Watching brief	
Title	Marburg Virus Disease Outbreak in Guinea, August 2021
Authors	Jessica Yang, The Garvan Institute of Medical Research
Date of first report of the outbreak	6/8/2021
Disease or outbreak	Marburg Virus Disease (MVD), formerly known as Marburg Virus Haemorrhagic Fever
Origin (*country, city, region*)	Tèmessadou M'boke, prefecture of Guéckédou, Nzerekore health district, Guinea
Suspected Source (specify food source, zoonotic or human origin or other)	The Egyptian fruit bat (EFB) (*Rousettus aegyptiacus*) is the known reservoir host of the virus (1, 2). In previous outbreaks, cases have been linked to mines or caves inhabited by infected bats (3). Investigations to identify the source of this outbreak are ongoing (4).
Date of outbreak beginning	9/8/2021
Date outbreak declared over	16/9/2021
Affected countries & regions	Guinea
Number of cases (specify at what date if ongoing)	1 confirmed case. 1 death.
Clinical features	The incubation period is 3-21 days (5). Following the incubation period, the onset of clinical signs and symptoms is divided into 3 phases: 1. Generalisation (Day 1-4): symptom onset occurs abruptly with patients displaying generic flu-like symptoms such as high fever, chills, severe headache, myalgia, odynophagia, vomiting and diarrhoea (5, 6). Patients may develop pharyngitis, enanthem, dysphasia, leukopenia, thrombocytopenia, lymphadenopathy and a maculopapular rash (5).

	2. Early organ (Day 5-13): many initial symptoms continue to worsen. Patients can experience neurological symptoms, dyspnoea, abnormal vascular permeability, haemorrhagic manifestations and multi-organ dysfunction (5). 3. Late organ/convalescence (Day 13+): patients either succumb to illness or recover. Fatalities usually occur 8-16 days following symptom onset and are due to multi-organ failure and shock (5). Recovering patients can experience exhaustion, peeling skin at rash sites, myalgia, sweating, partial amnesia and secondary infections (5).
Mode of transmission (dominant mode and other documented modes)	Zoonotic: Bats shed virus through their saliva, urine and faeces (2, 7, 8). Transmission can occur when people come into close contact with bat excrements, by eating contaminated fruit that bats have fed on or through bat bites during hunting (2). Contact with spill-over hosts such as non-human primates e.g. African Green Monkey (*Cercopithecus aethiops*) also poses a transmission source (9, 10). Human-to-human: Transmission is through direct contact (via skin abrasion or mucous membrane) with blood or other bodily fluids (urine, stool, saliva, tears, breast milk or sweat) from an infected individual or contaminated materials and surfaces (e.g. bedding or clothing) (5, 9, 10). Transmission through infected semen has also been documented 7 weeks following clinical recovery (11). Healthcare workers caring for patients can contract disease via needlestick injuries from contaminated injection equipment, and funerals also pose a transmission risk when there is direct contact with the body of the deceased (9).
Demographics of cases	The index case was a 46-year-old male farmer, who was a resident of the Temessadou M´Boké village in Guinea.
Case fatality rate	The CFR is uncertain because only one confirmed case has died. The CFR from previous outbreaks ranged from 23% (Germany-Serbia) to 90% (Angola 2004-2005) (9).
Complications	Complications of MVD can lead to severe haemorrhagic fever, causing multi-organ failure and death.

Available prevention	There are currently no licenced vaccines, however there are 3 potential vaccines in Phase I clinical trials (cAd3, MARV DNA and MVA-BN-Filo) and one is scheduled for a Phase II/III clinical trial (MVA-BN-Filo) (6, 12). Since there are no available vaccines, preventing disease includes the following measures (13): 1. Community engagement and education about infection prevention and transmission, such as avoiding contact with the body fluids of suspected or confirmed cases, employing safe practices during funerals/burial rituals, and practicing good hand hygiene. 2. Encouraging people to seek medical care immediately (at the nearest health facility) if they exhibit symptoms. 3. Educating recovered male patients about potential sexual transmission (14). Safe sex and maintaining good hygiene practices should be adhered to for 12 months following symptom onset or two negative results for MV are obtained (14). 4. Minimising contact with wildlife and handling with gloves and other protective clothing. 5. Avoiding consumption of raw meat and thoroughly cooking animal products prior to consumption.
Available treatment	Currently no antiviral treatments are approved to treat MVD (9). There are various pharmaceutical treatments in development, which include small molecule inhibitors, immnotherapeutics, antiviral nucleoside analogs, phosphorodiamidate morpholino oligomers and lipid-encapsulated small interfering RNAs (6). Current available treatment focuses on treating symptoms with aggressive supportive care. This includes oral or intravenous fluids to replace electrolytes, blood or blood products, maintaining oxygen levels and treating any infections (9, 15).
Comparison with past outbreaks	There have been 12 outbreaks of MVD since it was first described in 1967 when laboratory workers in Germany and Serbia (former Yugoslavia) became infected from African Green Monkeys imported from Uganda (3). Outbreaks have occurred sporadically and have been observed in Zimbabwe (1975), Kenya (1980 and 1987), the Democratic Republic of Congo (1998-2000), Angola (2004-2005) and Uganda (2007, 2012, 2014, 2017) (3). In 2008, two tourists returning to the USA and Netherlands were infected following their travels in Uganda (3).

