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WHAT'S NEW IN INTENSIVE CARE

# Severe SARS-CoV-2 infections: practical considerations and management strategy for intensivists

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On December 31, 2019, China reported cases of respiratory illness in humans appearing first in Wuhan, Hubei Province, that involved a novel coronavirus SARS-CoV-2 (aka 2019-nCoV). This new emergency is a zoonotic disease with unknown animal reservoir and with evidence of person-to-person transmission [1]. The basic reproductive number of this infection is estimated to be 2.2 (95% CI, 1.4–3.9) [2].

## Etiological agent and epidemiology

The new agent causing this pneumonia, a coronavirus (SARS-CoV-2), was identified and sequenced [3] and diagnostic tests were developed [4]. On January 30, 2020, the World Health Organization issued a worldwide public health alert on the emergence of a new epidemic viral disease. On February 3, 2020, 17,391 confirmed cases (153 cases outside of China) have been reported (https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports/). The overall mortality rate of affected patients is difficult to assess at this time, because of the lack of a reliable denominator. Severe forms represent 14% of the reported cases, and the overall mortality is around 2% of the confirmed cases. To date, 153 cases have been reported in 23 countries outside China (overall, 24 cases in Europe), most of them being imported cases: tourists coming from China, or China-originating persons returning to their country of residence after traveling to visit family in Wuhan or other Chinese regions. In Europe, at least three cases in Germany and one case in France involved patients with no history of travel to China. The German case occurred after exposure to an asymptomatic contact coming from China [5].

## Clinical features

To date, the ECDC criteria to require diagnostic testing for suspected cases are patients with acute respiratory infection (requiring hospitalization or not) in the 14 days prior to the onset of symptoms with at least one of the following epidemiological criteria being present: close contact with a confirmed or probable case of SARS-CoV-2 infection (COrona VIrus Disease 2019, COVID-19) (or) history of travel to China (or) having worked in or having attended a health care facility where patients with SARS-CoV-2 infections were being treated (https://www.ecdc.europa.eu/en/case-definition-and-european-surveillance-human-infection-novel-coronavirus-2019-ncov).

## Incubation period and clinical description

The mean incubation period was 5.2 days (95% confidence interval [CI], 4.1–7.0), with the 95th percentile of the distribution at 12.5 days [2]. Early signs included non-specific influenza-like symptoms [6]. Data from a series of 99 Chinese patients with COVID-19 pneumonia, diagnosed in all patients by real-time reverse-transcriptase polymerase chain reaction (rRT-PCR), have already been published. Three patients out of four received oxygen therapy, 13% had non-invasive ventilation and 4% invasive ventilation, 9% required renal replacement therapy and 3% extracorporeal membrane oxygenation. According to the authors, 11% of these hospitalized patients

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worsened within a short period of time and died of multiple organ failure [6]. Although these preliminary data are insufficient to draw a clinical overview of the patients affected with this viral respiratory illness novel to humans, it is obvious that COVID-19 could cause severe respiratory failure requiring ICU admission. The first experiences of our Chinese colleagues are described in this journal [7].

Four cases have already been admitted in Bichat-Claude Bernard reference hospital in Paris, including 2 cases in the medical ICU. Clinical presentation based on our experience and available data are depicted on Fig. 1.

## Management

There are several challenges that intensivists have to face when caring for a patient suspected of infection with an emerging pathogen such as SARS-CoV-2, both in terms of management of the patient, particularly regarding laboratory tests and diagnostic radiologic procedures, and of healthcare workers' protection and unit organization. Based on previous outbreaks due to emerging coronavirus, MERS and SARS, droplets are likely the major mode of transmission. Transmission from contaminated fomites close to the infected patient is also possible. Airborne transmission has been suspected, especially during invasive respiratory procedures. Personal protective equipment should, therefore, protect from droplets, contact and airborne transmission (see supplemental dress and undress procedures associated with photos and videos). The survival time of coronavirus on dry surfaces is no longer than 4 h, requiring regular environmental cleaning. A coordinated and multidisciplinary management between ICU, infectious diseases (ID) and infection control specialists, and also the institution, is of paramount importance. A trained supervisor is critical to ensure safe practices and reassure the ICU team.

