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EDITORIALS

Clinical features of covid-19

The wide array of symptoms has implications for the testing strategy

Pauline Vetter *medical doctor*[1 2 3], Diem Lan Vu *medical doctor*[2 3 4], Arnaud G L'Huillier *medical doctor*[3 5], Manuel Schibler *medical doctor*[2 3 4], Laurent Kaiser *professor*[1 2 3 4], Frederique Jacquerioz *medical doctor*[3 6 7]

[1]Geneva Centre for Emerging Viral Diseases, Geneva University Hospitals, 1211 Geneva 14, Switzerland; [2]Division of Infectious Diseases, Geneva University Hospitals, 1211 Geneva 14, Switzerland; [3]Laboratory of Virology, Geneva University Hospitals, 1211 Geneva 14, Geneva, Switzerland.; [4]University of Geneva, Faculty of Medicine, 1205 Geneva, Switzerland; [5]Pediatric Infectious Diseases Unit, Department of Child and Adolescent Medicine, Geneva University Hospitals and Medical School, Geneva, Switzerland; [6]Division of Tropical and Humanitarian Medicine, Geneva University Hospitals, 1211 Geneva 14, Geneva, Switzerland; [7]Primary Care Division, Geneva University Hospitals, 1211 Geneva 14, Geneva, Switzerland.

In January 2020, coronavirus SARS-CoV-2 was identified as the cause of an outbreak of severe pneumonia, now known to be a complication of the coronavirus disease 2019 (covid-19).[1] Since then, the spread of covid-19 has increased exponentially, with the World Health Organization declaring a pandemic on 11 March.[2] By 15 April, more than 1 900 000 cases and 123 000 deaths had been reported worldwide.[3]

Severe acute respiratory illness with fever and respiratory symptoms, such as cough and shortness of breath, comprise the working case definition used to select people for viral testing. This strategy captures typical symptomatic presentation, but imperfectly identifies unusual manifestations, such as patients without respiratory symptoms or only very mild symptoms. One widely cited modelling study concluded that up to 86% of cases might have been missed in China,[4] and reports of patients with unusual presenting symptoms are rising worldwide.

Non-respiratory symptoms

Case series report gastrointestinal symptoms in 2-40% of patients,[5 6] and diarrhoea can be the initial manifestation of infection.[7] Whether SARS-CoV-2 leads to such symptoms directly by infecting the gastrointestinal tract, indirectly by neurological involvement,[8] or through production of cytokines remains unknown. Viral RNA has been detected in stool samples, sometimes at high levels.[9] This raises the possibility of faecal-oral transmission,[10] which would have clear implications for infection control.

Taste or olfactory disorders were noted in up to 53% of the cases in a small cohort from Italy,[11] and new anosmia is being proposed as a criterion for testing, especially in young people with few other symptoms.[12] In one woman with covid-19, magnetic resonance imaging showed bilateral inflammatory obstruction of the olfactory clefts[13] with no abnormalities of olfactory bulbs and tracts. Complete characterisation of patients with covid-19 and anosmia needs further research, however, as this usually transient observation is described after many respiratory viral infections.[12] Animal models indicate that coronaviruses might track into the brain via the olfactory nerve or bulb or both, causing neuronal damage or death.[14]

Recent case series from China and the US describe other neurological symptoms among patients with covid-19, including ischaemic or haemorrhagic stroke, dizziness, headache, musculoskeletal disturbance, altered mental state, Guillain-Barré syndrome, or acute necrotising encephalopathy, without proof of direct viral invasion into the brain.[15-17] Systematic testing for SARS-CoV-2 should be considered in patients with acute neurological events during the pandemic.

Cardiovascular events that have been associated with covid-19 in preliminary observations include myocardial injury, especially in patients with severe infections,[18] myocarditis[19] and myopericarditis with reduced systolic function ,[20 21] cardiac arrhythmias,[22] heart failure, and misdiagnosis as acute coronary syndrome. Covid-19 was associated with a hypercoagulable state in a retrospective cohort study from China, probably increasing the risk for venous thromboembolic events including pulmonary embolus.[23] Chest pain should therefore alert clinicians to the possibility of covid-19.

Finally, ocular manifestations such as conjunctival hyperaemia, chemosis, and increased secretions, were reported in up to 32% of infected patients in a Chinese case series, and SARS-CoV-2 RNA could be detected in tears.[24]

Diagnosis might be particularly complicated in specific populations: children frequently have milder disease than adults, with few or no symptoms.[25] It's not yet clear why SARS-CoV-2 may minimally infect children, lead to asymptomatic infection, or give rise to atypical symptoms that are missed by the conventional case definition.

Correspondence to: P Vetter pauline.vetter@hcuge.ch

Infectious diseases might be harder to identify in older people, whose symptoms could be masked. A mild pneumonia might cause only fever, a fall, or confusion, leading to misdiagnosis. Diagnostic delay has serious consequences for older adults, including increased mortality and nosocomial transmission.[26] The threshold for testing should be lowered in this vulnerable group.

Few or no symptoms

Risk of transmission by people with few or no symptoms remains to be quantified. Case reports indicate that runny nose or sore throat can be isolated symptoms.[30] Testing strategies that exclude patients with few symptoms are likely to miss a substantial proportion of cases.

Similar viral loads have been documented in the upper respiratory tract of both symptomatic and asymptomatic cases[27] and in the presymptomatic phase.[28] In one quarantined cruise ship, up to 50% of positive cases were asymptomatic or presymptomatic at the time of testing.[29]

Available evidence from observational and modelling reports indicates that up to 12% of transmission occurs before an index case develops symptoms.[31 32] This has important implications for the effectiveness of any testing strategy and for contact tracing and containment measures. To curtail active transmission of SARS-CoV-2, testing should be extended far beyond people who fit a narrow case definition and other populations currently considered at risk. The current strategy will not capture the full picture, missing a substantial number of patients with atypical presentations or few symptoms. Worse, restrictive testing criteria could lead to unrecognised cases transmitting the virus in healthcare settings or the community and to delays in appropriate patient triage and management.

Broad population screening for SARS-CoV-2 infections, isolation of confirmed cases through contact tracing and quarantine combined with social distancing, and large serological studies will be critical to slowing the spread of covid-19.

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