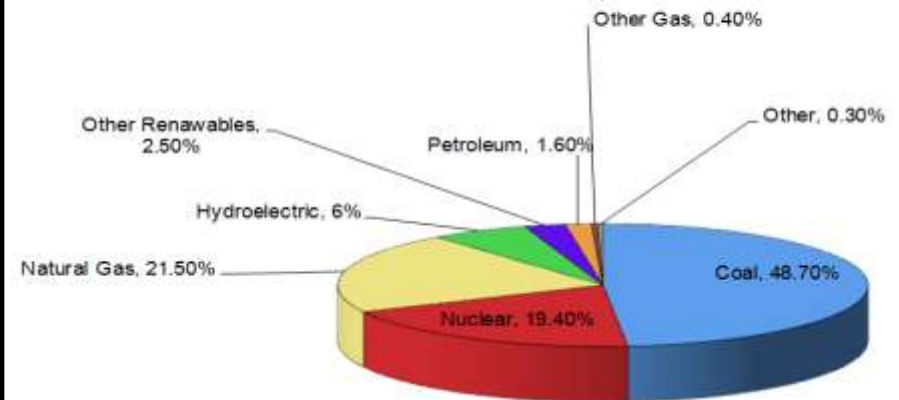
- limited plan for sustained air, maritime, rail and road supply networks
- US industry comprises 3 million workers but accorded no priority in national response plans
- ill-defined plans for prioritization of fuel supplies

Vulnerability of Global, National and Local Supply Chains in a Major Epidemic/Pandemic

Energy



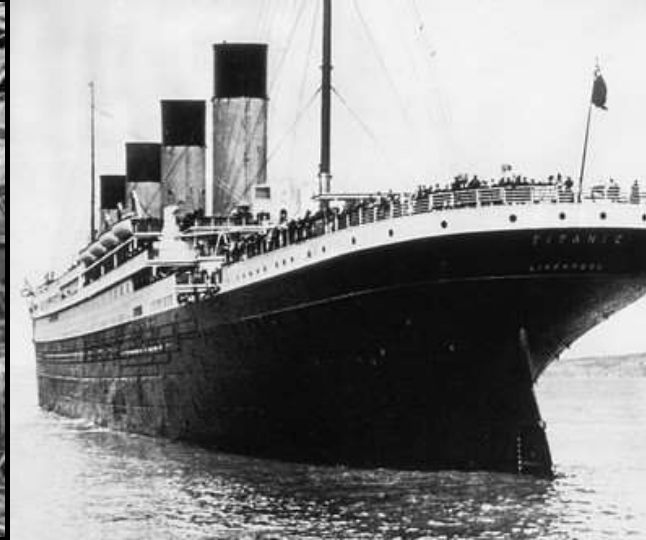
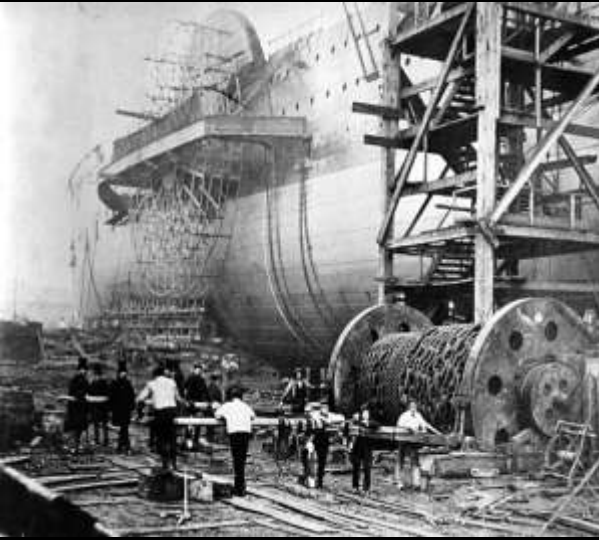
Net Power Generation in the US by Fuel Source, 2007



