MATRIC NUMER; 16/MHS06/053

COURSE CODE; MLS 406

COURSE TITILE; VIROLOGY

VIROLOGY OPEN TEST

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

Answer

Introduction

Coronaviruses belong to the largest group of viruses called the Nidovirales order. Members of this order include the Coronaviridae, Arteriviridae, and Roniviridae families. The Coronvirinae are one of two subfamilies in the Coronaviridae family. Coronavirinae are further subdivided into for groups, the alpha, beta, gamma, and delta coronaviruses. Nowadays, these viruses are divided using phylogenetic clustering. These virus families have animal and human hosts. The Middle Eastern Respiratory Syndrome Coronavirus (MERS-CoV) and Severe Acute Respiratory Coronavirus (SARS-CoV) are examples.

Coronavirus disease (COVID-19) is an infectious disease caused by a newly discovered coronavirus. Most people infected with the COVID-19 virus will experience mild to moderate respiratory illness and recover without requiring special treatment. Older people, and those with underlying medical problems like cardiovascular disease, diabetes, chronic respiratory disease, and cancer are more likely to develop serious illness.

ETIOLOGY

Coronaviruses are enveloped single-stranded RNA viruses that are zoonotic in nature and cause symptoms ranging from those similar to the common cold to more severe respiratory, enteric, hepatic, and neurological symptoms. Other than SARS-CoV-2, there are six known coronaviruses in humans: HCoV-229E, HCoV-

OC43, SARS-CoV, HCoVNL63, HCoV-HKU1, and MERS-CoV . COVID -19 strain has been known to be similar to the SARS virus. It is believed thst this strain underwent a mutation from a zoonotic strain found in a bat, transmitted to another intermediate host, which is a Pangolin, and mutated enough to be able to cause an infection in man, known as COVID-19 infection.

ORIGIN

Coronaviruses are common in certain species of animals, such as cattle and camels. Although the transmission of coronaviruses from animals to humans is rare, this new strain likely came from bats, though one study suggests pangolins may be the origin. Chinese-based researchers say they think the pangolin — a scaly, otherwise harmless mammal that eats ants — may have spread the virus to humans.

Researchers had shown previously that the new coronavirus is most similar to two other bat viruses; in fact, its genomic similarity to these viruses is 88%, which led scientists to believe that bats carried the new virus. Whereas, genomic sequencing was used to compare the DNA of the new coronavirus in humans with that in animals and found a 99% match with pangolins which is a higher DNA match than that of the bat, making the probability that the origin of this particular strain of Corona virus, the COVID-19, most likely originate from pangolins.

STRUCTURE

Nidoviruses contain an infectious, linear, positive-sense RNA genome that is capped and polyadenylated. Based on their genome size, nidoviruses are divided into two groups large and small nidoviruses. Coronaviruses are named for the crown-like spikes on their surface. There are four main sub-groupings of coronaviruses, known as alpha, beta, gamma, and delta.They have enveloped virions (virus particles) that measure approximately 120 nm (1 nm = 10^{-9} metre) in diameter. Club-shaped glycoprotein spikes in the envelope give the viruses a crownlike, or coronal, appearance. The nucleocapsid, made up of a protein shell known as a capsid and containing the viral nucleic acids, is helical or tubular. The coronavirus genome consists of a single strand of positive-sense RNA (ribonucleic acid).

Coronaviruses possess an unusual large RNA genome as well as a unique replication strategy.

Common features of coronaviruses include

(i) a highly conserved genomic organization with a large replicase gene preceding structural and accessory genes,
(ii) Expression of many non-structural genes by ribosomal frameshifting,
(iii) Several unique of unusual enzymatic activities encoded within the large replicase-transcriptase polyprotein, and
(iv) Expression of downstream genes by synthesis of 3'-nested sub-genomic mRNAs.
The typical organization of the genome is
5'-leader-UTR-replicase-S(Spike)-E(Envelope)-M(Membrane)-N(Nucleocapsid)-3'-UTR-poly(A) tail. Accessory genes are interspersed within the structural genes at the 3'-end of the genome.
The synthesis of polypeptide 1ab (pp1ab) involves programmed ribosomal frame shifting during translation of open-reading frame 1a (orf1a). Frame shifting results in a new reading frame that produces a trans-frame protein product.
U_UUA_AAC is a universal frame-shifting site

