Ebola Virus Infection in Dogs and Pigs

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Five Species of Ebola Viruses

- Enveloped RNA virus related to Marburg virus
- Genus: *Ebolavirus* (5 species)
  - Pathogenic for humans (Africa)
    - Zaire ebolavirus (ZEBOV)
    - Sudan ebolavirus
    - Tai forest ebolavirus
    - Bundibugyo ebolavirus
  - Not pathogenic for humans; pathogenic for non-human primates (Philippines, China)
    - Reston ebolavirus (REBOV)
Ebola Virus Antibody Prevalence in Dogs and Human Risk

- Serologic survey of dogs in highly infected areas during 2001-2002 Ebola Zaire outbreak in Gabon
- IgG ELISA
  - 159 dogs in epidemic area – 25.2% positive
  - 66 dogs in villages with human cases and animal source – 31.8% positive
  - 102 dogs in France – 2% positive (false)

Symptoms were not observed in any of these dogs
Blood samples were negative by PCR

“Although dogs can be asymptomatically infected, they may excrete infectious viral particles in urine feces and saliva for a short period before virus clearance, as observed experimentally in other animals.”
CDC Website: Questions and Answers about Ebola and Pets

- CDC Website: [http://www.cdc.gov/vhf/ebola/transmission/qas-pets.html](http://www.cdc.gov/vhf/ebola/transmission/qas-pets.html)

  “CDC is currently working with the USDA, the AVMA, and many other partners to develop additional guidance for the U.S. pet population”

Discovery of Swine as a Host for the Reston ebolavirus

*Barrette et al, Science 325:204-206, 2009*

PIADC, CDC and Philippines BIA

- Swine serum and tissue samples from Philippines submitted to FADDL in 2008

- Highly pathogenic PRRS virus and PCV2 isolated

- Cytopathic virus also isolated in VERO cells (non-permissive to PRRSV)

- Microarray revealed Reston Ebola
Discovery of Swine as a Host for the
Reston ebolavirus
Barrette et al, Science 325:204-206, 2009
PIADC, CDC and Philippines BIA

- Reston Ebola was found only in samples also positive for PRRSV
- Genomes of three virus isolates were significantly divergent from each other, suggesting that they have been circulating for several years

Discovery of Swine as a Host for the
Reston ebolavirus
Barrette et al, Science 325:204-206, 2009
PIADC, CDC and Philippines BIA

- Six (of 141) serum samples of people working with pigs in Philippines had antibody to REBOV
- No evidence of disease in humans
A Seroepidemiologic Study of *Reston ebolavirus* in Swine in the Phillipines
(Sayama et al, BMC Vet Res 2012; 8:82)

- 215 swine sera from two REBOV affected farms in 2008
  - ~70% positive for REBOV antibodies by multiple serodiagnostic systems
- 98 swine sera from non-epizootic region
  - All negative

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Ebola Reston Virus Infection of Pigs: Clinical Significance and Transmission Potential
(Marsh et al, JID 2011:204 S804-S809)

- Experimental challenge with REBOV in 16 five week old pigs
- Replication of virus in internal organs and viral shedding from nasopharynx and feces in absence of clinical signs
- Virus present in skeletal muscle
- Virus clearance associated with seroconversion occurring within 10 to 12 days after challenge – no virus persistence
Ebola Reston Virus Infection of Pigs: Clinical Significance and Transmission Potential

(Marsh et al, JID 2011:204 S804-S809)
Australian Animal Health Laboratory and CDC

- Concurrent respiratory infection may facilitate transmission
- “...asymptomatic infection of pigs with REBOV occurs ... animals so affected pose a transmission risk to farm, veterinary, and abattoir workers.”

