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WHAT'S NEW IN INTENSIVE CARE

COVID-19: a novel coronavirus and a novel challenge for critical care

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In December 2019, several cases of pneumonia of unknown etiology were reported in Wuhan, Hubei Province, China, and were linked to Huanan Seafood Wholesale Market [1–3]. The disease which is now called COVID-19 is caused by a novel coronavirus, labeled as SARS-CoV-2, which was discovered through whole-genome sequencing, polymerase chain reaction (PCR) and culture of bronchoalveolar lavage fluid obtained from affected patients [1, 4]. This virus, which is the seventh coronavirus that has been proven to infect humans, has 75–80% genomic similarity to the severe acute respiratory syndrome coronavirus (SARS-CoV), 50% to the Middle East Respiratory syndrome coronavirus (MERS-CoV) and 96% to a bat coronavirus and uses the same cell receptor, angiotensin-converting enzyme II (ACE2), that is used by SARS-CoV [1, 4, 5].

As of March 1, 2020, 87 137 confirmed COVID-19 cases were reported to the World Health Organization (WHO) from China and 53 other countries [6, 7]. Among the 79 394 confirmed cases in China, there were 2838 deaths [6, 7] With the expectation that these numbers are likely to increase, there are increasing global concerns about the outbreak, particularly for the intensive care community [8].

This is the third coronavirus that has emerged in the past 2 decades, causing multinational outbreaks and carrying substantial morbidity and mortality [9, 10]. While there are distinct features for each of these outbreaks (Table 1), the ongoing COVID-19 outbreak brings to intensivists and the critical care community similar challenges to what was faced with SARS and MERS outbreaks, and there are multiple lessons that can be learned [11, 12].

The biggest challenge to intensivists at this point is when to suspect COVID-19. At present, limited specific data are available on the clinical characteristics and natural course of critically ill patients with COVID-19 [13, 14]. In a study of 138 patients with 2019 nCoV, 36/138 were admitted to the ICU and they were significantly older than patients who did not require ICU admission (median of 66 compared to 51 years) and were more likely to have underlying comorbidities (72% compared to 37%). In the ICU, 11% of patients received high-flow nasal cannula and 15 (44%) received noninvasive ventilation. Invasive mechanical ventilation was required in 17 patients (47%), 4 of whom received extracorporeal membrane oxygenation as rescue therapy [15]. Interestingly, 44% were reported to develop arrhythmias in the ICU. In another study of 52 critically ill adult patients, the mean age was 60 years, with 40% of patients had at least one chronic illness. Of these patients, 67% developed ARDS, 29% acute kidney injury, 23% cardiac injury and 29% liver dysfunction. Invasive or noninvasive mechanical ventilation was required in 71% of patients. By day 28, 62% of patients died [16]. The majority of the severely ill cases have been in adults, with very limited data on pediatric infections with severe illness thus far.

Like MERS and SARS, there are no distinguishing clinical features of COVID-19 and symptoms overlap greatly with other severe acute respiratory infections [13, 14, 17]. Clinical characterization protocols are currently being collected on patients around the world to better define the disease, its natural history, and specific risk factors for worsened outcomes.

Suspicion of the disease is especially difficult in areas where the disease has been rare up to now, although public health vigilance is currently heightened to inform testing strategies. Therefore, clinicians have to rely on the

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Table 1 Comparison between COVID-19 and the other two coronaviruses infections, the Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS) [4,13–17,26]

	COVID-19	MERS	SARS
Epidemiologic links	Wuhan, China	Arabian Peninsula	Guangdong, China
Animal host	Unclear, bat suspected	Dromedary camel	Civet cats and bats suspected
Human–human transmission	Yes	Yes	Yes
Nosocomial transmission	Yes	Yes	Yes
Risk to healthcare workers	Yes	Yes	Yes
Countries with reported cases	54	27	26
Number of cases	85,403 as of March 1, 2020	2494	8437
Clinical features of critically ill patients			
Age, years	60	58	57
Comorbid conditions	40%	80%	++
ARDS/pneumonia	Main feature	Main feature	Main feature
Shock and multiorgan failure	Yes	Yes	Yes
Invasive mechanical ventilation	42%	85%	76%
Vasopressors	35%	79%	44%
Renal replacement therapy	17%	49%	11%
Mortality	Still being defined to 62%	67%	34%

epidemiological link as outlined in the current COVID-19 case definition, such as travel history to affected areas, although this is liable to change as spread continues. During MERS and SARS outbreaks, delayed or even missed diagnoses have led to exposing many other patients, visitors and healthcare workers to the infection. Additionally, the currently available testing has not been formally validated for sensitivity and until more data are available negative PCR needs to be interpreted in clinical context and with caution [17, 18].

Having a plan for surge capacity

Outbreaks can lead to significant increase in the need for ICU beds, but may simultaneously reduce the available beds. The SARS outbreak in Toronto led to 10-day closure of 38% of a tertiary care university ICU beds primarily due to lack of staff because of illness or quarantine [19]. Hence, hospitals should always have plans to augment ICU bed capacity, which may include by transforming general wards into ICUs [20].

