The Challenge of Global Preparedness For Outpacing Infectious and Parasitic Diseases

Dr. George Poste, Chief Scientist, Complex Adaptive Systems Initiative Del E. Webb Chair in Health Innovation Arizona State University

george.poste@asu.edu

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

- Commercial globalization plus urbanization and industrialization of developing countries
- Climate change, competition for non-renewable resources and environmental sustainability
- Social and economic inequities and fundamentalism as drivers of political instability
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

<table>
<thead>
<tr>
<th>Disease</th>
<th>Burden</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-AIDS</td>
<td>84.5 million</td>
</tr>
<tr>
<td>Neglected Tropical Diseases</td>
<td>56.6 million</td>
</tr>
<tr>
<td>Malaria</td>
<td>46.5 million</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>34.7 million</td>
</tr>
</tbody>
</table>

Hotez PJ, Molyneux DH, Fenwick A, Ottesen E, Ehrlich Sachs S, Sachs JD
Emerging Infections:
The Evolving Nature of Human Infectious and Parasitic Diseases

Mark Woolhouse Univ. Edinburgh

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

One Objective

One Health

Human Health

Ecosystem Health

Animal Health
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
"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?

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

Sir John Beddington
UK Government’s Chief Scientific Adviser
GovNet SDUK09
The Global Food Supply and Food Borne Pathogens

- Food chain increasingly complex, international and inter-dependent
- Food production over next 25 years ≅ 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

- Agricultural Firm, MX
- Agricultural Firm, Michoacan, MX
- Broker, Nuevo Leon, MX
- Distributor/Repacker/Broker, Nuevo Leon, MX
- Agricultural Firm, Mexico
- Growing Facility, Nuevo Leon, MX
- Agricultural Firm, Guadalajara, Mexico
- Agricultural Firm, Tamaulipas, MX
- Agricultural Firm, Mexico
- Grower, Tamaulipas, MX
- Positive sample found
- traceback of positive sample
- distribution from grower, Tamaulipas, MX

Food & Agriculture Commodity Flow System Labor Inputs/Outputs Input/Process/Output Diagram
Production Inputs - Livestock & Crop Production - Food Processing - Food Distribution Wholesale - Food Service

18
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

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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

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

US Importations (2006) LEMIS Data

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 deaths
- accounts for 5% of 9 million new cases of TB
- 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)
- recent WHO/IUATLD Global Surveillance report indicated 7.5% (301/4012) of MDR TB to be XDR
- around 40,000 XDR-TB cases emerge every year

“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
The First Global Map of the Distribution of Human Diseases: Friedrich Schnurrer’s ‘Charte Uber die Geographische Ausebreitung der Krankheiten’ (1827)
Surveillance Systems for the Rapid Detection and Control of Infectious and Parasitic Diseases

- Signatures of Pathogenic Organisms
- Global Network of Surveillance and Diagnostic Testing Systems
- Rapid Analysis and Response to Diagnostic and Surveillance Information

Profile | Sense | Act
Global Disease Surveillance

EMERGEncy ID NET

World Health Organization

Public Health Department's Surveillance

Infectious Diseases Society of America

HealthMap

Global Disease Alert Map

U.S. Influenza Sentinel Provider Surveillance Network

DoD - GEISWeb

Global Emerging Infections System

GIDEON

Quarantine Activity Reporting System (QARS).

BioPortal

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

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not be full agreement.
The Increasing Importance of Geodemographic Information Systems (GIS) in Global Public Health
Geodemographic Information Systems (GIS): Real-Time, Front Line, Ground Zero Data from Field Sampling and Sentinels
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
Use of GIS for Management of Population Movement, Healthcare Facilities and Supply Chains for Optimum Bioincident Control
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
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

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

\[
\frac{dY_i(t)}{dt} = X(t) \left( \beta_i Y_i(t) + \phi \sum_{j=1}^{4} Y_j(t) \right) - \sigma Y_i(t) - \mu Y_i(t)
\]

\[
\frac{dZ_i(t)}{dt} = \sigma Y_i(t) - Z_i(t) \left( \beta_i Y_i(t) + \phi \sum_{j=1}^{4} Y_j(t) \right) - \mu Z_i(t)
\]

\[
\frac{dY_j(t)}{dt} = Z_j(t) \left( \beta_j Y_j(t) + \phi \sum_{i=1}^{4} Y_i(t) \right) - \sigma Y_j(t) - \mu Y_j(t)
\]

\[1 = X(t) + \sum_{i=1}^{4} Y_i(t) + \sum_{j=1}^{4} Z_j(t) + \sum_{i,j=1}^{4} Y_{ij}(t) + Z(t)\]
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

Population

Critical occupations
- Deployed forces
- Critical healthcare
- EMS
- Fire
- Police

High risk population
- Pregnant women
- Infants
- Toddlers

Critical occupations
- Military support
- Border protection
- National Guard
- Intelligence services
- Other natl. security
- Pharmacists
- Mortuary services
- Community services
- Utilities
- Communications
- Critical govt.

