

## Editorial

# Travellers give wings to novel coronavirus (2019-nCoV)

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This virus can fly. For the third time in less than two decades the world is confronting a deadly and disruptive epidemic caused by a coronavirus.<sup>1,2</sup> The first was the severe acute respiratory syndrome (SARS) in 2002–2003. The second started unfolding in 2012 caused by the Middle East respiratory syndrome coronavirus (MERS-CoV). SARS was contained through consistent, compulsive application of traditional public health measures (surveillance, detection, isolation of infected persons and quarantine of exposed). MERS still smolders (about 2500 cases confirmed globally) but has remained largely confined to the Middle East except for one well-documented outbreak (186 cases) traced to a traveller returning to South Korea from the Middle East.<sup>3</sup> Both SARS and MERS have been associated with nosocomial transmission and super-spreader events, in which a single person infected many others.<sup>4</sup> In December 2019, a cluster of pneumonia cases was reported to be linked to a seafood market in Wuhan, China. Now the world is confronting the emergence of 2019-nCoV, and on 30 January 2020, the World Health Organization declared it to be a Public Health Emergency of International Concern.

Coronaviruses, enveloped RNA viruses with surface spikes, infect a wide range of animals and humans. They can cause mild, self-limited upper respiratory infections in humans (the common cold). A few coronaviruses, normally carried by apparently healthy animals, can be lethal if they infect humans. For many viruses that primarily infect animals but can spill over into the human population, humans are dead-end hosts. Examples include the rabies virus and most hantaviruses. With these, transmission to other humans does not occur, or does so rarely.

Then there are the exceptions. Some animal viruses that have crossed the species barrier to infect humans, such as the human immunodeficiency virus (HIV), the Ebola virus, and certain coronaviruses, have the capacity to spread from human-to-human and to cause lethal disease. Most are RNA viruses, prone to mutation and with the capacity to adapt to a new host. The route of spread depends on the virus, but these viruses have caused major, disruptive epidemics or pandemics. When they first infect humans, typically no treatment or vaccine exists, so early generations of spread can be dramatic, devastating, and lethal, as observed with HIV and Ebola virus.

Lethality and transmissibility are not necessarily linked, and lethality depends on the host species. The H5N1 influenza virus causes high mortality in domestic poultry and severe disease and death in humans, yet is poorly transmitted from human to human. Most influenza viruses that cause seasonal influenza are highly transmissible but overall have low mortality. Nevertheless, they still cause substantial burden through global spread.

The frequency of spillover events from animals to humans has increased in recent decades. Reasons include the large interface between humans and wild animals and food animals. Clearing lands for agriculture and development, building dams and other land use changes have disrupted animal habitats, displaced animal populations and led to human–animal contact.<sup>5</sup> Humans have also created the perfect scenario for spillover events—large live animal markets selling multiple species of wild and domestic animals in proximity to large populations of densely housed humans who are extensively connected by air, land and water to the rest of the world. Even though spillover events of viruses that have the capacity to kill humans may be rare, the world today has expanded the opportunities for such events.

Research since the SARS epidemic of 2002–2003 has revealed that bats carry multiple coronaviruses that have the potential to infect humans.<sup>6</sup> The angiotensin converting enzyme 2 (ACE2), found in the lower respiratory tract of humans, has been identified as a receptor used for cell entry for the SARS CoV.<sup>7</sup> Recent research suggests that the 2019-nCoV also uses the ACE2 receptor.<sup>1</sup>

Wuhan combines multiple elements favourable for emergence and spread of a zoonotic virus. As the largest city (11 million) in central China, it is a major transport hub and centre for industry and commerce. It is where the Yangtze and Han rivers intersect and is home to the largest train station, biggest airport and largest deep-water port in central China. About 30 000 passengers fly from Wuhan daily to destinations throughout the world. In 2018, >24.5 million passengers passed through the airport. China's high-speed train network stretched to about 35 000 km by the end of 2019. Bullet trains handled 2.31 billion passenger trips in 2019.

An analysis of 2018 passenger volumes originating from Wuhan International Airport between January and March found

that Bangkok, Hong Kong, Tokyo and Taipei received the largest volumes.<sup>8</sup> As of 28 January 2020, Thailand, Hong Kong and Japan had confirmed the largest number of 2019-nCoV cases outside of China. These countries all have high Infectious Disease Vulnerability Index (IDVI) scores that suggest greater capacity to respond to outbreaks.<sup>9</sup> The IDVI is a validated tool that estimates a country's capacity to manage infectious disease threats and includes metrics defining health care, public health, demographics, economics, political and other factors.

