

Emerging Disease Notice

Philippines: Reston Ebolavirus in Swine and Humans

Summary

In 2008, the Philippine government submitted samples from swine affected by unknown pathogens to the USDA APHIS Foreign Animal Disease Diagnostic Laboratory (FADDL) at Plum Island, New York. Tests revealed two known swine viruses and a strain of Ebolavirus (Reston subtype) that had never before been found in pigs or implicated in any livestock diseases¹. Reston ebolavirus (REBOV) is highly pathogenic for some primates, but transmission to humans working with infected animals has been rare and has caused little or no apparent illness. A few exposed animal workers have produced antibodies to the virus. Epidemiological studies are underway in the Philippines, and U.S. health agencies are conducting research and developing diagnostic tests for REBOV in swine. The United States does not import live pigs or pork products from the Philippines, and at this time, the outbreak does not appear to present an animal or human health threat to the United States. More research is needed to fully evaluate the importance of Reston ebolavirus to swine and human health.

Introduction

In October 2008, APHIS Veterinary Services (VS) notified the Philippines Chief Veterinary Officer (CVO) that Ebolavirus (Reston subtype) had been identified in six of 24 swine diagnostic samples submitted by the Philippines to the APHIS VS Foreign Animal Disease Diagnostic Laboratory (FADDL) at Plum Island. The samples had previously tested positive for porcine reproductive and respiratory syndrome virus (PRRSV) and circovirus-type 2, findings which were shared with the Philippines in August and September, 2008. The U.S. Centers for Disease Control (CDC) confirmed the REBOV in swine samples and asked that the Philippines Ministry of Health be notified because of the potential for the virus to infect humans handling the animals.

The Philippines CVO officially notified the OIE of an outbreak of atypical PRRSV in December 2008. In its report, the Philippine government stated that REBOV had coincidentally been found in some pigs, but that the virus did not appear to be a public health threat. Officials quarantined two commercial hog farms in Bulacan and Pangasinan provinces where REBOV had been identified, and they suspended trade of live pigs and

swine products. Additional samples were collected and tested from pigs and humans, and the government invited an international team of animal and human health experts to conduct an epidemiological investigation and risk assessment, which is ongoing.

This is the first time Reston ebolavirus has been identified in livestock. The only other animal isolations of this virus were from monkeys originating in the Philippines and imported to laboratories in the United States and Europe between 1989 and 1996. In addition, several workers who had close contact with sick primates or sick pigs were asymptotically infected.

Incident History and Status

In July 2008, the Philippine Department of Agriculture, Bureau of Animal Industry, requested FADDL diagnostic support for an investigation of a swine disease outbreak occurring in the Philippines since late spring of 2007. The outbreak was characterized by sudden increase in mortality among piglets in Pandi municipality (Bulacan province) and morbidity of all age-classes of pigs in Manaoag municipality (Pangasinan province). Clinical signs suggested an atypical infection, possibly involving multiple pathogens including PRRS virus, porcine circovirus type 2, and classical swine fever virus.

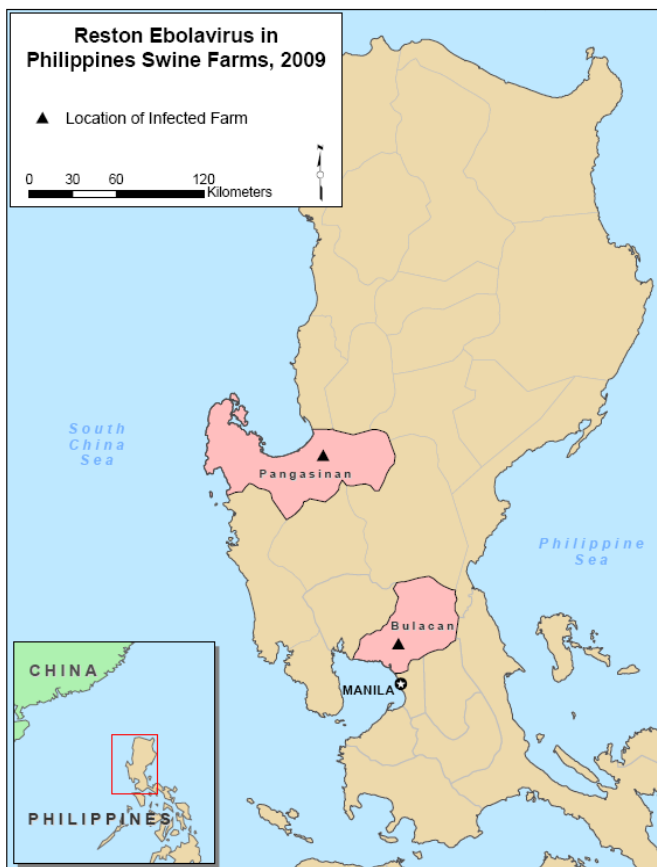
FADDL staff agreed to assist in the investigation and received samples collected from five Philippine farms between September 2007 and June 2008. Diagnostic testing, which began in August 2008, found the samples were positive for porcine circovirus type 2 and atypical PRRS virus but negative for classical swine fever and African swine fever viruses. The PRRSV gene sequence was 98% homologous to a highly pathogenic strain of PRRSV recently linked to widespread epizootics of blue ear disease among swine in China and Vietnam. (For a discussion of these epizootics, see http://www.aphis.usda.gov/vs/ceah/cei/taf/emergingdiseasenotice_files/prrschinavietnam2007.pdf).

