Topic: A COMPREHENSIVE REVIEW Covid-19

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REVIEW

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (WHO, 2020). The disease was first identified in December 2019 in Wuhan, the capital of China's Hubei province, and has since spread globally, resulting in the ongoing 2019–20 coronavirus pandemic (WHO, 2020). As of February 2020 and based on 55924 laboratory confirmed cases, typical signs and symptoms includes: fever(87.9%), dry cough(67.7%), sore throat (13.9%), head ache(13.6%), vomiting(5%), nasal congestion(4.8%), diarrhea(3.7%), arthralgia(14.8%), hemoptysis(0.9%) and conjunctiva congestion(0.8%). (WHO).

Other symptoms may include fatigue, muscle pain, sore throat, loss of smell and abdominal pain The time from exposure to onset of symptoms is typically around five days, but may range from two to 14 days. While the majority of cases result in mild symptoms, some progress to viral pneumonia and multi-organ failure (WHO, 2020). As of 9 April 2020, more than 1.5 million cases have been reported in more than 200 countries and territories, resulting in more than 89,900 deaths. (Johns, 2020). More than 339,000 people have recovered (Johns, 2020). The virus is mainly spread during close contact and by small droplets produced when those infected cough, sneeze, or talk (WHO, 2020). These droplets may also be produced during breathing; however, they rapidly fall to the ground or surfaces and are not generally spread through the air over large distances. People may also become infected by touching a contaminated surface and then their face (WHO, 2020). The virus can survive on surfaces for up to 72 hours.( National Institutes of Health, 2020). Coronavirus is most contagious during the first three days after onset of symptoms, although spread may be possible before symptoms appear and in later stages of the disease (WHO, 2020). The standard method of diagnosis is by real-time reverse transcription polymerase chain reaction (rRT-PCR) from a nasopharyngeal swab (WHO, 2020). The infection can also be diagnosed from a combination of symptoms, risk factors and a chest CT scan showing features of pneumonia (Jin *et al.,*2019). Recommended measures to prevent infection include frequent hand washing, social distancing (maintaining physical distance from others, especially from those with symptoms), covering coughs and sneezes with a tissue or inner elbow and keeping unwashed hands away from the face (WHO, 2020). The use of masks is recommended for those who suspect they have the virus and their caregivers (WHO, 2020). Recommendations for mask use by the general public vary, with some authorities recommending against their use, some recommending their use and others requiring their use (Tait and Robert, 2020). Currently, there is no vaccine or specific antiviral treatment for COVID-19 (WHO, 2020). Management involves treatment of symptoms, supportive care, isolation and experimental measures (CDC, 2019). The World Health Organization (WHO) declared the 2019–20 coronavirus outbreak a Public Health Emergency of International Concern (PHEIC) (Mahtani *et al*., 2020) on 30 January 2020 and a pandemic on 11 March 2020 (WHO, 2020). Local transmission of the disease has been recorded in many countries across all six WHO regions.

Signs and symptoms

Fever, Dry cough, Fatigue, Sputum production, Loss of smell, Shortness of breath, Muscle or joint pain, Sore throat, Headache, Chills, Nausea or vomiting Nasal congestion.Those infected with the virus may be asymptomatic or develop flu-like symptoms, including fever, cough, fatigue, and shortness of breath (Chen *et al.,* 2019). Emergency symptoms include difficulty breathing, persistent chest pain or pressure, confusion, difficulty waking and bluish face or lips; immediate medical attention is advised if these symptoms are present (CDC, 2020). Less commonly, upper respiratory symptoms, such as sneezing, runny nose or sore throat may be seen. Symptoms such as nausea, vomiting and diarrhoea have been observed in varying percentages (Huang *et al.,* 2020). Some cases in China initially presented only with chest tightness and palpitations (CDC, 2020). In March 2020 there were reports indicating that loss of the sense of smell (anosmia) may be a common symptom among those who have mild disease, (Iacobucci and Gareth, 2020). Although not as common as initially reported (Palus and Shannon, 2020). In some, the disease may progress to pneumonia, multi-organ failure and death (WHO, 2020). In those who develop severe symptoms, time from symptom onset to needing mechanical ventilation is typically eight days (CDC, 2020). As is common with infections, there is a delay between the moment when a person is infected with the virus and the time when they develop symptoms. This is called the incubation period. The incubation period for COVID-19 is typically five to six days but may range from two to 14 days (WHO, 2020). 97.5% of people who develop symptoms will do so within 11.5 days of infection (Lauer *et al*., 2020).

Virology

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel severe acute respiratory syndrome coronavirus, first isolated from three people with pneumonia connected to the cluster of acute respiratory illness cases in Wuhan (CDC, 2020). All features of the novel SARS-CoV-2 virus occur in related coronaviruses in nature (Anderson *et al*., 2020). Outside the human body, the virus can be killed with even household soap.

