

# Marburg virus

**Marburg virus** ..... 3

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In 1967 there was an epidemic of Marburg virus infection among laboratory staff in Marburg, Germany. These people worked with African green monkeys (*Cercopithecus aethiops*), imported from Uganda. Some people in Frankfurt and Belgrade, Yugoslavia, who encountered the same batch of animals also fell ill. In all, 32 people were affected: 26 primary infections and 6 secondary infections. The mortality rate of the primary infections was 25%. In the next few years a few sporadic cases were seen in Zimbabwe ('75), Kenya ('80 and '87) and a laboratory infection in Russia ('87). In 1999 and 2000 multiple cases were diagnosed in the north east of Congo, in the area of Watsa and Durba. Infection occurred mainly in gold miners, working in very primitive conditions in old mines. There had probably already been a low level of transmission in this area for some considerable time (maybe even years). Social unrest and armed conflicts in the area hindered local research. The end of the epidemic coincided with the flooding of the mine.

Early 2005 there was a large epidemic in Uige, Northern Angola, with 374 cases (initial case fatality rate 92%). It was the largest Marburg epidemic to date (the initial estimate was above 400 cases). Two viral subtypes are responsible for all described outbreaks: MARV (Marburg virus), RAVV (Ravn virus) which both diverge from the prototype Marburg virus variant Musoke (MARV/Mus) by < 10% at nucleotide level. There are very probably other subtypes as well. In 2007, it was found that certain fruit bats (*Rousettus aegyptiacus*) were carrying Marburg viral RNA as well as antibodies against the virus. It seems more and more likely that bats form the reservoir, although more research is needed. In 2009, the successful isolation of infectious Marburg virus was reported from caught healthy Egyptian rousettes (*Rousettus aegyptiacus*). This isolation strongly suggests that Old World fruit bats are involved in the natural maintenance of marburgviruses and makes bats the prime suspect as reservoir for Ebola virus, though the latter has never been cultured from bats. Further studies are necessary to establish whether Egyptian rousettes are the actual hosts of MARV and RAVV or whether they get infected via contact with another animal and therefore serve only as intermediate hosts. Experimentally infected bats developed relatively low viremia lasting at least 5 days but remained healthy and didn't develop any notable gross pathology. The virus also replicated to high titers in major organs (liver and spleen) and organs that might possibly be involved in virus transmission

In 2008 a Dutch tourist became infected after visiting a cave in Uganda. She became sick after her return home and subsequently died in the Netherlands. Also, in 2008 an American tourist developed chills and diarrhoea, severe leukopenia, massively elevated transaminases, coagulation problems, pancreatitis and renal failure after a similar voyage. The diagnosis of Marburg infection was obtained in retrospect, when she was informed of the death of the above-mentioned Dutch tourist. In October

2012, the disease flared-up in Uganda, short after an outbreak of Ebola virus. The clinical signs and symptoms are similar to Ebola (see further). There is no effective treatment.

At present, an experimental vaccine against Marburg has been developed. It is based on a live attenuated recombinant vesicular stomatitis virus, a well-known pathogen of horses, bovines and pigs. The gene coding for Marburg glycoprotein was inserted into the viral genome (similar work was performed with the Ebola Zaire virus). Experiments in monkeys showed a good humoral and cellular immune response and protection against infection with wild type virus. There was no cross-protection against other filoviruses, such as Ebola virus. So far, the vaccine has shown no evidence of pathogenicity in four species of animals (mouse, guinea pig, goat, monkey).

In 2012 it was demonstrated that macaque monkeys could be protected from Marburg virus disease by post-exposure treatment with hyperimmune serum (Marburg virus-specific IgG). No clinical human trials have been performed to date. On the basis of efficacy in nonhuman primates and pharmacokinetic data in humans, AVI-7288 – a phosphorodiamidate morpholino oligomer with positive charges that targets the viral messenger RNA that encodes Marburg virus (MARV) nucleoprotein – has potential as postexposure prophylaxis for MARV infection in humans.