### Patient management

Decision of ICU admission and discharge should be discussed daily in closed collaboration with ID physicians.

If COVID-19 is suspected, the patient must be placed in a single room and all principles of infection prevention and control (IPC) should be taken as for confirmed cases (eSupplement Table 1). Diagnostic testing, if not already performed at patient admission, is the first task for intensivists. Etiologic diagnosis relies on rRT-PCR assays. Specimens from upper and if possible lower respiratory tracts should be collected (lower respiratory specimens likely have a higher diagnostic value). Upper respiratory tract specimens are obtained through nasopharyngeal swab, oropharyngeal swab, or nasopharyngeal aspirate or nasal wash. As per the lower respiratory tract samples, a bronchoalveolar lavage (BAL) fluid specimen is possible but it is not recommended due to the high risk that bronchoscopy poses to ICU staff. Plugged telescopic catheter specimen with or without mini-BAL, endotracheal aspirate, or expectorated sputum should be preferred. Additional specimens of blood, urine and feces and any other site if appropriate could be considered for delayed testing.

Based on the previous experiences on MERS, if the initial testing is negative in a patient who is strongly

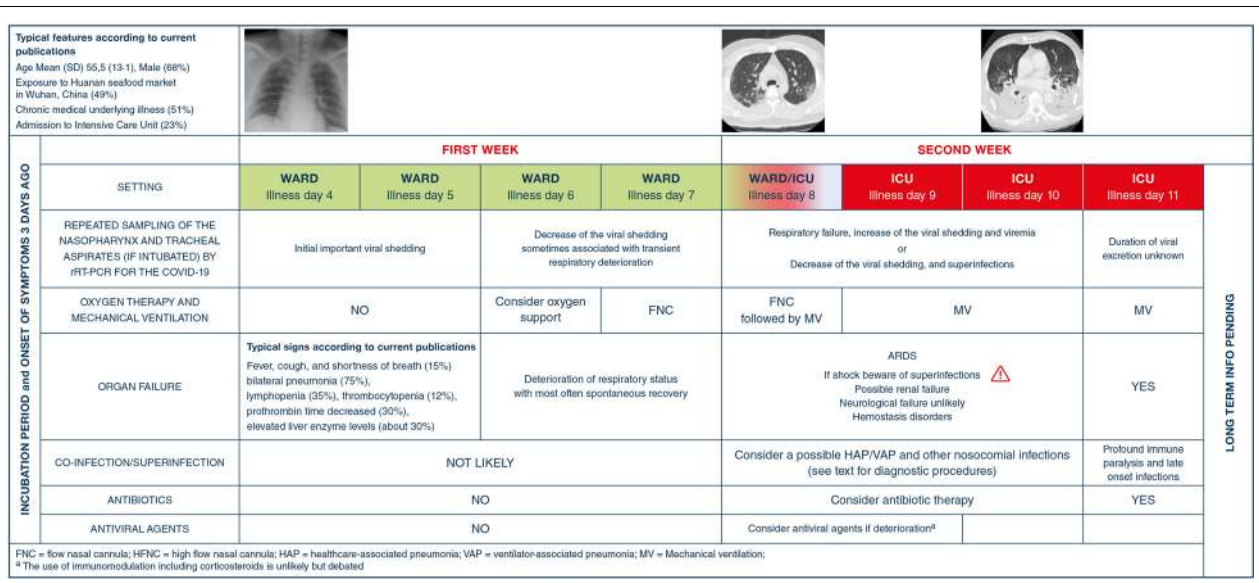


**Fig. 1** Global picture of severe cases

suspected to have SARS-CoV-2 infection, it is recommended to perform a repeated test (multiple respiratory tract sites including nose, sputum, and endotracheal aspirate) (https://www.ecdc.europa.eu/sites/default/files/documents/nove-coronavirus-infection-prevention-control-patients-healthcare-settings.pdf).

