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continuity of sleep in both groups. Finally, daytime sleepiness is usually present less often (and if present, is less severe) in elderly patients with OSA syndrome, and elderly patients can cope better with sleepiness symptoms because they are often not in full-time work. Older apnoeic patients screened and recruited in this study were far from representative of the whole panel of older apnoeic patients seen in routine clinical practice. Many elderly apnoeic patients have no daytime sleepiness and consult for other symptoms—eg, nocturia, severe snoring, waking with feelings of choking, or minor memory complaints—or OSA is discovered by chance after onset of stroke or heart attack. It is difficult to determine the benefit of CPAP in the non-sleepy elderly apnoeic patients complaining about non-specific symptoms associated with unrefreshing sleep. In the study, the number of women is low, and thus the underrepresentation of women reduces the generalisation of the results obtained in men. We know that daytime sleepiness, according to an equivalent severity of apnoea or hypopnea, is often less severe in women than in men.<sup>1</sup> This difference in clinical presentation is important to consider in the detection and treatment of all apnoeic patients.

The quality of the work in this study is remarkable and encourages continued high-quality controlled clinical trials in the specialty of sleep-related breathing disorders in elderly people; a disorder that can affect a third of patients aged 68 years or older and that might significantly accelerate cognitive decline in undiagnosed and untreated patients.

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## Dromedary MERS-CoV replicates in human respiratory tissues

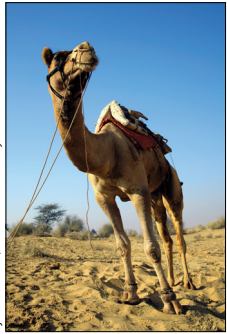
Since its discovery in the autumn of 2012, Middle East respiratory syndrome coronavirus (MERS-CoV) has caused more than 800 laboratory-confirmed cases of human infection, with a case-fatality rate of about a third.<sup>1</sup> Patients admitted to hospital with MERS are characterised by symptoms of severe pneumonia, often accompanied by renal failure. However, mild and asymptomatic infections have been reported, especially in secondary cases. Dromedary camels have been identified as the putative source of human MERS-CoV infections, although nosocomial transmission is increasingly reported. So far, all cases of human

MERS-CoV infection were identified in Middle Eastern countries, or in individuals who had recently travelled from that area.

At present, endeavours to control this emerging pathogen target two main efforts. First, identification of the source of zoonotic MERS-CoV infections might guide control strategies at the human–animal interface. Second, source and contact tracing in combination with hygiene and isolation measures will restrict human-to-human transmission of MERS-CoV. Although MERS-CoV is phylogenetically related to bat  $\beta$ -coronaviruses, epidemiological investigations

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have provided evidence that contact with livestock, especially dromedary camels, represents a risk factor for infection; serological and virological data have shown the circulation of MERS-CoV in dromedary camels in the Middle East and beyond.<sup>2-4</sup>

In *The Lancet Respiratory Medicine*, Renee Chan and colleagues<sup>5</sup> provide additional support for the putative role of dromedary camels as the direct source of MERS-CoV infections in human beings, by showing that Saudi and Egyptian isolates of MERS-CoV from dromedary camels replicate in tissues of the human respiratory tract. MERS-CoV isolates from Saudi Arabia were phylogenetically closely related to human isolates, whereas those from Egypt were genetically divergent from previously characterised MERS-CoV isolates. Nonetheless, MERS-CoV isolates of either origin replicated in primate cell cultures and in human bronchus and lung explants at similar levels as did a human MERS-CoV isolate. The tropism of both dromedary camel and human MERS-CoV isolates included bronchial non-ciliated epithelial cells, alveolar type II pneumocytes, and lung endothelial cells, in accordance with the distribution of the MERS-CoV cellular receptor, dipeptidyl-peptidase-4.<sup>6</sup> The MERS-CoV viruses studied were all weak inducers of innate immune responses in a human cell line, further suggesting phenotypic similarities between camel and human MERS-CoV viruses.

