

TOPIC: COVID-19

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NAME: ZUBAIRU KAMARU MAHMUD

DEPARTMENT: HUMAN ANATOMY

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LECTURER: MR EDEM EDEM

COMPREHENSIVE REVIEW OF THE AETIOLOGY OF COVID-19

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). Common symptoms include fever, cough and shortness of breath (WHO, 2020). Other symptoms may include fatigue, muscle pain, diarrhea, sore throat, loss of smell and abdominal pain (Hopkins and Claire, 2020). The time from exposure to onset of symptoms is typically around five days, but may range from two to 14 days (Velavan and Meyer, 2020). 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).

Transmission



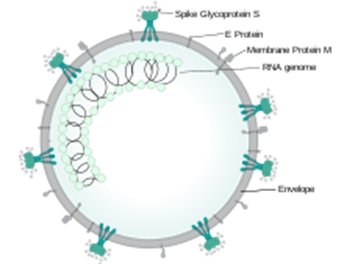
Respiratory droplets produced when a man is sneezing visualised using Tyndall scattering

Some details about how the disease is spread are still being determined (CDC, 2020). The WHO and the US Centers for Disease Control and Prevention (CDC) say it is primarily spread during close contact and by small droplets produced when people cough, sneeze or talk; (CDC, 2020) with close contact being within 1–3 m (3 ft 3 in–9 ft 10 in) (WHO, 2020). A study in Singapore found that an uncovered cough can lead to droplets travelling up to 4.5 meters (15 feet) (Loh *et al.,* 2020). A second study, produced during the 2020 pandemic, found that advice on the distance droplets could travel might be based on old 1930s research which ignored the protective effect and speed of the warm moist outbreath surrounding the droplets. This study found that an uncovered cough or sneeze can travel up to 8.2 metres (27 feet) (Bourouiba and Lydia, 2020).

Respiratory droplets may also be produced while breathing out, including when talking. Though the virus is not generally airborne (WHO, 2020). The National Academy of Science has suggested that bioaerosol transmission may be possible and air collectors positioned in the hallway outside of people's rooms yielded samples positive for viral RNA (NAP, 2019).The droplets can land in the mouths or noses of people who are nearby or possibly be inhaled into the lungs (CDC, 2020). Some medical procedures such as intubation and cardiopulmonary resuscitation (CPR) may cause respiratory secretions to be aerosolised and thus result in airborne spread (IPC, 2019). It may also spread when one touches a contaminated surface, known as fomite transmission, and then touches ones eyes, nose or mouth (WHO, 2020). While there are concerns it may spread by feces, this risk is believed to be low (WHO, 2020).

detectable for one day on cardboard, for up to three days on plastic (polypropylene) and stainless steel (AISI 304) and for up to four hours on 99% copper (Van *et al.,* 2020). This, however, varies based on the humidity and temperature (Moriyama *et al.,* 2020). Surfaces may be decontaminated with a number of solutions (within one minute of exposure to the disinfectant to achieve a 4 or more log reduction), including 78–95% ethanol (alcohol used in spirits), 70–100% 2-propanol (isopropyl alcohol), the combination of 45% 2-propanol with 30% 1-propanol, 0.21% sodium hypochlorite (bleach), 0.5% hydrogen peroxide, or 0.23–7.5% povidone-iodine. Soap and detergent are also effective if correctly used; soap products degrade the virus' fatty protective layer, deactivating it, as well as freeing them from skin and other surfaces.[63] Other solutions, such as benzalkonium chloride and chlorhexidine gluconate (a surgical disinfectant), are less effective (Kampf *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 (Andersen *et al*., 2020). Outside the human body, the virus is killed by household soap, which bursts its protective bubble (Salehi *et al.,* 2020).

Diagnosis



test kit for COVID-19 (CDC, 2020).

The WHO has published several testing protocols for the disease (WHO, 2020). The standard method of testing is real-time reverse transcription polymerase chain reaction (rRT-PCR). (CDC, 2020). The test is typically done on respiratory samples obtained by a nasopharyngeal swab, however a nasal swab or sputum sample may also be used (CDC, 2020). Results are generally available within a few hours to two days (Brueck, 2020). Blood tests can be used, but these require two blood samples taken two weeks apart and the results have little immediate value (CDC, 2020). Chinese scientists were able to isolate a strain of the coronavirus and publish the genetic sequence so laboratories across the world could independently develop polymerase chain reaction (PCR) tests to detect infection by the virus (Cohen and Normile, 2020). As of 4 April 2020, antibody tests (which may detect active infections and whether a person had been infected in the past) were in development, but not yet widely used (Petherick and Anna, 2020). The FDA approved the first point-of-care test on 21 March 2020 for use at the end of that month (CDC, 2020).