Vaccine

There is no available vaccine, but various agencies are actively developing vaccine candidates. There are three vaccination strategies being investigated. First, researchers aim to build a whole virus vaccine. The use of such a virus, be it inactive or dead, aims to elicit a prompt immune response of the human body to a new infection with COVID-19. A second strategy, subunit vaccines, aims to create a vaccine that sensitises the immune system to certain subunits of the virus. In the case of SARS-CoV-2, such research focuses on the S-spike protein that helps the virus intrude the ACE2 enzyme receptor. A third strategy is that of the nucleic acid vaccines (DNA or RNA vaccines, a novel technique for creating a vaccination). Experimental vaccines from any of these strategies would have to be tested for safety and efficacy (Chen *et al.,* 2020). On 16 March 2020, the first clinical trial of a vaccine started with four volunteers in Seattle. The vaccine contains a harmless genetic code copied from the virus that causes the disease (Roberts, 2020). A key challenge for vaccine development for SARS-COV-2, SARS-COV, and MERS-COV is the phenomenon of antibody dependent enhancement.

PATHOGEGENESIS AND HISTOPATHOLOGICAL FEATURES

Clinical features: Public Health England (PHE) has outlined criteria to assess possibility of COVID-19 infection in patients (HSE, 2020). These criteria are the same when the patient is deceased with the exception that the timelines given in the guidance refer to the time prior death or onset of relevant symptoms before death where known.

If it is considered that COVID-19 may have been related to death by these criteria, the choice of either to perform a full postmortem or an examination is limited only to retrieving the samples required to verify COVID-19 infection. This decision must be made according to the individual case and should include the requirements of the coroner or any pertinent individuals. A staged postmortem may also be considered. This involves taking only diagnostic samples initially and later considering or a more complete autopsy after the results of these diagnostic tests are available. This staged technique is recommended if possible.

Macroscopic features: the macroscopic features of COVID-19 are likely to be in the chest and may include pleurisy, pericarditis, lung consolidation and pulmonary oedema. Lung weight may be increased above normal. It should be noted a secondary infection may be superimposed on the viral infection that can lead to purulent inflammation more typical of bacterial infection (Osborn *et al*., 2020).

Microscopic findings*:* a recent article described the early histopathological features in COVID-19 in two patients who underwent surgical resections for lung adenocarcinoma but were later discovered to have had COVID-19 at the time of the operation (Tian *et al.,* 2020). The findings were non-specific and included oedema, pneumocyte hyperplasia, focal inflammation and multinucleated giant cell formation while no hyaline membranes were seen (Tian *et al.,* 2020). Given that these patients were asymptomatic with respect to COVID-19 at the time of the operation, these are likely to reflect only early changes of acute lung injury in the infection In another case, a 50-year-old man died from severe COVID-19 infection and more marked histopathological findings were noted (Xu *et al.*, 2020). Samples were taken by postmortem biopsy, and a description of the gross postmortem findings is not given, although multiple ground glass opacities were noted on chest X-ray. The microscopic findings included diffuse alveolar damage with exudates (Xu *et al.,* 2020). The inflammation was predominantly lymphocytic, and multinucleated giant cells were seen alongside large atypical pneumocytes, although no definitive viral inclusions were noted. Microvesicular steatosis with mild inflammation was noted in the liver, although it was unclear whether this was related to the virus or iatrogenic. The features are very similar to those seen in SARS and MERS-coronavirus infections (Ding *et al.,* 2003).

Molecular immune pathogenesis and diagnosis of COVID-19

Highlights

The highly pathogenic SARS-CoV-2 appearing in December 2019 can cause COVID-19 and even death in infected persons.

Coronavirus infections led to the damage of lung, while imbalanced and excessive immune responses may cause pneumonia.

RT-PCR and CT scans are significant for the diagnosis of SARS-CoV-2 infection, and drugs and vaccines against SARS-CoV-2 are being developed.

Coronavirus disease 2019 (COVID-19) is a kind of viral pneumonia with an unusual outbreak in Wuhan, China, in December 2019, which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The emergence of SARS-CoV-2 has been marked as the third introduction of a highly pathogenic coronavirus into the human population after the severe acute respiratory syndrome coronavirus (SARS-CoV) and the Middle East respiratory syndrome coronavirus (MERS-CoV) in the twenty-first century. In this minireview, we provide a brief introduction of the general features of SARS-CoV-2 and discuss current knowledge of molecular immune pathogenesis, diagnosis and treatment of COVID-19 on the base of the present understanding of SARS-CoV and MERS-CoV infections, which may be helpful in offering novel insights and potential therapeutic targets for combating the SARS-CoV-2 infection.

