Emerging Microbial Threats: Issues, Challenges, and Opportunities at the Human-Animal-Ecosystem Interface

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Disclosure

No conflicts with this presentation
OUTLINE

- Identify factors contributing to infectious disease emergence and spread
- Discuss recent examples of disease emergence from animal reservoirs
- Describe challenges in zoonotic disease detection and response
- Review current efforts to strengthen global capacity for early detection, response, and control of emerging diseases

Crude Death Rate* for Infectious Diseases
United States, 1900-1996

*Per 100,000 population per year.

MMWR 1999;48:621-48
“...One can think of the middle of the twentieth century as the end of one of the most important social revolutions in history, the virtual elimination of the infectious disease as a significant factor in social life.”

Burnet, 1962

IOM Definition of Emerging Infections

New, reemerging or drug-resistant infections whose incidence in humans has increased within the past two decades or whose incidence threatens to increase in the near future.

1992
Factors Contributing to the Emergence of Infectious Diseases

1992
- Human demographics and behavior
- Technology and industry
- Economic development and land use
- International travel and commerce
- Microbial adaptation and change
- Breakdown of public health measures

2003
- Human susceptibility to infection
- Climate and weather
- Changing ecosystems
- Poverty and social inequality
- War and famine
- Lack of political will
- Intent to harm

Institute of Medicine
Human Demographics and Behavior

Trends in Global Population


- Less developed countries
- More developed countries

Source: US Bureau of the Census
### Number and Location of Megacities* by Setting and Year, 1950–2025

<table>
<thead>
<tr>
<th>Year</th>
<th>Number</th>
<th>Number (%) in developing world</th>
</tr>
</thead>
<tbody>
<tr>
<td>1950</td>
<td>2</td>
<td>0(0)</td>
</tr>
<tr>
<td>1975</td>
<td>3</td>
<td>1(33)</td>
</tr>
<tr>
<td>2007</td>
<td>19</td>
<td>14(74)</td>
</tr>
<tr>
<td>2025</td>
<td>27</td>
<td>21(78)</td>
</tr>
</tbody>
</table>

* >10 million people

Source: UN Dept of Economic and Social Affairs, World Urbanization Prospects: 2007 Revision

### World Meat Consumption Projections from 1983-2017

![Graph showing world meat consumption projections from 1983 to 2017](image)

*Achieving Sustainable Global Capacity for Surveillance and Response to Emerging Diseases of Zoonotic Origin. IOM Forum on Microbial Threats Workshop Summary, 2008*
Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: a molecular, biological, and epidemiological study

Kathleen E. N. C. L. A. C. A. N. S. S. G. N. S. D. N. M. 1 (New Delhi metallo-β-lactamase-1) in Enterobacteriaceae

- NDM-1 (New Delhi metallo-β-lactamase-1) in Enterobacteriaceae
- Pan-resistant except tigecycline and colistin
- Clonally diverse strains
- Most on plasmids and transferable
- Some infections associated with medical tourism

Lancet Inf Dis 2010; 10:597–602
New Delhi: 171 surface water (SW) and 50 tap water (TW) samples
- NDM-1 gene in 51 (30%) of SW and 2 of 50 (4%) of TW samples
- NDM-1 gene found in 11 “new” species of bacteria

*Lancet Inf Dis 2011; 11:355–362*
Lack of Political Will – Human Disease

Polio: Obstacles keep eradication out of reach

Polio spreading from Kano has reinfected >20 countries from West Africa to Indonesia

Lack of Political Will – Zoonotic Disease

Early Cases of SARS: Guangdong Province, China

Nov 16, 2002: first known cases of atypical pneumonia in Foshan

Feb 11-12, 2003: China reports 305 cases of acute respiratory syndrome in Guangdong Province
**Carlo Urbani**
President of the Italian Chapter of Doctors without Borders

- French Hospital in Hanoi, Vietnam, early March 2003: Dr. Urbani called to evaluate American businessman who had fallen ill with “bad case of influenza”
- The patient had been in “Hotel M” in Hong Kong
- Dr. Urbani realized that the patient did not have flu, but probably a new highly contagious disease; he notified WHO, and an investigation began
- Bangkok, Thailand, late March: Dr. Urbani presented with dyspnea, fever, myalgias, thrombocytopenia, leukopenia

- Fever persisted
- Respiratory distress worsened
- Patient died on day 19
### SARS Coronavirus

