TOPIC: AETIOLOGY OF COVID-19

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**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 2019–2020 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. 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). More than 1.5 million cases have been reported in more than 200 countries and territories, resulting in more than 89,900 deaths. More than 339,000 people have recovered. 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 mostly 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). 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. 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. 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). 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).

**Transmission**

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). 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). 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). It may also spread when one touches a contaminated surface, known as fomite transmission, and then touches one’s eyes, nose or mouth (WHO, 2020). While there are concerns it may spread by faeces, 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. 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.

**Diagnosis**

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). 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. 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).

**PATHOGEGENESIS**

Patients with COVID-19 show clinical manifestations which include fever, nonproductive cough, dyspnea, myalgia, fatigue, normal or decreased leukocyte counts, and radiographic evidence of pneumonia (Xiaowei et al., 2020). Which are similar to the symptoms of SARS-CoV and MERS-CoV infections (Xiaowei et al., 2020). Other 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. 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. The findings were non-specific and included oedema, pneumocyte hyperplasia, focal inflammation and multinucleated giant cell formation while no hyaline membranes were seen. 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. 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. The inflammation was predominantly lymphocytic, and multinucleated giant cells were seen alongside large atypical pneumocytes, although no definitive viral inclusions were noted.

**HISTOPATHOLOGY OF COVID-19**

The pathological features of COVID-19 greatly resemble those seen in SARS and Middle Eastern respiratory syndrome (MERS) coronavirus infection (Zhe Xu et al., 2020). In addition, the liver biopsy specimens of the patient with COVID-19 showed moderate micro vesicular steatosis and mild lobular and portal activity (Zhe Xu et al., 2020), indicating the injury could have been caused by either SARS-CoV-2 infection or drug-induced liver injury (Zhe Xu et al., 2020). Moreover, there was an increased concentration of highly pro inflammatory CCR6+ Th17 in CD4 T cells Additionally, CD8 T cells were found to harbor high concentrations of cytotoxic granules, in which 31·6% cells were perforin positive, 64·2% cells were granulysin positive, and 30·5% cells were granulysin and perforin double-positive (Zhe Xu et al., 2020) Our results imply that over activation of T cells, manifested by increase of Th17 and high cytotoxicity of CD8 T cells, accounts for, in part, the severe immune injury in this patient.

Although corticosteroid treatment is not routinely recommended to be used for SARS-CoV-2 pneumonia (Zhe Xu et al., 2020), according to our pathological findings of pulmonary oedema and hyaline membrane formation, timely and appropriate use of corticosteroids together with ventilator support should be considered for the severe patients to prevent ARDS development. Lymphopenia is a common feature in the patients with COVID-19 and might be a critical factor associated with disease severity and mortality (Zhe Xu et al., 2020). Our clinical and pathological findings in this severe case of COVID-19 can not only help to identify a cause of death, but also provide new insights into the pathogenesis of SARS-CoV-2-related pneumonia, which might help physicians to formulate a timely therapeutic strategy for similar severe patients and reduce mortality (Zhe Xu et al., 2020).

**CURRENT POTENTIAL THERAPIES OF COVID-19**

Some medical professionals recommend paracetamol (acetaminophen) over ibuprofen for first-line use. 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. There is no proof that any drug can cure or prevent infection with the coronavirus (Denise et al., 2020). But in the face of an exploding pandemic with a frightening death toll, people are desperate for a bit of hope, a chance to believe there is something that will help (Denise et al., 2020).

**Personal protective equipment**

Precautions must be taken to minimize the risk of virus transmission, especially in healthcare settings when performing procedures that can generate aerosols, such as intubation or hand ventilation. 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 facemask, Gown, Medical gloves, Eye protection. 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. Staying aware of the current situation and actively working to maintain your overall health and wellbeing are the best steps to take right now.

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