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Crimean–Congo haemorrhagic fever: test early with ROTEM?

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See **Articles** page 862

In their observational cohort study published in *The Lancet Infectious Diseases*, Tom Fletcher and colleagues[1] used rotational thromboelastometry (ROTEM) to better understand the coagulopathy of Crimean–Congo haemorrhagic fever.

Crimean–Congo haemorrhagic fever is the most widespread tick-associated viral fever. Its clinical presentation ranges from non-symptomatic to massive haemorrhage leading to a high degree of morbidity and even death. The physiopathology of haemostatic disorders in haemorrhagic fevers is not completely elucidated; however, decreased platelet count and function have been described.[2,3] Because the severity of haemostatic impairment is frequently not reflected by standard coagulation tests, a quick and easy assessment of functional haemostasis by ROTEM might facilitate identification of patients at high risk of mortality even before the underlying virus is confirmed by more sophisticated methods such as PCR. This approach is even more important since timely treatment seems to mitigate symptoms, improving the outcome and decreasing mortality. This is especially important for low-income countries where health care is not always easily accessible or available, and diagnostic and treatment options are restricted.

In perioperative medicine, ROTEM has been used as a point-of-care test for blood coagulation for more than a decade. Although the tests do not identify a specific disease mechanism or a single coagulation factor deficit, they allow early and fast estimation of the coagulation capacity and consequently targeted treatment of the haemorrhage. In addition to estimating bleeding risk or guiding haemostatic therapy in critically ill patients, we recently showed the potential of such tests in predicting mortality in a cohort of patients with sepsis.[4]

It therefore makes sense to use ROTEM as an early warning tool when Crimean–Congo haemorrhagic fever is suspected, with the purpose of detecting the most severe cases and minimising delays in starting treatment and in adopting isolation measures and transferring high-risk patients to specialised units. This approach could be optimised by use of a schematic approach, with ROTEM tests done in a standardised manner at fixed time intervals, since coagulopathy in Crimean–Congo haemorrhagic fever seems to be a dynamic process, similar to sepsis. According to the findings of Fletcher and colleagues,[1] who did ROTEM in patients within the first 48 h of admission to hospital, patients with moderate to severe Crimean–Congo haemorrhagic fever had coagulopathy with prolonged initiation of coagulation and decreased clot amplitude mainly due to the platelet component. The clot firmness decreased after the first 48 h of illness, reaching the lowest values on days 4–6 and increasing after the first week of illness with all samples taken in the convalescence phase showing normal results.

For patients with Crimean–Congo haemorrhagic fever, a prognostic score including ROTEM and possibly platelet function tests could be developed, allowing not only better selection of high-risk patients but also targeted management of bleeding and a method to

monitor the success of therapy, since surviving patients show complete normalisation of ROTEM variables.

Unfortunately, ROTEM is not designed to deliver answers to the underlying mechanism leading to bleeding. In Crimean–Congo haemorrhagic fever, bleeding and coagulopathy seem to be related to platelet disorders, whereas in sepsis the consumption coagulopathy and disseminated intravascular coagulation are the main causes of bleeding. ROTEM also has some intrinsic blind spots: platelet function and the effect of von Willebrand factor are not adequately reflected by this method, but could have a role in viral haemorrhagic fever. The performance of viscoelastic tests for clot lysis assessment is also limited, with a low sensitivity for detection of hyperfibrinolysis and hypofibrinolysis.[5,6] For a better understanding of bleeding induced by Crimean–Congo haemorrhagic fever, research with additional tests such as platelet function tests and a more sensitive evaluation of clot stability is needed.

Nonetheless, the results of this global haemostatic assessment could be incorporated in an algorithm allowing timely detection of the most critically ill patients while also offering the possibility of targeted treatment of bleeding, which is a common cause of death and organ dysfunction in patients with viral haemorrhagic fever.

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Emergence of human monkeypox in west Africa

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See **Articles** page 872

Human monkeypox is a zoonotic disease that is endemic to central and western Africa. It is caused by an orthopoxvirus that was first identified in captive monkeys in 1958, and in a child from DR Congo in 1970. There are two variants of the virus: the Congo Basin clade and the west African clade. Unlike the variola virus, the monkeypox virus has a wide range of hosts and a reservoir in wild animals.[1]

Monkeypox mainly affects people living in the Congo Basin, where its incidence has increased since the 1980s.[1,2] An eight-times increase in incidence, partly due to active surveillance, was reported in DR Congo from 1981 to 1986.[1,3] Incidence of the disease then decreased substantially in the country until 1996–97, when more than 400 cases were identified during an outbreak. This outbreak was followed by other outbreaks with hundreds of cases in DR Congo in the 2000s,[1,4,5] when smaller outbreaks were also reported in Republic of the Congo and Sudan.[6,7] In west Africa, only sporadic cases were identified in Côte d'Ivoire, Liberia, Nigeria, and Sierra Leone between 1970 and 1981, which led to the hypothesis that the west African clade had little or no propensity for human-to-human transmission.[2]

In *The Lancet Infectious Diseases*, Adesola Yinka-Ogunleye and colleagues[8] provide a definitive picture of a large monkeypox outbreak (122 confirmed or probable cases) that occurred in Nigeria in 2017–18. The first case, an 11-year-old boy from the south–south region, was identified in September, 2017.[9] The peak of the outbreak was in October, 2017, but cases continued to occur until September, 2018. Confirmed cases of monkeypox virus infection were recorded in 17 states. Three states accounted for 66 (54%) of the 122 confirmed or probable cases. The viral strains that caused the outbreak were similar to those previously detected in the same area in 1971.[10]

The large size of the outbreak and the geographical spread of the cases could be explained by multiple