

EDITORIALS

Novel coronavirus: how much of a threat?

We know the questions to ask; we don't yet have many answers

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A third case of novel coronavirus (NCoV) infection was reported by the Health Protection Agency (HPA) on 15 February 2013, part of a family cluster of three cases in the West Midlands, England.¹ This means that 13 cases have been laboratory confirmed worldwide since September 2012. Four cases have been diagnosed in the United Kingdom, and seven patients, including one in the UK, have died.² The index patient in the recent UK cluster had travelled to Saudi Arabia and Pakistan in the 10 days before the onset of disease, whereas the second and third cases were family members who had not been abroad and probably acquired their infection after contact with the index case. The earlier UK case was a previously well adult transferred to intensive care in London from Qatar with severe respiratory illness in September 2012.³ What have we discovered about this new pathogen from the few cases so far reported? Is this likely to represent a global public health threat akin to that from severe acute respiratory syndrome (SARS) coronavirus?

Human coronaviruses, first identified in the 1960s, are part of a diverse group of viruses found in humans and animals. In humans these RNA viruses typically cause respiratory illnesses ranging from the common cold, caused by a group of seasonal coronaviruses (229E and OC43), to the severe respiratory disease caused by the recently recognised SARS coronavirus responsible for the global outbreak in 2002-03.

What can we say about the source of NCoV? Other than the patients who acquired the infection through contact with a confirmed case in the UK, all others became unwell in the Middle East, suggesting this region as the source, although the full geographical extent is unknown. Although NCoV is genetically similar to other coronaviruses present in bats,⁴ the reservoir remains unknown, as does its route of transmission to humans and risk factors for human infection. One possibility is that the virus circulates in one or more animal groups and is transmitted intermittently to humans as a sporadic zoonotic infection. This could be by direct contact with the natural animal reservoir, by indirect transmission through an intermediate host, or through food or environmental contamination.

How is the virus transmitted and what is the spectrum of illness in humans? Might transmission be sustained in the human population with widespread asymptomatic infection or only

mild symptoms, enabling the illness to go mostly undetected? And might the infection have been circulating undetected for some time? The limited information we have indicates that person-to-person transmission is unusual. The 13 recent cases were confirmed after the development of a diagnostic test in September 2012.⁵ Five were sporadic, with no associated human cases. The remainder occurred in three clusters with limited chains of transmission: two cases in one cluster in an intensive care unit in Jordan,⁶ and the others in two family clusters of three cases each in Saudi Arabia and the UK. Extensive follow-up of close contacts of the first patient diagnosed in the UK (HPA, unpublished data),³ and of a patient transferred from Qatar to Germany,⁷ detected no secondary cases using virological and serological endpoints.

What is the spectrum of illness? Evidence to date suggests that infection usually results in a severe illness. All but one of the 13 cases have been severe enough to require hospital admission and 11 have needed intensive care. Follow-up of close contacts of the index case in the recent UK cluster has identified a single case of a mild respiratory illness with detection of NCoV in sputum.⁸ However, intensive clinical, virological, and serological follow-up of close contacts of two previous cases failed to find evidence of mild or asymptomatic infection.^{3,7}

The World Health Organization has provided guidance on surveillance to detect possible cases of this novel virus.⁹ Recognising such cases in the UK requires clinical and public health vigilance, combined with rapid microbiological investigation to rule out other causes and to confirm NCoV infection.¹⁰ Patients need supportive clinical care. No recognised effective treatment is yet available, although possible interventions that need to be investigated in clinical trials include convalescent plasma from recovered cases, antiviral therapies used for other viral infections, or immune modulatory agents. Strict infection control needs to be rapidly instituted for confirmed cases to prevent onward spread, and close contacts need to be identified and followed up.¹¹ If respiratory illness occurs in the 10 days after last exposure in a close contact the contact should be isolated and investigated urgently for NCoV infection.

Further work needs to be undertaken rapidly to fill the gaps in our knowledge of the clinical, virological, and epidemiological aspects of this infection, as world experience remains limited. In view of the apparent high case fatality ratio and lack of known treatments, confirmed cases need to be studied in detail to gain a better understanding of the natural course of infection in human hosts, the potential therapeutic options, and the nature of genetic variation between different strains to help piece together the origin of this viral infection. Although resource intensive, close follow-up of cases and contacts is needed to help understand the spectrum of illness and risk of infection in those exposed. Work is also needed to identify potential reservoirs of infection, risk factors for infection, and the prevalence of NCoV infection among people with acute respiratory illness in the Middle East and elsewhere. The question of whether this is a new virus in humans, or a newly recognised virus infection that has been undetected for some time, should also be investigated.

It is not yet clear whether a low level of sporadic infections with occasional limited person-to-person spread will continue to occur, or whether case numbers will build as a prelude to sustained transmission in the human population. The global experience of SARS is a salutary reminder of the devastation that can result from a newly emerging infection capable of human-to-human transmission. Improvements in diagnostic technologies and application of infection control lessons learnt from SARS have contributed to the response to NCoV infection. Until answers to some of these questions are available it is essential to maintain the current high level of vigilance for cases,

to intensively investigate all cases and their contacts, and to share the information rapidly.

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