**Matric No:** 16/MHS06/036

**Course Code:** MLS 406 (Virology)

**Virology Open Test**

Discuss the origin, etiology, structure and pathophysiology of COVID-19.

**Answers**

**Coronavirus disease 2019 (COVID-19)** is an infectious respiratory disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) a novel betacoronavirus of the same subgenus as SARS-CoV. The disease was first identified in December 2019 in Wuhan, the capital of China’s Hubei province, and has since spread globally with clinical manifestations ranging from mild respiratory symptoms to severe pneumonia and a fatality rate estimated around 2%, resulting in the ongoing 2019-2020 coronavirus pandemic. 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.

**Origin**

The coronavirus disease 2019 (COVID-19) is a highly transmittable and pathogenic viral infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which emerged in Wuhan, China and spread around the world. At the end of 2019, Wuhan an emerging business hub of China experienced an outbreak of a novel coronavirus that killed more than eighteen hundred and infected over seventy thousand individuals within the first fifty days of the epidemic. This virus was reported to be a member of the β group of coronaviruses. The novel virus was named as Wuhan coronavirus or 2019 novel coronavirus (2019-nCov) by the Chinese researchers. The International Committee on Taxonomy of Viruses (ICTV) named the virus as SARS-CoV-2 and the disease as COVID-19. The virus infected 120,000 individuals with mortality rate of 2.9% across 109 countries till date. This shows that the transmission rate of SARS-CoV-2 is higher than SARS-CoV and the reason could be genetic recombination event at S protein in the RBD region of SARS-CoV-2 may have enhanced its transmission ability.

Recently, by the end of 2019, WHO was informed by the Chinese government about several cases of pneumonia with unfamiliar etiology. The outbreak was initiated from the Hunan seafood market in Wuhan city of China and rapidly infected more than 50 people. The live animals are frequently sold at the Hunan seafood market such as bats, frogs, snakes, birds, marmots and rabbits. On 12 January 2020, the National Health Commission of China released further details about the epidemic, suggested viral pneumonia. From the sequence-based analysis of isolates from the patients, the virus was identified as a novel coronavirus. Moreover, the genetic sequence was also provided for the diagnosis of viral infection. Initially, it was suggested that the patients infected with Wuhan coronavirus induced pneumonia in China may have visited the seafood market where live animals were sold or may have used infected animals or birds as a source of food. However, further investigations revealed that some individuals contracted the infection even with no record of visiting the seafood market. These observations indicated a human-to-human spreading capability of this virus, which was subsequently reported in more than 100 countries in the world. The human-to-human spreading of the virus occurs due to close contact with an infected person, exposed to coughing, sneezing, respiratory droplets or aerosols. These aerosols can penetrate the human body (lungs) via inhalation through the nose or mouth or inoculation by touching the eyes, nose or mouth with infected hands.

Genomic analysis revealed that SARS-CoV-2 is phylogenetically related to severe acute respiratory syndrome-like (SARS-like) bat viruses, therefore bats could be the possible primary reservoir. The intermediate source of origin and transfer to humans is not known, however, the rapid human to human transfer has been confirmed widely. There is no clinically approved antiviral drug or vaccine available to be used against COVID-19.

**Etiology**

The disease is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It is primarily spread between people during close contact and via respiratory droplets from coughs and sneezes. A study investigating the rate of decay of the virus found no viable viruses after four hours on copper, 24 hours on cardboard, 72 hours on stainless steel, and 72 hours on plastic. However, detection rates did not reach 100% and varied between surface type (limit of detection was 3.33 x 100.5 TCID50 per liter of air for aerosols, 100.5 TCID50 per milliliter of medium for plastic, steel, and cardboard, and 101.5 TCID50 per milliliter of medium for copper). The virus has also been found in faeces, and transmission through faeces is being researched.

The disease spreads faster where people are close together or travel between areas. Travel restrictions can reduce the basic reproduction number (R0) from 2.35 to 1.05, allowing the epidemic to be more manageable.