	The most notable outbreak in history is the Angola outbreak (252 cases, 227 deaths, CFR=90%), which occurred in the Uige Province and began in October 2004 (16). It was the first outbreak in an urban setting and the majority (75%) of cases were observed in children under 5-years-old, a pattern not observed in earlier epidemics (17). The severity of this outbreak was largely due to delays in the initial response and also fear and misinformation within the community (16). The source of this outbreak was never identified.
Unusual features	• This is the first outbreak in Guinea and West Africa. Previous outbreaks were in southern and eastern Africa (3). • The source of infection in the current outbreak is unknown. There are ongoing activities to capture and sample bats in the local regions of Temessadou M´Boké, Baladou Pébal and Koundou (4). • The index cases' travel history and contact information is unavailable. The gentleman presented to a local health centre on the 1/8/21 with fatigue, abdominal pain, fever, headache and bleeding gums (18). He passed away the following day in his village and an investigative team was deployed to collect samples (18). Real-time PCR conducted on the 3/8/21 was positive for MVD and negative for Ebola virus (18).
Critical analysis	**<u>Disease control</u>** Guinea's success in containing the outbreak can be attributed to the preparedness and rapid response from health officials (19). Given the similarities between Ebola virus disease (EVD) and MVD, the Ebola control system Guinea, built after the 2014-2016 Ebola outbreaks, has been crucial in this operation (19). This enabled a well-coordinated effort of national health officials together with experts from WHO in the investigation of the outbreak, rapid emergency response, contact tracing as well as active searching for cases in the community and in health facilities, engaging with the community about risks, infection and control activities, and setting up strong surveillance both within Guinea as well point of entry to neighbouring countries (18, 19). The same region has also just seen the end of a 4-month Ebola outbreak that was declared over in June 2021 (20). The community would have been aware of viral haemorrhagic fever and understood the precautions and procedures to follow to minimise transmission. Consequently, this may have also contributed to the individual case in this outbreak. **<u>MV spill-over into humans</u>**

The source of the outbreak is still unknown. However, a study by Amman et al., (21) found MV that was genetically similar to the Angola strain actively circulating in EFB colonies in several locations in Sierra Leone. Two of the locations were found to border Guinea and were relatively close to Guéckédou (Figure 1) (21). Infected bats from these locations could be potential sources of the Guinea outbreak.

Figure 1. Map of Sierra Leone and Guinea showing locations where populations of MV positive EFB were discovered and their proximity to Guéckédou, Guinea (21). Image sourced from Google Maps (22).

In addition, time of year may also influence whether a spill over event will occur. Seasonal patterns of active MV circulating in EFBs have been found to fluctuate with breeding patterns. In the adult population there is a baseline level of circulating MV (2.4-2.5%) (21, 23). Following the breeding and birthing season there is an increase in the number of juvenile bats and an increase in the proportion of active infection (12.4%) in juveniles (6-months-old) (23). These spikes in MV were found to coincide with periods of historical outbreaks. Likewise, the current Guinea outbreak, which began in August also falls within this period of increased risk of human infection.

Key questions	• Where did the farmer contract the infection? • How closely is this viral strain related to viral strains from previous outbreaks? • What is the outcome of environmental investigations of the source? • If the source is from bats, where were the bats from? Is this the same colony which caused the recent Ebola outbreak in Guinea? • Were there cases of MV which were missed because of the recent Ebola virus epidemic? Do they confirm every case of Ebola virus? Would they have tested for MV? Is it possible to have coinfection with the two viruses.
References	1. Ross A. Guinea records probable case of Ebola-like Marburg virus 2021 [Available from: https://www.reuters.com/business/healthcare-pharmaceuticals/guinea-records-probable-case-ebola-like-marburg-virus-2021-08-06/. [Accessed 5th September, 2021]. 2. Centers for Disease Control and Prevention (CDC). Deadly Marburg Virus Found in Sierra Leone Bats 2018 [Available from: https://www.cdc.gov/media/releases/2018/p1220-marburg-found-in-bats.html. [Accessed 11th October, 2021]. 3. Centers for Disease Control and Prevention (CDC). History of Marburg Virus Disease (MVD) Outbreaks 2021 [Available from: https://www.cdc.gov/vhf/marburg/outbreaks/chronology.html. [Accessed 26th September, 2021]. 4. World Health Organisation (WHO). Marburg virus disease - Guinea 2021 [Available from: https://www.who.int/emergencies/disease-outbreak-news/item/marburg-virus-disease---guinea. [Accessed 24th of September, 2021]. 5. Brauburger K, Hume AJ, Mühlberger E, Olejnik J. Forty-five years of Marburg virus research. *Viruses*. 2012;4(10):1878-927. DOI: https://doi.org/10.3390/v4101878. 6. Kortepeter MG, Dierberg K, Shenoy ES, Cieslak TJ. Marburg virus disease: A summary for clinicians. *International Journal of Infectious Diseases*. 2020;99:233-42. DOI: https://doi.org/10.1016/j.ijid.2020.07.042. 7. Amman BR, Jones MEB, Sealy TK, Uebelhoer LS, Schuh AJ, Bird BH, et al. Oral shedding of Marburg virus in experimentally infected Egyptian fruit bats (Rousettus aegyptiacus). *Journal of Wildlife Diseases,*. 2015;51(1):113-24. DOI: https://doi.org/10.7589/2014-08-198. 8. Pawęska JT, Storm N, Markotter W, Di Paola N, Wiley MR, Palacios G, et al. Shedding of Marburg Virus in Naturally Infected Egyptian Rousette Bats, South Africa, 2017. *Emerging Infectious*

