

# OUTBREAK INVESTIGATION REVEALS “SUPER-SPREADER” POTENTIAL OF ANDES VIRUS

## STUDY COULD INFORM CONTROL MEASURES FOR COVID-19, OTHER DISEASES

By Caree Vander Linden, USAMRIID PAO

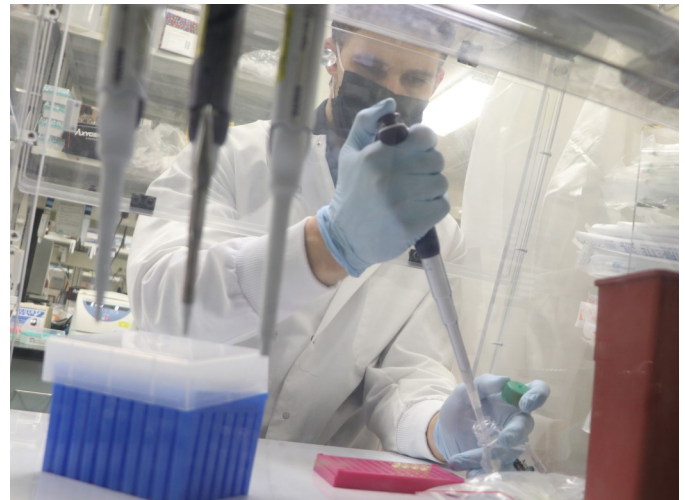
“Super-spreader” events and extensive person-to-person contact propelled an outbreak of hantavirus pulmonary syndrome in a small village in Argentina from 2018-2019, according to research published Dec. 3 in *The New England Journal of Medicine*.

In the paper, an international scientific team reports the genetic, clinical, and epidemiologic features of the outbreak caused by the Andes virus, a member of the hantavirus family. The group’s analysis could aid clinicians and public health officials in managing outbreaks of other viral diseases with similar transmission patterns, including COVID-19.

Andes virus is carried by wild rodents native to South America, and people can be infected through exposure to infected animals or their droppings. Like other hantaviruses, Andes virus infection can lead to a severe and often fatal respiratory disease in humans, called Hantavirus Pulmonary Syndrome (HPS). Importantly, Andes virus is the only hantavirus known to spread person to person. Those who come into direct contact with an infected individual or their body fluids, or who spend time in close proximity to an ill person, may also become infected. Currently, no licensed vaccines or drugs are available to treat the disease.

According to the study, led by scientists at the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) and Administración Nacional de Laboratorios e Institutos de Salud Dr. Carlos G. Malbrán (ANLIS), large social events and high viral load in infected individuals fueled person-to-person transmission of the Andes virus during the outbreak. Researchers teamed up with local health authorities to piece together a near-complete epidemiological “picture” reconstructing specific transmission events for the 34 confirmed cases. They traced the outbreak’s origin to a single spillover event, and documented a 32 percent case fatality rate overall.

While person-to-person spread of Andes virus was first described in 1996, the recent outbreak had the most extensive recorded human-to-human transmission of the virus seen to date. The team’s genomic analysis showed a striking similarity between the 2018-2019 and 1996 outbreak sequences. Understanding which genomic



Dr. Nicholas Di Paola, a National Research Council Fellow, prepares Andes virus sequencing libraries for complete genome characterization at the U.S. Army Medical Research Institute of Infectious Diseases, Fort Detrick, Md.

*Photo by John W. Braun Jr., USAMRIID Visual Information Office*

“signatures” correspond to the mechanisms necessary for person-to-person transmission may help scientists to develop new therapeutics to treat Andes virus infection.

Researchers found that droplets or aerosolized viral particles may have been routes of infection during the extensive person-to-person transmission of the 2018-2019 outbreak. They also noted that symptoms presented anywhere between 9 and 40 days after the infection took place. However, the authors pointed out that there might be a narrow window of infectiousness. Transmission often occurred on the first day of fever presentation in an infected patient. Interestingly, there was no clear association between the individuals transmitting the virus and their disease severity.