Diagnostic guidelines released by Zhongnan Hospital of Wuhan University suggested methods for detecting infections based upon clinical features and epidemiological risk. These involved identifying people who had at least two of the following symptoms in addition to a history of travel to Wuhan or contact with other infected people: fever, imaging features of pneumonia, normal or reduced white blood cell count or reduced lymphocyte count (Jin *et al.,* 2020).

A March 2020 review concluded that chest X-rays are of little value in early stages, whereas CT scans of the chest are useful even before symptoms occur (Salehi *et al.,* 2020). Typical features on CT include bilateral multilobar ground-glass opacificities with a peripheral, asymmetric and posterior distribution (Salehi *et al.,* 2020). Subpleural dominance, crazy paving (lobular septal thickening with variable alveolar filling) and consolidation develop as the disease evolves (lee *et al*., 2020). As of March 2020, the American College of Radiology recommends that "CT should not be used to screen for or as a first-line test to diagnose COVID-19" (ACR, 2020).

Reinfection

As of March 2020, it was unknown if past infection provides effective and long-term immunity in people who recover from the disease (BSI, 2020). Immunity is seen as likely, based on the behaviour of other coronaviruses, but cases in which recovery from COVID-19 have been followed by positive tests for coronavirus at a later date have been reported (Omer *et al.,* 2020). These cases are believed to be worsening of a lingering infection rather than re-infection (Omer *et al*., 2020).

Epidemiology

Several measures are commonly used to quantify mortality (PFE, 2020) These numbers vary by region and over time and are influenced by the volume of testing, healthcare system quality, treatment options, time since initial outbreak and population characteristics such as age, sex and overall health. (Ritchie *et al*., 2020). In late 2019, WHO assigned the emergency ICD-10 disease codes U07.1 for deaths from lab-confirmed SARS-CoV-2 infection and U07.2 for deaths from clinically or epidemiologically diagnosed COVID-19 without lab-confirmed SARS-CoV-2 infection (WHO, 2020).

The death-to-case ratio reflects the number of deaths divided by the number of diagnosed cases within a given time interval. Based on Johns Hopkins University statistics, the global death-to-case ratio is 6.0% (89,915/1,502,618) as of 9 April 2020 (CSSE, 2020). The number varies by region (Lazzerini *et al*., 2020).

Other measures include the case fatality rate (CFR), which reflects the percent of diagnosed individuals who die from a disease, and the infection fatality rate (IFR), which reflects the percent of infected individuals (diagnosed and undiagnosed) who die from a disease. These statistics are not time bound and follow a specific population from infection through case resolution. A number of academics have attempted to calculate these numbers for specific populations (Castiglione *et al.,* 2020). In the epicentre of the outbreak in Italy, Castiglione d'Adda, a small village of 4500, 80 (1.8%) are already dead. Most people in the village appear to have developed antibodies and plausible immunity, most did so without being diagnosed, and many did not have symptoms (Castiglione *et al*., 2020). An investigation is underway to test the entire population to learn more about the disease (Galli *et al.,* 2020).

Non-Human Cases

While the disease is believed to be zoonotic in origin, humans appear to be capable of transmitting the virus to some other animals as well. A domestic cat in Liège was tested positive after it started showing symptoms (diarrhoea, vomiting, shortness of breath) a week later than its owner, who was also positive. Tigers at the Bronx Zoo tested positive for the virus and showed symptoms of COVID-19, including a dry cough and loss of appetite (Goldstein and Joseph, 2020)

Nomenclature

The World Health Organization announced in February 2020 that COVID-19 is the official name of the disease. World Health Organisation chief Tedros Adhanom Ghebreyesus explained that CO stands for corona, VI for virus and D for disease, while 19 is for when the outbreak was first identified: 31 December 2019 (NCD, 2020). The name had been chosen to avoid references to a specific geographical location (e.g. China), animal species or group of people, in line with international recommendations for naming aimed at preventing stigmatisation (WHO, 2020).

The virus that causes COVID-19 is named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (WHO, 2020). The WHO additionally uses "the COVID-19 virus" and "the virus responsible for COVID-19" in public communications (WHO, 2020). Coronaviruses were named in 1968 for their appearance in electron micrographs which was reminiscent of the solar corona, corōna meaning crown in Latin (Merriam, 2020). Both the disease and virus are commonly referred to as "coronavirus".

