ENDOTHELIOPTROPIC ELEPHANT HERPESVIRUS INFECTION

ANIMAL GROUP AFFECTED	TRANS-MISSION	CLINICAL SIGNS	FATAL DISEASE ?	TREATMENT	PREVENTION & CONTROL
Elephants	Unknown	Asian elephants: Ranging from silent infection, mucosal oral and vaginal vestibular lesions to acute mortality in young elephants, swollen blue tongue, edema of head and front legs; African elephants: nodules in the lungs, skin and the vestibulum vaginae; occasionally fatal	high mortality in mostly young Asian elephants, two lethal cases in young African elephants with a high suspicion of other illness and/or altered immune status.	In a few cases early treatment with famciclovir has been considered to be effective. Supportive therapy for shock is important	Reduce stressful situations in the elephant group. May be prudent to separate Asian and African elephants However more and more cases are being reported in Asian elephants without primary or secondary contact between both species

Fact sheet compiled by
Willem Schaftenaar, Head of the Veterinary Dept. of the Rotterdam Zoo, The Netherlands

Last update
January 2009

Fact sheet reviewed by
C.Reid, Dept. Evolutionary Genetics, Inst. Zoo and Wildlife Research, Berlin, Germany
L. Richman, Dept. of Pathology, National Zoological Park, Washington DC, USA

Susceptible animal groups
Asian elephants (*Elephas maximus*): all ages, but predominantly young animals are affected
African elephants (*Loxodonta africana*) occasionally lethal; minor lesions may be found in otherwise healthy animals.

Causative organism
Elephant Endotheliotropic herpesvirus. Based on viral DNA-sequences for the glycoprotein B variants, EEHV can be divided into EEHV-1 and EEHV-2; tEEHV1 is further divided into EEHV-1a and EEHV-1b. Recently the names Proboscivirus 1 and 2 have been introduced by the ICTV.
EEHV1: found in Asian and African elephant
EEHV2: only found in African elephants

Zoonotic potential
None known.

Distribution
Captive Asian elephants in zoos of North America and Europe (Switzerland, Germany, the Netherlands, UK) and the middle East. Fatal outbreaks amongst captive and wild elephants in South-east Asia and India have been confirmed. 2 cases of lethal EEHV2 in African elephants in North America.

Transmission
Unknown.
Close contact between both elephant species has been considered the major form of transmission. However, outbreaks in wild elephants in Asia strongly suggest that EEHV1 is indigenous in wild Asian elephants and endemic in range countries.

Incubation period
Unknown

Clinical symptoms

General information: the virus may be present in many elephants without being noticed (clinically silent). Sometimes a correlation between stress and cases of EEHV has been very suggestive. The disease presents as an acute hemorrhagic syndrome clinically similar to disseminated intravascular collapse and shock.

Asian elephant: Probably silent (in a latent state) in most adult elephants. Mucosal lesions in the oral cavity and vestibulum vaginae in a zoo herd of Asian elephants (n=4) were PCR-positive for EEHV1. The lesions remained PCR-positive for at least 1 week and healed completely in 6 weeks. No other clinical symptoms were observed. Young Asian elephants (2-8 years) are more susceptible to severe EEHV-associated disease (primary exposure?), sometimes showing lethargy, inappetence, leukopenia, cyanosis of the tongue and edema of the head and front legs. Death may occur within a few days or even hours. Stillborn or very weak neonate. One case of a subadult male: lethargy, complete inappetence, uremia (no leukopenia observed). A 42-yr-old female Asian elephant died a few months after another adult female (that originated from a herd that suffered an EEHV-case) was transferred to the zoo for the purpose of companionship.

African elephants: Nodules in lungs (EEHV2), skin (EEHV1) and patches of the vestibulum vaginae (EEHV1). Mortality associated with EEHV-2 in both cases.

Post mortem and microscopic findings

Cyanosis of the tongue; edema of the head and front legs. Inclusion bodies in endothelial cells of the heart, tongue, liver and other organs, severe haemorrhages due to blood vessel leakage. By electron microscopy, 80-92 nm diameter viral particles present within endothelial cells.

Diagnosis

PCR on swabs from mucosal lesions and whole blood (EDTA or heparin) of clinical cases.

Post-mortem: endothelial inclusion bodies. PCR on tissue samples (heart, muscle/tongue, liver, spleen). In African elephants: PCR on nodules of affected tissues.

Serologic tests for EEHV are still in the validation stages:

Experimental polyvalent antibody-ELISA (MAP7 based): currently used in the USA (Laura Richman/Erin Latimer, Smithsonian National Zoological Park, USA).

