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Editorial

The re-emergence of Marburg virus Disease in West Africa: how prepared is the sub-region for preventing recurrent zoonotic outbreaks?

On 13 February 2023, Equatorial Guinea confirmed its first-ever outbreak of Marburg virus disease (MVD) [1]. This latest outbreak in Kié-Ntem province, north of Equatorial Guinea, was linked to 9 deaths among 25 suspected cases. This is the third country in West Africa, in 18 months, to report MVD outbreak since it was first detected in Guinea in August 2021 [2] and Ghana in June 2022 [3].

Since its first detection in Europe in 1967, during two outbreaks occurring simultaneously in Marburg and Frankfurt in Germany, and in Belgrade, Yugoslavia (now Serbia), all but one of the other outbreaks were reported in Africa [4]. Since 1975, 15 separate reports of human MVD cases have come from South Africa (1975 – 3 cases), Kenya (1980 – 2 cases, 1987 – 1 case), Russia (1990 – 1 case), Democratic Republic of Congo (1998-2000 – 154 cases), Angola (2000-2005 – 252 cases), Uganda (2007 – 4 cases, 2017 – 4 cases), USA, ex Uganda (2008 – 1 case), Netherlands-ex Uganda 2008 – 1 case), Uganda (2014 – 1 case), Guinea (2021 – 1 case) and Ghana (2022 – 3 cases) [1-3,5]. The largest outbreak reported in Angola in 2004 had led to 227 deaths among 252 cases [5].

Like Ebola virus, the Marburg virus is a member of the Filoviridae family and MVD is as deadly as Ebola virus disease with case-fatality rates reaching 90% [5]. Marburg virus can be transmitted to humans from fruit bats and spread through direct contact with bodily fluids of infected people. Symptoms of MVD include high fever, severe headache and malaise. Many patients develop severe haemorrhagic symptoms within seven days. In Africa, where febrile illnesses are common, distinguishing MVD clinically from malaria, meningitis, typhoid fever, and other viral haemorrhagic fevers can be challenging. Marburg virus can be detected using serum neutralisation tests, antigen-capture detection tests, antibody-capture ELISA, RT-PCR assay, and virus isolation by cell culture [2]. These diagnostic methods require good laboratory infrastructure and well-trained personnel in settings with continuous power supply, and an efficient cold chain for samples and reagents.

West Africa is now on high alert after three outbreaks of MVD and one outbreak of Ebola (in Cote D'Ivoire in August 2021) since August 2021 [6]. The control mechanisms in place for Ebola in Guinea, Liberia and Sierra Leone have effectively informed protocols for an emergency response to the Marburg virus. Efficient tools are crucial to detect the emergence and spread of new pathogens, drug resistance mechanisms, providing evidence for implementing public health control measures. For this, molecular diagnostics and genotyping of pathogens have become indispensable tools to both improve clinical management and limit further spread. The rapid detection of the Marburg virus in laboratories in West Africa when the outbreaks occurred and the emergency responses by health authorities demonstrated the degree to which laboratory capacities have been strengthened in the past 10 years. During the Ebola outbreak between 2013 and 2016, the three most affected countries – Guinea, Liberia and Sierra Leone – lacked the technical capacities such that diagnostics and bioinformatics had been performed through parachute research [7].

The basic reproduction number for MVD of 1.59 [8] implies that large outbreaks are less probable but outbreaks in the Democratic Republic of the Congo (1998–2000), Angola (2004–05) and West Africa (2021–2023) showed that areas with weak health systems, especially during conflict/post-conflict are vulnerable to frequent and substantial outbreaks. Africa CDC was founded in 2016 because of the West Africa Ebola epidemics, as a specialised technical institution that supports public health initiatives of member states of the African Union. In partnership with World Health Organization Regional Office for Africa (WHO-AFRO) and other organisations, it has strengthened the capacity and capability of Africa's public health institutions as well as partnerships, ensuring that African countries can detect and respond quickly and effectively to disease threats and outbreaks, based on data-driven interventions and programmes.

