right and left heart catheterisations and more subtle imaging techniques[12] might be able to better differentiate pulmonary hypertension due to left heart disease from PAH.

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CG declares that he has no conflicts of interest. IML has served as a consultant and as a member of scientific advisory boards for Actelion, Bayer-Schering, and Novartis. She has also been an investigator in trials involving these companies and has received research grants from these companies.

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Emerging respiratory viral infections: MERS-CoV and influenza

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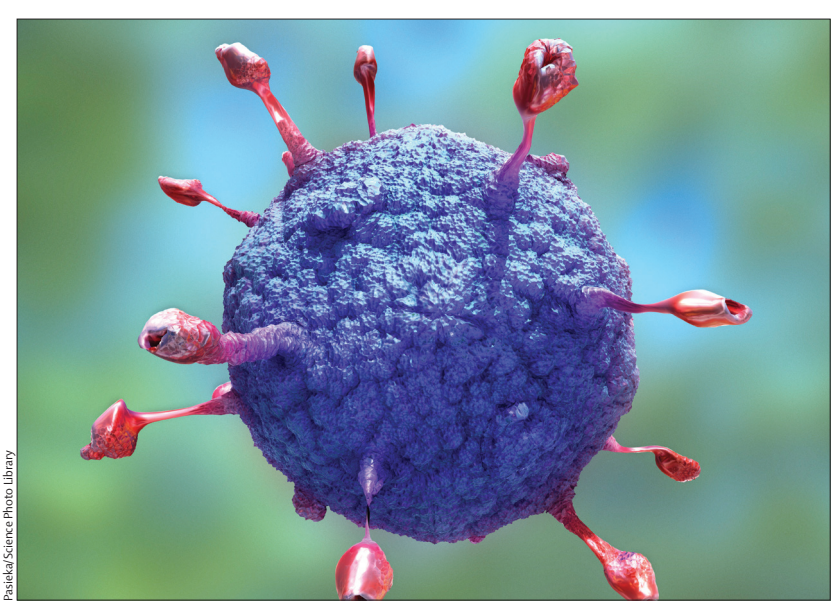
Each year, the world faces the rising burden of viral respiratory infections. These infections are of major importance to public health because of the lack of specific therapeutic and preventive measures, and, more specifically, the lack of vaccines for most of these viruses.[1]

In 2013, the emergence of three new respiratory viruses—varian influenza virus (H3N2v), H7N9, and Middle East Respiratory Syndrome coronavirus (MERS-CoV)—was of particular concern. These viruses all have the potential to cause widespread pandemics with substantial morbidity and mortality. The two influenza viruses (variant influenza virus and H7N9) were reported to cause, potentially severe, disease in human beings.

Infection with MERS-CoV was initially described in a patient from Saudi Arabia and then retrospectively identified in patients from Zarqa, Jordan.[2,3] As of Dec 2, 2013, 163 cases of infection with MERS-CoV have been reported, with 71 fatalities.[4] MERS-CoV can cause sporadic infection, infection among families, and, of particular concern, infection among health-care workers.[5] The largest outbreak of MERS-CoV was described in Al-Hasa, the eastern province of Saudi Arabia.[5] Fever and cough was present in most cases, with shortness of breath in almost half of all cases, and gastrointestinal symptoms in about a third. A study of the largest reported outbreak of MERS-CoV[6] estimated the median incubation period to be 5·2 days (95% CI 1·9–14·7), and reported a high rate of person-to-person transmission in 21 of 23 cases in health-care settings.[6] Case-fatality rate was high (65%) in this outbreak.[7] Of more than 417 household and health-care contacts, symptoms of MERS-CoV developed in only seven people.[6] A subsequent large-scale phylogenetic analysis of 21 genome sequences and inclusion of the previous nine published MERS-CoV genomes showed that multiple introductions of MERS-CoV and lower R_0 values were possible.[7] Thus MERS-CoV has not yet reached pandemic potential. Transmission within Saudi Arabia was consistent with movement of an animal reservoir, animal products, or infected people. The source of the infection has yet to be identified, although bats and camels have been implicated.