Experimental antibody-ELISA (glycoprotein B based): still in process of validation at the Erasmus Medical Centre (Byron Martina, Rotterdam, the Netherlands) and the Leibniz Institute for Zoo and Wildlife Research (C. Reid, Berlin, Germany).

Material required for laboratory analysis

Daily collected swabs from mucosal lesions, immediately stored in virus buffer medium; EDTA or Heparin blood. Tissues: heart, liver, kidney, spleen, muscle, blood vessels, tongue (fresh or frozen; for retrospective studies formalin-fixated material has also been used thought it is not preferred).

Relevant diagnostic laboratories

Dr. C. Reid and Dr. J.Fickel, Dept. Evolutionary Genetics, Inst. Zoo and Wildlife Res., A.-Kowalke-Str. 17, 10315 Berlin, Tel. +49 (0)30 5168726

Prof. Dr. A.D.M.E. Osterhaus and Dr. B. Martina, Erasmus Medical Centre, virology department, Dr. Molewaterplein 50, 3015 GE Rotterdam, Tel: +31-10-4088066

Any relevant virology laboratory should be able to run the PCR. For information about the primers, each of the above mentioned laboratories should be consulted.

Treatment

Mucosal lesions without other symptoms do not seem to pose a health risk to the animal and need no treatment. Contact animals may be at risk during this excretion phase and should be monitored carefully. Immediately after the onset of general clinical symptoms, famciclovir should be given either orally or per rectum. In the latter case, the drug should be mixed with a gel (ultrasound gel) and rubbed gently into the mucosa of the rectum after cleaning and flushing of the rectum.

Dose of famciclovir:

First day: 15 mg/kg BW, followed after 8 and 16 hours by 8 mg/kg BW

Following 10-15 days: 5-10 mg/kg BW BID

The anti-viral drug administration should be combined with supportive therapy against shock.

Prevention and control in zoos

Stress is considered by some to be the most important factor to trigger clinical disease.

Stress factors may include: weaning, birth, movement of animals, introduction of new animals, ranking order related problems in the group.

Asian and African elephants should not be kept in close contact with each other.

Especially in young and subadult Asian elephants any undetermined general illness should be suspected and treated like an EEHV-infection.

Risk factors: movement of elephants to known 'infected' herds. Introduction of a carrier elephant.

Suggested disinfectant for housing facilities

- Lysol and Bleach containing agents are known to kill viruses, follow manufacturers instructions to prevent

toxicity or overexposure to keeps and animals

Notification

- Testing, diagnostics and other procedures regarding EEHV can be financially incorporated under the umbrella of the ongoing EEHV Research Project funded by the Alexander von Humboldt Foundation
Contact : C Reid, DVM, PhD, Institute for Zoo and Wildlife Research, Alfred Kowalke Str 17, 10315 Berlin Germany, +49-30-516-8722 cell phone +49 178 186 0147, email reid@izw-berlin.de

Guarantees required under EU Legislation

-

Guarantees required by EAZA Zoos

-

Measures required under the Animal Disease Surveillance Plan

-

Measures required for introducing animals from non-approved sources

-

Measures to be taken in case of disease outbreak or positive laboratory findings

-

Conditions for restoring disease-free status after an outbreak

-

Contacts for further information

Catherine E Reid, DVM, PhD, Institute for Zoo and Wildlife Research, Alfred Kowalke Str 17, 10315 Berlin Germany, +49-30-516-8722 cell phone +49-178-186-0147, email reid@izw-berlin.de
L. K. Richman, DVM, PhD, DACVP, Smithsonian, National Zoological Park, +1-202-633-4252 or =1-301-253-8723
E. Latimer, M.S., Smithsonian, National Zoological Park, (202) 633-4252 or (703) 855-9611
W. Schaftenaar, DVM, Rotterdam Zoo. P.O. box 532, 3000 AM, Rotterdam, The Netherlands, +31-10-4431485