Reston Virus in Domestic Pigs in China

(Pan et al, Arch Virol 2014;159:1129-1132)
Peoples Republic of China

- 137 spleen samples from pigs that died of PRRSV on 3 farms in Shanghai
- 4/137 positive for Reston ebolavirus by RT-PCR
- All co-infected with PRRSV and under 8 weeks old
- One sequence was most closely related to Philippines REBOV, other 3 more distantly related to Philippines REBOV and to each other
Replication, Pathogenicity, Shedding, and Transmission of Zaire ebolavirus in Pigs
(Kobinger et al, JID 2011:204:200-208)
CFIA and others, Winnipeg, Canada

- Demonstrated that pigs (3 to 5 weeks old) are susceptible to mucosal challenge with ZEBOV and can develop severe respiratory disease which is transmitted to pen mates (more severe in older pigs)

- Virus replicated in macrophages, pneumocytes and endothelial cells of lung

- “In contrast to the severe systemic syndrome often leading to shock and death in primates, pigs developed a respiratory syndrome that could be mistaken for other porcine respiratory diseases.”

Transmission of Ebola virus from pigs to non-human primates
CFIA and others, Winnipeg, Canada

- Oronasal challenge of six 4 week old pigs with Zaire ebolavirus. Four Macaques in same room, no direct contact

- Increase in respiratory rate and in rectal temperatures of pigs was observed between 5 and 7 days post infection. All piglets apparently recovered from the disease by 9 dpi.
Transmission of Ebola virus from pigs to non-human primates
CFIA and others, Winnipeg, Canada

- Zaire ebolavirus was transmitted from pigs to all four cynomolgus macaques without direct contact
- Transmission between macaques in similar housing conditions was never observed
- Design and size of the animal cubicle did not allow to distinguish whether the transmission was by aerosol, small or large droplets in the air, or droplets created during floor cleaning

Immunopathogenesis of Severe Acute Respiratory Disease in Zaire ebolavirus-Infected Pigs
(Nfon et al, PLoS ONE 8(4): e61904)
CFIA and others, Winnipeg, Canada

- May be important age differences: 4 week old piglets had mild to moderate clinical signs while 6 week old piglets had rather severe respiratory distress
- “Genes for proinflammatory cytokines, chemokines and acute phase proteins, known to attract immune cells to sites of infection, were upregulated in the lungs, causing the heavy influx of cells into this site.”
  - Age difference may be related to innate immune ability to generate a cytokine storm
Vaccines and Diagnostics for Transboundary Animal Diseases


- Workshop, Ames, Iowa, September 17-19, 2012
  - Funded by Department of Homeland Security, Science and Technology Directorate

- Review of Ebola Virus Infections in Domestic Animals

- Ebola: Facing a New Transboundary Animal Disease
  (Feldmann et al, Dev Biol 2013; 135:201-209)
  - Diagnostics
  - Vaccines

Additional Information

- Updated CFSPH Fact Sheet: Ebolavirus and Marburg Virus Infections (111 references)
  - http://www.cfsph.iastate.edu/Factsheets/pdfs/viral_hemorrhagic_fever_filovirus.pdf

- OIE Terrestrial Animal Health Code
  - No information on Ebola
Association of Reston ebolavirus with Arterivirus infection

- Discovery of Reston ebolavirus in Macaques in Reston, VA 1989
  - Co-infected with simian hemorrhagic fever virus
  - Arteriviridae genus Arterivirus

- Reston ebolavirus in Philippines and China
  - All pigs were co-infected with Porcine Reproductive and Respiratory Syndrome Virus
  - Arteriviridae genus Arterivirus

Factors to Consider

- Ebola viruses are Biosafety Level 4 Select Agents (including REBOV which is non-pathogenic for humans or swine)

- Greatly restricts ability to conduct animal studies

- Diagnostic testing in BL2 laboratories?
Factors to Consider

• Where can diagnostic samples be submitted from domestic animals for Ebola serology, PCR, virus isolation?
  – CDC or NIH labs?
  – NVSL or NAHLN labs?
  – Validation of assays for use in domestic animals?

Factors to Consider

• Dogs vs. commercial swine vs. backyard swine vs. feral swine?
  – Personal protective equipment?
  – Euthanasia?
  – Carcass disposal?
  – Feces/Manure disposal?
Factors to Consider

- Ebola Zaire vs. Ebola Reston?

- Ebola Reston has apparently been circulating in the Philippines and in China for several years with no evidence of health impacts on humans

Communication Points

- Being developed by CDC, USDA, AVMA and others
CDC Website: Questions and Answers about Ebola-Reston Virus in Pigs, Philippines

- CDC Website:

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