“This important observation indicates that, regardless of the severity of the disease, all HPS cases should be equally managed concerning their potential for virus transmission,” said Gustavo Palacios, Ph.D., co-senior author of the paper and Division Chief of Molecular Biology at USAMRIID. “Furthermore, we need to re-evaluate the threat that this virus poses. The lack of existing medical countermeasures, super-spreading potential, and high case-fatality rate all should raise concern.”

These findings could potentially help clinicians and public health officials deal with future outbreaks. As

*(Continued on page 2)*

(Continued from page 1)

with the preventive measures currently being practiced for COVID-19, social distancing and the use of appropriate personal protective equipment were effective in controlling transmission. Moreover, widespread contact tracing and self-quarantining led to a detectable decrease in transmission.

“Although less than 10 percent of cases occurred in hospital settings, the threat to clinicians and hospital staff must not be underestimated,” said Valeria Martinez, Ph.D., of ANLIS, co-first author of the study. “Doctors should remember that in the 1996 outbreak, many health care personnel got sick, and some died, when the appropriate personal protective equipment was not used.”

According to the authors, the study also examined cytokines within patients to determine the types of immunological responses present in people with HPS caused by Andes virus. Cytokines are proteins that aid cell-to-cell communication in immune responses. They concluded that there was no clear mechanism, but more of a broad and dysfunctional immunologic response among patients.

“We hope that by further exploring this apparent immune dysregulation, we will expand our knowledge of how different hantavirus species cause hantavirus pulmonary syndrome,” said co-author Mariano Sanchez-Lockhart, Ph.D., of USAMRIID. “Gaining a better understanding of how our immune system tackles Andes virus infection will certainly help clinicians to better manage severe cases and pave the way for new therapeutic interventions.”

Based on their comprehensive data, the team confirmed the necessity to study the patterns of Andes virus emergence, super-spreading, person-to-person transmission, and pathology to improve public health response strategies. “The breadth of techniques and expertise used to piece together person-to-person transmission and super-spreading events could be applied beyond Andes virus outbreaks,” said co-author Peter Larson, Ph.D., of USAMRIID. “We hope this approach serves as a model for future investigations of person-to-person transmission and for the identification of super-spreading events.”

According to Palacios, the investigative foundation for this work was built and tested by USAMRIID’s Center for Genome Sciences during outbreaks of Ebola virus disease in Western Africa and the Democratic Republic of the Congo, as well as the introduction of Zika virus into the United States. “While we are proud of this work and our track record, we believe this is only the beginning,” said Palacios. “Having a comprehensive approach to track spillover events is a long-term goal we strive for every day.”

First authors on the study are Valeria Martinez and Daniel Alonso of Administración Nacional de Laboratorios e Institutos de Salud Dr. Carlos G. Malbrán, and Nicholas Di Paola and Unai Pérez-Sautu of USAMRIID. The senior authors are Claudia Perandonos and Gustavo Palacios.

#### Reference:

Martinez, Di Paola, Alonso, Perez-Sautu et al. “Super-Spreaders” and Person-to-Person Transmission of Andes Virus in Argentina: *The New England Journal of Medicine*. Published Dec. 3, 2020. DOI: 10.1056/NEJMoa2009040

#### Authors:

V.P. Martinez, N. Di Paola, D.O. Alonso, U. Perez-Sautu, C.M. Bellomo, A.A. Iglesias, R.M. Coelho, B. Lopez, N. Periolo, P.A. Larson, E.R. Nagle, J.A. Chitty, C.B. Pratt, J. Diaz, D. Cisterna, J. Campos, H. Sharma, B. Dighero-Kemp, E. Biondo, L. Lewis, C. Anselmo, C.P. Olivera, F. Pontoriero, E. Lavarra, J.H. Kuhn, T. Strella, A. Edelstein, M.I. Burgos, M. Kaler, A. Rubinstein, J.R. Kugelman, M. Sanchez-Lockhart, C. Perandonos, and G. Palacios.

#### Funding:

This research was supported by the Ministerio de Salud y Desarrollo Social de la Nación Argentina; the Administración Nacional de Laboratorios e Institutos de Salud (ANLIS) Dr. Carlos Malbrán; the Chemical and Biological Incident Preparedness and Response Program; and the National Institute of Allergy and Infectious Diseases.

