

European Commission

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Human cases of infection by Ebola-Reston, Philippines 31st March 2009

1. INTRODUCTION

Human cases of infection by Ebola Reston have recently been described in the Philippines.

2. EBOLA VIRUS, SUBTYPE RESTON

The Filovirus family includes the Marburg virus (identified in 1967) and Ebola (1976), which may cause viral haemorrhagic fevers (VHF).

- The Ebola-Reston (EBO-R) virus is one of five known species of Ebola virus.
- Three of these Ebola species (*Zaïre, Sudan* and *Bundibugyo*) have caused VHF epidemics associated with a high case-fatality ratio (CFR) in humans. The *Côte d'Ivoire* species has caused a single, isolated human case (who survived).
- Clinical signs of EBO-R infection :
 - In the long-tailed macaque¹: haemorrhagic syndrome with a CFR of approximately 80%;
- In the pig : unknown. EBO-R has been isolated simultaneously with Porcine Respiratory and Reproductive Syndrome (PRRS) Virus during high-CFR epizootics in the Philippines ; its exact causative role in the observed clinical syndrome is under study ;
- In man: no know clinical sign.

• **Incubation of EBO-R:** Not precisely documented to date. It lasts 2-21 days in case of infection by one of the 4 Ebola species know to be pathogenic in humans.

• **Geographic distribution:** EBO-R has been isolated on several occasions in the Philippines. Its exact area of spread, however, remains unknown.

3. DOCUMENTED EVENTS OF EBO-R TRANSMISSION FROM MONKEYS TO HUMANS (USA, EUROPE)

Between 1989 and 1996, six events have been described which involved transmission from monkeys imported from the Philippines to the USA and Europe. (Table 1). Investigations identified a common source : a monkey breeding and export facility (Ferlite Farms) located in Calamba, Laguna Province, 40 km south of Manila, Philippines (Figure 1).

Reston (Virginia, USA), 1989

- The virus was first isolated in 1989 in a monkey (*Macaca fascicularis*).
- 100 monkeys had been exported from Calamba to an animal quarantine centre in Reston, Virginia (USA) in October, 1989.
- The high mortality observed among these monkeys after their arrival in the USA (60 died, the

others were put down) led to an investigation being conducted :

- Tests conducted by the centre veterinarian showed that 3 out of 10 monkeys tested were infected by Simian Haemorrhagic Fever (SHF virus, not known to be transmissible to humans).
- An Ebola-like filovirus was fortuitously identified in 12 monkeys tested in two separate groups from two separate areas of the centre.
- 149 centre employees exposed to these monkeys were subsequently monitored (Table 1) :
 - None of the employees developed signs of infection;
- Anti-EBO-R IgG antibodies were found in 4 (2.7%) of them;
- One developed detectable EBO-R viraemia following percutaneous exposure (cut with a scalpel during autopsy of a monkey) but did not develop any symptoms.

Philadelphia (Pennsylvania, USA) 1989

- The investigation conducted in the USA after the Reston incident found another group of monkeys imported from the Calamba farm to an animal quarantine centre in Pennsylvania (USA).
- Several of these monkeys had died and EBO-R virus was identified.
- No EBO-R infection was clinically or biologically identified in centre employees.

• Reston (Virginia) et Alice (Texas, USA), 1990

- In January 1990, the Calamba farm exported 100 monkeys to the Reston centre and 100 others in another quarantine facility in Alice (Texas, USA).
- Between 01/02/90 and 15/03/90, 46 of 52 monkeys died in a quarantine zone.
- The 6 remaining monkeys were positive for EBO-R (some were also infected by SHF virus).
- Two (symptom-free) human cases were biologically identified among centre staff.

Siena (Italy), 1992

- 55 monkeys were exported from Ferlite Farms to Italy in March, 1992.
- 8 of these monkeys died between March and April and the rest were put down.
- EBO-R was identified in 3 monkeys.
- No clinical or biological signs of EBO-R infection were detected among 16 human contacts.

Alice (Texas, USA) 1996

- In March, 1996, two monkeys in another group of 100 monkeys exported from Ferlite Farms to the Alice (Texas) facility died of confirmed EBO-R infection. Monkeys were also infected by SHF.
- No case of EBO-R infection was identified in eight exposed staff of the quarantine facility.

¹ *Macaca fascicularis*, also known as Crab-eating Macaque

 Furthermore, a systematic serostudy in 55 animal keepers of the CDC (Atlanta, USA), laboratories in the absence of a suspected epizootic outbreak found one (1.8%) asymptomatic human case.

4. DOCUMENTED EVENTS OF EBO-R TRANSMISSION TO HUMANS (PHILIPPINES)

• 1989 - 1996 : Transmission by monkeys

- The Ferlite Farms monkey breeding and export centre, located in Calamba, Laguna Province, Philippines (cf. Figure 1) housed monkeys bred in captivity or captured in the wild, principally on the island of Mindanao.
- Following the events described in the USA in 1989-1990, most of the Farm's monkeys were put down.
- Between 1989 and 1996, serosurveys conducted in the Philippines identified five animal farm staff with anti-EBO-R antibodies who had contacts with sick or dead long-tailed macaques. All were employees of Calamba farms, the only monkey export centre where EBO-R had been identified (Table 1).
- An investigation was conducted in the Philippines in 1996 after cases were documented in Alice (Texas, USA). Results showed that:
- Many monkeys had died during the preceding weeks and some had been infected by EBO-R;
- Among the 18 screened employees of the Farm, one case of infection (symptom-free and previously identified during the 1992 serosurvey) was confirmed. No other case of EBO-R infection was found among 228 staff of other primate export centres in the area;
- Four persons had been exposed only to Farm staff presenting or who had presented anti-EBO-R antibodies: none of them had biological signs of infection.
- The Ferlite Farms primate facility was definitively shut down following the 1996 transmission event.

