

Editorial

Monkeypox: Another Virus Gone Viral!



Monkeypox virus is a double-stranded DNA virus belonging to the *Orthopoxvirus* genus, which also includes variola (smallpox), vaccinia, and cowpox viruses. The virus can be transmitted to humans from animals and is therefore a zoonotic disease. In humans, Monkeypox transmission occurs from direct or indirect contact with the body fluids or infected lesions or via respiratory droplets. The symptoms in infected individuals are very similar to those seen in the past in smallpox patients, although it is clinically less severe.

The name monkeypox originates from the initial discovery of the virus in monkeys in 1958. A few years later, the disease was considered endemic in central and west African countries. Since then, sporadic cases, related to travel, were reported globally. In May 2022, outbreaks of the virus were reported in nonendemic countries. As of August 15, 2022, the Centers for Disease Control and Prevention (CDC) has reported over 38,000 confirmed cases in 387 countries worldwide, with the United States, Spain, Germany, and the United Kingdom having the largest number of reported cases (Fig. 1). The ensuing deaths prompted the World Health Organization (WHO) to declare Monkeypox virus a global health emergency.

There are two clades of monkeypox virus: West African clade and the Congo Basin (Central African) clade, that were recently renamed by the WHO as clade I and clade II, respectively. The differences in clinical presentation of the two known clades of the orthopoxvirus genome structure suggest that changes among a relatively small number of Open Reading Frames (ORFs) can be attributed to proteins that modulate viral pathogenesis or host response.^{1,2} Sequencing studies suggest that the current outbreak is likely due to a virus from clade I (West African clade), which is often associated with milder disease and apparent human-to-human transmission.³

On May 17, 2022, the CDC developed, and the Food and Drug Administration cleared, the Non-variola Orthopoxvirus Real-time PCR Primer and Probe Set (nonvariola Orthopoxvirus assay) for testing through

the Laboratory Response Network (LRN) member laboratories.⁴ This polymerase chain reaction (PCR) diagnostic assay detects most commonly known human pathogenic Orthopoxviruses (eg, Vaccinia, Cowpox, and Monkeypox viruses) but not Variola virus, the causative agent of smallpox. The assay uses two sets of PCR primers and probes. One set of primers targets the Orthopoxvirus DNA polymerase gene (E9L; GenBank L22579). The second set amplifies the human RNase P gene as an internal control in monitoring specimen quality. Results of this assay are for the potential identification of nonvariola Orthopoxvirus DNA. Since the primers are not specific for monkeypox, positive results must be interpreted in conjunction with clinical presentation for the presumptive diagnosis and treatment of monkeypox. Confirmation of monkeypox is obtained from appropriate state or national public health authorities, including the CDC.

From the laboratory diagnostic perspective, rapid testing for the monkeypox virus did not ramp up fast enough to clamp down community spread of the virus. Testing for Orthopoxviruses beyond LRN members is just starting to establish itself, and screening sites are still trying to launch high-throughput testing. Furthermore, even though effective vaccines for monkeypox were available, the short supply and lack of organization affected access especially to high-risk individuals. The bottom line is we are still floundering at handling emerging pandemics. Mobilizing rapid testing and enhancing preventative measures to nip the problem in the bud continue to be daunting to health care. Emerging infections have gone viral over the past 3 years, and molecular testing methodologies can offer a clear path to identify and possibly control further infections.

Helen Fernandes, PhD

Department of Pathology and Cell biology
Columbia University Irving Medical Center
New York, NY 10032, USA

E-mail address: hf2340@cumc.columbia.edu

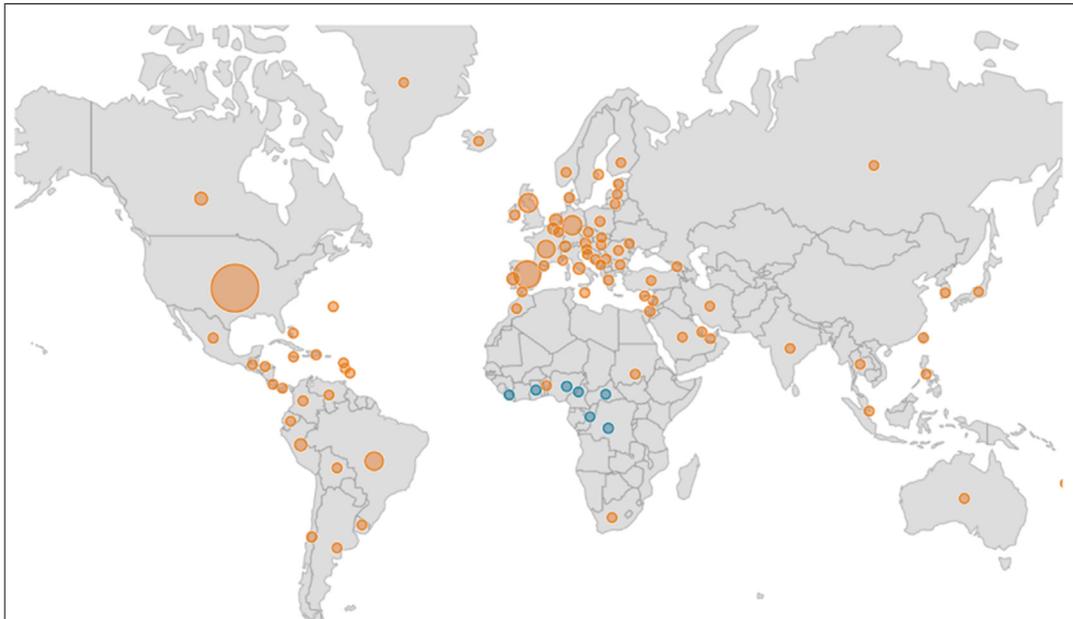


FIG. 1 Distribution of Monkeypox virus infections worldwide. (From 2022 Monkeypox Outbreak Global Map. Centers for Disease Control and Prevention. <https://www.cdc.gov/poxvirus/monkeypox/response/2022/world-map.html>. Published August 4, 2022.)

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- 3 Isidro J, Borges V, Pinto M, et al. Phylogenomic characterization and signs of microevolution in the 2022 multi-country outbreak of monkeypox virus. *Nat Med* 2022;28(8): 1569–72. <https://doi.org/10.1038/s41591-022-01907-y>.
- 4 Test procedure: non-variola orthopoxvirus generic real-time PCR test. Available at: <https://www.cdc.gov/poxvirus/monkeypox/pdf/Non-variola-Orthopoxvirus-Generic-Real-Time-PCR-Test.pdf>. Accessed August 16, 2022.