References

1. Fickel, J., D. Lieckfeldt, L.K. Richman, W.J. Streich, T.B. Hildebrandt, C. Pitra. 2003. Comparisson of glycoprotein B variants of the endotheliotropic elephant herpesvirus (EEHV) isolated from Asian elephants. Vet. Microbiol. 91:11-21.
2. Fickel, J., L. K. Richman, A. Reinsch, R. Montali, W. Schaftenaar, F. Göritz, T. B. Hildebrandt, and C. Pitra. 2001. A variant of the endotheliotropic herpesvirus in Asian elephants *(Elephas maximus)* in European zoos. Vet. Micrbiol. 82: 103-109.
3. Jacobson, E.R., J. P. Sundberg, J. M. Gaskin, G. V. Kollias, and M. K. O'Banion. 1986. Cutaneous papillomas associated with a herpes virus-like infection a herd of captive African elephants. JAVMA 189: 1075-1078.
4. McCully, R. M., P. A. Basson, J. G. Pienaar, B. J. Erasmus, and E. Young. 1971. Herpes nodules in the lung of the African elephant (*Loxodonta africana* [Blumenbach, 1797]). Onderstepoort J. Vet. Res. 38: 225-236.
5. Ossent, P., F. Guscetti, A. E. Metzler, E. M. Lang, A. Rübel, and B. Hauser. 1990. Acute and fatal herpes virus infection in a young Asian elephant (*Elephas maximus*). Vet. Path. 27: 131-133.
6. Richman, L. K., R. J. Montali, R. C. Cambre, J. Lehnhardt, M. Kennedy, S. Kania, and L. Potgieter. 1996. Endothelial inclusion body disease: a newly recognized fatal herpes-like infection in Asian elephants. Proc. An. Conf. AAZV. pp. 483-486.
7. Richman, L., R. J. Montali, T. B. Hildebrandt, J. Fickel, D. L. Schmitt, and G. S. Hayward. 1999. Status of a new, fatal herpes virus disease of elephants in North America and Europe. Verh. Erkr. Zoot. 39: 17-21.
8. Richman, L. K., R. J. Montali, R. C. Cambre, D. Schmitt, D. Hardy, R. L. Garber, T. Hildebrandt, J. Fickel, W. Schaftenaar, and G.S. Hayward. 1999. Clinical and pathological aspects of a fatal herpes virus disease in Asian (*Elephas maximus*) and African Elephants (*Loxodonta africana*). Proc. AAZV. Pp. 263-265.
9. Richman, L. K., R. J. Montali, R. L. Garber, M. A. Kennedy, J. Lehnhardt, T. Hildebrandt, D. Schmitt, D. Hardy, D. J. Alcendor, and G. S. Hayward. 1999. Novel endotheliotropic herpes viruses fatal for Asian and African elephants. Science 283: 1171-1176.
10. Richman, L. K., R. J. Montali, R.C. Cambre, D. Schmitt, D. Hardy, T. Hildebrandt, R. G. Benbis, F. M. Hamzeh, A. Shakolahi, and G. S. Hayward. 2000. Clinical and pathological findings of a newly recognized disease of elephants caused by endotheliotropic herpes viruses. J. Wildl. Dis. 36: 1-12.
11. **Reid CE**, **Hildebrandt TB**, **Marx N**, **Hunt M**, **Thy N**, **Reynes JM**, **Schaftenaar W**, **Fickel J**. **Endotheliotropic elephant herpes virus (EEHV) infection. The first PCR-confirmed fatal case in Asia.** Vet Q. 2006 Jun;28(2):61-4.
12. Reid CE, Martina, BEE, Schaftenaar W, Osterhaus, ADME Development of a recombinant protein based ELISA for the detection of EEHV: an improvement on the peptide based ELISA to increase

sensitivity, specificity and reproducibility In: Proceedings of the 2008 International Elephant Conservation and Research Symposium: 62, 24-26 November, Pattaya, (Thailand).
13. Schmitt, D. L. and D. G. Hardy. 1998. Use of famciclovir for the treatment of herpes virus in an Asian elephant. J. El. Man. Ass. 9: 2, 103-104.
14. Schaftenaar, W., J. M. C. H. Mensink, A. M. de Boer, T. B. Hildebrandt, and J. Fickel. 2001. Successful treatment of a subadult Asian bull elephant (*Elephas maximus*) infected with the endotheliotropic elephant herpes virus. Verh. Erkr. Zoot. 40: 141-146.
15. *Schaftenaar, W., Reid, C. Martina, B., Osterhaus A.D.M.E.* 2008. Epithelial lesions in a group of captive Asian elephants (*Elephas maximus*) associated with the endotheliotropic elephant herpes virus. In: Proceedings of the 2008 International Elephant Conservation and Research Symposium: 64, 24-26 November, Pattaya, (Thailand).
16. Schmitt, D. L., D. G. Hardy, R. J. Montali, L. K. Richman, W A. Lindsay, and R. Isaza. 1999. Use of famciclovir for the treatment of herpes virus in Asian elephants. Verh. Erkr.. Zoot. 39: 23-25.
17. Notes from the EEHV-workshop, September 28-30, 2005; Houston (Texas) USA.
18. *Zachariah, A. et al.* 2008. Fatal endotheliotropic elephant herpes virus mortality in free ranging and captive Asian elephants in South India. In: Proceedings of the 2008 International Elephant Conservation and Research Symposium: 60, 24-26 November, Pattaya, (Thailand).