Covid-19: a puzzle with many missing pieces
Better information on epidemiology, pathogenesis, and treatments are urgent priorities

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By 15 February 2020, 51 800 cases of the novel coronavirus disease (formerly known as 2019-nCoV and renamed covid-19), including more than 1600 deaths, had been confirmed in China, mainly in Hubei province. A further 526 laboratory confirmed cases have been reported across 25 other countries.1 As is usual in the early phase of a disease outbreak, the alarm was raised as a result of the most severe cases, and the first reports describe severe pneumonia in patients admitted to hospital.2 In a linked paper, Xu and colleagues (doi:10.1136/bmj.m606) report a case series of 62 patients (median age 41 years) admitted to hospital in the Zhejiang province with laboratory confirmed infection with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), the virus responsible for covid-19.3 All the patients presented with respiratory symptoms, fever or flu-like illness, or both, and all had travelled to Wuhan or been in contact with a patient with confirmed covid-19 while staying in Wuhan. All but one had radiologically confirmed pneumonia, but only one patient was subsequently admitted to an intensive care unit and none has died, similar to other reports describing less severe disease.4,5

Among cases reported to the World Health Organization, 15% are severe, 3% are critical, and 82% are mild (press conference WHO, 7 February 2020. https://twitter.com/WHO/status/1225797786903277568). The estimated overall case fatality rate is around 2% but outside of Hubei province the figure is around 0.05 or less, not so far from the mortality observed with seasonal influenza. We should not be lulled into inaction by this low fatality rate, however: no cross protection by a common analogue, is active against covid-19 in vitro9,10 and has been shown to be safe in Ebola trials.10,11 HIV antiproteases, with or without

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inhaled interferon, are currently being tested against the Middle East respiratory syndrome coronavirus (MERS-CoV). Evaluations during the 2002-03 SARS outbreak were, however, inconclusive.

Surprisingly, anti-influenza drugs umifenovir and oseltamivir are also under investigation, despite the lack of biological rationale. Monoclonal antibodies as passive prophylactic or therapeutic immunotherapy are an attractive option, although antibodies used to treat respiratory syncytial virus or influenza have not been successful so far. Steroids and methylprednisolone seem to be used frequently, but they prolong viral shedding in patients with MERS-CoV and WHO advises against their use in COVID-19, except for patients with an associated acute respiratory distress syndrome. Other interventions under evaluation include hydroxychloroquine, vitamin C, and elements of Chinese medicine. With any antiviral treatments, timely administration before complications develop will be crucial.

Randomised controlled trials of the most promising treatments are a leading priority, and, hopefully, the road to an effective treatment and vaccine will not be too long. But despite the urgency generated by the emergence of a new disease, health providers and researchers must maintain a rigorous evidence based approach underpinned by sound ethical rules. “First, do no harm” must still be the guiding principle.

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