Our Vulnerability to Animal Diseases: Zoonotic Diseases and their Potential for Infecting Humans

James A. Roth, DVM, PhD, DACVM
Center for Food Security and Public Health
College of Veterinary Medicine
Iowa State University
Newly Emergent Zoonotic Diseases Since 1982

Emerging and Re-emerging Disease Timeline

2005
Avian Influenza (H5N1) spreads to Europe and Africa
Streptococcus suis in China

2003
SARS, Monkeypox
First case of BSE in U.S.

1998
Nipah virus in swine and humans in Malaysia

1996
Variant Creutzfeldt-Jakob Disease (vCJD) in humans in U.K.

1986
First case of BSE in the UK

1982
E. coli 0157:H7
Lyme Disease (Borrelia burgdorferi)

2007 and Beyond
???

2004
Avian Influenza (H5N1) in East Asia, Asia, Eurasia

1999
West Nile Virus in the U.S.

1997
First human cases of Avian Influenza (H5N1) - Hong Kong

1993
Hantavirus (Sin Nombre Virus)
Four corners region of the U.S.

1983
HIV in the United States
Factors contributing to continuing emergence/re-emergence of diseases

- Overpopulation
- Intensive animal agriculture
- Increased “backyard” animal production
- Wildlife/domestic animal/human interactions
- Interspecies transfer of pathogens
- Changing ecosystems
- Global warming
- Globalization
Major Biological Crises

- Plague (Black Death) in Europe
  - 1/3 to 2/3 died
- Smallpox in native Americans
  - 50% to 80% died
- AIDS
  - 25 million deaths worldwide
  - 39 million living with HIV
- ???
Potential Zoonotic Biological Crises in Food Producing Animals

- Ruminants
  - Rift Valley Fever
- Swine
  - Nipah virus
  - Swine influenza virus
- Poultry
  - Highly Pathogenic Avian influenza
Rift Valley Fever

- Phlebovirus (Bunyaviridae)
- Arthropod vector
  - Most commonly mosquito
- Acute febrile disease
  - Sheep, cattle, goats
  - High abortion rates and death in young
- Can affect humans, cats, dogs
Rift Valley Fever
Animal Disease

<table>
<thead>
<tr>
<th>Mortality 100%</th>
<th>Severe Illness Abortion Mortality</th>
<th>Severe Illness Viremia Abortion</th>
<th>Infection Viremia</th>
<th>Refractive to Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lambs</td>
<td>Sheep</td>
<td>Monkeys</td>
<td>Horses</td>
<td>Rodents</td>
</tr>
<tr>
<td>Calves</td>
<td>Cattle</td>
<td>Camels</td>
<td>Cats</td>
<td>Rabbits</td>
</tr>
<tr>
<td>Kids</td>
<td>Goats</td>
<td>Rats</td>
<td>Dogs</td>
<td>Birds</td>
</tr>
<tr>
<td>Puppies</td>
<td>Humans</td>
<td>Squirrels</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kittens</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Some rodents</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
Human Disease

- Incubation period: 2-6 days
  - Inapparent or flu-like signs
    - Fever, headache, myalgia, nausea, vomiting
    - Recovery in 4-7 days
  - Severe disease in 1%
    - Retinopathy
    - Hemorrhagic fever
    - Encephalitis
- Overall mortality ~1%
Transmission to Humans

- **Vector-** mosquito
- **Direct contact or aerosolization**
  - Tissue or body fluids of infected animals
  - Aborted fetuses
  - Slaughter, necropsy
- **Oral**
  - Drinking unpasteurized milk from an infected animal
- **Person-to-person transmission** rare
Distribution of Rift Valley Fever
Rift Valley Fever Current Outbreak

- November 2006 to present
- As of April 2007, 989 human cases reported in Kenya, Tanzania and Somalia with 246 deaths
- Control efforts implemented including restricting movement or slaughter of animals, vaccination of livestock, insect vector control and public education
Reservoirs for RVF

- Mosquitoes – *Aedes* species
  - Transovarial transmission
  - Eggs dormant in soil for long periods

- Ruminants are amplifying host

- Humans have high enough viremia to transmit
  - Incubation period 2 to 6 days
Reducing the Global Threat of RVF

- Investment in safe and effective vaccines for ruminants and man

- Vaccinating ruminants would greatly reduce the need to vaccinate people

- Making vaccines available to endemic countries will reduce the threat of global spread
Rift Valley Fever Vaccine

- No vaccine in US for animals or people
- MP12: a mutagen-attenuated modified live vaccine candidate
- Developed by USAMRIID
  - Protected pregnant cows, neonatal calves, and steers from virulent challenge
  - Safe in neonatal lambs, fetal and neonatal calves, pregnant cows
Nipah Virus Outbreak