To date, about 140 disease outbreaks occur in Africa annually [9]. Genomic surveillance is critically important for early notification and control of outbreaks. Huge gaps exist in genomics and bioinformatic capacities in national institutions and a highly skilled workforce is required in all African sub-regions for the incorporation of pathogen genomics into the existing disease surveillance systems. Evidently, there is a need to strengthen south-north and south-south partnerships and collaborations to enable a coordinated approach to pathogen diagnostics and response to outbreaks to be developed. In 2019, the Africa Pathogen Genomics Initiative (PGI) was launched by the Africa CDC Institute for Pathogen Genomics to support public health pathogen genomics and bioinformatics, maximising the benefits of next-generation genomic sequencing tools across Africa. Before the COVID-19 outbreak, 72% of Africa's genome sequencing capacity was concentrated in four countries: South Africa, Kenya, Nigeria and Morocco [9]. Filling the gap in sequencing and related technologies would accelerate the

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generation of the scientific evidence needed for health systems to better prevent, identify and track these outbreaks.

Currently, 20 national public health and research institutions across Africa have facilities for pathogen genomic surveillance, including hubs in eleven member states of the African Union. The regional hubs are strategically located to serve national public health institutions of neighbouring countries to reduce specimen shipping time and costs. Three out the 9 regional hubs/specialised centres namely, African Centre of Excellence for Genomics of Infectious Diseases (ACEGID), Noguchi Memorial Institute for Medical Research (NMIMR), University of Ghana and Institute Pasteur, Dakar, are in West Africa. These hubs are well equipped with advanced sequencing platforms. Supported by Africa CDC, these institutions are working closely with key partners including the WHO AFRO to improve technical capabilities across the entire West-Africa. Through this initiative, a coordinated Africa-wide effort has contributed to the scientific understanding of the evolution and spread of SARS-CoV-2 variants during the peak of COVID-19 pandemic [9,10]. Other programmes in diagnostic capacities and laboratory systems in West Africa are organised by the West Africa Health Organisation (WAHO) and the Third Country Laboratory Training (TCTP) funded by the Japan International Cooperation Agency and based at the NMIMR. Scientists in West Africa are now better prepared to perform research in emerging infections than during the Ebola epidemics in West Africa starting from 2013. Within 48 hours of the suspected outbreaks of MVD in West Africa, scientists in Guinea, Ghana and Senegal were able to confirm infection with the Marburg virus.

Prophylaxis and therapy are the other major challenges, as no vaccines or antiviral treatments have been approved to date to treat MVD. An effective MVD vaccine for the protection of healthcare workers and ring vaccination of contacts, such as that implemented during the recent Ebola outbreaks in Guinea, could be an important addition to the available tools for the fight against the outbreak**.** Several vaccines to prevent MVD are at various stages of development, such as the candidate modified chimpanzee adenovirus vaccine by Sabin Vaccine Institute (Washington DC, USA); candidate human adenovirus vaccine by Janssen (Beerse, Belgium); and candidate vaccines being developed by the Public Health Vaccines (PHV) (Massachusetts, USA), the International Aids Vaccine Initiative (IAVI) (New York City, USA) and Auro Vaccines (Pearl River, New York), based on the weakened forms of vesicular stomatitis virus as vector [11–13]. The first-in-human trial of a cAd3-Marburg vaccine showed the candidate vaccine to be safe and immunogenic, with a safety profile like previously tested cAd3-vectored filovirus vaccines [14]. The ongoing MVD outbreak in Equatorial Guinea has led WHO to convene a MVD expert group meeting in Geneva, Switzerland on February 14th, 2023, which has discussed the logistics of testing the vaccines, although, like previous outbreaks, effective infection control measures such as quarantine are anticipated to end the outbreak before vaccines can be administered.

