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in countries with larger drug-resistant tuberculosis patient cohorts will require considerable and concerted efforts, including quicker diagnosis, increased treatment coverage, and better surveillance data.

Notably, there are limited data available to assess temporal trends in drug-resistant tuberculosis in high tuberculosis burden countries with concomitant high HIV prevalence. In South Africa, estimated tuberculosis incidence is declining by 0.5% annually, most likely driven by increased coverage of antiretroviral treatment for HIV.⁷ By contrast, drug-resistant tuberculosis as a proportion of tuberculosis increased between two national surveys in 2001 and 2012, primarily driven by an increase in rifampicin mono-resistant tuberculosis.⁸ Systematic reviews suggest an association between HIV and drug-resistant tuberculosis, with increased risks of drug-resistant tuberculosis in individuals who are tuberculosis treatment naive, suggesting a stronger association for transmitted resistance than acquired.⁹ However, HIV infection has also been associated with increased drug-resistance acquisition during tuberculosis treatment.⁹ Taken together, these data suggest that any association between HIV and drug-resistant tuberculosis depends on the epidemiological setting and highlight the necessity of improved tuberculosis drug-resistance surveillance in settings with a high HIV prevalence.⁹

Until 2018, recommended treatment for drug-resistant tuberculosis required lengthy courses of often toxic and ineffective drugs, with a treatment success of approximately 50%. However in the past 2–3 years, new and repurposed drugs have become available, allowing for shorter, all-oral, and more effective drug-resistant

tuberculosis treatment regimens.¹⁰ These regimens, combined with rapid diagnostics, offer the potential for improved treatment access even in the most resource-constrained settings. However, such scale-up will require substantial commitment, both on the part of governments of high-burden countries and global funders, if we are to avert a situation in which drug-resistant tuberculosis becomes the new normal.

We declare no competing interests.

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Confronting the persisting threat of the Middle East respiratory syndrome to global health security

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The Middle East respiratory syndrome coronavirus (MERS-CoV) is a priority zoonotic pathogen of humans highlighted in the WHO research and development blueprint list requiring urgent action¹ because it has epidemic potential, a high fatality rate with no specific treatment or vaccine, and a wide geographical distribution of the host reservoir of dromedary camels in the Middle East, Africa, and Asia.²

Globally, as of May 31, 2019, 2442 laboratory-confirmed MERS cases, with 842 deaths (case-fatality ratio of 34.5%), had been reported to WHO since September, 2012.³ 2031 of these cases occurred in Saudi Arabia and the largest outbreak outside the Middle East occurred in South Korea in May, 2015, with 186 cases reported between May 15 and July 6, 2015, showing its epidemic potential.⁴ An upsurge in the

number of MERS cases has been seen in Saudi Arabia and Oman, with 189 cases reported between July, 2017, and June, 2018, compared with 126 cases between January and March, 2019.³ Worryingly, although MERS-CoV continues to circulate in the Middle East, progress in advancing priority research and development on the epidemiology, rapid diagnostics, treatments, and vaccines, including regional One Health activities⁵ have been slow. Importantly, despite many WHO MERS expert group and other stakeholder meetings that have defined priority research needs, major knowledge gaps remain in the epidemiology, transmission, pathogenesis, and phylogenetic evolution of MERS-CoV.^{6,7}

Major opportunities for appropriate longitudinal and cross-sectional studies to fill these gaps from the recurrent community and nosocomial outbreaks of MERS in Saudi Arabia are being missed. By contrast, several studies done after the 2015 MERS outbreak in South Korea yielded important epidemiological, clinical, virological, and management outcome data.⁸ MERS-CoV sequence variants were detected during the South Korean outbreak, with some mutations incorporated into the circulating virus. Remarkably, the most extensively studied mutations, which occurred in the surface glycoprotein were not predicted.⁸ The surface glycoprotein is crucial for virus entry and during the severe acute respiratory syndrome epidemic it evolved to bind more tightly to its cellular receptor. By contrast, changes detected in MERS-CoV-surface glycoprotein appeared to decrease binding and were expected to decrease virulence and transmissibility;⁸ however, these changes could be beneficial to the MERS-CoV by facilitating evasion of the antibody response.

