

Filoviruses (Infection with)

Aetiology Epidemiology Diagnosis Prevention and Control
Potential Impacts of Disease Agent Beyond Clinical Illness References

AETIOLOGY

Classification of the causative agent

Filoviruses are enveloped, non-segmented, negative-sense, single-stranded RNA, pleomorphic viruses that are capable of causing viral haemorrhagic fevers predominantly in humans and non-human primates (NHPs). Within *Filoviridae* there are three genera: *Cuevavirus*, *Marburgvirus* and *Ebolavirus*. They are genetically similar to other *Mononegavirales* (families *Paramyxoviridae*, *Rhabdoviridae*, *Filoviridae*, and *Bornaviridae*) but stand apart due to their unusual filamentous morphology and capacity to cause destructive and highly fatal disease in humans and NHPs.

The genus *Ebolavirus* consists of 6 species: Ebola virus, Sudan virus, Tai Forest virus, Reston virus, Bombali virus, and Bundibugyo virus. *Marburgvirus* and *Cuevavirus* each consist of one species, *Marburg marburgvirus* and *Lloviu cuevavirus* (LLOV), respectively.

Filoviruses are zoonotic and are classified as Biosafety Level 4 (BSL4) agents. They are not listed by the OIE.

Resistance to physical and chemical action

Temperature:	Incineration, autoclaving on a waste cycle (121°C for 30 minutes), and boiling water are effective decontamination methods
pH:	Not determined
Chemicals/Disinfectants:	Hospital-grade bleach, detergents, solvents, alcohols, ammonia products/quaternary ammonium compounds, and aldehydes are effective disinfectants
Survival:	Heat, sunlight, UV light, and gamma radiation inactivate the virus.

EPIDEMIOLOGY

Hosts

- Humans
- Non-human primates (NHPs)
 - Gorillas (*Gorilla gorilla*)
 - Chimpanzees (*Pan* spp.)
 - Macaques (*Macaca* spp.)
 - African green monkeys (*Chlorocebus* spp., formerly *Cercopithecus* spp.)
 - Baboons (*Papio* spp.)
- Pigs (*Sus* spp.)
- Bats are believed to be reservoir hosts
 - Ebola virus has been detected in *Hypsignathus monstrosus*, *Epomops franqueti*, and *Myonycteris torquata* by PCR
 - Antibodies to Filoviruses have been detected in *Rousettus leschenaulti*, *Pipistrellus pipistrellus*, and *Myotis* spp.
 - Bombali virus has been identified in *Mops condylurus* and *Chaerephon pumilus*.
- Duikers (*Cephalophus* spp.)

- Other mammals (domestic cats and dogs) have been infected with Filoviruses but have not developed clinical disease

Transmission

- Direct contact with broken skin or mucous membranes
 - In NHPs, the virus is shed from all body surfaces including skin.
- Contact with contaminated surfaces, vegetation, or fomites
- Aerosol transmission is possible but its role in transmission varies by viral species.
- Virions cannot be transmitted until an individual has developed clinical signs.

Sources

- Bodily fluids such as urine, saliva, feces, vomit, breast milk, semen
 - In humans and other primates, semen and breast milk may contain virus even after the resolution of clinical disease. It is not known whether these fluids harbor virions in swine.
- Contaminated fomites
- Infected humans, bats, pigs, or NHPs
 - Contact with infected carcasses
 - Handling and consuming meat from an infected animal

Occurrence

Filoviruses originate from tropical Africa and the Philippines. Clinical disease is associated with contact with other infected individuals or contact with contaminated waste products including water.

DIAGNOSIS

The incubation period can range from 2-21 days depending on the particular viral species. Infected humans and NHPs die within 6-9 days of the onset of clinical disease.

Clinical diagnosis

Ebolavirus disease (EVD) and Marburg haemorrhagic fever virus (MARV) are clinically similar, highly virulent zoonotic diseases with case fatality rates surpassing 50% in humans and approaching 100% in NHPs. Development of clinical disease is sudden and non-specific: fever, headache, malaise, myalgia, nausea, and vomiting (including haematemesis) are most common, and infected individuals decline over the course of days. Profuse bleeding from venipuncture sites and haemorrhagic lesions are common. Affected individuals are bradycardic and weak, and exhibit weight loss and delirium/amnesia during periods of severe illness. Disseminated intravascular coagulation is a common terminal event.