During the initial outbreak in Wuhan, China, the virus and disease were commonly referred to as "coronavirus" and "Wuhan coronavirus" (McNeil *et al*., 2020). In January 2020, WHO recommended 2019-nCov and 2019-nCoV acute respiratory disease as interim names for the virus and disease in accordance with 2015 guidance against using locations in disease and virus names (WHO, 2020). The official names COVID-19 and SARS-CoV-2 were issued on 11 February 2020 (WHO, 2020).

Vaccine

There is no available vaccine, but various agencies are actively developing vaccine candidates. Previous work on SARS-CoV is being utilised because SARS-CoV-2 and SARS-CoV both use the ACE2 receptor to enter human cells (Cascella *et al.,* 2020). 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.,* 2020).

Mortuary factors

Adequate ventilation is need where HG3 autopsies are being performed with enough separation from the rest of the mortuary. Either whole room ventilation or down-drafts at the work stations are acceptable (Lucas, 2010) Any electric bone saws used should have a vacuum that isolates aerosolised particles. It is preferable to have an isolated high-risk facility for performing HG3 autopsies, although this is not compulsory (HSE, 2020). All essential equipment should be brought at the start of the postmortem examination (eg, sample receptacles, culture bottles and so on) to eliminate the need to leave and re-enter the workspace. Further information may be found in the appropriate National Health Service guidance documents (NBS, 2005).

The team available for these high-risk, postmortem examinations best includes the pathologist, the anatomic pathology technician (APT) and a third circulator. The presence of a circulator is beneficial but not essential (HSE, 2020). Suitably experienced autopsy pathology trainees (as assessed by senior staff) may be involved in HG3 autopsies with adequate supervision. No specific infection risk to pregnant trainees has been identified; however, they may decide not to undertake autopsy work, and this should be discussed with the deanery.

Performance of the autopsy in HG3 infections

Several techniques undertaken at autopsy can reduce the risks encountered by HG3 infections. Personnel must be adequately trained. For APTs, this exposure should be in line with their curriculum and standardised training under the Royal Society for Public Health. For pathology trainees, this is at the discretion of senior staff. Sharps injuries can be reduced by minimising sharps in the workspace, using round-ended scissors, blunt-ended PM40 blades and having only a single operator working in the body cavity at a time (Osborn *et al.,* 2020). Fresh organs should be sliced while being stabilised with a sponge on a solid surface. Needles should be placed in sharps bins and never resheathed.

Molecular immune pathogenesis and diagnosis of COVID-19

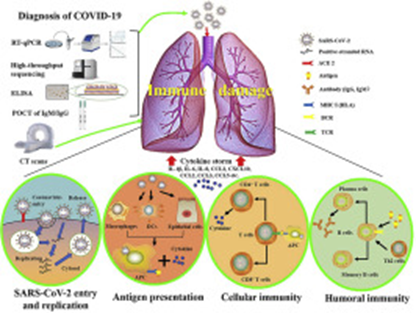
Highlights

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.