A clinical and epidemiological analysis of 47 cases showed that infection with MERS-CoV occurred

predominantly in men,[5] although this finding did not hold after an interim analysis of 133 cases.[8] Most patients who were initially infected with MERS-CoV had underlying comorbid medical conditions and laboratory testing showed that most of these cases had raised concentrations of lactate dehydrogenase and aspartate aminotransferase associated with thrombocytopenia and lymphopenia.[5] In preparation for the Hajj this year, the largest recurring religious mass gathering worldwide, the Saudi Ministry of Health recommended that certain individuals postpone their participation. Groups particularly at risk from infection include pregnant women, children younger than 12 years, adults older than 65 years, and those with chronic or acute diseases. The concern over the pandemic potential of MERS-CoV was estimated in two recent publications.[9] In one optimistic view,[9] the estimated MERS-CoV R_0 was 0·69 compared with the R_0 for prepandemic severe acute respiratory syndrome-coronavirus of 0·80. This optimistic estimate downplayed the possibility of a MERS-CoV pandemic, which supported the recommendations of the Third Meeting of the International Health Regulations Emergency Committee,[10] that MERS-CoV does not warrant international measures to curtail Hajj-related travel. Sporadic cases MERS-CoV continue to be reported, and thus continued vigilance and further studies are needed to close the knowledge gap in MERS-CoV epidemiology and clinical presentations.[5]



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A novel avian-origin influenza A virus, H7N9, was initially described in human beings in China on March 30, 2013. At that time, three patients developed fatal pneumonia and were subsequently diagnosed as infected with H7N9.[11,12] Since this initial description, H7N9 has resulted in 139 infections and 45 fatalities.[13] Review of the initial 111 patients with H7N9 infection[14] showed a high rate of admission to intensive-care units (76·6%) with a mortality rate of 27%. Infected patients were older adults with a median age of 61 years, with twice as many men infected than women. It is also interesting to note that most patients infected with H7N9 had a pre-existing medical condition. Subsequent analysis of 136 laboratory confirmed cases showed a mortality bias toward men older than 50 years.[15] Of the total cases, 7% were reported in individuals younger than 20 years, with no fatal cases in this age group.[15]

The emergence of these viral respiratory infections (H7N9 and MERS-CoV) showed a similar initial pattern: the predominant involvement of older men and the presence of comorbid conditions in most cases. This pattern seems to be due to recognition bias, because younger cases are now being identified who have no underlying medical conditions. In facing future challenges of emerging respiratory viruses such as influenza there is a clear need for the development of effective influenza vaccines that target the conserved antigenic structures of influenza virus. Continued contact of humans with animals creates an added risk of development of zoonotic diseases, adaptation of the new virus rendering it infectious to humans, and possible efficient transmission of these viruses among the human population.

The emergence of respiratory viruses that cause significant disease in human beings is a major risk to the global economy and the health of the human population. The potential effect of newly discovered viruses calls for a better understanding of the human–animal interface, the development of rapid diagnostic tests, and effective antiviral and immunomodulatory therapies.[13] The eradication of respiratory viruses is not possible and thus the development of effective vaccines directed against the conserved antigens of these viruses would be extremely welcome. Finding predictors of severe disease and the initiation of antiviral drugs early in the course of many respiratory viral infections might prove to be beneficial.

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Tuberculosis: progress and challenges in product development and delivery

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Although global tuberculosis control is improving, progress remains slow; about 1·3 million people died of tuberculosis in 2012, more deaths than from any other single infectious agent (other than HIV).[1] WHO emphasised two major challenges in 2013: identifying and treating the "missing 3 million" people who develop active tuberculosis every year and whose condition never becomes known to national tuberculosis control programmes; and the crisis of multidrug-resistant (MDR) tuberculosis, in which three of four people with MDR tuberculosis are never diagnosed, and less than half of those diagnosed are successfully treated.[1]

New diagnostics, drugs, and vaccines are crucial for transformational progress. 2013 heralded both progress and disappointment in these areas. In diagnostics, progress was made in the global scale-up of Xpert MTB/RIF (Cepheid Inc, Sunnyvale, CA, USA), a molecular test for tuberculosis that also enables rapid detection of resistance to rifampicin. More than 4 million MTB/RIF cartridges had been procured under concessional pricing as of September, 2013, and a US$25·9 million UNITAID project was announced in March, 2013, for rollout in 21 countries.[2] Based on new evidence, WHO recommended in October, 2013, that Xpert MTB/RIF be used as the initial diagnostic test in adults and children with presumed MDR tuberculosis or HIV-associated tuberculosis (and, conditionally, for all forms of tuberculosis), as well as for diagnosis of certain types of extrapulmonary tuberculosis.[3]

The first randomised trial of Xpert MTB/RIF was published in October, 2013.[4] This pragmatic, multicentre trial of nurse-led Xpert MTB/RIF versus sputum-smear microscopy in people with symptoms of tuberculosis presenting to primary care clinics in four African countries showed Xpert MTB/RIF to be more accurate than smears and more effective in leading to same-day treatment initiation. However, the primary outcome of tuberculosis-related morbidity was equivalent between the two arms, as was treatment initiation by 56 days.[4] The authors postulated that this lack of difference in morbidity was the result of high empirical treatment rates among smear-negative individuals with ongoing symptoms. Results from additional trials in Brazil and

Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.