During initial testing of the Philippine swine samples, FADDL scientists noticed that some of the cell cultures were affected by an unknown pathogen. To resolve these unexplained cases, the scientists employed a new investigational tool being developed to identify unknown or emerging viral pathogens. Termed a panviral microarray, this tool consists of tens of thousands of viral genetic sequences microscopically arranged on a slide so as to bind with matching amplified viral genetic material (DNA) extracted from samples. The microarray analysis revealed a strong indication of an Ebola-like virus related to the Reston subtype. Further testing by polymerase chain reaction (PCR) showed that the

genetic sequence from the samples was more than 95% similar to previous REBOV isolates.

Because REBOV is classified as a biosafety level 4 select agent, samples were transferred to the CDC's Special Pathogens Branch in Atlanta, Georgia. Identification of the virus as REBOV was confirmed by Ebola-specific real-time reverse transcription (RT)-PCR analysis, antigen enzyme-linked immunosorbent assay, immunohistochemistry, and virus isolation².

Reston ebolavirus is considered less pathogenic to humans than the four other known strains of Ebolavirus. Three of these strains – Zaire, Sudan, and Bundibugyo – have caused deadly outbreaks of Ebola hemorrhagic fever in Africa, killing up to 90% of those infected³. A fourth strain – Côte d'Ivoire (Ivory Coast) ebolavirus – caused a single case of nonfatal hemorrhagic fever in a person and is considered potentially lethal. All five strains are treated as hazardous because there are no effective vaccines or antiviral treatments.



As part of its ongoing health investigation of REBOV, the Philippine government collected blood samples from 141 people who may have been exposed to the virus on infected pig farms or associated facilities. To date, six people have tested positive for antibodies to REBOV². All were reportedly healthy during the preceding 12 months. Blood tests on more than 1,000 pigs at the two affected commercial farms were negative. These preliminary findings confirmed the possibility of pig-to-human transmission of REBOV. Contact with infected pigs, or with their blood and fluids, is the presumed route of exposure. The Philippine Department

of Health is conducting broader surveillance of farmers in the region, including testing of stored samples.

Clinical Picture in Non-human Primates, Humans and Swine

This is not the first time Reston ebolavirus has been found in the Philippines. The virus was discovered in 1989 during an outbreak of viral hemorrhagic fever among captive macaque monkeys imported from the Philippines to a quarantine facility at Reston, Virginia, USA⁴. REBOV later was detected in macaques imported from the Philippines to the United States in 1990¹, to Italy in 1992⁵, and again to the United States in 1996⁶. The virus was also isolated from monkeys at the Philippine export facility^{7,8}. Many of the monkeys became ill and died as a result of REBOV infection⁷. The Philippines is a major world exporter of macaques, which are used extensively in biomedical research⁹.

As of March 2009, 15 human infections with REBOV have been documented: four were animal caretakers at the Reston primate facility in 1989-1990¹, five were animal handlers at the Philippines primate export facility⁸, and six were the recently-identified hog farm employees and slaughterhouse workers in the Philippines. All the infected workers developed REBOV-specific antibodies, and one U.S. worker who accidentally cut himself on an infected scalpel blade became viremic. None showed any signs of illness. These asymptomatic cases imply that while humans may become infected with Reston ebolavirus, it does not cause disease in people. Nevertheless, the virus is still considered a potential human pathogen.

There have been no other published reports of REBOV infecting swine, thus its clinical importance in pigs is unknown. The recent epizootic among pigs in the Philippines is thought to have been caused by highly pathogenic PRRSV, either alone or in combination with other swine pathogens. Some of the swine samples from the Philippines outbreak were co-infected with PRRSV and REBOV, and according to CDC researchers, the distribution of the Reston virus in lung and lymph tissue was similar to that of fatal Ebolavirus infections in primates. A definitive answer to the role that REBOV plays in swine disease will likely come only through carefully controlled experiments, in which pigs are infected with virus in a highly biosecure environment.