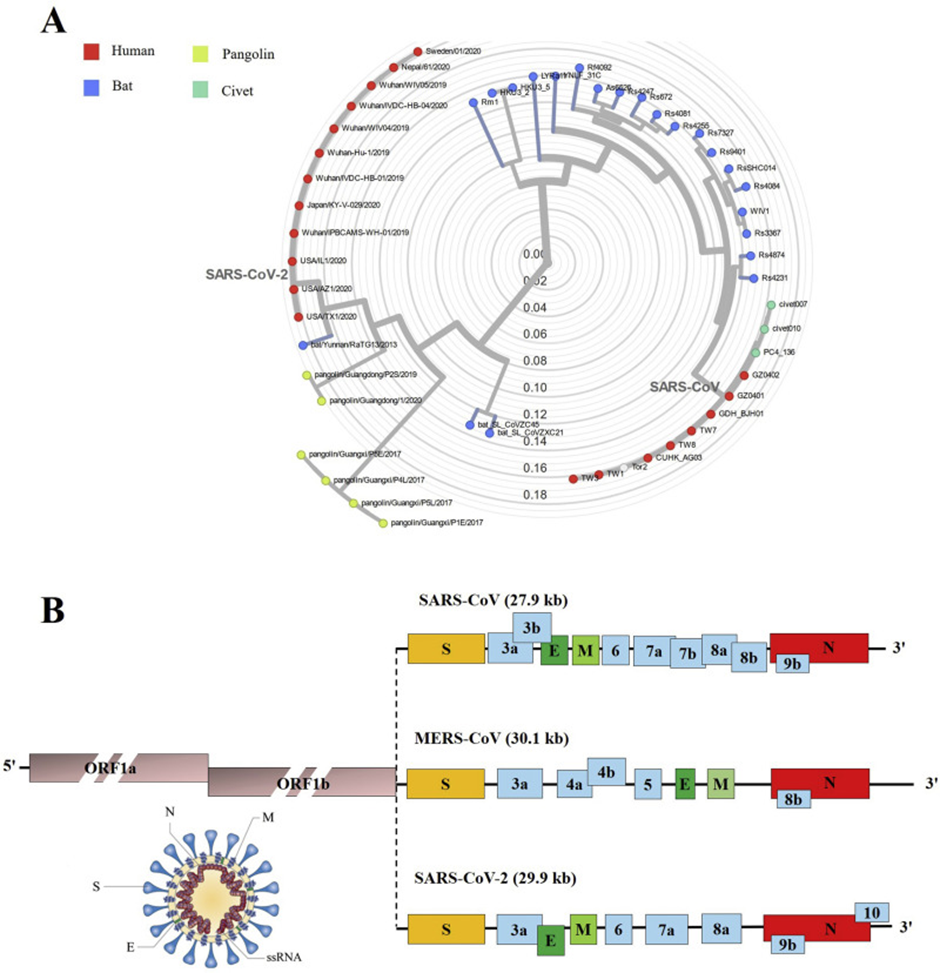
RT-PCR and CT scans are significant for the diagnosis of SARS-CoV-2 infection, and drugs and vaccines against SARS-CoV-2 are being developed.

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.



Virology of SARS-CoV-2

Coronaviruses are enveloped viruses with a positive sense single-stranded RNA genome (26–32 kb) (Wong *et al*., 2016). Four coronavirus genera (α, β, γ, δ) have been identified so far, with human coronaviruses (HCoVs) detected in the α coronavirus (HCoV-229E and NL63) and β coronavirus (MERS-CoV, SARS-CoV, HCoV-OC43 and HCoV-HKU1) general (Perlman and Netland, 2009). In late December 2019, patients presenting with cough, fever, and dyspnea with acute respiratory distress syndrome (ARDS) due to an unidentified microbial infection were reported in Wuhan, China. Virus genome sequencing of five patients with pneumonia hospitalized from December 18 to December 29, 2019, revealed the presence of a previously unknown β-CoV strain in all of them (Lu *et al*., 2020). This isolated novel β-CoV shows 88% identity to the sequence of two bat-derived severe acute respiratory syndromes (SARS)-like coronaviruses, bat-SL-CoVZC45 and bat-SL-CoVZXC21, and about 50% identity to the sequence of MERS-CoV (Lu *et al.,* 2020). The novel β-CoV was then named “SARS-CoV-2” by the International Virus Classification Commission.



(A) This phylogeny shows evolution of SARS-like β-coronaviruses including samples from human (n = 20), bat (n = 22), civet (n = 3) and pangolin (n = 6). The phylogenetic tree of complete genome sequences of coronaviruses was obtained and analyzed with Nextstrain (https://github.com/blab/sars-like-cov). (B) Coronaviruses form enveloped and spherical particles of 100–160 nm in diameter. They contain a positivesense single stranded RNA (ssRNA) genome of 26–32 kb in size. In SARS-CoV, MERS-CoV and SARS-CoV-2, the 5′-terminal two-thirds of the genome ORF1a/b encodes polyproteins, which form the viral replicase transcriptase complex. The other ORFs on the one-third of the genome encode four main structural proteins: spike (S), envelope (E), nucleocapsid (N) and membrane (M) proteins, as well as several accessory proteins.

Patients with COVID-19 show clinical manifestations including fever, nonproductive cough, dyspnea, myalgia, fatigue, normal or decreased leukocyte counts, and radiographic evidence of pneumonia (Wang *et al.,* 2020), which are similar to the symptoms of SARS-CoV and MERS-CoV infections (Guan *et al*., 2020). Hence, although the pathogenesis of COVID-19 is poorly understood, the similar mechanisms of SARS-CoV and MERS-CoV still can give us a lot of information on the pathogenesis of SARS-CoV-2 infection to facilitate our recognition of COVID-19. Clinical diagnosis of COVID-19 is mainly based on epidemiological history, clinical manifestations and some auxiliary examinations, such as nucleic acid detection, CT scan, immune identification technology (Point-of-care Testing (POCT) of IgM/IgG, enzyme-linked immunosorbent assay (ELISA)) and blood culture. However, the clinical symptoms and signs of patients infected with SARS-CoV-2 are highly atypical, including respiratory symptoms, cough, fever, dyspnea, and viral pneumonia. Therefore, auxiliary examinations are necessary for the diagnosis of COVID-19, just as the epidemiological history.

