**NAME: WILLIAMS WENDY**

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TEST:

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

Answer:

The corona virus also known as COVID-19 is an infectious disease caused by a new virus; 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. It is one of a group of viruses causing a range of diseases from common cold to other complex conditions. Individuals with the corona virus either recover from the virus or die.

**ETIOLOGY:**

The corona virus is similar to the SARS virus (severe acute respiratory distress syndrome) the corona virus has a zoonotic effect that means they are first developed in animal before humans. SARS was discovered in 2002 on the surface of bats as its reservoir host and then it mutated and affected‘civet’ and it later affected humans. It is caused by a respiratory related infection. In 2012 another form of the virus detected it was called the MERS (Middle Eastern respiratory syndrome). It was able to mutate from the surface of bats through to its intermediate host this time suspected to be as camels and then to humans. The corona virus known as COVID-19 attaches itself to the surface of bats as its reservoir host and then to an animal known as ‘pangolin’ that serves as its intermediate host and then it attacks humans.

Epidemiology: However the case fatality rate of the corona virus which follows the formulae; no of deaths/total no number of cases \*100= 3.7%. As the denominator increases the case fatality rate will decrease. They are many people who are asymptomatic with the virus that means they show little or no symptoms of the virus. The bat is the known reservoir of the virus through which it passes to an intermediate host and then to humans. Furthermore the reproductive ratio that means the degree of spreadibility entails the ability of an infected person to infect other people. The reproductive ratio has been estimated to 2-3 that means an infected person can transmit the infection to at least 2-3 persons at a time when the droplet comes in contact to their mucus membrane. It however has a wide reproduction rate compared to other viruses.

**ORIGIN:**

In 2003, the Chinese population was infected with a virus causing Severe Acute Respiratory Syndrome (SARS) in Guangdong province. The virus was confirmed as a member of the Beta-coronavirus subgroup and was named SARS-CoV . The infected patients exhibited pneumonia symptoms with a diffused alveolar injury which lead to acute respiratory distress syndrome (ARDS). SARS initially emerged in Guangdong, China and then spread rapidly around the globe with more than 8000 infected persons and 776 deceases. A decade later in 2012, a couple of Saudi Arabian nationals were diagnosed to be infected with another coronavirus. The detected virus was confirmed as a member of coronaviruses and named as the Middle East Respiratory Syndrome Coronavirus (MERS-CoV). The World health organization reported that MERS-coronavirus infected more than 2428 individuals and 838 deaths. MERS-CoV is a member beta-coronavirus subgroup and phylogenetically diverse from other human-CoV. The infection of MERS-CoV initiates from a mild upper respiratory injury while progression leads to severe respiratory disease. Similar to SARS-coronavirus, patients infected with MERS-coronavirus suffer pneumonia, followed by ARDS and renal failure.

Recently, by the end of 2019, WHO was informed by the Chinese government about several cases of pneumonia with unfamiliar origin. The outbreak was initiated from the Hunan seafood market in Wuhan city of China and rapidly infected more than 50 peoples. 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 the human spreading capability of this virus, which was subsequently reported in more than 100 countries in the world. The human to the 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.

**STUCTURE**:

The corona virus comprises of the nucleocapsid protein, the envelop glycoprotein, the RNA, the spikes proteins, the membrane glycoproteins and the lipid bilayer. The coronavirus spike protein is a multifunctional molecular machine that mediates coronavirus entry into host cells. It first binds to a receptor on the host cell surface through its S1 subunit and then fuses viral and host membranes through its S2 subunit. Two domains in S1 from different coronaviruses recognize a variety of host receptors, leading to viral attachment. The spike protein exists in two structurally distinct conformations, prefusion and postfusion. The transition from prefusion to postfusion conformation of the spike protein must be triggered, leading to membrane fusion. Coronaviruses are large, enveloped, positive-stranded RNA viruses. They have the largest genome among all RNA viruses, typically ranging from 27 to 32 kb. The genome is packed inside a helical capsid formed by the nucleocapsid protein (N) and further surrounded by an envelope. Associated with the viral envelope are at least three structural proteins: The membrane protein (M) and the envelope protein (E) are involved in virus assembly, whereas the spike protein (S) mediates virus entry into host cells. Some coronaviruses also encode an envelope-associated hemagglutinin-esterase protein (HE). Among these structural proteins, the spike forms large protrusions from the virus surface, giving coronaviruses the appearance of having crowns (hence their name; *corona* in Latin means crown). In addition to mediating virus entry, the spike is a critical determinant of viral host range and tissue tropism and a major inducer of host immune responses. The coronavirus spike contains three segments: a large ectodomain, a single-pass transmembrane anchor, and a short intracellular tail. The ectodomain consists of a receptor-binding subunit S1 and a membrane-fusion subunit S2. Electron microscopy studies revealed that the spike is a clove-shaped trimer with three S1 heads and a trimeric S2 stalk. During virus entry, S1 binds to a receptor on the host cell surface for viral attachment, and S2 fuses the host and viral membranes, allowing viral genomes to enter host cells. Receptor binding and membrane fusion are the initial and critical steps in the coronavirus infection cycle; they also serve as primary targets for human inventions.