**Structure**



**Structure of Coronavirus disease 2019 (COVID-19)**

**Pathophysiology**

The **lungs** are the organs most affected by COVID-19 because the virus accesses host cells via the enzyme Angiotensin Concertin Enzyme Type 2 (ACE2), which is most abundant in the type II alveolar cells of the lungs. The virus uses a special surface glycoprotein called a “spike” (peplomer) to bind to the ACE2 and is then engulfed into the host cell. On entering the cell, it releases **RNA** (*Positive Sense Single Stranded RNA, +ssRNA*) into the cytoplasm of the type II pneumocytes which uses the host cell ribosomes and translates them into proteins and uses the enzyme RNA-dependent RNA polymerase (RDRP) to synthesize more +ssRNA. Enzyme called Proteinases which are specific are used to cleave the poly-proteins into the different viral components that make up the nuclear capsid, enzymes and spike proteins.

The cells RDRP and the cells ribosomes are used to make proteins that make up components of the viral protein structure. Synthesis of lots of +ssRNA are incorporated into the combination of nuclear capsid, spike proteins and enzymes and are then budded off of the type II pneumocyte making lots of virus particles which in the process destroys the cell. Damage to the cell results in the release of specific inflammatory mediators which stimulates the macrophages to secrete specific cytokines – Interleukine-1 (IL-1), Interleukine-6 (IL-6) and TNF-α that cause problems. The cytokines enter the bloodstream and cause vasodilation – Smooth Muscle dilates but increases the capillary permeability by causing endothelial cells to contract.

This results in the fluid, plasma leaking into the interstitial spaces potentially the alveoli. Accumulation of fluid outside the alveoli leads to compression of the alveoli. Some fluids also try to get into the alveoli and as this accumulates causes **Alveolar Edema** which causes the surfactant to drown out.

**NB:** Surfactant decrease surface tension within the alveoli and reduces collapsing pressure.

Drowning out the surfactant causes increase in surface tension. Laplace law states that:

**P = 2T / R**

As surface tension increases, the collapsing pressure increases resulting in alveolar collapse which increases **Work of Breathing**.

Accumulation of fluid outside the alveolar impairs the respiratory membrane allowing for gas exchange, decrease in gas exchange leads to **Hypoxemia** which is very dangerous especially when it becomes refractory.

All the inflammatory mediators bring in lots of neutrophils which come to the site of the inflammation and due to the numerous inflammations they try to destroy the virus. When they start to try to destroy the virus, they release **Reactive Oxygen Species** and **Proteases** which might destroy some of the virus but also end up damaging the type I and type II alveoli cells which leads in reduction in gas exchange and reduced surfactant levels respectively. As all the cells start to get destroyed, they get sloughed off to the center of the alveolus. In the center of the alveolus, there is fluid, protein deposition, cellular debris – type I and type II pneumocyte cellular debris, macrophages, neutrophils leading to a **Consolidation**. This consolidation also alters gas exchange leading to hypoxemia. The Reactive Oxygen Species damages the type I and type II alveolar cells leading to alveolar collapse also.

The release of lots of IL-1 and IL-6 travels to the CNS where the hypothalamus is and controls temperature. IL-1, IL-6 and TNF-α when in high concentrations communicates to the hypothalamus to release specific prostaglandins like PG2 and this resets the thermostat and thereby increases body temperature which leads to **Fever** – one of the most common symptoms. Consolidations and accumulation of these contents inside the alveolus starts to degrade and this gives a **Cough** response which releases productive mucus.

Inflammation of the lung becomes severe and starts leaching into the bloodstream and spreading the Systemic Inflammatory Response starts carrying all over to different parts of the body. This inflammation with the lungs leads to SIRS or starts off as ARDS and progresses to SIRS which potentially leads to septic shock. If the inflammation spreads throughout the circulatory system, it causes increased capillary permeability within the systemic circulation and as fluids start leaking out and start accumulating within the tissue spaces, the **blood volume** decreases and vasodilation of the blood vessels leading to a decrease in **total peripheral resistance** which all lead to reduced **Blood Pressure** – Hypotensive leading to a decrease in the **Perfusion** to multiple different organs leading to **Multiple System Organ Failure (MSOF)**.

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