

Conclusion. PEP with a combination of oral ribavirin and lopinavir/ritonavir appears to be effective and generally safe for preventing MERS-CoV infection after high-risk exposure in healthcare workers.

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2492. Clinical, Virologic, and Immunologic Characteristics of Zika Virus Infection in a Cohort of US Patients

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Background. The clinical, virologic and immunologic characteristics of Zika virus (ZIKV) infections in US patients are poorly defined.

Methods. US patients with suspected Zika virus (ZIKV) infection were enrolled and clinical data and specimens were prospectively collected. Body fluids were tested for ZIKV RNA by PCR and blood was tested using serologic and cellular immune assays. Findings from those with confirmed ZIKV infections (cases) and ZIKV-negative controls were compared.

Results. We enrolled 45 cases and 14 controls. The most commonly reported symptoms among cases and controls were maculopapular rash (97.8% and 81.8%), fatigue (86.7% and 81.8%) and arthralgia (82.2% and 54.5%), respectively. The sensitivity and duration of detection by PCR were highest in whole blood samples (94% of 35 cases who had samples collected up to day 79 post illness onset were positive); strikingly, 84% of those were still positive at 65–79 days post illness onset (Figure 1). ZIKV neutralizing antibodies were detected in all cases and none of the controls, and titers were significantly higher in dengue virus (DENV)-experienced subjects than in DENV-naïve ones (Figure 2). Among cases, anti-ZIKV IgG antibodies were also significantly higher in DENV-experienced patients, while anti-ZIKV IgM antibodies were no higher in DENV-experienced compared with naïve ones. Using intracellular cytokine staining, the highest frequencies of T cells producing IFN- γ , IL-2 and/or TNF- α were against the NS1, NS3, and NS5 proteins for CD4+ T cells, and against the E, NS3, and NS5 proteins for CD8+ T cells (Figure 3).

Conclusion. Detection of ZIKV RNA was more frequent and much more prolonged in whole blood samples compared with other body fluids. Diagnostic molecular assays on this easily obtained fluid should be prioritized for point-of-care development. Robust cellular responses to E, NS3 and NS5 proteins could have implications for vaccine development.

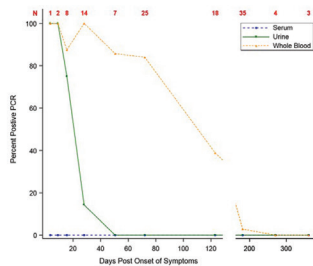


Figure 1. Percent of Zika virus infected patients with a positive PCR in whole blood, urine and serum by day post onset of symptoms. N represents the number of subjects with the specified body fluid at the specified time point.

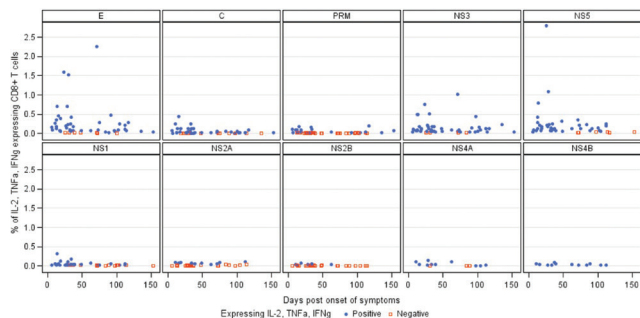


Figure 2. Percent of CD8+ T cells expressing IL-2, TNF- α and IFN- γ following stimulation with the specified proteins in cases (positive) and controls (negative).

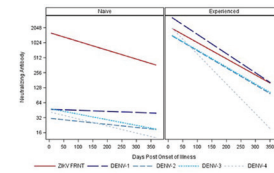


Figure 3. Neutralizing antibody titers by days post onset of illness in Dengue virus-naïve and experienced patients with confirmed Zika virus infection. FRNT=focus reduction neutralizing test.

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2493. Marburg Virus Disease: Virulence of Angola vs. Musoke Strain in Cynomolgus Macaques

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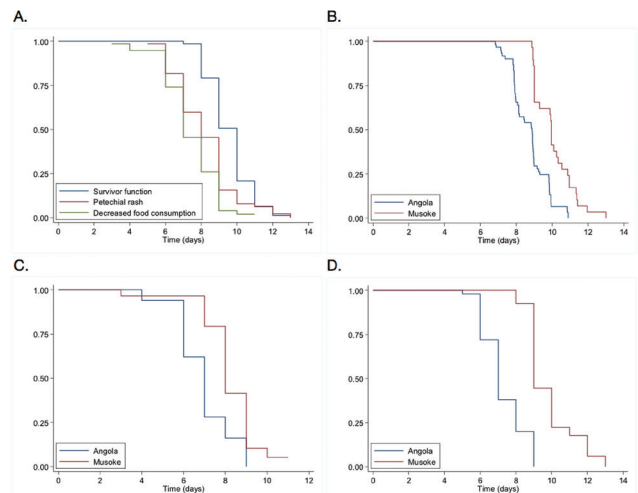
Background. From 2004 to 2005, an outbreak of Marburg virus, a filovirus, in Angola led to a case-fatality rate of 90 percent. However, little information is available regarding the virulence of the Angola strain from this outbreak compared with the virulence of other strains. Therefore, we sought to assess time to selected outcomes in non-human primates (NHPs) experimentally infected with either Angola or Musoke Marburg strains.

Methods. Between 2012 and 2017, nine therapeutic trials at the US Army Medical Research Institute of Infectious Diseases were conducted in *Macaca fascicularis* monkeys challenged with 1 to 10,000 plaque forming units of Marburg virus administered intramuscularly. The current study population was comprised of 90 control NHPs, of which, 61 were administered Angola strain in four separate trials and 29 with Musoke strain in five trials. Clinical responses including development of rash and oral intake were collected following infection. The primary outcome of interest was time to death or euthanasia post-inoculation between strains evaluated using Cox proportional hazards regression. Secondary endpoints included time to development of a petechial rash and time to decreased appetite.

Results. Following Marburg virus challenge, all NHPs died and most NHPs experienced decreased food consumption (97%), and petechial rash (96%). The median time to death for Angola-infected NHPs was 8.9 days (25th, 75th percentiles: 7.9, 9.3), whereas Musoke-infected NHPs survived for a median of 10.0 days (25th, 75th percentiles: 9.0, 10.9) (Figure 1). Irrespective of strain, petechial rash was preceded by decreased food consumption by 0.7 days (SD 1.5) on average. Angola strain was associated with statistically significant earlier death (adjusted HR = 21.8; 95% CI: 8.9, 53.2), earlier development of petechiae (adjusted HR = 17.6; 95% CI: 7.0, 44.5) and earlier loss of appetite (adjusted HR = 5.8; 95% CI: 2.9, 11.7).

Conclusion. This was the first study to compare survival and clinical characteristics in NHPs between these strains. Despite sharing the similar genetic lineage, our data strongly supports increased virulence of Angola strain compared with Musoke strain. Pathophysiological mechanisms involved in increased virulence require further study.

Figure 1. Kaplan Meier survival curves in *Cynomolgus macaques* for A) overall time to death, petechial rash, and decreased food consumption (n=77); B) time to death by strain (n=90); C) time to decreased food consumption by strain (n=79); D) time to petechial rash by strain (n=77).



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