**Negative stain**  
**In Vero E6 cells**

<table>
<thead>
<tr>
<th>Antigenic Group</th>
<th>Virus</th>
<th>Host</th>
<th>Respiratory Syndrome</th>
<th>Enteric Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>TGEV</td>
<td>pig</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td></td>
<td>FIPV</td>
<td>cat</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>II</td>
<td>HCV-229E</td>
<td>human</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>HCV-OC43</td>
<td>human</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>III</td>
<td>MHV</td>
<td>mouse</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>III</td>
<td>IBV</td>
<td>hen</td>
<td></td>
<td>yes</td>
</tr>
</tbody>
</table>

**Chain of transmission among guests at Hotel M—Hong Kong, 2003**

Data as of March 28, 2003

- 4 HCWs
- 37 HCWs
- 99 HCWs (includes 17 medical students)
- 0 HCWs
- 28 HCWs
- 4 other Hong Kong Hospitals
- 156 close contacts of HCWs and patients
- 34 HCWs
- Hotel M
- 2 close contacts
- 10 HCWs
- Hotel 1 HK
- Hotel 2 HK
- Hotel 3 HK
- Guangdong Province, China
- 4 family members
- 2 family members
- Unknown number close contacts
- 37 close contacts
- 34 HCWs
- 2 close contacts
- unknown
- HCWs
- HCV
- SARS CoV
- FIPV
- HCV
- IBV
- MHV
- TGEV

*Health-care workers; † All guests except G and K stayed on the 9th floor of the hotel. Guest G stayed on the 14th floor, and Guest K stayed on the 11th floor; ‡ Guests L and M (spouses) were not at Hotel M during the same times as Index Guest A but were at the hotel during the same times as Guests G, H, and I who were ill during this period.*
Severe acute respiratory syndrome coronavirus-like virus in Chinese horseshoe bats


Department of Microbiology, Research Centre of Infectious and Emerging, New Key Laboratory of Emerging Infectious Diseases, and Department of Pathology, University of Hong Kong, Queen Mary Hospital, Pokfulam, Hong Kong Special Administrative Region, China

*Corresponding author. Email: lacagief@hku.hk

Abstract

Although the finding of severe acute respiratory syndrome coronavirus (SARS-CoV) in caged palm civets from live animal markets in China has provided evidence for inter-species transmission in the genesis of the SARS epidemic, subsequent studies suggested that the civet may have served only as an amplification host for SARS-CoV. In a serosurvey study for CoV in non-caged wildlife from the wild areas of the Hong Kong Special Administrative Region, we identified a CoV closely related to SARS-CoV, CoV HKU3. Phylogenetic analysis of the S gene of this virus showed that it has a SARS-CoV-like S gene and is closely related to SARS-CoV. In addition, the protein X, the essential protein for SARS-CoV replication, was conserved. Collectively, these findings suggest that this novel virus, named SARS-CoV-like virus (S-CoV), is a natural reservoir of S-CoV, and may be a potential reservoir for zoonotic SARS-CoV.

Methods

Molecular Identification. The study was approved by the Research Committee of Food and Health.

PNAS 2005;102:14040-5

Animal photos courtesy of Dr. Yi Guan
Hong Kong University, and badgers.org.uk

References

“The SARS experience ... made one lesson clear early in its course: inadequate surveillance and response capacity in a single country can endanger national populations and the public health security of the entire world.”

Heymann D, Rodier G. Emerg Infect Dis 2003
Orthopox virus
- First identified in non-human primates, but reservoir is rodents
- 1st human illness seen in 1970 in Congo during smallpox eradication era
- Clinical features similar to smallpox
- Lower mortality (<10%); less efficient person-to-person transmission
- All previous disease in West and Central Africa
- Understudied; smallpox vaccine appears cross-protective

Monkeypox

Case
- A 30-year-old woman developed sore throat, headache, fever, malaise and a small painless papule on her left cheek
- Within 48 hours, throat soreness and malaise worsened and additional lesions developed
Primary inoculation lesion at site of prairie dog bite

Secondary lesions

The Washington Post, June 9, 2003
Movement of Imported African Rodents to Animal Distributors and Distribution of Prairie Dogs from an Animal Distributor Associated with Human Cases of Monkeypox*

**As of July 8, 2003. Does not include one probable human case from Ohio; investigation ongoing.**

**Identified as distributor C in MMWR 2003;52:561-4.**

**Identified as distributor D in MMWR 2003;52:561-4.**

**Identified as distributor B in MMWR 2003;52:561-4.**

**Includes 2 persons who were employees at IL-1.**

? - date of shipment unknown

1 PD traced

200 prairie dogs (PDs) at facility

* 50 Gambian giant rats (GR)
* 53 rope squirrels (RS)
* 2 brushtail porcupines (BP)
* 47 tree squirrels (TS)
* 100 striped mice (SM)
* 510 dormice (DM)