Epidemiology – Potential Reservoirs and Pathways for Transmission

The ecology of filoviruses, which includes Ebola and Marburg viruses, is poorly understood. Various animal species have been proposed as potential reservoir hosts¹⁰. Disease investigations in the Central African rainforest linked the first human cases of Ebola infection to contact with wild mammals that were hunted or found sick or dead⁹. The virus then passed to other people through contact with infected patients and corpses. Bats have been implicated as sources of filovirus infection

based on epidemiological links between human disease and habitats where bats were present¹¹. Detection of asymptomatic infections in fruit-eating bats bolsters this hypothesis^{12,13}. The existence of amplifying hosts has also been theorized¹¹. Gorillas and chimpanzees are highly susceptible to Ebolavirus but appear to be indicators of viral circulation rather than important factors in maintaining Ebolavirus cycles in nature¹⁴.

Reston ebolavirus is the only known filovirus of Asian origin⁹. It is unclear how and when this virus may have spread to monkeys or pigs in the Philippines, although phylogenetic analysis of samples from swine suggests that REBOV may have been circulating since, and possibly even before, it was first discovered among imported monkeys². As with other filoviruses, bats may represent potential reservoir hosts of REBOV.

During the initial outbreaks of REBOV in U.S. primate facilities, the virus moved between animal rooms, suggesting the possibility of aerosol spread. However, this mode of transmission is unproven and there is no evidence of aerosol spread outside a laboratory setting¹. During an outbreak of Zaire ebolavirus in Africa, dogs were exposed to the virus and developed asymptomatic infections after feeding on infected dead animals¹⁵. The role of pigs and other species in the REBOV outbreak in the Philippines is still under investigation.

Animal Trade and Health Risks

Movement of animals and their products through trade is a potential pathway for the spread of animal diseases. In response to the REBOV situation, the Philippines temporarily halted all swine and pork exports from the country. The Philippines ranks 14th in world swine stocks¹⁶ with approximately three-fourths of the country's 12-13 million pigs raised in backyard operations¹⁷. Philippine swine and pork exports more than tripled between 2005 and 2007 (US\$ 1.4 to 5.1 million), comprising 1.1-1.2% of global swine exports¹⁸.

U.S. import practices, together with the Philippines ban on swine and pork exports, provide an effective regulatory barrier against entry of Reston ebolavirus into the United States. According to the National Center for Import and Export, the United States does not import live pigs or embryos, swine semen, fresh pork or pork byproducts, or cooked/processed swine meat from the Philippines. Processed pork byproducts from the Philippines are eligible to enter the United States if they meet all mitigation requirements for foreign animal diseases including foot-and-mouth disease, swine vesicular disease, and classical swine fever. Required mitigations such as formalin and heat treatment for these pathogens would also inactivate REBOV.

Disease protections for nonhuman primates have also been strengthened in the United States. Since 1975, the CDC has prohibited the importation of primates except for scientific, educational or exhibition purposes. Imported primates are required to be held in quarantine for at least 31 days following U.S. entry¹⁹. In 1990, after

REBOV was identified in the shipment of Philippine monkeys, CDC published guidelines fortifying quarantine and transport rules for imported primates. New mandatory disease control measures included testing for REBOV⁹. Additional import restrictions and permit requirements were placed on species thought to be susceptible to filovirus infection¹⁹. In 1994 the Philippines banned export of wild-caught monkeys and applied a 45-day quarantine period prior to exporting primates⁸.

Human Health Consequences

Despite studies showing that REBOV does not sicken people, exposure to infected animals or foods remains a safety concern. The epidemiology and pathogenesis of this virus are poorly understood, and the potential impacts of REBOV on children, pregnant women and immune-compromised people are unknown²⁰. At least three of the five known strains of Ebolavirus are lethal to humans. As a consequence, all diagnostic specimens suspected of containing Ebola viruses are handled with extreme care and only by laboratories with the highest levels of biosecurity approval. Even in the absence of identified risks, officials advise careful meat handling, rigorous personal hygiene, and cooking of pork to proper temperatures. The Philippines Department of Agriculture has advised the public to buy meat only from sources certified by its National Meat Inspection Services.

Conclusion

At this time, Reston ebolavirus in the Philippines does not appear to be a health threat to the United States. The origin of this virus is a mystery and more research will be needed to assess its role, if any, in swine disease. Understanding where REBOV resides in nature, how pigs become infected, and the extent and consequences of spillover into humans will be necessary to develop appropriate animal and public health responses⁹. The Philippine government is coordinating an international effort to test swine populations and animal workers and to look for REBOV reservoirs. Sampling of wildlife in affected areas may yield further clues to the virus' origin. It is fortunate that none of the human exposures to REBOV infection have resulted in clinical illness. While this virus appears less harmful to people than other Ebola strains, more study is needed to fully assess its importance to animal and human health.

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