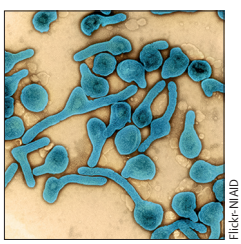
Reconsidering the incubation period of Marburg virus disease



Flickr-NIAID

Lancet Infect Dis 2022

Published Online
September 26, 2022
https://doi.org/10.1016/
S1473-3099(22)00647-8

Several outbreaks of Marburg virus disease (MVD) with a total of 475 cases have been reported globally so far. Although some of these cases were zoonotic, two larger outbreaks with human-to-human transmission occurred in the Democratic Republic of the Congo (154 cases) and in Angola (252 cases).[1]

In August 2022, Ghana announced that the country can again be regarded to be free of MVD.[2,3] The control of such outbreaks crucially depends on knowing the incubation period: it establishes which contacts of known cases should be traced, how long they need to be quarantined, and when a country can be declared free of MVD; and it also helps to identify zoonotic reservoirs. Although the onset of the disease is easily recognised, the time of infection (which is needed to calculate the incubation period) can only be established for patients with very short exposure windows. Especially for newly emerging and rare infections, initial outbreak investigations are caught in a vicious circle: some previous knowledge should be used to establish when and from whom new patients might have acquired their infection.

Estimates on the MVD incubation period have, thus, been highly influenced by the original outbreak in Marburg, Germany, in 1967, where laboratory workers were exposed to infected monkey organs for several weeks.[4] The time of infection could be narrowed down in only four of 21 cases, and was argued to be 5–7 days. All these patients had direct contact with blood; those with a short incubation period were infected by contaminated broken glass or needles, suggesting an initial viral load that might have been much higher than found after human-to-human transmission.

At the same time, six more MVD cases occurred in Frankfurt, Germany, after contact with the blood from infected monkeys; in this outbreak, the incubation period was narrowed down to 7–9 days.[5] This interval coincided with that of patients from Kenya, where the infection occurred in the hospital or at a funeral and patients had either skin contact with infected blood or got infected from highly contagious cases or corpses.[6] Based on the original outbreak and on information that has been gathered during subsequent outbreaks, the incubation period of MVD is believed to last for 5–10 days (range, 3–21), yet newer evidence from Angola and from the latest outbreak in Ghana shows that this range has been underestimated.[7,8]

One of the reasons for this might be that historic estimates ignore the route of transmission and the infecting viral load, which might influence the duration of the incubation period.[1] Two patients from Angola who were infected by human-to-human transmission had an incubation period of at least 23 and 26 days,[7] contradicting the previous upper limit of 21 days.

Observations from the latest outbreak in Ghana provide further evidence of a longer incubation period. The index patient of the Ghana outbreak developed MVD on June 24, 2022, two days after returning from travel to the western region of Ghana, where he had entered abandoned mines (such places had previously been associated with zoonotic MVD reservoirs).[9] His son and wife had contact with him from his return to their home on June 22, until his burial on June 27. After completing a 21-day quarantine period and daily monitoring, they developed symptoms on July 17 (for the son) and July 21 (for the wife), and were diagnosed with MVD.[2,8,10] Because the wife became symptomatic only 4 days after her son, it is highly unlikely that he infected her. Hence, the incubation period of the son was 21–24 days, and that of his mother was 25–28 days. These two secondary infections provide further evidence for an extended incubation period after human-to-human transmission.

Together with the two documented patients infected by household transmission in Angola who had an incubation period of 21 or more days, the recent outbreak in Ghana shows that new estimates of the incubation period of MVD that account for the route of infection are urgently needed. A thorough study of the clinical records of all previous outbreaks, which is less biased towards the assumption of a short incubation period of 5–9 days, would be necessary to obtain adequate estimates and to inform public health policy.

We declare no competing interests.

*Kristan A Schneider, Joseph H Kofi Bonney, Chrysantus Kubio, Gordon A Awandare, Martin Eichner
kristan.schneider@hs-mittweida.de

Department of Applied Computer and Bioscience, Hochschule Mittweida, Mittweida 09648, Germany (KAS); Department of Virology, Noguchi Memorial Institute for Medical Research (JHKB), and the West African Centre for Cell Biology of Infectious Pathogens (GAA), University of Ghana, Legon, Ghana;

Savannah Regional Health Directorate, Ghana Health Service, Damongo, Ghana (CK); Institute for Clinical Epidemiology and Applied Biometrics, University of Tübingen, Tübingen, Germany (ME); Epimos, Bischofsheim in der Rhön, Germany (ME)

1 Brauburger K, Hume AJ, Mühlberger E, Olejnik J. Forty-five years of Marburg virus research. *Viruses* 2012; **4:** 1878–927.

2 Ghana News Agency. Marburg: Ghana is free—GHS. 2022. https://gna.org.gh/2022/08/marburg-ghana-is-free-ghs/ (accessed Aug 21, 2022).

3 Ghana Health Service. Recovery of the last case of Marburg virus disease in Ghana. 2022. https://ghs.gov.gh/ooboxyky/2022/08/Press-Release-Update-on-MVD-final.pdf (accessed July 9, 2022).

4 Martini GA. Marburg virus disease. Clinical syndrome. In: Martini GA, Siegert R (eds). Marburg Virus Disease. Berlin, Heidelberg; Springer, 1971.

5 Stille W, Böhle E, et al. Über eine durch Cercopithecus aethiops übertragene Infektionskrankheit. *Dtsch Med Wochenschr* 1968; **93:** 572–82 (in German).

6 Smith DH, Johnson BK, Isaacson M, et al. Marburg-virus disease in Kenya. *Lancet* 1982; **1:** 816–20.

7 Pavlin BI. Calculation of incubation period and serial interval from multiple outbreaks of Marburg virus disease. *BMC Res Notes* 2014; **7:** 906.

8 Ghana Health Service. Update on Marburg virus disease outbreak in Ghana. 2022. https://ghs.gov.gh/ooboxyky/2022/08/Press-Release-Marburg-Virus-Disease_Final_20220728_15_36Hours.pdf (accessed July 9, 2022).

9 Bausch DG, Nichol ST, Muyembe-Tamfum JJ, et al. Marburg hemorrhagic fever associated with multiple genetic lineages of virus. *N Engl J Med* 2006; **355**: 909–19.

10 WHO. Marburg virus disease - Ghana. 2022. https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON402 (accessed Aug 21, 2022).