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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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

spillover events from animal reservoirs throughout the country and, potentially, human-to-human transmission. Whether enhanced surveillance after the first case reports contributed to the identification of otherwise undiscovered cases remains undefined. However, the detection, for the first time, of cases in travellers from Nigeria is an unprecedented event.[11]

Among all cases, 36 (30%) reported contacts with people with similar symptoms, but an epidemiological link with a confirmed case was not always established. Clustering of cases was reported in households and in a prison facility, with no link between clusters. Two cases were reported among health-care workers. Genomic analysis of viral isolates provided further evidence that multiple introductions of the virus were followed by secondary (ie, human-to-human) transmission, especially in overcrowded settings such as the prison. In DR Congo, secondary transmission accounted for up to 28% of cases in one study,[3] and secondary attack rates among unvaccinated household contacts were as high as 50%.[5]

Although in a previous study[12] children were most commonly infected by human monkeypox, in the 2017–18 Nigerian outbreak most cases occurred in young adults. This finding suggests a lack of cross-protection because of an increasing number of people not vaccinated against smallpox or waning immunity to smallpox. The case-fatality rate of 6% reported by Yinka-Ogunleye and colleagues is consistent with the range of 1–10% reported in previous outbreaks,[13] in which the lowest rates were probably a result of misdiagnosis with cocirculating varicella. Four of the seven deaths in Yinka-Ogunleye and colleagues' study occurred in people with HIV, suggesting that immunosuppression could be associated with severe human monkeypox disease.

The characteristics of the 2017–18 outbreak suggest that the strains of monkeypox virus in west Africa could sustain epidemic events. Although west Africa was previously considered to be at low risk of a human monkeypox outbreak, small-scale serosurveys have shown similar seroprevalence of anti-orthopoxvirus antibodies among young people living at forest margins in Ghana and in Republic of the Congo, and a shipment of animals from Ghana was the source of the human monkeypox outbreak that occurred in the USA in 2003.[2]

Vaccination was not discussed by Yinka-Ogunleye and colleagues. Although anti-smallpox vaccines might protect against monkeypox virus infection, severe adverse reactions in people with HIV limit the use of traditional vaccines containing replication-competent vaccinia virus, and few data on attenuated third-generation vaccines are available. However, vaccination has been offered to health-care workers during periods of sustained transmission of human monkeypox virus in DR Congo.[14]

Since October, 2018, sporadic cases of monkeypox have been reported in Nigeria. Although a study[6] done in the Congo Basin detected chains of transmission of up to seven generations, monkeypox outbreaks are usually self-limiting, and consistently have a basic reproductive number of less than 1.

In summary, the outbreak of human monkeypox in Nigeria was to some extent unexpected and suggests changes in monkeypox virus epidemic dynamics in west Africa. The determinants of human monkeypox emergence in Nigeria, including distribution of animal reservoirs and changes in human behaviour, need to be identified.

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Anal cancer risk: HPV-based cervical screening programmes

Similar to cervical cancer, most anal cancers (89–100%) are induced by persistent infections with high-risk human papillomavirus (HPV), especially HPV16.[1] Anal cancer accounts for only 4% of all malignancies of the lower alimentary tract, but its incidence is rising in high-income countries. For the USA, increasing average annual percentage changes of 2·1 for men and 2·9 for women have been reported.[2] About 8300 new anal cancer cases are diagnosed in the USA each year, with higher incidence rates in women than in men.[3] Similar numbers have been estimated for Europe.[4] More than one-third of patients with anal cancer die within 5 years after diagnosis.[3] Several risk groups for anal cancer have been identified, such as men who have sex with men, transplant recipients, people with HIV/AIDS, and women with a history of HPV-induced cervical, vaginal, or vulvar cancer.[3] The latter group has an increased incidence (three to 22 times) of anal cancer, compared with the general population.[3]

Anogenital HPV-induced cancers are largely preventable by prophylactic vaccination of HPV-naive individuals (primary prevention) or by screening for precancers (secondary prevention).[5,6] For cervical cancer, population-based cytology screening has been replaced by primary HPV screening or by co-testing (HPV and cytology) in several countries.[6] By contrast, anal cancer screening has been recommended only for high-risk groups, such as HIV-positive individuals, especially men who have sex with men.[7,8] However, the evidence of benefit has yet to be established in ongoing prospective studies.[7]

In a study in *The Lancet Infectious Diseases*, Chunqing Lin and colleagues[9] have shown that data available from routine HPV-based cervical screening programmes can be used to define anal cancer risk profiles in the participating women. Lin and colleagues did a retrospective collaborative pooled meta-analysis, including individual-level data from 36 studies with 13 427 women for whom paired anal and cervical samples were available. They found that cervical HPV16 is strongly associated with anal HPV16. 41% of HIV-negative women with cervical HPV16 also had anal HPV16, compared with 2% of those without cervical HPV16 (prevalence ratio [PR] 16·5); in HIV-positive women, these values were 46% and 11% (PR 4·4). Anal precancer (high-grade squamous intraepithelial lesion [HSIL]) was associated with cervical high-risk HPV and with cervical HSIL, regardless of HIV status. One quarter of older women (aged ≥45 years) with cervical HPV16 had anal HPV16-associated HSIL (25% of HIV-negative women, 23% of HIV-positive women).[9]

Notwithstanding the divergent progression rates of anal HSIL to invasive cancer reported in the literature[7], the findings of Lin and colleagues[9] have important public health implications. Anal cancer screening might be advisable in all women with cervical high-risk HPV infection (irrespective of their HIV status), particularly if the detected HPV-type is HPV16. Furthermore, a diagnosis of cervical HSIL or cancer seems to be a strong determinant for anal HSIL, also in HIV-negative women (PR 23·1). In HIV-positive women, anal HSIL was found in 25% of patients with cervical HSIL, but also in 7% of those with normal cervical cytology. Similarly, 8% of HIV-positive women without cervical high-risk HPV infection had anal HSIL. This finding could argue for anal cancer screening in more HIV-positive women than only in those with HPV-associated dysplasia.[8] Anal cancer screening algorithms for both HIV-negative and HIV-positive women could possibly be further refined by incorporating additional risk factors, such as smoking or sexual practices.[3]

Similar to anal cancer, incidence rates of HPV-associated oropharyngeal cancer are steadily increasing, especially in men, but also in women.[2] It would be interesting to analyse whether the cervical markers described by Lin and colleagues (HPV16 positivity, HSIL, and cancer)[9] are also associated with an increased risk for HPV-induced oropharyngeal cancer. Such studies could be done in countries that maintain comprehensive

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