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**COURSE: ANA 404(HISTOPATHOLOGYS); WRITE A COMPREHENSIVE REIEW OF THE AETIOLOGY OF COVID-19**

**PATHOGENEIS OF COVID-19**

Coronavirus is one of the major pathogens that primarily targets the human respiratory system. Previous outbreaks of coronaviruses (CoVs) include the severe acute respiratory syndrome (SARS)-CoV and the Middle East respiratory syndrome (MERS)-CoV which have been previously characterized as agents that are a great public health threat. In late December 2019, a cluster of patients was admitted to hospitals with an initial diagnosis of pneumonia of an unknown etiology. These patients were epidemiologically linked to a seafood and wet animal wholesale market in Wuhan, Hubei Province, China (Bogoch *et al.,* 2020). Early reports predicted the onset of a potential Coronavirus outbreak given the estimate of a reproduction number for the 2019 Novel (New) Coronavirus (COVID-19, named by WHO on Feb 11, 2020) which was deemed to be significantly larger than 1 (ranges from 2.24 to 3.58), (S. Zhao *et al.,* 2020).

 The severe symptoms of COVID-19 are associated with an increasing numbers and rate of fatalities specially in the epidemic region of China. On January 22, 2020, the China National Health Commission reported the details of the first 17 deaths and on January 25, 2020 the death cases increased to 56 deaths. The percentage of death among the reported 2684 cases of COVID-19 was approximately 2.84% as of Jan 25, 2020 and the median age of the deaths was 75 (range 48–89) years (W. Wang *et al.,* 2020).

Patients infected with COVID-19 showed higher leukocyte numbers, abnormal respiratory findings, and increased levels of plasma pro-inflammatory cytokines. One of the COVID-19 case reports showed a patient at 5 days of fever presented with a cough, coarse breathing sounds of both lungs, and a body temperature of 39.0 °C. The patient's sputum showed positive real-time polymerase chain reaction results that confirmed COVID-19 infection. The laboratory studies showed leucopenia with leukocyte counts of 2.91 × 10^9 cells/L of which 70.0% were neutrophils. Additionally, a value of 16.16 mg/L of blood C-reactive protein was noted which is above the normal range (0–10 mg/L). High erythrocyte sedimentation rate and D-dimer were also observed (J. Lei *et al.,* 2020). The main pathogenesis of COVID-19 infection as a respiratory system targeting virus was severe pneumonia, RNAaemia, combined with the incidence of ground-glass opacities, and acute cardiac injury. Significantly high blood levels of cytokines and chemokines were noted in patients with COVID-19 infection that included IL1-β, IL1RA, IL7, IL8, IL9, IL10, basic FGF2, GCSF, GMCSF, IFNγ, IP10, MCP1, MIP1α, MIP1β, PDGFB, TNFα, and VEGFA. Some of the severe cases that were admitted to the intensive care unit showed high levels of pro-inflammatory cytokines including IL2, IL7, IL10, GCSF, IP10, MCP1, MIP1α, and TNFα that are reasoned to promote disease severity (C. Huang *et al.,* 2020).

**HISTOPATHOLOGICAL FEATURES OF COVID-19**

COVID-19 is caused by SARS-CoV-2, a betacoronavirus. It is comprised of a single-stranded ribonucleic acid (RNA) structure that belongs to the Coronavirinae subfamily, part of the Coronaviridae family.Sequence analysis of SARS-CoV-2 has shown a structure typical to that of other coronaviruses (Fig. 2), and its genome has been likened to a previously identified coronavirus strain that caused the SARS outbreak in 2003 [54]. Structurally, the SARS coronavirus (SARS-CoV) has a well-defined composition comprising 14 binding residues that directly interact with human angiotensin-converting enzyme 2. Of these amino acids, 8 have been conserved in SARS-CoV-2 [55]. In humans, coronaviruses were thought to cause mild respiratory infections until the identification of SARS-CoV and MERS coronavirus (MERS-CoV). Although the exact pathophysiological mechanisms underlying the emergence of SARS-CoV-2 are unknown (due to pending laboratory trials), genomic similarities to SARS-CoV could help to explain the resulting inflammatory response that may lead to the onset of severe pneumonia [55]. Until these laboratory trials are initiated, the precise mechanism of SARS-CoV-2 remains hypothetical.