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_(medical)) 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)

Preventive measures to reduce the chances of infection include staying at home, avoiding crowded places, washing hands with soap and water often and for at least 20 seconds, practising good respiratory hygiene and avoiding touching the eyes, nose or mouth with unwashed hands (CDC, 2020). The CDC recommends covering the mouth and nose with a tissue when coughing or sneezing and recommends using the inside of the elbow if no tissue is available (CDC, 2020). They also recommend proper hand hygiene after any cough or sneeze (CDC, 2020). Social distancing strategies aim to reduce contact of infected persons with large groups by closing schools and workplaces, restricting travel and cancelling mass gatherings (Maragakis, 2020) Distancing guidelines also includes that people stay at least 6 feet (1.8 m) apart (Parker and Tara, 2020).

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).

According to the WHO, the use of masks is recommended only if a person is coughing or sneezing or when one is taking care of someone with a suspected infection (WHO, 2020). Some countries also recommend healthy individuals to wear face masks, including China (HNC, 2020) Hong Kong, Thailand, Czech Republic, and Austria. In order to meet the need for masks, the WHO estimates that global production will need to increase by 40%. Hoarding and speculation have worsened the problem, with the price of masks increasing sixfold, N95 respirators tripled, and gowns doubled (WHO, 2020). Some health experts consider wearing non-medical grade masks and other face coverings like scarves or bandanas a good way to prevent people from touching their mouths and noses, even if non-medical coverings would not protect against a direct sneeze or cough from an infected person.

Those diagnosed with COVID-19 or who believe they may be infected are advised by the CDC to stay home except to get medical care, call ahead before visiting a healthcare provider, wear a face mask before entering the healthcare provider's office and when in any room or vehicle with another person, cover coughs and sneezes with a tissue, regularly wash hands with soap and water and avoid sharing personal household items (CDC, 2020). The CDC also recommends that individuals wash hands often with soap and water for at least 20 seconds, especially after going to the toilet or when hands are visibly dirty, before eating and after blowing one's nose, coughing or sneezing. It further recommends using an alcohol-based hand sanitiser with at least 60% alcohol, but only when soap and water are not readily available (CDC, 2020).

For areas where commercial hand sanitisers are not readily available, the WHO provides two formulations for local production. In these formulations, the antimicrobial activity arises from ethanol or isopropanol. Hydrogen peroxide is used to help eliminate bacterial spores in the alcohol; it is "not an active substance for hand antisepsis". Glycerol is added as a humectant (WHO, 2020).

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).

Personal protective equipment

Precautions must be taken to minimise the risk of virus transmission, especially in healthcare settings when performing procedures that can generate aerosols, such as intubation or hand ventilation (Cheung *et al*., 2020). For healthcare professionals caring for people with COVID-19, the CDC recommends placing the person in an Airborne Infection Isolation Room (AIIR) in addition to using standard precautions, contact precautions and airborne precautions (CDC, 2020)

CDC outlines the specific guidelines for the use of personal protective equipment (PPE) during the pandemic.The recommended gear includes: Respirator or facemaskGownMedical glovesEye protection

When available, respirators (instead of facemasks) are preferred. N95 respirators are approved for industrial settings but the FDA has authorised the masks for use under an Emergency Use Authorisation (EUA). They are designed to protect from airborne particles like dust but effectiveness against a specific biological agent is not guaranteed for off-label uses.When masks are not available, the CDC recommends using face shields or, as a last resort, homemade masks (CDC, 2020).

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.

Options for ARDS

Therapy

Recommendations

High-flow nasal oxygen

For SpO2 <93%. May prevent the need for intubation and ventilation

Tidal volume

6mL per kg and can be reduced to 4mL/kg

Plateau airway pressure

Keep below 30 cmH2O if possible (high respiratory rate (35 per minute) may be required)

Positive end-expiratory pressure

Moderate to high levels

Prone positioning

For worsening oxygenation

Fluid management

Goal is a negative balance of 0.5–1L per day

Antibiotics

For secondary bacterial infections

Glucocorticoids

Not recommended

Experimental treatment

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.

In this special resource section, you'll learn about coronaviruses, find resources related to the current outbreak, and discover the steps you should take to prepare your family should a viral outbreak happen in your community.

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.

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