- 1998-1999, Malaysia
  - Respiratory and neurologic syndrome in swine
  - Encephalitis in humans
    - More than 250 cases
    - More than 100 deaths
  - Initially mistaken for Japanese encephalitis
  - Discovered new Paramyxovirus
Nipah Virus

- Virus isolated in March 1999
- Quick national response with international assistance
- 1.1 million pigs culled (out of 2.4 million total)
- No new cases in Malaysia since 1999
Reservoir

- Flying foxes (fruit bats)
  - Carry the virus
  - Are not affected
  - Virus found in
    - Urine
    - Partially eaten fruit
  - Migratory
From Tambun, Nipah spread through infected pigs to farms in Penang, Perak, Selangor, Malacca, Negri Sembilan and Johor. Farmers in Tambun had "fire sales" to get rid of pigs.
Nipah Field Investigations- Malaysia
Nipah Virus in Bangladesh

- Outbreaks of respiratory disease, high fever, unconsciousness, vomiting, headache
- 2002 to present
- Confirmed to be Nipah virus infection by CDC
- Believed to be oral transmission from contaminated fruit
- Human to human transmission
Rational Design of Marker Vaccine for Nipah Virus

- **Vaccine**
  - Live virus vector expressing the Nipah F and G genes

- **Companion Diagnostic Test**
  - ELISA test for antibody vs Nipah N protein
Major Challenges for Nipah Vaccine Development

- Biosafety level 4 pathogen
- Access to viral genetic material
- Foreign animal disease
- Recombinant vaccine work in BL2+ lab and BL3 Ag animal facility
- USDA Import permits
- Proprietary rights to vaccine vectors
- USDA APHIS Center for Veterinary Biologics approval for vaccine transport, use, and export
- Permission of State Veterinarian
- Funding
Nipah Virus Vaccine and Companion Diagnostic Test Development

- Collaborative project between
  - ISU College of Veterinary Medicine
  - Veterinary Research Institute of Malaysia
  - US Centers for Disease Control and Prevention
  - USDA Plum Island Animal Disease Center
  - USDA APHIS National Veterinary Services Laboratories
  - Merial Animal Health
  - Canadian Food Inspection Agency
Influenza Overview

- Avian influenza in birds
  - Low pathogenic (H1 to H16)
  - High pathogenic (H5 or H7)
  - High pathogenic H5N1, Asia

- Influenza in humans
  - Seasonal influenza (H1, H2, H3)
  - Pandemic influenza
    - 1918, 1957, 1968, 2???
  - Pandemic avian influenza H5N1
Influenza A Viruses

- Mutate frequently
  - Antigenic drift
    - Point mutations accumulated during virus replication
  - Antigenic Shift
    - Hybrid virus emerges when a cell is infected with two different influenza viruses
      - Human, avian, swine, equine
    - Transfer of an Influenza virus to a different species
Countries with H5N1 Avian Influenza and Human Deaths (both cumulative)

- **Countries with H5N1 avian influenza in animals**
- **Human Deaths** (in 12 countries)

<table>
<thead>
<tr>
<th>Year</th>
<th>Countries</th>
<th>Human Deaths</th>
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<tbody>
<tr>
<td>2003</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>2004</td>
<td>9</td>
<td>36</td>
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<td>2005</td>
<td>16</td>
<td>78</td>
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<td>2006</td>
<td>55</td>
<td>158</td>
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<tr>
<td>2007</td>
<td>60</td>
<td>191</td>
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Through June 30
Interspecies Transmission of Influenza Viruses
Stopping Emerging Diseases at their Source
Essential Elements to Avoid and Manage Biological Crises

Accelerate the application of modern science to improve diagnostics, vaccines, and anti-virals
  - Increase funding
  - Streamline regulatory hurdles

One medicine, one world, approach to diseases
  - Human medicine, veterinary medicine, public health

International collaboration
  - Led by international organizations
  - Funded by developed world
  - Government agency, private sector and university collaboration

Strengthen public health infrastructure and veterinary services in all nations
Funding Sources for Center for Food Security and Public Health Zoonotic Disease Projects

- USDA
  - Agriculture Research Service
  - Animal and Plant Health Inspection Service
  - Foreign Agriculture Service
  - Cooperative State Research, Extension, and Education Service
  - Risk Management Agency
- HHS
  - Centers for Disease Control and Prevention
  - National Institute of Allergy and Infectious Diseases
Questions?

The Gentle Doctor by Christian Peterson
Iowa State University, College of Veterinary Medicine