**THE CURRENT POTENTIAL THERAPIES TO ADDRESS COVID-19**

The person-to-person transmission of COVID-19 infection led to the isolation of patients that were administered a variety of treatments. At present, there are no specific antiviral drugs or vaccine against COVID-19 infection for potential therapy of humans. The only option available is using broad-spectrum antiviral drugs like Nucleoside analogues and also HIV-protease inhibitors that could attenuate virus infection until the specific antiviral becomes available. The treatment that have so far been attempted showed that 75 patients were administrated existing antiviral drugs. The course of treatment included twice a day oral administration of 75 mg oseltamivir, 500 mg lopinavir, 500 mg ritonavir and the intravenous administration of 0·25 g ganciclovir for 3–14 days (N. Chen *et al.,* 2020). Another report showed that the broad-spectrum antiviral remdesivir and chloroquine are highly effective in the control of 2019-nCoV infection in vitro. These antiviral compounds have been used in human patients with a safety track record. Thus, these therapeutic agents can be considered to treat COVID-19 infection (M. Wang *et al.,* 2020). Furthermore, there are a number of other compounds that are in development. These include the clinical candidate EIDD-2801 compound that has shown high therapeutic potential against seasonal and pandemic influenza virus infections and this represents another potential drug to be considered for the treatment of COVID-19 infection (M. Toots *et al.,* 2020). Along those lines, until more specific therapeutics become available, it is reasonable to consider more broad-spectrum antivirals that provide drug treatment options for COVID-19 infection include Lopinavir/Ritonavir, Neuraminidase inhibitors, peptide (EK1), RNA synthesis inhibitors. It is clear however, that more research is urgently needed to identify novel chemotherapeutic drugs for treating COVID-19 infections. In order to develop pre-and post-exposure prophylaxis against COVID-19, there is an urgent need to establish an animal model to replicate the severe disease currently observed in humans. Several groups of scientists are currently working hard to develop a nonhuman primate model to study COVID-19 infection to establish fast track novel therapeutics and for the testing of potential vaccines in addition to providing a better understanding of virus-host interactions.

**FUTURE OF COVID-19 ON PUBLIC HEALTH**

First, close monitoring is needed of changes in epidemiology and of the effectiveness of public health strategies and their social acceptance.

Second, continued evolution is needed of enhanced communication strategies that provide general populations and vulnerable populations most at risk with actionable information for self-protection, including identification of symptoms, and clear guidance for treatment seeking.

Third, continued intensive source control is needed in the epicentre in China—ie, isolation of patients and persons testing positive for COVID-19, contact tracing and health monitoring, strict health facility infection prevention and control, and use of other active public health control interventions with continued active surveillance and containment activities at all other sites where outbreaks are occurring in China.

Fourth, continued containment activities are needed around sites outside China where there are infected people and transmission among contacts, with intensive study to provide information on transmissibility, means of transmission, and natural history of infection, with regular reporting to WHO and sharing of data.

Fifth, intensified active surveillance is needed for possible infections in all countries using the WHO-recommended surveillance case definition.11

Sixth, preparation for resilience of health systems in all countries is needed, as is done at the time of seasonal influenza, anticipating severe infections and course of disease in older people and other populations identified to be at risk of severe disease.

Seventh, if widespread community transmission is established, there should then be consideration of a transition to include mitigation activities, especially if contact tracing becomes ineffective or overwhelming and an inefficient use of resources. Examples of mitigation activities include cancelling public gatherings, school closure, remote working, home isolation, observation of the health of symptomatic individuals supported by telephone or online health consultation, and provision of essential life support such as oxygen supplies, mechanical ventilators and extracorporeal membrane oxygenation (ECMO) equipment.

Eighth, serological tests need to be developed that can estimate current and previous infections in general populations.

Finally, continued research is important to understand the source of the outbreak by study of animals and animal handlers in markets to provide evidence necessary for prevention of future coronavirus outbreaks.

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