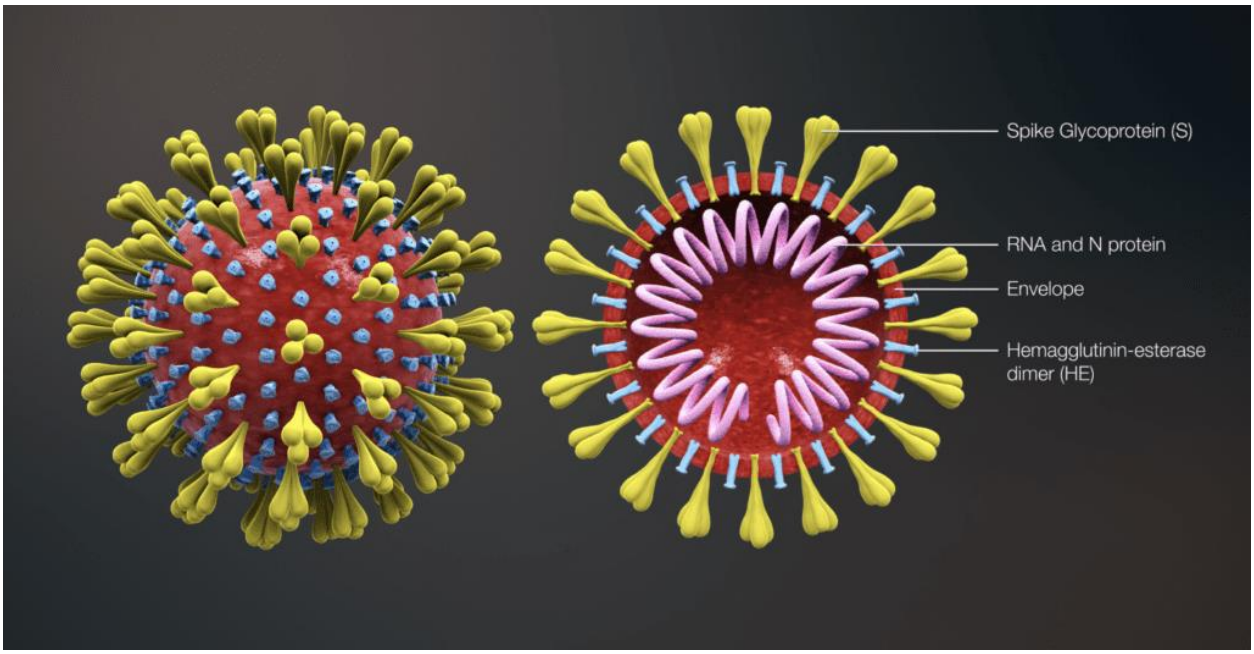

DIAGRAM OF COVID-19 STRUCTURE

PATHOPHYSIOLOGY

The viral agent gain access into the body through two main ways which are

a. fecal oral route

b. respiratory droplets inhaled and inoculated into mucosae

The virus gets into the body and affects the respiratory tract, most particularly the alveoli. In the alveoli, the virus attaches to the type II pneumocytes which is responsible for the production of surfactant that functions as a surface tension reducer in the alveoli. The S- spike proteins bind to specific receptor sites on the type 2 pneumocyte (ACE2). The virus then becomes engulfed into the cell n releases its RNA for replication to occur. The RNA is transcribed using the ribosome of the host cell and then translated which produces polyproteins. These polyproteins are converted into key components of the virus by the enzyme proteins. As replication occurs, the cells are being destroyed and begin to malfunction. The polyproteins cause an inflammatory response and this stimulates the macrophages. The macrophages activate IL-1,IL-6 and TNC- alpha which cause the blood vessels to dilate increasing capillary permeability causing the plasma to leak into the interstitial layer, compressing the alveoli surrounding while also trying to gain access into the alveoli. During this process the concentration of the surfactant begins to reduce by drawing out the surfactant hence increasing surface tension which leads to alveoli collapse leading to a decrease in gaseous exchange causing shortness of breath. The inflammatory mediator (IL1,6 and tumor necrotic factor alpha) attract neutrophils to the site of inflammation trying to destroy the virus by releasing specific substances. In the process of destroying the virus the pneumocytes, (types I&II) are also destroyed leading to poor gaseous exchange and poor surfactant production increasing surface tension and eventually collapsing the alveoli. As the cells are getting destroyed they are being moved to the center, accumulating and forming a consolidation which alters a gaseous exchange leading hypoxemia. The accumulation also results in the coughing of mucous fluids. When the interleukins released in large amounts, the can travel as far as the CNS through the blood and when this occurs the hypothalamus is affected. These mediators cause the hypothalamus to release specific prostaglandins like PGE2 which affect the thermostat causing rise in temperature,

which then leads to fever. Also, the accumulation of substances in the alveoli, when they start to degrade, are going to be coughed up, together with productive mucus. Because of the poor gaseous exchange in the alveoli, the partial pressure of oxygen the lungs (Po2), is low, and when this happens, the chemoreceptors are stimulated and in reflex stimulate the sympathetic nervous system which increases heart rate, Also, in attempt of the SNS to resolve the low oxygen level by increasing the oxygen level, there will be an increase in respiratory rate. The inflammation becomes severe if the immune system cannot fight the virus and hence the inflammation begins to spread leading to systemic inflammatory response syndrome which may lead to septic shock. The blood vessels begin to increase capillary permeability, causing leakage of fluids and accumulating in tissue spaces, decreasing the blood volume, total peripheral resistance is reduced also due to vasodilation and this leads to low blood pressure, leading to perfusion of organs and then multiple organ failure. Some of the organs affected include the kidney, which will be indicated by high creatinine and bun, and the liver which would present with elevated liver enzyme levels (ALT,AST) and bilirubin levels. Without subsequent resolution of the inflammation, multiple system organ failure will occur leading to death of the patient.

References;

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