Many lessons were learned from the SARS outbreak almost 20 years ago. The virus causing the cluster of pneumonia cases in December 2019 in Wuhan was identified and sequenced promptly, and genetic sequences were shared with the global community in early January 2020.<sup>2</sup> What was not apparent—or not shared initially—was that the virus was spreading from human to human. After initial reassurances that no human-to-human spread was occurring, infections exploded in many locations and the virus has now infected thousands in China and has spread to more than 24 countries—a number that continues to increase. Local transmission is also occurring outside of China.

The size and reach of today's global travel network means that locally emerging pathogens have the capacity to disperse rapidly. The greatest danger is posed by pathogens that can spread by the respiratory route, especially if airborne spread occurs. Other factors that make control of a pathogen more difficult include transmissibility during asymptomatic, mild or pre-symptomatic periods. A long infectious period also makes control more challenging. The virus that has emerged in Wuhan combines characteristics that do not bode well for the human population. Based on the first 425 confirmed cases in Wuhan, the mean incubation period was 5.2 days (potential range 2–14 days), the number of cases doubled every 7.4 days, and each case was estimated to infect 2.2 others.<sup>10</sup> This basic reproductive number is similar to an estimate of 2.6 (uncertainty range: 1.5–3.5) reached by researchers with simulated epidemic trajectories using a mathematical model.<sup>11</sup> Modelling results suggest that control measures would need to block >60% of transmission to control the outbreak.<sup>11</sup> Based on observations with SARS and other infections, the basic reproductive number may decrease as people become aware of the threat of infection and change behaviour, but the basic reproductive number must drop <1 to stop the epidemic. The analysis based on the model suggests there will be ongoing sustained transmission in the absence of effective interventions.

A simulation study to assess the effectiveness of airport exit screening concluded that >60% of infected travellers would not be detected using plausible assumptions based on the current situation.<sup>12</sup> The simulation was based on early and incomplete information but uses the best estimates available to date. Entry screening could detect a larger number of infections because of the potential for developing symptoms during the flight, especially during long flights. The investigators conclude that exit or entry airport screening for symptoms and use of thermal scanners is unlikely to detect a sufficient proportion of those infected to prevent entry of infection into new areas.

SARS-CoV generally caused fever before being transmissible, so fever was used as a marker to track and contain it. Preliminary information with 2019-nCoV suggests the clinical spectrum of

**Box 1.** Reliable public websites for updates on 2019 Wuhan novel coronavirus outbreaks

Source	Web link
World Health Organization	<a href="https://www.who.int/">https://www.who.int/</a>
Centers for Disease Control and Prevention	<a href="https://www.cdc.gov/coronavirus/2019-ncov/index.html">https://www.cdc.gov/coronavirus/2019-ncov/index.html</a>
CDC Travelers' Health Branch, Travel Health Notices	<a href="https://wwwnc.cdc.gov/travel">https://wwwnc.cdc.gov/travel</a>
International Society of Infectious Diseases Program for Monitoring Emerging Diseases (ProMED)	<a href="https://promedmail.org/">https://promedmail.org/</a>

infection is milder and that asymptomatically infected individuals may be able to transmit infection. Whether and how often this occurs remains to be confirmed. Given the absence of vaccines or treatment at present, detection and isolation of cases will be the primary tool to control spread. Although work has already begun on therapeutics and vaccines, good medical care will be the mainstay of management in the near term. Early observations suggest that older individuals and those with chronic diseases will likely bear the greatest burden of disease.

Research is urgently needed to define the clinical spectrum, effective screening approaches, incubation and infectivity periods, routes of human-to-human transmission, best infection control and management practices and potential specific treatment modalities. Bats are the likely reservoir host,<sup>13</sup> but it is essential to identify any amplifying or transmitting animal hosts and alternative routes of transmission to humans.

Travellers have already played a central role in the dispersal of this virus. Accurate diagnostic tests are not yet available to all who need them. It is desirable to focus resources on the most vulnerable places and populations. For example, among the top 20 countries receiving air travellers from Wuhan, Bali, Indonesia ranks lowest on the IDVI.<sup>8</sup> Can the IDVI be used to identify places needing more support?<sup>9</sup> Analysis of commercial air traffic can help to identify cities and regions most likely to receive infected travellers.<sup>8</sup> Many issues relevant to travellers will require constant updating with the best, current information on transmissibility, spread and vulnerability (see Box 1).

The wet market in Wuhan has been closed for the time being, but large numbers of similar markets exist elsewhere. Major threats to human health have come from animal viruses that have infected humans. Although one can never eliminate all contact with animal viruses, it is time to develop guidelines to markedly reduce the extensive contact with wild animal tissues, excreta and fluids that occurs with the handling, butchering and selling multiple species of animals for food. A One Health perspective is needed to integrate data from human and animal health and develop policies that protect and preserve the health of multiple populations.

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