Severe acute respiratory syndrome coronavirus (SARS-CoV), which emerged in China about a decade ago, was also related to bat  $\beta$ -coronaviruses. Angiotensin-converting enzyme 2 (ACE2) was identified as its functional receptor.<sup>7</sup> Wild carnivores sold at live-animal markets for human consumption were implicated as intermediary hosts for SARS-CoV between bats and human beings. These animals included masked palm civets (*Paguma larvata*), raccoon dogs (*Nyctereutes procyonoides*), and Chinese ferret badgers (*Melogale moschata*).<sup>8</sup> The spike proteins of SARS-CoVs isolated from these animals and from early zoonotic cases mediated more efficiently infection of cells expressing palm-civet ACE2 than infection of cells expressing human ACE2.<sup>9</sup> Subsequent evolution of the receptor-binding domain of SARS-CoV spike protein enhanced SARS-CoV infection efficiency of human cells, probably contributing to its increased human-to-human transmissibility, resulting in the emergence of a pandemic threat.

The tropism of both dromedary camel and human MERS-CoV for the human lower respiratory tract could well account for the alveolar damage and pneumonia in severe human cases. However, naturally infected camels apparently show little disease.<sup>3</sup> Studies of the pathogenesis of MERS-CoV infection in camels are awaited to identify possible differences in within-host virus distribution patterns between the animal and human hosts, as was reported for SARS-CoV.<sup>9</sup> Ex-vivo cultures of, for example, lung slices are useful and could be further standardised for quantitative assessment of virus tropism. Because MERS-CoV seems to be endemic in dromedary camels, such differences could provide clues about their ability to be transmitted within and between species. One remarkable difference between SARS-CoV and MERS-CoV is in their tropism within the human respiratory tract, targeting ciliated and non-ciliated epithelial cells, respectively. Interestingly, a similar difference in tropism between human and zoonotic influenza A viruses correlates with their transmissibility among human beings.<sup>10</sup>

After the outbreak of SARS, global collaboration under WHO guidance (initiated in March, 2003) resulted in the identification of SARS-CoV as the causative agent within a month. This knowledge allowed the implementation of effective intervention strategies that terminated chains of human-to-human transmission and the associated pandemic threat within 3 months. The functional receptor of the SARS-CoV was identified soon thereafter,<sup>7</sup> leading to improved understanding of the pathogenesis of SARS-CoV infection and its evolution towards efficient human-to-human transmissibility. A decade later, MERS-CoV was identified as the aetiological agent of MERS within 2 weeks of the discovery of the new illness. Its receptor was also reported soon thereafter.<sup>6</sup> Reported human-to-human transmission of MERS-CoV in household and health-care settings is worryingly reminiscent of the situation at the start of the SARS epidemic. Building on lessons learned from the successful combat against the emerging SARS pandemic, studies such as that reported by Chan and colleagues—addressing questions about MERS-CoV pathogenesis and epidemiology at the human-animal interface—could well contribute to an equally successful interruption of the emerging MERS

epidemic, one step ahead of its development into a pandemic threat.

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ADMEO reports a patent, owned by Erasmus Medical Centre regarding MERS-CoV pending as a co-inventor. LAR declares no competing interests.

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## Breaking new ground to promote change

In this issue of *The Lancet Respiratory Medicine*, we publish a Commission entitled “Respiratory risks of household air pollution in low and middle income countries”. With around 3 billion people exposed to the threat of such pollution every day and its consequent effects on respiratory symptoms and disease, this was an obvious topic to cover as our first Commission. We were delighted to work with the authors of this project, and would like to especially acknowledge the efforts of the two senior authors, Prof Stephen B Gordon and Prof William J Martin II, who have ensured that the paper came to fruition. The problem of household air pollution is most prevalent in low-income and middle-income countries, hence the focus of the report, but high-income

countries do not escape unscathed, as emphasised by a linked comment from Dr Neil Schluger. *Lancet* group Commissions have at their core the philosophy of promoting change, and we hope that the Commission, and its associated content, will provide the impetus to drive change and tackle what is a preventable, but devastating, burden on the health of the world’s population, not least in terms of the morbidity and mortality associated with acute and chronic respiratory diseases.

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## Household air quality in high-income countries: forgotten but not gone



A great deal of the burden of lung disease in the world has been linked to factors in the environment.<sup>1</sup> The Commission<sup>2</sup> in *The Lancet Respiratory Medicine* highlights that household air pollution, which is produced by the use of biomass (or solid) fuels, is one of the biggest threats to lung health. Most of the burden of household air pollution is noted in low-

income and middle-income countries, where solid fuels are routinely used by most of the population for cooking and heating. However, high-income countries also have substantial problems related to indoor air quality, although the nature of the threat is somewhat different. Some of this burden is related to pockets of solid fuel consumption in poor regions of otherwise

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