Table 1: Available data on nine symptom-free cases of Ebola-Reston (EBO-R) transmission from monkeys to humans, 1989-1996 (Source : literature, WHO and <u>CDC</u>)*.

Place an year of event	N Exposed	N infected (%)
Reston (USA), 1989	149	4 (2.7%)
Philadelphia (USA), 1989	- 29**	0* <i>(0%)</i>
Reston and Alice (USA), 1990		
Siena (Italy), 1992	16	0 (0%)
Philippines, 1989-1990	18	3 (16.7%)
Philippines, 1992	21	2 (9.5%)
Alice, 1996	10	0 <i>(0%)</i>
Philippines, 1996	18	0 (0%)
Total	261	9 (3.4%)

* ELISA results were retained when available and IFAT results (considered to have low specificity) were disregarded; ** Computed data: 178 exposed staff in total in the USA between 1989 and 1990, including 149 in Reston in 1989. The remaining 29 persons were exposed in Philadelphia and in Reston and Alice, USA, in 1990.

Figure 1 : Geographic location of Ebola-Reston transmission events, Philippines, 1989-2008.



• 2007 - 2008 : Transmission by pigs

- In 2007-2008, unexplained pig deaths were reported in the Philippines.
- Investigations conducted around the affected pig farms found EBO-R virus in sick pigs in September 2007 in Pangasinan province and in May and June in Bulacan province (Fig. 1).
- Samples taken from 28 sick pigs were analysed. Several were positive for Porcine Respiratory and Reproductive Syndrome (PRRS) Virus and six (from two distinct pig farms) were positive for EBO-R.
- The EBO-R virus isolated in pigs in 2008 is considered similar to, yet different, from the strains isolated in monkeys in 1989, 1992 and 1996.
- Furthermore, among 141 personnel exposed to sick pigs in the two affected pig farms or employed in nearby slaughterhouses, six (4.2%) were anti-EBO-R antibody-positive :
 - The owner of a backyard herd in Valenzuela City (Greater Manila);
 - Three workers : two from a pig farm in Bulacan and one from another pig farm in Pangasinan, (both farms were shut down after EBO-R was identified in pigs in 2008);
 - 1 slaughterhouse employee in Pangasinan
 - 1 slaughterhouse employee in Cabanatuan, Nueva Ecija province.
- According to Filipino authorities, none of these six persons had presented significant symptoms during the previous 12 months.

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5. EBOLA VIRUSES, ANIMAL RESERVOIRS AND TRANSMISSION

- Fruit bats are thought to play a significant role (reservoir) in maintaining the transmission cycle of Filoviruses on the African continent, considering:
- Human cases of Ebola or Marburg viral haemorrhagic fevers after contacts with bats or their droppings in African caves;
- Recent studies showing that certain bats which had been captured alive had signs of infection with Ebola or Marburg viruses ;
- That bat infected experimentally with Ebola become viraemic for that virus but do not systematically die of the infection.
- Bats therefore seem to be both a reservoir and a vector for Filoviruses in Africa. Spillover cases occur in other mammal species after accidental exposure to bats' blood or body fluids (droppings, eating soiled fruit or bats themselves) (Figure 2).
- Infection by the Ebola virus is well documented in other species: in Africa, human epidemics have occurred following contact with sick or dead chimpanzees, gorillas and other primates, forest antelopes or porcupine.
- The pig herds involved in the 2008 EBO-R epizootics in the Philippines are located very near to fruit orchards which harbour many bats.
- Furthermore, the role of bats in the transmission of emerging viruses in pig farms is well documented (Nipah virus, for example).

COMMENTS

The 2007-2008 events in the Philippines are the first documented EBO-R outbreaks in pigs. Many of these pigs, however, were coinfected by other viruses known for their high degree of pathogenicity in these animals. It is therefore important to precisely document and quantify Ebola-Reston's - highly likely - specific pathogenicity in pigs.

Since the identification of the Ebola-Reston virus in the USA in 1989 to date, transmission to humans has been documented in 15 cases, all of whom have remained symptom-free. All these human cases had been exposed to animals in which EBO-R circulation had been evidenced (9 cases among 261 persons exposed to monkeys - see Table 1 - and 6 cases among 141 persons exposed to pigs). There are no epidemiological data regarding possible transmission to humans outside of these events revealed by animal outbreaks in the USA, in several parts of the Philippines and in Europe.

Considering the important role played by fruit bats in Filovirus transmission in Africa as well as transmission of other viruses to pigs in Asia, the role of bats in the transmission of EBO-R is suspected. Further studies are ongoing to document the epidemiology of Ebola-Reston and the exact role played by bats (reservoir, amplification, transmission) in the 2007-2008 outbreaks documented in pigs in the Philippines.

Data available to date do not indicate that this emerging phenomenon constitutes a major threat to public health at this point. As specific surveillance data are lacking, however, wider circulation of EBO-R and the occurrence of symptomatic or severe cases cannot be formally excluded. Further elements must lead to caution: the symptom-free Ebola-Reston infections which occurred following contact with animals or their blood or body fluids were described in healthy workers; there are no data on the symptoms which EBO-R may cause in more vulnerable persons. Furthermore, there are no available data on the circulation of this Filovirus in animals or in humans in the rest of the Philippines or in other countries or the region.

Several Ebola species have a high degree of pathogenicity in humans. In the absence of extensive and specific epidemiological data, the progression of the Ebola-Reston virus must be studied in animals and humans with the utmost attention.

Figure 2 : Geographic spread of Ebola viral haemorrhagic fever hotspots in the Old World and spread of fruitbats of the Pteropodidae family (adapted from <u>WHO</u>).