TX-1**

4/9/03

GR

4/11/03

SM

3/15/03

DM

TX-2

NJ

RS, BP, TM, RM

TX-3

IA†

GR, DM

TX-4

TX-5

DM

DM

TX-6

TX-7

TX-8

TX-9

TX-10

IL-1§

IL-2

DM

DM

DM

IL-3

IL-4

DM

DM

Japan

DM

SC

No human cases

IL-5

DM

KS

No human cases

IN

DM

MO

Human cases: 2 confirmed

MN

DM

SC

No human cases

MI

No human cases

MI

No human cases

MN

DM

WI

DM

WI

DM

IL-1

DM

IL-2

DM

IL-3

DM

IL-4

DM

Japan

DM

TX-8

TX-9

TX-10

IL-2

DM

4/28/03

5/12/03

6/1/03

4/25/03

4/9/03

4/2/03

4/11/03

4/2/03

4/26/03

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4/26/03

4/26/03
Annual Global Trade in Exotic Animals

- 4 million birds
- 640,000 reptiles
- 40,000 primates
- Illegal trade unknown – estimate $4-6 billion

Vigilance

- The “Alert” Physician
- The “Alert” Veterinarian
- The “Alert” Pathologist / Laboratorian
- The “Alert” Research Scientist
- The “Alert” Public Health Official

Public Health Dispatch

West Nile Virus Infection in Organ Donor and Transplant Recipients — Georgia and Florida, 2002

On August 23, 2002, the Georgia Division of Public Health (GDPH) and CDC were notified of two cases of unexplained fever and encephalitis in recipients of organ transplants from
Five Stages through which Pathogens of Animals Evolve to Cause Diseases Confined to Humans

Clin Infect Dis 2010; 50(12):1636-1640

- Systematic literature review: 1,399 human pathogens
- 87 (6%) first reported since 1980; 58 (67%) viruses, mostly RNA
- Global distribution
- Majority from animal reservoirs
Global trends in emerging infectious diseases

Kate E. Jones, Nikki G. Patel, Marc A. Levy, Adam Storeygard, Deborah Balk, John L. Gittleman, Peter Daszak

Emerging infectious diseases (EIDs) are a significant burden on global economies and public health. Their emergence is thought to be driven largely by socio-economic, environmental and ecological factors. But no one has explicitly analysed these linkages to understand global temporal and spatial patterns of EIDs. Here we analyse a database of 1,000 EID events (emergence of EIDs or between 1980 and 2004) and demonstrate non-random global patterns. EID events have been significantly over time after controlling for reporting bias, with their peak incidence in the 1990s concurrent with the HIV/AIDS pandemic. EID events are dominated by avian (68.0% of EIDs); the majority of these (57.3%) originate in wildlife (for example, avian acute respiratory virus, H5N1 virus) and are increasing significantly over time. We find prios pathogens constitute only 28.4% of EID events, in contrast to previous analyses which suggest the 50-65% of emerging pathogens are viruses or prions and 16-30% bacteria or rickettsiae. This follows up an analysis of each individual pathogen and incudes strain as a separate pathogen in our database, and reflects more accurately the true significance of antimicrobial drug resistance for global health, in which different pathogens strains can cause separate significant outbreaks. In broad consensus, with previous studies on the characteristics of emerging human pathogens, we find the percentages of EID events caused by either pathogens types to be 18.7% for prions, 4.9% for fungi and 3.4% for helminthes (see Supplementary data and Supplementary Table 7 for detailed summaries on recent studies)

- Review of 335 emerging disease events, 1940-2004
- Non-random global distribution
- 60% from animal reservoirs; 72% of those from wildlife
- Identification of geographic hot spots

Nature 2008;451:990-93

Economic Impact of Recent Zoonotic Epidemics

Infectious Disease Movement in a Borderless World. IOM Forum on Microbial Threats Workshop Summary, 2010
“Human and animal health are inextricably linked. They always have been. They always will be.”

James H. Steele
1913 -
Chief, Veterinary Public Health Division, CDC
Assistant Surgeon General for Veterinary Affairs, USPHS

Calvin Schwabe
1927 – 2006
Professor of Veterinary Medicine

“One Health”

Humans
Domestic Animals
Wildlife
Ecosystems

http://www.onehealthcommission.org/
• 13 zoonoses responsible for ~2.4 B cases & ~2.2 M deaths/yr; foodborne disease #1

• Majority in low or middle income countries

• Greatest impact on poor livestock keepers

• High burden countries include India, China, Bangladesh, Ethiopia, Nigeria, Pakistan, DR Congo, & Tanzania