Viral shedding may vary with time; therefore, repeated sampling is recommended for confirmed cases. The prognostic value of the evolution of viral shedding is still unknown.

The initial diagnosis testing should include a search for other respiratory pathogens, including blood cultures, sputum culture, providing that specimens are handled according to biosafety practices. Point-of-care testing is useful to quicken biological surveillance, but a limited number of tests are available. When cultures can not be performed because of biosafety issues, multiplex PCR is instrumental for bacterial infections identification. Bronchoscopy is acceptable, but it should be discussed when concerns regarding other diagnoses are high.

There are no reasons to limit care intensity for patients infected with SARS-CoV-2. However, procedures ranging from bronchoscopy to extracorporeal membrane oxygenation, to transporting patient outside the ICU or to surgery, should be discussed collectively on a case-by-case basis. Apart from the vital emergency, these procedures should be anticipated.

### Infection prevention and control (IPC)

An important component of IPC is staff education and preparation.

IPC strategies have been adapted from IPC for probable or confirmed cases of Middle East respiratory syndrome coronavirus (MERS-CoV), and they are likely to evolve rapidly as new information is collected.

Patient should be ideally placed in a negative pressure isolation room. Healthcare staff should use contact, airborne and droplet precautions (see ESM).

In the event of a massive influx of patients, the preventive measures will have to be degraded. Without a doubt, the most important component of personal protective equipment is wearing a fit-tested FFP2 (or equivalent) face mask (see ESM).

## Treatment

If the diagnosis is uncertain or if a co-infection is suspected, empirical therapy for community-acquired pneumonia should be considered, using antibiotics with activity against both typical and atypical respiratory pathogens.

In ARDS patients, superinfection is often associated with shock and multiple organ failure. Etiologic agents vary with the patients' country of origin but uncommon pathogens such as *Acinetobacter baumannii* and *Aspergillus fumigatus* have been collected [6]. There is no effective disease-specific treatment or vaccine. However, experimental drugs and drug combinations such as remdesivir, lopinavir–ritonavir, or lopinavir–ritonavir and interferon Beta-1b are under investigation and may be considered for compassionate use in severely ill patients [8]. It has been shown that remdesivir and interferon Beta-1b have superior antiviral activity to LPV and RTV in vitro [8].

In view of the high amount of cytokines induced by SARS-CoV, MERS-CoV and SARS-CoV-2 infections [9], corticosteroids were frequently used for the treatment of patients with severe illness, the reduction of the inflammatory-induced lung injury being the expected benefit. However, current evidence suggests that corticosteroids did not have an effect on mortality, but rather delayed viral clearance [10]. Moreover, the increase in the viral load and viremia argue against their use. Therefore, systemic corticosteroids should not be given routinely, according to WHO interim guidance.

### Discharge to the isolation room

Discharge from the ICU to an isolation room in the ward has no specificity compared to another patient admitted to the ICU. According to the World Health Organization, more comprehensive information about the mode of transmission of the SARS-CoV-2 infection is required to define the duration of the precautions set-up.

#### Electronic supplementary material

The online version of this article (https://doi.org/10.1007/s00134-020-05967-x) contains supplementary material, which is available to authorized users.

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#### Compliance with ethical standards

#### Conflicts of interests

The authors declare no conflict of interest linked to the submitted work. Outside the submitted work: JFT declares research grants from Pfizer, Merck, 3M, Astellas, Biomerieux; scientific Board participation with Maat Pharma, Merck, Bayer pharma, Medimune, Gilead, VenatoRx, Nabriva, Paratek; lecture fees for Merck, Pfizer, Biomerieux.

