

Biodefense solutions to protect our nation

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CONTACT: Caree Vander Linden (301) 619-2285 Caree.VanderLinden@us.army.mil

Post-Exposure Antibody Treatment Protects Primates from Ebola, Marburg Viruses

Army scientists have demonstrated, for the first time, that antibody-based therapies can successfully protect monkeys from the deadly Ebola and Marburg viruses. In addition, the animals were fully protected even when treatment was administered two days post-infection, an accomplishment unmatched by any experimental therapy for these viruses to date. The work appears in this week's electronic edition of *Proceedings of the National Academy of Sciences*.

The filoviruses, Ebola and Marburg, cause hemorrhagic fever with human case fatality rates as high as 90 percent. They are a global health concern and are considered potential biological threat agents. Currently there are no available vaccines or therapies approved for use in humans, making the development of such products a high priority.

In the article, John M. Dye, Andrew S. Herbert, William D. Pratt, and colleagues from the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) describe using antibody from monkeys that had previously survived challenge with lethal doses of filoviruses under controlled laboratory conditions. These survivors had developed high levels of antibody to ward off disease. Investigators collected blood serum from these animals, purified it and tested it for virus-neutralizing activity before commencing with their work.

In the first study, monkeys infected with Marburg virus were treated with antibody 15 to 30 minutes post-exposure, with additional treatments on days 4 and 8. The animals were completely protected, with no signs of disease or detectable levels of virus in their bloodstreams. Furthermore, all the monkeys generated an immune response to Marburg virus and survived subsequent re-challenge with the virus.

In the next set of studies, monkeys were infected with either Ebola or Marburg virus and treatments were delayed 48 hours, with additional treatments on days 4 and 8 post-exposure. The delayed treatments protected both sets of animals from challenge. In each group, two of the three animals had no clinical signs of illness following treatment, with the third developing mild symptoms followed by full recovery.

For nearly a decade, the filovirus research community has disregarded antibody-based therapies due to numerous failed attempts to protect monkeys against filovirus challenge, according to Dye.

"The use of antibodies as a treatment for infectious diseases is a well-established technology, with multiple products having received approval from the Food and Drug Administration," said Dye. "With these findings, we have provided proof-of concept that antibody-based therapies can indeed be used to effectively treat filovirus infections."

Dye said the USAMRIID team is hopeful that its work will open new avenues for development of filovirus therapies for human use.

USAMRIID's mission is to protect the warfighter from biological threats and to be prepared to investigate disease outbreaks or threats to public health. Research conducted at USAMRIID leads to medical solutions—vaccines, drugs, diagnostics, and information—that benefit both military personnel and civilians. The Institute plays a key role as the lead military medical research laboratory for the Defense Threat Reduction Agency's Joint Science and Technology Office for Chemical and Biological Defense. USAMRIID is a subordinate laboratory of the U.S. Army Medical Research and Materiel Command.

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Reference: Postexposure antibody prophylaxis protects nonhuman primates from filovirus disease. John M. Dye, Andrew S. Herbert, Ana I. Kuehne, James F. Barth, Majidat A. Muhammad, Samantha E. Zak, Ramon A. Ortiz, Laura I. Prugar, and William D. Pratt: *PNAS Early Edition* (published online at www.pnas.org/cgi/doi/10.1073/pnas.1200409109).

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