• Hot spots for emergence in US & UK also

Prediction Considerations

- **Hot spots**
  - e.g., rainforests, megacities

- **Hot reservoirs**
  - e.g., bats, pigs, prairie dogs

- **Hot settings**
  - e.g., wet markets

- **Hot vectors**
  - e.g., Aedes albopictus

- **Hot vehicles**
  - e.g., bush meat
Swine Flu Names Evolving Faster Than Swine Flu Itself

Science 2009;324:811

Emerging Pandemic Threats Program

UC Davis-Led Team Selected to Implement USAID Wildlife Surveillance Project to Detect and PREDICT Emerging Infectious Diseases

- 5-year, $400 million effort
- Launched in FY10
- Focus on early identification of and response to dangerous pathogens in animals (especially wildlife) before transmission to humans
Opportunities to Prevent, Detect, and Respond to the Emergence and Transmission of Zoonotic Diseases

*Sustaining Global Surveillance and Response to Emerging Zoonotic Diseases. IOM Forum on Microbial Threats Workshop Summary, 2009*

**FIGURE E.1:** Early Control of Zoonotic Disease Is Both Cost-effective and Prevents Human Disease

*Source: Adapted from IOM (2009).*

*World Bank Report Number 69145-GLB, 2012*
Common Ground for Medical and Veterinary Communities

- Avian, animal, and pandemic influenza
- Other zoonotic diseases including those associated with exotic pet and wildlife trade
- Foodborne disease
- Healthcare-associated infections
- Antimicrobial resistance
- Blood, organ, tissue safety
- Neglected tropical diseases
- Pathogen discovery / new diagnostics
- Disease eradication
- Biosafety / Biosecurity
- Bioterrorism / Biodefense

Future Challenges

- Another Influenza Pandemic
- Antimicrobial Resistance
- International Foodborne Disease Outbreaks
- Urban Yellow Fever in Latin America or Asia
- Microbial Etiologies of Chronic Diseases
- The Unexpected
“At the same time, I am somewhat bemused by the number of ‘experts’ who appear regularly in the public media and predict—with virtual certainty—that H5N1 will be the next pandemic strain—and soon! Lifelong students of this disease are much more humble about their predictions!”

Theodore C. Eickhoff, M.D.
Chief Medical Editor
Infectious Disease News
December 2005;18:4
“A robust public health system—in its science, capacity, practice, and through its collaborations with clinical and veterinary medicine, academia, industry and other public and private partners—is the best defense against any microbial threat.”

Opportunities

International Health Regulations (2005)
www.who.int/csr/ihr/en/

- Timely reporting
- Information sharing
- Laboratory capacity
IHR 2005: “Faster, Stronger, Broader”

- Goal: prevent international spread of disease
- Not a surrogate for national surveillance and response systems
- But all Member States must be able – in a timely way – to detect, assess, report, and respond to public health risks / emergencies of international concern

Public Health Emergency of International Concern (PHEIC)

- Decision instrument
- Immediate notification of even one case:
  - Smallpox
  - Poliomyelitis
  - SARS
  - Influenza caused by new subtypes
- Notification determined by assessment:
  - Cholera
  - Pneumonic plague
  - Yellow fever
  - Viral hemorrhagic fever (Ebola, Marburg, Lassa)
  - West Nile fever
  - Others of national/regional concern (e.g., dengue, Rift Valley fever)
• From July 2007 – December 2011, 105 countries reported 222 potential PHEICs*

• United States reported 24
  • 12 due to new influenza virus subtypes
  • 10 of other 12 caused by microbes
    – 7 by zoonotic pathogens (5 Salmonella)
    –* Public Health Emergency of International Concern

Emerg Infect Dis 2012; 18:1047-53

Lessons Learned and Future Needs

• Vigilance
• Strengthened surveillance and public health laboratory capacity
• Better predictive capability
• Multidisciplinary partnerships
• Improved coordination, proactive communication, and avoidance of stigmatization
• Transparency and sustained political will (locally, nationally, regionally and globally)
• Address research, training, and education priorities
Focus on threats or disease activity affecting humans, animal, or plants to achieve early detection and situational awareness and enable better decision making

- All hazards approach
- Guiding Principles
  - Leverage existing capabilities
  - Embrace all-of-nation approach
  - Add value for all participants
  - Maintain global health perspective

Conclusions

- Trends in factors favor microbes
- New threats will emerge; many will be zoonotic
- Vigilant frontline healthcare workers will continue to have a critically important role in recognition of emerging diseases
- History: travel, work, hobbies, animal contact
- Surveillance is critical to achieving public health security; improving national and international surveillance capabilities should be priorities for national health and security policy
- Helping individual countries improve their surveillance capacities will benefit all countries
Expect the Unexpected

Complacency

http://www.cdc.gov/eid
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