Infection prevention and control

Nosocomial transmission to other patients and transmission to HCWs has been a major feature of both outbreaks of SARS, MERS and now COVID-19 [15, 21]. In one report, 41% of hospitalized COVID-19 cases were acquired in hospital, including patients who were already hospitalized for other reasons and healthcare workers [15]. ICU personnel need to follow strict isolation precautions in the ICU to protect personnel, other patients and visitors. Current recommendations are to follow contact and droplet precautions and airborne precautions when performing aerosol-generating procedures [22]. With concerns that the virus remains viable in inanimate environments for a sustained period, special attention needs to be paid to environmental disinfection in the ICU [12, 22]. Intensive care physicians should be sure to keep informed of the evolving knowledge and liaise with their local public health authorities to inform local infection control strategies.

The consumption of supplies required for infection control, such as medical masks and N95 masks, alcohol-based hand rub and surface disinfectant, increases substantially during outbreaks [12]. Ensuring an adequate supply chain from the manufacturer through to frontline staff is crucial to reduce nosocomial transmission.

Staff protection

Protecting the workforce is another critical challenge. Sick leaves increase during outbreaks as healthcare workers with respiratory symptoms are requested to stay home until results of testing become available and because of contact tracing of infected patients [12]. Caring for infected patients represents a substantial exposure risk for ICU staff because of high and prolonged exposure to critically ill patients who presumably have higher viral shedding. Severe infections and deaths have occurred among healthcare workers with MERS, SARS and now COVID-19, exerting significant psychosocial stress on the staff. During the SARS and MERS outbreaks, healthcare workers reported concerns for their own or their

family's health and described painful experiences of fear, anxiety and even social prejudice and stigmatization [23].

Learning more about COVID-19

As a novel infectious disease, there is an urgent unmet need to conduct research to determine optimal treatment including specific antiviral therapy, the role of modulation of the immune system, and how best to provide support for failed organ systems. At the time of writing this paper, there are > 160 registered randomized and non-randomized studies (http://www.chictr.org.cn/searchproj en.aspx and http://apps.who.int/trialsearch/default.aspx) for treatment of COVID-19 using a variety of interventions including corticosteroids, different combinations of ribavirin, lopinavir/ritonavir, chloroquine, hydroxychloroquine, interferons and other agents. An RCT is being conducted using remdesivir for severe COVID-19 (NCT04257656).

Many lessons have been learned from previous outbreaks of emerging infectious diseases, as the research response has often been insufficient to answer questions relevant to optimal clinical practice due to the long lead times that are necessary to design, implement, obtain approval, and recruit patients into randomized controlled trials [24]. For COVID-19, the World Health Organization in collaboration with the Global Research Collaboration for Infectious Disease Preparedness (GLOPID-R) has organized the Global Research and Innovation Forum in February 11–12, 2020 to identify the urgent priorities for research in aspects related to the outbreak including clinical characterization, therapeutics and diagnostics, among other priorities. The REMAP-CAP (Randomized, Embedded, Multifactorial Adaptive Platform Trial for Community-Acquired Pneumonia) is designed as an adaptive pre-planned, pre-approved platform trial for ICU patients with severe community-acquired pneumonia. The trial is recruiting currently at 52 sites in 13 countries on 3 continents with a further 35–40 sites being activated (https://www.remapcap.org) [25]. The trial is multifactorial, meaning it can analyze the independent effect of multiple interventions and their interactions and utilizes frequent analyses using Bayesian statistics to report results as soon as there is sufficient statistical confidence regarding superiority, inferiority or equivalence of interventions that are being evaluated [25]. Urgent modifications are being made to the protocol of REMAP-CAP to make it suitable to evaluate the effect of a range of interventions that may be active against this COVID-19. If COVID-19 becomes widespread, there are plans to substantially increase the number of sites that can participate in REMAP-CAP.

The COVID-19 that has currently affected tens of thousands of patients and continues to spread is a major concern for ICU physicians around the world. Preparedness activities must include examining surge capacity, reviewing infection control protocols, and evaluating laboratory diagnostics. Learning from the experiences of past coronavirus outbreaks will greatly improve our ability to respond effectively, ensuring that we provide the best possible care to infected patients while simultaneously protecting ourselves and our communities.

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Compliance with ethical standards

Conflicts of interest

Dr. Arabi is the principal investigator on a clinical trial for lopinavir/ritonavir and interferon in Middle East respiratory syndrome (MERS) and that he was a nonpaid consultant on antiviral active for MERS-coronavirus (CoV) for Gilead Sciences and SAB Biotherapeutics. Dr. Arabi, Murthy, and Prof Webb are investigators on REMAP-CAP and are board members of the International Severe Acute Respiratory and emerging Infection Consortium (ISARIC).

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