High risk population
- Infant contacts
- High risk children

High risk population
- High risk adults
- Elderly

Rest of population
123 million

24 million

64 million

74 million

15 million

Tier 1
Tier 2
Tier 3
Tier 4

Vaccination tier

Tier
### Healthcare Delivery in a Major Epidemic/Pandemic: Defining Surge and Resiliency Capacities

#### Site of Care

<table>
<thead>
<tr>
<th>Site of Care</th>
<th>Level of Care</th>
<th>Inpatient</th>
<th>Ambulatory</th>
<th>Decedent</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>ICU</td>
<td>Med/Surg</td>
<td>Diag/Treat</td>
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<tr>
<td>Acute care hospitals</td>
<td></td>
<td>Red</td>
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<tr>
<td>Rehab hospitals</td>
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<tr>
<td>Mobile field hospitals</td>
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<tr>
<td>Nursing homes</td>
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<tr>
<td>Urgent care centers</td>
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<td>Community health centers</td>
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<td>Home health agencies</td>
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<tr>
<td>Community medical practices</td>
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<tr>
<td>Emergency medical services</td>
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<tr>
<td>School-based health centers</td>
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<tr>
<td>University health services</td>
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<tr>
<td>Occupational medicine services</td>
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<tr>
<td>Tribal health services</td>
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<tr>
<td>Households</td>
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<tr>
<td>Other non-traditional sites</td>
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</tbody>
</table>

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


• 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

- “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
• 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

- 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

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

Maps of energy-related infrastructure and fuel sources in the United States.
Communication of Risk to the Public

Homeland Security Advisory System

Severe
Severe risk of terrorist attacks

High
High risk of terrorist attacks

Elevated
Significant risk of terrorist attacks

Guarded
General risk of terrorist attacks

Low
Low risk of terrorist attacks
The Unsinkable Ship

Media Sensationalism

The Economist
- Obama's first 100 days
- Latin America's economic resilience
- Pakistan attacks the Taliban
- Wall Street's angry shareholders
- The dancing parrot

The New Yorker
- The pandemic threat
- How scared should you be?

Swine Flu Panic Timeline
- Last Week: AHHHHHH!
- This Week: EH...
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”


![Graph showing the number of new antibacterials approved by FDA for systemic (non topical) use from 1983-1987 to 2003-2007. The number of approvals decreases over time.]
“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
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
Re) Building an International Public Health Infrastructure

Un Grand Fléau
LA TUBERCULOSE

 SMALLPOX

 痘種來速

 傳染者痘種不

 OH BOY! WHAT A BREAK. THIS IS WHERE I COME IN!

 KEEP OUT MALARIA MOSQUITOES
 REPAIR YOUR TORN SCREENS

 ERADICATE POLIO

 KICK POLIO OUT OF KENYA

 NATURAL IMMUNIZATION DAYS
 TAKE YOUR CHILD BELOW 5 YEARS TO THE NEAREST IMMUNIZATION CENTRE
 PROTECT YOUR CHILD WITH

 SIFILIS

 CURACIÓN ABSOLUTAMENTE EFÍCICA
 EN 7 DÍAS

 SUPPORT
 MEN: MAKE A DIFFERENCE!
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)
From Nibbling at the Edges to Engagement in the Root Causes

- ill-defined performance metrics and technology transfer processes
- political correctness (PC)

- tractable, actionable, measurable policies
- accountability

- 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
- Vulnerabilities created by highly variable national and global preparedness capabilities
- Prioritizing global health as a key component in investment, trade, diplomacy and military policies
- Political will, investment and trans-generational commitment to build resilient systems
The Ten Great U.S. Public Health Achievements of the 20th Century

<table>
<thead>
<tr>
<th>#1</th>
<th>vaccination</th>
<th>#6</th>
<th>safer foods</th>
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<tbody>
<tr>
<td>#2</td>
<td>motor vehicle safety</td>
<td>#7</td>
<td>maternal and infant health</td>
</tr>
<tr>
<td>#3</td>
<td>safer workplaces</td>
<td>#8</td>
<td>family planning</td>
</tr>
<tr>
<td>#4</td>
<td>infection control</td>
<td>#9</td>
<td>fluoridation</td>
</tr>
<tr>
<td>#5</td>
<td>CAD / stroke</td>
<td>#10</td>
<td>anti-tobacco actions</td>
</tr>
</tbody>
</table>

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

- 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