Leukopenia is apparent early in disease but is followed by a robust neutrophilia with a left shift. There is little inflammatory infiltration into sites of hepatic parenchymal necrosis. Macrophages, monocytes, and dendritic cells are important sites of viral replication; they disseminate the virus and produce cytokines that contribute to a pro-inflammatory state, which facilitates further replication. Lymphocytes experience extensive apoptosis which induces a lymphopenia that often progresses to lymphoid depletion.

The pathology and clinical signs observed in humans and NHPs are very similar. Reston virus has been detected in cases of porcine reproductive and respiratory syndrome (PRRS), but its pathologic role is not completely understood.

Pigs are able to shed virus, but they rarely develop haemorrhagic fever syndromes - infections in swine are generally not well characterized. LLOV is only known to infect bats; very little is otherwise known about the virus.

Lesions

- Maculopapular rash
- Widespread haemorrhage, petechiae, and ecchymoses
 - Haemorrhagic pharyngitis
 - Melaena in the gastrointestinal tract
- Hepatic necrosis
- Conjunctivitis

Differential diagnoses

- Lassa fever virus
- Dengue virus-induced haemorrhage
- *Bunyavirus* infection
- Typhoid fever (*Salmonella typhi*)
- Influenza
- Gastroenteritis

Laboratory diagnosis

Due to zoonotic potential and public health risks, tests should be performed in laboratories suitable for handling BSL4 agents whenever possible.

Samples

For isolation of agent

- Bodily fluids; blood is preferred
- Mucosal swabs

Serological tests

- Blood

Procedures

Identification of the agent

- Virus isolation
- Polymerase chain reaction (PCR)
- Immunohistochemistry (IHC)
- Electron microscopy
 - Virions have a peculiar pleomorphic, filamentous shape

Serological tests

- Antigen capture enzyme-linked immunosorbent assay (ELISA)
- IgM or IgG antibody capture ELISA

PREVENTION AND CONTROL

Sanitary prophylaxis

- Always wear personal protective equipment (PPE) when handling infectious tissues, contaminated objects, or cleaning contaminated areas.
 - Gloves (+/- puncture-resistance), face-shield, goggles, water-resistant gown
- Practice effective handwashing techniques to rid skin of dirt, blood, and other materials. Follow with alcohol-based hand sanitizers or 0.05% chlorine solution.
- Contain all contaminated waste as close to its source as possible.
- Whenever possible, utilize a BSL4 equipped with a Class II Biosafety cabinet to perform laboratory tests.
- Necropsies of carcasses are considered high-risk and warrant the use of extensive PPE including watertight clothing, face shields, and personal air filtration systems. Utilize disposable instruments.
 - It is highly recommended that individuals performing this type of work be adequately trained on proper technique and safety precautions.
- Utilize proper PPE before handling bats or their droppings in areas where Filoviruses are endemic.

Medical prophylaxis

- Experimental Ebola virus vaccines are currently being employed for humans on an “expanded access” or “compassionate use” basis.
- A recombinant MARV vaccine is being developed utilizing a vesicular stomatitis virus vector.
- There is currently no medical prophylaxis for LLOV.
- Milk and semen may contain virus after clinical disease has resolved; secretions should be tested before continuing with relevant swine or NHP husbandry practices.

POTENTIAL IMPACTS OF DISEASE AGENT BEYOND CLINICAL ILLNESS

Risks to public health

- *Cuevavirus* is only known to infect bats and is therefore unlikely to be a risk to public health.
- *Marburgvirus* and *Ebolaviruses* are zoonotic, virulent, and highly lethal.
 - Reston virus is nonpathogenic to humans but is pathogenic to NHPs.

Risks to agriculture

- There is currently insufficient understanding of Reston virus infection in pigs to determine its risk to the swine industry. Natural infections appear to be uncommon but have been associated with some cases of PRRS.

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The OIE will periodically update the OIE Technical Disease Cards. Please send relevant new references and proposed modifications to the OIE Science Department (scientific.dept@oie.int). Last updated 2019. Written by Marie Bucko and Samantha Gieger with assistance from the USGS National Wildlife Health Center.