MERS-CoV transmission occurs in community or household settings or in health-care facilities.^{2,3} Nosocomial outbreaks were a major feature but have decreased due to increased awareness and implementation of infection control measures.¹⁰ Although zoonotic transmission from camels is thought to be the primary mode of transmission, a substantial proportion of patients describe no camel contact.^{2,6,10,11} MERS-CoV infection of camels throughout Africa is common, although no convincing serological or virological evidence exists of human MERS-CoV infection in Africa.^{11,12} The key questions are why did human MERS-CoV infection only begin in the Middle East in 2012 and not in Africa? And how do patients without contact with camels acquire the disease? Sequence analysis of

MERS-CoV isolated from patients in the Middle East revealed mutations in the virus, most of which were transient with reversion to wild type sequence,⁹ which is inconsistent with continuing adaptation to humans. Many of the virus variants were observed circulating in camels at the same time,¹³ suggesting continuing camel-to-human transmission, which might have obscured adaptive changes in the human virus. Small differences in sequences were observed when east African and Saudi Arabian MERS-CoV isolates were compared, with more substantial differences observed when compared with west African MERS-CoV, including deletions detected in west African MERS-CoV.¹² These differences might contribute to diminished transmission; however, another possibility is that differences might occur in human–camel contact in Africa versus the Middle East. Camel workers and owners have close contact with camels and thus have increased prevalence of MERS-CoV immunopositivity (3–67%) than the general population (0–15%).^{14,15} Camel workers have mild or subclinical disease, and they might transmit MERS-CoV either directly or indirectly to more susceptible individuals (eg, those with comorbidities) who would present as sporadic cases.

These studies point to several directions for priority research and interventions to decrease the persistent threat of MERS-CoV transmission. First, continuous sequence analysis of MERS-CoV in endemic countries is needed to establish viral evolution, as was the case in the South Korean outbreak. Second, increased understanding of camel–human interactions and patterns of camel grazing in Africa and the Middle East could provide insight into transmission differences. Third, an effective vaccine for humans is the best way to prevent spread of MERS but logistical issues because of the small number of sporadic MERS cases in different geographical locations need to be overcome. Alternatively, vaccination of juvenile camels might block transmission. Fourth, development of antiviral and other therapies for MERS-CoV would improve patient outcomes and, by decreasing virus burden, could decrease transmission. Finally, continued efforts to educate camel workers about infection control measures, such as handwashing and wearing protective gear when handling camels, especially juvenile ones with upper respiratory tract infections, will be crucial in minimising transmission.

The persistence of MERS-CoV transmission in the Middle East 7 years after it was first discovered, and

the many unanswered questions regarding MERS^{6,7} that have been raised recurrently at WHO MERS expert group annual meetings, now require a major change from the current status quo. If we are to prevent MERS-CoV evolving into the next global pandemic, serious financial and political commitments, especially from MERS-endemic countries, are needed to establish and take forward an effective multidisciplinary One Health consortia to establish more effective multidisciplinary research collaborations.

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Amoebic liver abscess: a neglected tropical disease

Neglected tropical diseases (NTD) are diverse and affect more than a billion people, causing considerable social disruption in some of the poorest economies of the world. Although coordinated global strategies have been developed and implemented for the prevention and control of NTDs,¹ the WHO list of NTDs omits an important disease: intestinal amoebiasis caused by *Entamoeba histolytica*, a silent killer in many low-income countries. *E histolytica* is the second leading cause of parasitic diseases globally² and causes substantial morbidity and mortality through invasive amoebic colitis and amoebic liver abscess.

Patients with intestinal amoebiasis remain predominantly as asymptomatic carriers and invasiveness

occurs only in a few individuals. Methodological difficulties result in variable estimates of the prevalence of intestinal amoebiasis, ranging from around 8–14%^{3,4} to as high as 40%.⁵ In an era of global travel, *E histolytica* is the third most frequently isolated intestinal pathogen among travellers returning from low-income countries to higher-income countries presenting with infectious gastrointestinal disease.⁶ The heavy burden of this intestinal pathogen becomes a greater threat to human life when invasiveness results in amoebic liver abscess. Amoebic liver abscess is the most common form of extra-intestinal amoebiasis and the fourth leading cause of mortality worldwide due to any parasitic infection, with an estimated 50 000 deaths annually caused