Pathology



* [Macroscopy](https://en.wikipedia.org/wiki/Macroscopic_scale): [pleurisy](https://en.wikipedia.org/wiki/Pleurisy), [pericarditis](https://en.wikipedia.org/wiki/Pericarditis), [lung consolidation](https://en.wikipedia.org/wiki/Lung_consolidation) and [pulmonary oedema](https://en.wikipedia.org/wiki/Pulmonary_oedema)
* Four types of severity of [viral pneumonia](https://en.wikipedia.org/wiki/Viral_pneumonia) can be observed:
	+ minor [pneumonia](https://en.wikipedia.org/wiki/Pneumonia): minor serous [exudation](https://en.wikipedia.org/wiki/Exudate), minor [fibrin](https://en.wikipedia.org/wiki/Fibrin) exudation
	+ mild pneumonia: [pulmonary oedema](https://en.wikipedia.org/wiki/Pulmonary_oedema), [pneumocyte](https://en.wikipedia.org/wiki/Pneumocyte) [hyperplasia](https://en.wikipedia.org/wiki/Hyperplasia), large atypical [pneumocytes](https://en.wikipedia.org/wiki/Pneumocyte), interstitial [inflammation](https://en.wikipedia.org/wiki/Inflammation) with [lymphocytic](https://en.wikipedia.org/wiki/Lymphocytic) [infiltration](https://en.wikipedia.org/wiki/Infiltration_%28medical%29) and [multinucleated giant cell](https://en.wikipedia.org/wiki/Giant_cell) formation
	+ severe pneumonia: [diffuse alveolar damage](https://en.wikipedia.org/wiki/Diffuse_alveolar_damage) (DAD) with diffuse [alveolar](https://en.wikipedia.org/wiki/Pulmonary_alveolus) [exudates](https://en.wikipedia.org/wiki/Exudates). DAD is the cause of [acute respiratory distress syndrome](https://en.wikipedia.org/wiki/Acute_respiratory_distress_syndrome) (ARDS) and severe [hypoxemia](https://en.wikipedia.org/wiki/Hypoxemia).
	+ healing pneumonia: [organisation](https://en.wikipedia.org/wiki/Healing) of [exudates](https://en.wikipedia.org/wiki/Exudate) in [alveolar cavities](https://en.wikipedia.org/wiki/Pulmonary_alveolus) and [pulmonary interstitial fibrosis](https://en.wikipedia.org/wiki/Pulmonary_fibrosis)
	+ [plasmocytosis](https://en.wikipedia.org/wiki/Plasma_cell) in [BAL](https://en.wikipedia.org/wiki/Bronchoalveolar_lavage)
* [Blood](https://en.wikipedia.org/wiki/Blood): [disseminated intravascular coagulation](https://en.wikipedia.org/wiki/Disseminated_intravascular_coagulation) (DIC); leukoerythroblastic reaction
* [Liver](https://en.wikipedia.org/wiki/Liver): microvesicular [steatosis](https://en.wikipedia.org/wiki/Steatosis)

As a vaccine is not expected until 2021 at the earliest, (Grenfell and Drew, 2020) a key part of managing COVID-19 is trying to decrease the epidemic peak, known as "flattening the curve" (Anderson *et al*., 2020). This is done by slowing the infection rate to decrease the risk of health services being overwhelmed, allowing for better treatment of current cases and delaying additional cases until effective treatments or a vaccine become available (Anderson *et al*., 2020).

Current management therapies

Medications

Some medical professionals recommend paracetamol (acetaminophen) over ibuprofen for first-line use (Day and Michael, 2020). The WHO does not oppose the use of non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen for symptoms, (WHO, 2020) and the FDA says currently there is no evidence that NSAIDs worsen COVID-19 symptoms.

While theoretical concerns have been raised about ACE inhibitors and angiotensin receptor blockers, as of 19 March 2020, these are not sufficient to justify stopping these medications (de Simone and Giovanni, 2020). Steroids, such as methylprednisolone, are not recommended unless the disease is complicated by acute respiratory distress syndrome (Vetter *et al*., 2020).

### APN01

A clinical trial is set to start soon in China to examine the potential of a drug called [APN01](https://pipelinereview.com/index.php/2020022673884/Proteins-and-Peptides/APEIRONs-respiratory-drug-product-to-start-pilot-clinical-trial-to-treat-coronavirus-disease-COVID-19-in-China.html) to fight the novel coronavirus. The scientists who first developed APN01 in the early 2000s discovered that a certain protein called ACE2 is involved in [SARS](https://www.healthline.com/health/severe-acute-respiratory-syndrome-sars) infections. This protein also helped protect the lungs from injury due to respiratory distress.