**PATHOPHYSIOLOGY**:

This entails how the virus is transmitted including the pathologic effect of the virus and the physiologic effect of the virus. However the series interval is the period of time when the symptoms starts to when the initially infected person infects another person. The shorter the series interval the less risk of the viral infection. The series interval of COVID-19 is 5-7 days.

The most common means of infection is the respiratory droplets (air borne). It can be transmitted within the range of 3-6 feet from an infected person. The droplets of the infection can survive about 24 hours on surfaces. The air droplets can last in the air for about 3 hours being able to infect anyone that comes within that area. Asymptomatic individuals also have the ability to spread the virus. Once it gets into the respiratory system it attacks the alveolar and attaches to the type 2 pneumocyte cell. The surfactant helps to decrease the surface tension within alveolar and reduces the collapsing pressure. The virus has spike proteins on the body. The spikes of the virus bind on the specific receptors on the type2 pneumocyte binds on the ACE. This binding allows the virus to be engulfed and taken into the cell. Once it is the cell, it releases its single stranded RNA into the cytoplasm of the type 2pneumocyte. Once this is achieved, it can use the host cells ribosome then it can take mRNA and convert it into protein, this is called translation. When translation occurs the single stranded RNA would be converted to protein molecules thereby forming different poly protein molecules. The positive sense single RNA has the ability to use another enzyme called the RNA dependent polymerase i.e. it takes RNA and synthesis RNA. It takes SSSRNA and converts it into more RNA. Therefore SSSRNA with the ribosome cell would lead to the production of protein that will make component of viral structure. Protease is an enzyme that helps to bind the nucleocapsid that helps the formation of the virus. Polyproteins gets converted into all the components of the virus such as nucleocapsid, specific enzymes, and spikes proteins with the presence of the enzyme called protease. This process leads to the production of more viruses and causing damage in the type2 pneumocyte. The damage leads to a release in specific inflammatory mediators and this would stimulate macrophages, causing them to secret cytokines that cause more damage. These cytokines comprise of interleukin 1 and 6. Once they enter the blood stream they cause the endothelial cells to contract thereby increasing permeability causing vasodilation and increase in the capillary permeability. All the plasma will leak into the alveoli causing compression of the alveoli. The presence of fluid in the alveoli is going to cause alveoli oedema, making the alveoli to drown out the surfactant; the surfactant however helps the alveoli to decrease surface tension. The surface tension begins to go up and causing the collapsing of the alveoli. The collapse is going to lead to decreased gas exchange, hypoxemia and increased work of breathing. All the inflammatory mediators also bring in neutrophils. The neutrophils would want to destroy the virus by releasing reactive oxygen specie; this would also cause damage to the type1 and 2 cells alongside the virus. The alveolar would filled with macrophages, neutrophils, fluid, protein deposition, and type 1 and 2 pneumocytes causing consolidation. This would alter the gas exchange process leading to hypoxemia. The release of interleukin 1 and 6 in the blood stream can also travel to the nervous system affecting the hypothalamus, which controls the body temperature, stimulating it and causing it to release specific prostaglandins and it causes an increasing in the body temperature which leads to fever. During these series of processes occurring it can lead to inflammation of the lungs that can cause inflammatory response syndrome or it can lead to septic shock. It can also cause hypotension. This can affect the kidney leading to a high presence of creatine and lack of proper circulation in the kidney. The leaking out of blood and it accumulation in the tissues and vasodilation of the arteriole vessels can cause reduction of blood volume causing profusion to multiple organs resulting in multiple organ failure.

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