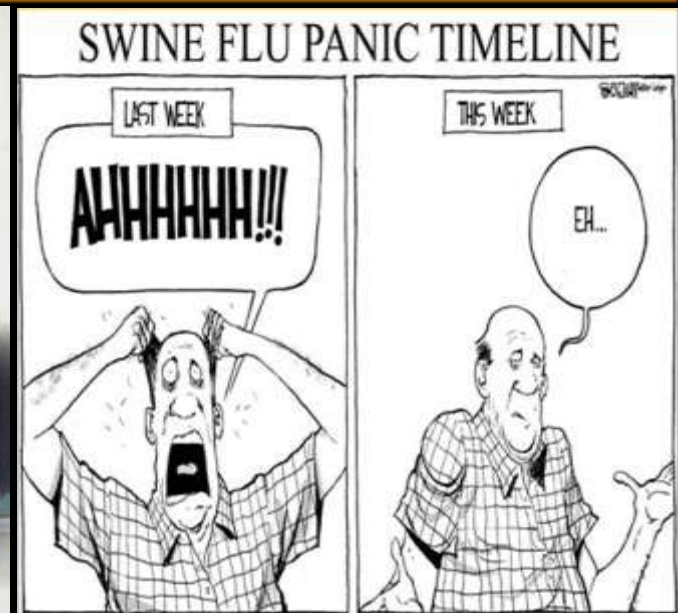
Communication of Risk to the Public



The Unsinkable Ship



Media Sensationalism



The Crucial Role of the Media in Incident Management



Pre-recorded Modules



Familiar (Trusted?) Face(s)



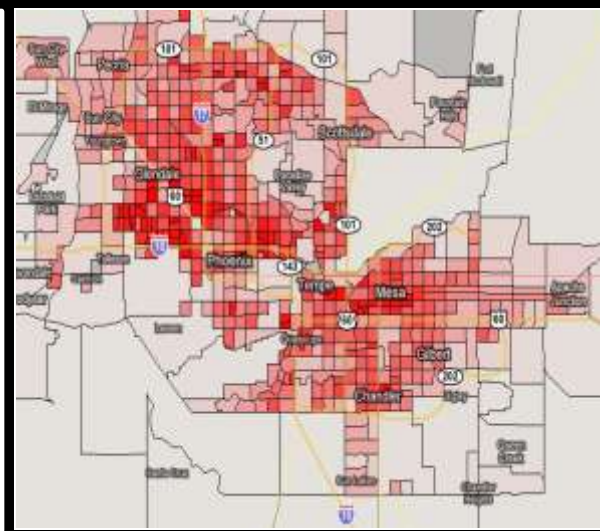
Credibility and Reality



Setting Examples to Limit Civil Disorder



Authoritative Leadership

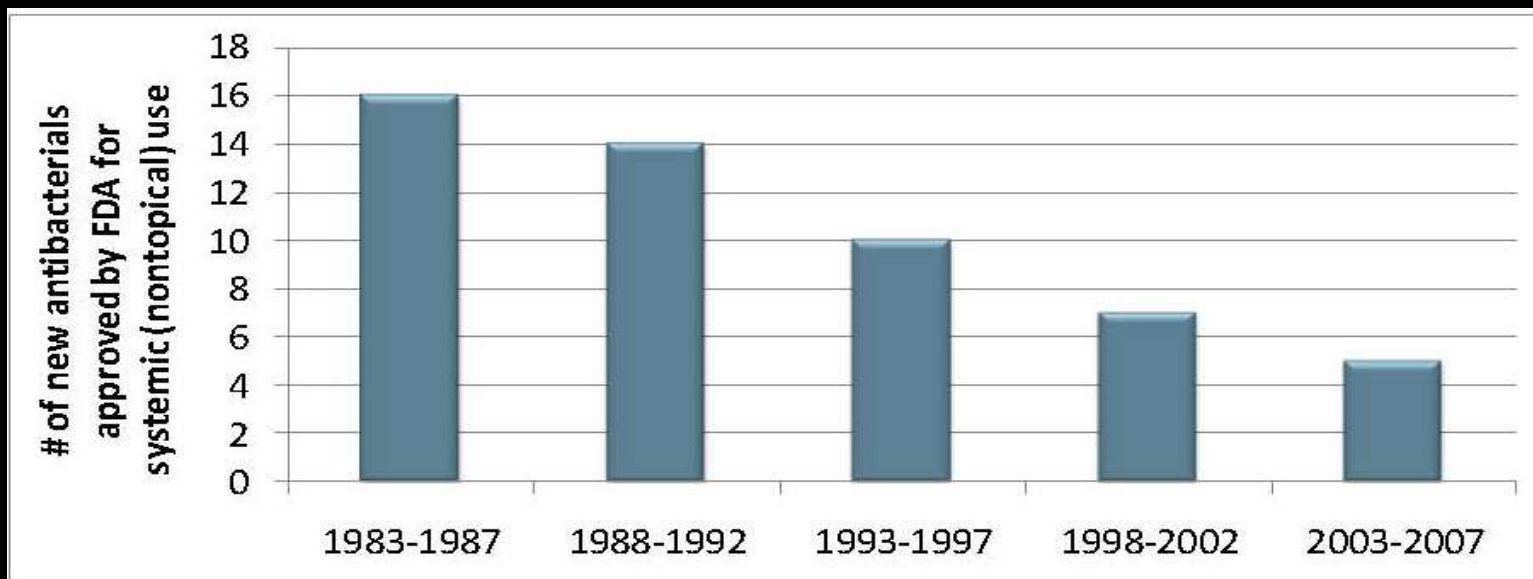


Community Cooperation

The Valley of Dearth: Declining Investment in Drug and Vaccine R&D to Combat Microbial and Parasitic Diseases