Diseases,. 2020;26(12):3051-5. DOI: https://doi.org/10.201/eid2612.202108.
9. World Health Organisation (WHO). Marburg virus disease 2021 [Available from: https://www.who.int/news-room/fact-sheets/detail/marburg-virus-disease. [Accessed 4th September, 2021].
10. Centers for Disease Control and Prevention. Marburg (Marburg Virus Disease): Transmission 2021 [Available from: https://www.cdc.gov/vhf/marburg/transmission/index.html. [Accessed 23rd September, 2021].
11. Martini GA. Marburg agent disease: in man. *Transactions of the Royal Society of Tropical Medicine & Hygiene,*. 1969;63(3):295-302. DOI: https://doi.org/10.1016/0035-9203(69)90001-7.
12. Outbreak News Today. Marburg vaccine: Walter Reed Army Institute of Research begins phase 1 clinical trial 2018 [Available from: http://outbreaknewstoday.com/marburg-vaccine-walter-reed-army-institute-research-begins-phase-1-clinical-trial-84079/. [Accessed 26th September, 2021].
13. World Health Organisation (WHO). Marburg Virus Disease – Guinea – Disease Outbreak News 2021 [Available from: https://who.africa-newsroom.com/press/marburg-virus-disease--guinea--disease-outbreak-news-18sep?lang=en. [Accessed 23rd September, 2021].
14. Diallo T. Guinea-Fièvre Marburg: the case of Guékédou confirmed by the Pasteur Institute in Dakar Guineenews.org2021 [Available from: https://guineenews.org/author/thierno/. [Accessed 4th September, 2021].
15. Ligon BL. Outbreak of Marburg hemorrhagic fever in Angola: a review of the history of the disease and its biological aspects. *Seminars in Pediatric Infectious Diseases,*. 2005;16(3):219-24. DOI: https://doi.org/10.1053/j.spid.2005.05.001.
16. Centers for Disease Control and Prevention. Outbreak of Marburg virus hemorrhagic fever--Angola, October 1, 2004-March 29, 2005. MMWR Morb Mortal Wkly Rep. 2005/04/01 ed2005. p. 308-9. PMID: 15800477.
17. Pearson H. Marburg's behaviour bewilders scientists 2005 [updated 2005/04/07. Available from: https://doi.org/10.1038/news050404-12.
18. World Health Organisation (WHO). Marburg virus disease - Guinea 2021 [Available from: https://www.who.int/emergencies/disease-outbreak-news/item/2021-DON331.
19. World Health Organisation (WHO). West Africa's first-ever case of Marburg virus disease confirmed in Guinea 2021 [updated 09 August 2021. Available from: https://www.afro.who.int/news/west-africas-first-ever-case-marburg-virus-disease-confirmed-guinea. [Accessed 11th October, 2021].
20. World Health Organisation (WHO). Ebola outbreak in Guinea declared over 2021 [Available from:

https://www.afro.who.int/news/ebola-outbreak-guinea-declared-over. [Accessed 10th October, 2021].
21. Amman BR, Bird BH, Bakarr IA, Bangura J, Schuh AJ, Johnny J, et al. Isolation of Angola-like Marburg virus from Egyptian rousette bats from West Africa. *Nature Communications*. 2020;11(1):510. DOI: https://doi.org/10.1038/s41467-020-14327-8.
22. Google Maps. Border of Sierra Leone and Guinea 2021 [Available from: https://www.google.com/maps/@8.6441034,-9.9934235,9.73z. [Accessed 17th October, 2021].
23. Amman BR, Carroll SA, Reed ZD, Sealy TK, Balinandi S, Swanepoel R, et al. Seasonal pulses of Marburg virus circulation in juvenile Rousettus aegyptiacus bats coincide with periods of increased risk of human infection. *PLoS Pathogens*. 2012;8(10):e1002877. DOI: https://doi.org/10.1371/journal.ppat.