The previous Ebola virus disease and the recent MVD outbreaks in West Africa highlight missed opportunities for rapid research during outbreaks. Planning and executing clinical research rapidly during new outbreaks can be difficult and protracted. Development of locally acceptable ethically sound research protocols including adaptive RCT designs, can and does delay rapid implementation of clinical research [15,16]. This emphasises why medical and scientific communities should work together to design and introduce specific pathways for optimal trial designs for evaluation of multiple products, and to put in place ethical standard and logistics framework for assessing novel diagnostics, treatments, and vaccines. African countries should continue to invest in health systems and improve disease surveillance. Benchmarking and the harmonisation of performance levels of health systems could strengthen capabilities and competences and potentially standardise responses to an outbreak when it occurs. In addition to the African CDC providing leadership, sub-regional bodies such as WAHO should lead the process. The WAHO has been involved in harmonisation of health curricula in West Africa to ensure that healthcare professionals have the same level of competence to treat infections and other illnesses in the sub-region. What is still missing is the uniform implementation of the harmonised curricula across the sub-region and also an equitable health system infrastructure. Equatorial Guinea would not have needed testing in Senegal, had the testing infrastructure and capability been present in the country. It is time for African Union Institutions, such as the African Peer Review Mechanism to conduct necessary reviews on health systems across the continent. Harmonisation of health systems is needed so that a unified highly-skilled approach can be adopted to prevent and manage future outbreaks in all sub-regions in Africa.

Author declarations

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References

[1] WHO. Equatorial Guinea confirms first-ever Marburg virus disease outbreak. https://www.afrowhoint/countries/equatorial-guinea/news/equatorial-guinea-confirms-first-ever-marburg-virus-disease-outbreak. 2023.
[2] Koundouno FR, Kafetzopoulou LE, Faye M, Renevey A, Soropogui B, Ifono K, et al. Detection of Marburg Virus Disease in Guinea. *N Engl J Med* 2022;**386**(26):2528–30.
[3] Hussain Z. Ghana declares its first outbreak of Marburg virus disease after two deaths. *BMJ* 2022;**378**:o1797.
[4] Slenczka W, Klenk HD. Forty years of marburg virus. *J Infect Dis* 2007;**196 Suppl 2**:S131–5.
[5] Farahat RA, Memish ZA. Re-emergence of Marburg virus and monkeypox in the shadow of COVID-19 pandemic: Current situation and implications - Correspondence. *Int J Surg* 2022;**106**:106923.
[6] Adepoju P. West Africa on alert for haemorrhagic fevers. *Lancet* 2021;**398**(10301):653.
[7] The Lancet Global Health. Closing the door on parachutes and parasites. *Lancet Glob Health* 2018;**6**(6):e593.
[8] Manno D. Developing a vaccine against Marburg virus disease. *Lancet* 2023;**401**(10373):251–3.
[9] Makoni M. Africa's $100-million Pathogen Genomics Initiative. *Lancet Microbe* 2020;**1**(8):e318.
[10] Tegally H, San JE, Cotten M, Moir M, Tegomoh B, Mboowa G, et al. The evolving SARS-CoV-2 epidemic in Africa: Insights from rapidly expanding genomic surveillance. *Science* 2022;**378**(6615):eabq5358.
[11] Harris E. Marburg Vaccine Safe, Immunogenic in Phase 1 Trial. *JAMA* 2023.
[12] Longini IM, Yang Y, Fleming TR, Munoz-Fontela C, Wang R, Ellenberg SS, et al. A platform trial design for preventive vaccines against Marburg virus and other emerging infectious disease threats. *Clin Trials* 2022;**19**(6):647–654.
[13] O'Donnell KL, Feldmann F, Kaza B, Clancy CS, Hanley PW, Fletcher P, et al. Rapid protection of nonhuman primates against Marburg virus disease using a single low-dose VSV-based vaccine. *EBioMedicine* 2023;**89**:104463.
[14] Hamer MJ, Houser KV, Hofstetter AR, Ortega-Villa AM, Lee C, Preston A, et al. Safety, tolerability, and immunogenicity of the chimpanzee adenovirus type 3-vectored Marburg virus (cAd3-Marburg) vaccine in healthy adults in the USA: a first-in-human, phase 1, open-label, dose-escalation trial. *Lancet* 2023;**401**(10373):294–302.
[15] Ippolito G, Lanini S, Brouqui P, Di Caro A, Vairo F, Abdulla S, et al. Ebola: missed opportunities for Europe-Africa research. *Lancet Infect Dis* 2015;**15**(11):1254–5.
[16] Ippolito G, Lanini S, Brouqui P, Di Caro A, Vairo F, Fusco FM, et al. Non-randomised Ebola trials–lessons for optimal outbreak research. *Lancet Infect Dis* 2016;**16**(4):407–8.