“Antimicrobial and vaccine development is in a state of crisis based on the status of the current pipeline for both naturally occurring infectious agents and those that might be intentionally released”

**US National Academies Institute of Medicine Report:
Microbial Threats to Health:
Emergence, Detection and Response 2003**



The Political and Economic Challenges of Drug and Vaccine R&D for Disease of the Developing World (DDW)



“Of course every complex problem has a simple solution, and its invariably wrong.”

H.L. Mencken (1935)

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

Chris Hentshel

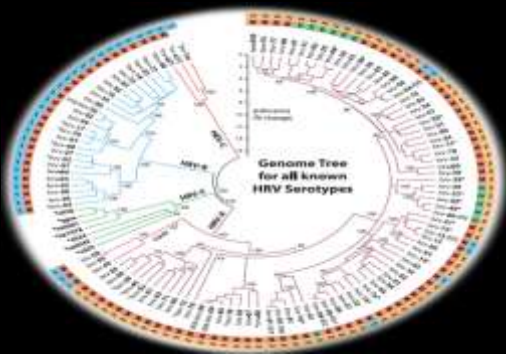
Medicines for Malaria Venture

Lancet (2004) 363, 2198

Maintaining Incentives for R&D Investment in Drugs, Vaccines and Diagnostics

- **low margins (vaccines and public tenders)**
- **tort liability (USA)**
- **escalating cost of clinical trials (regulatory creep)**
- **pricing barriers for new antibiotics (Europe)**
- **market failure (diseases of developing world)**

Crucial Needs for Improved Knowledge of Host-Pathogen Biology



- evolutionary analysis of the dynamics of viral disease
- role of super-shedders in epidemics/epizootics
- molecular biology of adaptive evolution to drugs
- defining protein tertiary structure “rule-sets” for epitope design and recognition in adaptive immunity
- pathogen modulation of host inflammatory and immune responses

INSTITUTE OF MEDICINE AND
NATIONAL RESEARCH COUNCIL
OF THE NATIONAL ACADEMIES

GLOBALIZATION, BIOSECURITY, AND THE FUTURE OF THE LIFE SCIENCES

THE ROYAL
SOCIETY
CELEBRATING 350 YEARS

New approaches to biological risk assessment



twenty ten | 350 years of
excellence in science

NATIONAL
SCIENCE
ADVISORY
BOARD FOR
BIOSECURITY

Strategic Plan for Outreach and Education On Dual Use Research Issues



Report of the National Science Advisory Board for Biosecurity (NSABB)

December 10, 2008

THE ROYAL
SOCIETY
CELEBRATING 350 YEARS

Synthetic biology

2-4 April 2008



scientific
DISCUSSION MEETING
SUMMARY

web.royalsociety.org

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EUROPEAN
COMMISSION
Community research