From recent research, it turns out that the 2019 coronavirus, like SARS, also uses the ACE2 protein to infect cells in humans. The randomized, dual-arm trial will look at the effect of the medication on 24 patients for 1 week. Half of the participants in the trial will receive the APN01 drug, and the other half will be given a placebo. If results are encouraging, larger clinical trials will be done.

### Favilavir

China has approved the use of the antiviral drug [favilavir](https://www.upi.com/Health_News/2020/02/17/China-approves-antiviral-favilavir-to-treat-coronavirus/5291581953892/) to treat symptoms of COVID-19. The drug was initially developed to treat inflammation in the nose and throat. Although the results of the study haven’t been released yet, the drug has supposedly shown to be effective in treating COVID-19 symptoms in a clinical trial of 70 people.

1. **Chloroquine/Hydroxychloroquine**

The president of the United States recently approved the drug to be used in a worst case scenario/clinical condition as there is no cure. There have been reports from a few patients who have recovered after being administered this drug, but some claim it is ineffective and has side effects that damage organs.

Mechanical ventilation

Most cases of COVID-19 are not severe enough to require mechanical ventilation (artificial assistance to support breathing), but a percentage of cases do. Some Canadian doctors recommend the use of invasive mechanical ventilation because this technique limits the spread of aerosolised transmission vectors. Severe cases are most common in older adults (those older than 60 years and especially those older than 80 years). Many developed countries do not have enough hospital beds per capita, which limits a health system's capacity to handle a sudden spike in the number of COVID-19 cases severe enough to require hospitalisation. This limited capacity is a significant driver of the need to flatten the curve (to keep the speed at which new cases occur and thus the number of people sick at one point in time lower). One study in China found 5% were admitted to intensive care units, 2.3% needed mechanical support of ventilation, and 1.4% died. Around 20–30% of the people in hospital with pneumonia from COVID-19 needed ICU care for respiratory support (CDC, 2020).

Acute respiratory distress syndrome

Mechanical ventilation becomes more complex as acute respiratory distress syndrome (ARDS) develops in COVID-19 and oxygenation becomes increasingly difficult. Ventilators capable of pressure control modes and high PEEP are needed to maximise oxygen delivery while minimising the risk of ventilator-associated lung injury (CDC, 2020) and pneumothorax. High PEEP may not be available on older ventilators.

No medications are approved to treat the disease by the WHO although some are recommended by individual national medical authorities. Research into potential treatments started in January 2020, and several antiviral drugs are in clinical trials (WHO, 2020). Although new medications may take until 2021 to develop (Lu, 2020) several of the medications being tested are already approved for other uses or are already in advanced testing (WHO, 2020). Antiviral medication may be tried in people with severe disease. The WHO recommended volunteers take part in trials of the effectiveness and safety of potential treatments.

After weeks of spreading throughout China and into several countries around the globe, the novel coronavirus (COVID-2019) has now been designated "a public health emergency of international concern." This announcement from the World Health Organization means that there is a greater probability for a much larger outbreak.

COVID-2019 is a potentially deadly and highly contagious virus that can be transmitted through human-to-human contact. It is called the novel coronavirus, because it is a new (novel) coronavirus that is still being examined. While researchers work to uncover the background of this outbreak and the impact of the resulting illness, it's important to remember that even though there are confirmed cases of COVID-2019 within the United States, the risk to the general American public is still considered low by the Centers for Disease Control. Staying aware of the current situation and actively working to maintain your overall health and wellbeing are the best steps to take right now.

As always, follow the guidelines and information provided by the agencies responsible for monitoring and responding to concerns of this nature. Trusting your family's health and wellbeing to untrusted sources of information may unnecessarily aggravate concerns or worry younger family members who do not have a full understanding of the situation.

**Personal Opinion on the future of COVID-19**

Pandemics involve multiple countries having sustained transmission of a pathogen, with no exclusion of minor Infections. The virus though highly fatal still has a very low percentage of death rates compared to the number of people infected (+/-10%). An implication is that countries should share data comfortably, so that we’ll have baselines for every emerging pandemic. Two key elements of pandemics are efficient transmission and disease severity. I could imagine grades of pandemics, based on statistic such as; the progressive surge capacity needed for personal protective equipment, diagnostic testing, ventilators, medical personnel and others essentials, the only uncertainties about pandemics are when and how severe. Albert Camus, in his allegorical novel, *The Plague*, said that regardless of the recurrence of pandemics *“... we find it hard to believe in ones that crash down on our heads from a blue sky”.* Therefore we shouldn’t be taken aback by pandemics.

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