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### References

1. Phan LT, Nguyen TV, Luong QC, Nguyen HT, Le HQ, Nguyen TT, Cao TM, Pham QD (2020) Importation and human-to-human transmission of a novel coronavirus in Vietnam. N Engl J Med. https://doi.org/10.1056/NEJMc2001272
2. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, Ren R, Leung KSM, Lau EHY, Wong JY, Xing X, Xiang N, Wu Y, Li C, Chen Q, Li D, Liu T, Zhao J, Li M, Tu W, Chen C, Jin L, Yang R, Wang Q, Zhou S, Wang R, Liu H, Luo Y, Liu Y, Shao G, Li H, Tao Z, Yang Y, Deng Z, Liu B, Ma Z, Zhang Y, Shi G, Lam TTY, Wu JTK, Gao GF, Cowling BJ, Yang B, Leung GM, Feng Z (2020) Early transmission dynamics in wuhan, china, of novel coronavirus-infected pneumonia. N Engl J Med. https://doi.org/10.1056/NEJMoa2001316
3. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, Zhao X, Huang B, Shi W, Lu R, Niu P, Zhan F, Ma X, Wang D, Xu W, Wu G, Gao GF, Tan W (2020) A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 382:727–733. https://doi.org/10.1056/NEJMoa2001017
4. Corman VM, Landt O, Kaiser M, Molenkamp R, Meijer A, Chu DK, Bleicker T, Brunink S, Schneider J, Schmidt ML, Mulders DG, Haagmans BL, van der Veer B, van den Brink S, Wijsman L, Goderski G, Romette JL, Ellis J, Zambon M, Peiris M, Goossens H, Reusken C, Koopmans MP, Drosten C (2020) Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. Euro surveillance 25:3
5. Rothe C, Schunk M, Sothmann P, Bretzel G, Froeschl G, Wallrauch C, Zimmer T, Thiel V, Janke C, Guggemos W, Seilmaier M, Drosten C, Vollmar P, Zwirglmaier K, Zange S, Wolfel R, Hoelscher M (2020) Transmission of 2019-nCoV infection from an asymptomatic contact in Germany. N Engl J Med. https://doi.org/10.1056/NEJMc2001468
6. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, Qiu Y, Wang J, Liu Y, Wei Y, Xia J, Yu T, Zhang X, Zhang L (2020) Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 395(10223):507–513. https://doi.org/10.1016/S0140-6736(20)30211-7
7. Liao X, Wang B, Kang Y (2020) Novel coronavirus infection during the 2019–2020 epidemic: preparing intensive care units-the experience in Sichuan Province, China. Intensive Care Med. https://doi.org/10.1007/s00134-020-05954-2
8. Sheahan TP, Sims AC, Leist SR, Schafer A, Won J, Brown AJ, Montgomery SA, Hogg A, Babusis D, Clarke MO, Spahn JE, Bauer L, Sellers S, Porter D, Feng JY, Cihlar T, Jordan R, Denison MR, Baric RS (2020) Comparative therapeutic efficacy of remdesivir and combination lopinavir, ritonavir, and interferon beta against MERS-CoV. Nature Commun 11:222
9. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z, Yu T, Xia J, Wei Y, Wu W, Xie X, Yin W, Li H, Liu M, Xiao Y, Gao H, Guo L, Xie J, Wang G, Jiang R, Gao Z, Jin Q, Wang J, Cao B (2020) Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 395(10223):497–506. https://doi.org/10.1016/S0140-6736(20)30183-5
10. Arabi YM, Shalhoub S, Mandourah Y, Al-Hameed F, Al-Omari A, Al Qasim E, Jose J, Alraddadi B, Almotairi A, Al Khatib K, Abdulmomen A, Qushmaq I, Sindi AA, Mady A, Solaiman O, Al-Raddadi R, Maghrabi K, Ragab A, Al Mekhlafi GA, Balkhy HH, Al Harthy A, Kharaba A, Gramish JA, Al-Aithan AM, Al-Dawood A, Merson L, Hayden FG, Fowler R (2019) Ribavirin and interferon therapy for critically ill patients with middle east respiratory syndrome: a multicenter observational study. Clin Infect Dis. https://doi.org/10.1093/cid/ciz544