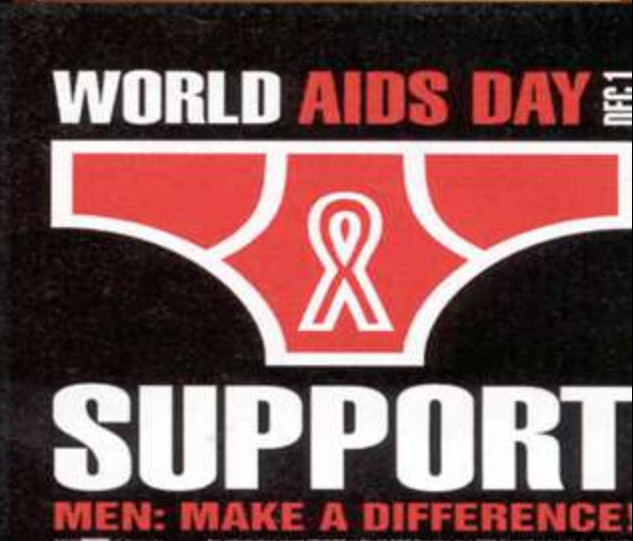
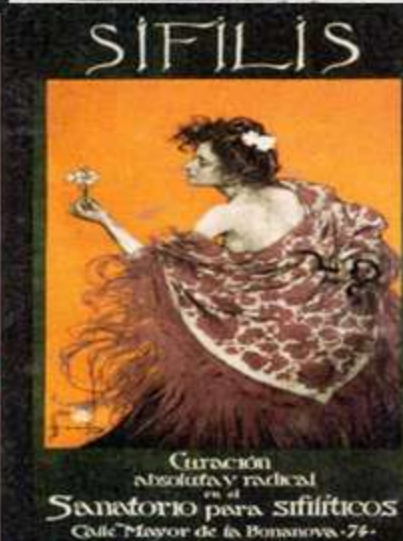
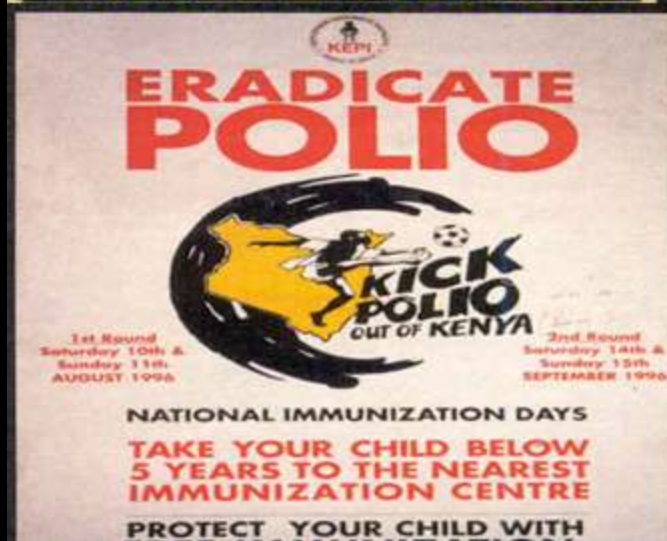
Parliamentary Office of
Science and Technology

postnote

July 2009 Number 340

THE DUAL-USE DILEMMA

Re) Building an International Public Health Infrastructure



Global Public Health: A Daunting Complex Systems Challenge

- **multi-dimensional, multi-disciplinary challenge**
- **complexity increased by disparate socio-economic, and technological capabilities in different geographies**



The Obligate Need for a Systems Approach



**Political Will and Commitments for
Infrastructure, Training, Research and Service**



One World: One Health: One Objective

Comfort and Complacency: The Enemies of Vigilance and Preparedness



**“But I must go and meet the danger there,
or it will seek me in another place,
and find me worse provided.”**

- William Shakespeare, Henry IV

Biosecurity: International Engagement, Commitment and Political Resolve

environmental
sustainability
and
non-
renewable
resources

global
public
health

political
instability
and
escalating
conflict

terrorism
and
international
security



Who Pays for Preparedness?



The Implications of Growing National Debt (G8)





Global Polio
Eradication Initiative

PMI Saving Lives in Africa
PRESIDENT'S MALARIA INITIATIVE



2



BILL & MELINDA
GATES foundation



THE
ROCKEFELLER
FOUNDATION



From Nibbling at the Edges to Engagement in the Root Causes

- ill-defined performance metrics and technology transfer processes



- tractable, actionable, measurable policies
- accountability

- political correctness (PC)



- purposeful commitment (the real PC)
- denunciation of corruption, ineptitude and activist extremism

From Nibbling at the Edges to Engagement in the Root Causes

- public health marginalized in foreign policy and international security policies



- prioritizing global health as a key component in investment, trade, diplomacy and military policies

- vulnerabilities created by highly variable national and global preparedness capabilities



- political will, investment and trans-generational commitment to build resilient systems

The Ten Great U.S. Public Health Achievements of the 20th Century

- | | |
|--------------------------------|--------------------------------------|
| #1 vaccination | #6 safer foods |
| #2 motor vehicle safety | #7 maternal and infant health |
| #3 safer workplaces | #8 family planning |
| #4 infection control | #9 fluoridation |
| #5 CAD / stroke | #10 anti-tobacco actions |

From: CDC MMWR 1999 48 (12) 241-43

The Greatest Global Public Health Achievements of the Early 21st Century (2000-2025)

- **mobilization of public-private partnerships**
 - **DDW, sanitation and safe water, education and e.literacy**
- **reconstruction of international public health surveillance and response capabilities**
- **“one health”: successful integration of diverse disciplines required to outpace infectious and parasitic diseases**
- **expanded portfolio of DDW drugs and vaccines**
- **containment of HIV, TB and malaria**
- **a safe food supply and enhanced agricultural/health self-sufficiency in DCs**
- **vigorous enforcement of BWC and prevention of bioterrorism**



**“Politics is the art of the possible,
the calculated science of survival”**

Prince Otto von Bismarck

***“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)**





Prof Joe Brownlie

DSc BVSc PhD FRCVS FRCPath DipECVP