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Editorial

The COVID-19 epidemic

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The current outbreak of the novel coronavirus SARS-CoV-2 (coronavirus disease 2019; previously 2019-nCoV), epi-centred in Hubei Province of the People's Republic of China, has spread to many other countries. On 30. January 2020, the WHO Emergency Committee declared a global health emergency based on growing case notification rates at Chinese and international locations. The case detection rate is changing daily and can be tracked in almost real time on the website provided by Johns Hopkins University [1] and other forums. As of midst of February 2020, China bears the large burden of morbidity and mortality, whereas the incidence in other Asian countries, in Europe and North America remains low so far.

Coronaviruses are enveloped, positive single-stranded large RNA viruses that infect humans, but also a wide range of animals. Coronaviruses were first described in 1966 by Tyrell and Bynoe, who cultivated the viruses from patients with common colds [2]. Based on their morphology as spherical virions with a core shell and surface projections resembling a solar corona, they were termed coronaviruses (Latin: corona = crown). Four subfamilies, namely alpha-, beta-, gamma- and delta-coronaviruses exist. While alpha- and beta-coronaviruses apparently originate from mammals, in particular from bats, gamma- and delta-viruses originate from pigs and birds. The genome size varies between 26 kb and 32 kb. Among the seven subtypes of coronaviruses that can infect humans, the beta-coronaviruses may cause severe disease and fatalities, whereas alpha-coronaviruses cause asymptomatic or mildly symptomatic infections. SARS-CoV-2 belongs to the B lineage of the beta-coronaviruses and is closely related to the SARS-CoV virus [3,4]. The major four structural genes encode the nucleocapsid protein (N), the spike protein (S), a small membrane protein (SM) and the membrane glycoprotein (M) with an additional membrane glycoprotein (HE) occurring in the HCoV-OC43 and HKU1 beta-coronaviruses [5]. SARS-CoV-2 is 96% identical at the whole-genome level to a bat coronavirus [4].

SARS-CoV-2 apparently succeeded in making its transition from animals to humans on the Huanan seafood market in Wuhan, China. However, endeavours to identify potential intermediate hosts seem to have been neglected in Wuhan and the exact route of transmission urgently needs to be clarified.

The initial clinical sign of the SARS-CoV-2-related disease COVID-19 which allowed case detection was pneumonia. More recent reports also describe gastrointestinal symptoms and asymptomatic infections, especially among young children [6]. Observations so far suggest a mean incubation period of five days [7] and a median incubation period of 3 days (range: 0–24 days) [8]. The proportion of individuals infected by SARS-CoV-2 who remain asymptomatic throughout the course of infection has not yet been definitely assessed. In symptomatic patients, the clinical manifestations of the disease usually start after less than a week, consisting of fever, cough, nasal congestion, fatigue and other signs of upper respiratory tract infections. The infection can progress to severe disease with dyspnoea and severe chest symptoms corresponding to pneumonia in approximately 75% of patients, as seen by computed tomography on admission [8]. Pneumonia mostly occurs in the second or third week of a symptomatic infection. Prominent signs of viral pneumonia include decreased oxygen saturation, blood gas deviations, changes visible through chest X-rays and other imaging techniques, with ground glass abnormalities, patchy consolidation, alveolar

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exudates and interlobular involvement, eventually indicating deterioration. Lymphopenia appears to be common, and inflammatory markers (C-reactive protein and proinflammatory cytokines) are elevated.

Recent investigations of 425 confirmed cases demonstrate that the current epidemic may double in the number of affected individuals every seven days and that each patient spreads infection to 2.2 other individuals on average (R0) [6]. Estimates from the SARS-CoV outbreak in 2003 reported an R0 of 3 [9]. A recent data-driven analysis from the early phase of the outbreak estimates a mean R0 range from 2.2 to 3.58 [10].

Dense communities are at particular risk and the most vulnerable region certainly is Africa, due to dense traffic between China and Africa. Very few African countries have sufficient and appropriate diagnostic capacities and obvious challenges exist to handle such outbreaks. Indeed, the virus might soon affect Africa. WHO has identified 13 top-priority countries (Algeria, Angola, Cote d'Ivoire, the Democratic Republic of the Congo, Ethiopia, Ghana, Kenya, Mauritius, Nigeria, South Africa, Tanzania, Uganda, Zambia) which either maintain direct links to China or a high volume of travel to China.

Recent studies indicate that patients ≥60 years of age are at higher risk than children who might be less likely to become infected or, if so, may show milder symptoms or even asymptomatic infection [7]. As of 13. February 2020, the case fatality rate of COVID-19 infections has been approximately 2.2% (1370/60363; 13. February 2020, 06:53 PM CET); it was 9.6% (774/8096) in the SARS-CoV epidemic [11] and 34.4% (858/2494) in the MERS-CoV outbreak since 2012 [12].

Like other viruses, SARS-CoV-2 infects lung alveolar epithelial cells using receptor-mediated endocytosis via the angiotensin-converting enzyme II (ACE2) as an entry receptor [4]. Artificial intelligence predicts that drugs associated with AP2-associated protein kinase 1 (AAK1) disrupting these proteins may inhibit viral entry into the target cells [13]. Baricitinib, used in the treatment of rheumatoid arthritis, is an AAK1 and Janus kinase inhibitor and suggested for controlling viral replication [13]. Moreover, one *in vitro* and a clinical study indicate that remdesivir, an adenosine analogue that acts as a viral protein inhibitor, has improved the condition in one patient [14,15]. Chloroquine, by increasing the endosomal pH required for virus-cell fusion, has the potential of blocking viral infection [15] and was shown to affect activation of p38 mitogen-activated protein kinase (MAPK), which is involved in replication of HCoV-229E [16]. A combination of the antiretroviral drugs lopinavir and ritonavir significantly improved the clinical condition of SARS-CoV patients [17] and might be an option in COVID-19 infections. Further possibilities include leronlimab, a humanised monoclonal antibody (CCR5 antagonist), and galidesivir, a nucleoside RNA polymerase inhibitor, both of which have shown survival benefits in several deadly virus infections and are being considered as potential treatment candidates [18]. Repurposing these available drugs for immediate use in treatment in SARS-CoV-2 infections could improve the currently available clinical management. Clinical trials presently registered at ClinicalTrials.gov focus on the efficacy of remdesivir, immunoglobulins, arbidol hydrochloride combined with interferon atomisation, ASC09F+Oseltamivir, ritonavir plus oseltamivir, lopinavir plus ritonavir, mesenchymal stem cell treatment, darunavir plus cobicistat, hydroxychloroquine, methylprednisolone and washed microbiota transplantation [19].

Given the fragile health systems in most sub-Saharan African countries, new and re-emerging disease outbreaks such as the current COVID-19 epidemic can potentially paralyse health systems at the expense of primary healthcare requirements. The impact of the Ebola epidemic on the economy and healthcare structures is still felt five years later in those countries which were affected. Effective outbreak responses and preparedness during emergencies of such magnitude are challenging across African and other lower-middle-income countries. Such situations can partly only be mitigated by supporting existing regional and sub-Saharan African health structures.

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