Virology open test

Mls 406

16/mhs06/024

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Write on etiology,origin,pathiophysiology and structure of Covid 19.

Answer

Introdution:

COVID-19 is an acute respiratory disease caused by novel coronavirus SARS-CoV-2  also known as 2019-nCoV. On March 11, 2020, the World Health Organization (WHO) characterized COVID-19 as a pandemic.Coronaviruses are a large family of viruses that are known to cause illness ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS).

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.COVID-19 coronavirus SARS-CoV-2 belongs to the Betacoronavirus genus originating from bats. Betacoronaviruses can infect mammals, are zoonotic pathogens, and can cause severe respiratory disease in humans. Other viruses in this family are SARS coronavirus and MERS coronavirus. COVID-19 (SARS-CoV-2) has approximately 79% sequence identical to SARS-CoV and 50% to MERS-CoV.In addition, homology modeling shows COVID-19 (SARS-CoV-2)  has a similar receptor-binding domain structure as SARS-CoV which suggests COVID-19 (SARS-CoV-2) uses ACE2 receptor in humans for infection.

Etiology of Covid 19:

Transmission pattern many domestic and wild animals, including camels, cattle, cats, and bats, may serve as hosts for coronaviruses. It is considered that, generally,

animal coronaviruses do not spread among humans.However, there are exceptions, such as SARS and MERS, which are mainly spread though close contact with infected people via respiratory droplets from cough or sneezing. With regard to COVID-19, early patients were reported to have some link to the Huanan Seafood Market in Wuhan, China, suggesting that these early infections were due to animal-to-person transmission. However, later cases were reported among medical staff and others with no history of exposure to that market or visiting Wu- han, which was taken as an indication of human-to- human transmission

Origin of Covid 19:

The coronavirus disease (COVID-19) has been identified as the cause of an outbreak of respiratory illness in Wuhan, Hubei Province, China beginning in December 2019. As of 31 January 2020, this epidemic had spread to 19 countries with 11 791 confirmed cases, including 213 deaths. The World Health Organization has declared it a Public Health Emergency of International Concern. The novel coronavirus originated from the Hunan seafood market at Wuhan, China where bats, snakes, raccoon dogs, palm civets, and other animals are sold, and rapidly spread up to 109 countries. The zoonotic source of SARS-CoV-2 is not confirmed, however, sequence-based analysis suggested bats as the key reservoir. DNA recombination was found to be involved at spike glycoprotein which assorted SARS-CoV (CoVZXC21 or CoVZC45) with the RBD of another Beta CoV, thus could be the reason for cross-species transmission and rapid infection. According to phylogenetic trees, SARS-CoV is closer to SARS-like bat CoVs.

Pathiophysiology of Covid 19:

Pathophysiology:

Mode of Transmission:

1.) Faecal oraL route

2.) Respiratory droplets through coughing or sneezing

-Spreads between 3.6ft.

-Lasts on a surface for 24hrs

-Airborne for 3 hrs

3.) Asymptomatic carriers

Viruses enters into the respiratory system attacks the alveoli by entering and attaching to the type 2 pneumocytes which are structures that produces surfactant while type 1 is for gas exchange.Surfactant decreases the surface tension within the alveoli and reduces the collapsing pressure

The virus has different types of spike protein and the most significantly is the S-Spike which binds on to specific receptors on the type 2 pneumocytes.This receptor is called angiotensin converting enzyme type 2(ACE-2). When it binds the virus to be engulfed and taken into the cell. Once it enters into the cell,it then releases it’s RNA (cause in the structure it has Positive Sense Single Stranded (PSSSRNA) into the cytoplasm of type 2 pneumocytes. Once it released it can use the host cells ribosomes by taking mRNA and convert it into protein(translation) then SSRNA can be converted into specific proteins molecules.PSSSRNA has the ability to use another enzymes called RNA Dependent RNA Polymerase which takes RNA and synthesizes it(SSRNA and converts into more RNA).Proteinase enzymes and specific types that are going to proteolytic clear polyproteins into different viral components making up nuclear capsid enzymes and spike proteins.

SSRNA combines with nuclear capsid enzymes and spike proteins which leaves destroying the type 2 pneumocytes and if damaged is caused it releases specific inflammatory mediators which stimulates the macrophage to secret specific cytokines that causes lot of problems:Interlukin 1,Interlukin 6 and Tumor Necrotic Factor Alpha which enters into the bloodstream and causes endothelial cells to undergo dilation(smooth muscles dilates while increasing capillary permeability by causing endothelial cells contraction increasing the permeability)this leads to vasodilation and increased capillary permeability.All fluids flow out and leaks into the alveoli while some of the fluid try entering the alveoli leading to increased alveoli edema drowning out the sulfactant decreases surface tension and collapsing alveoli impairing alveolar respiratory membrane for gas exchange leading to decreased gas exchange causing hypoxemia and increased work of breathing.All inflammatory mediators brings in a lot of neutrophils which tries to destroy the virus releasing reactogens species and proteases which ends up damaging type 1 and 2 alveoli cells.

The alveolar center is filled up as cells gets destroyed with fluid,protein deposition, debris of type 1 and pneumocytes,macrophages,neutrophils causing consolidation which alters gas exchange process leading to hypoxemia and alveoli collaps also.

Interlukin 1 and 6 released in large amount can travel via blood to CNS and hypothalamus to release specific prostaglandins like PG 2 which helps to reset the thermic thermostat increasing body temperature leading to fever.

Consolidation causes accumulation inside the alveoli and eventually starts to degrade leading to coughing which coughs off productive mucus.Hypoxemia stimulates chemoreceptors which triggers reflex resulting in stimulation of sympathetic nervous system(SNS) causing increased heart rate(IHR) and increased respiration rate(IRR).

Inflammation of the lungs becomes severe leaching into blood stream and spreading,systemic inflammatory response starts carrying it all over to different parts of the body.Systemic inflammatory respiratory syndrome (SIRS) can lead to septic shock if the inflammation spreads throughout the entire circulatory system causing increased capillary permeability with a new systemic circulation as fluids starts leaking out and accumulating within tissue spaces causing decrease in overall blood volume and vasodilation of vessels and decrease in total peripheral resistance leading to decrease blood pressure (hypothensive) and decrease perfusion to multiple organs leading to multiple system organ failure(MSOF).

Ability to get rid of creatinine and blood urine nitrogen is reduced as kidney is not getting enough blood flow leading to increased BUN and Cr to show kidney damage.

Liver is also damaged and starts releasing specific inflammatory enzymes like AST,ALT,Bilirubin or acute phase reactant proteins like CRP,fibrinogen,interlukin 6 which might all be elevated.

Incubation period is from 4 to 14 days.

Structure of Covid 19:

COVID-19 (SARS-CoV-2) Structure

The structure of COVID-19 (SARS-CoV-2) consists of the following: a spike protein (S), hemagglutinin-esterease dimer (HE),  a membrane glycoprotein (M), an envelope protein (E) a nucleoclapid protein (N) and RNA.

1. Spike protein (S) is heavily glycosylated, utilizes an N-terminal signal sequence to gain access to the ER and mediate attachment to host receptors. It is the largest structure and makes the distinct spikes on the surface of the virus. For most coronaviruses, S protein is cleaved by a host cell furin-like protease into two separate polypeptides S1 and S2.
2. RNA is the genome of the virus.
3. Nucleocapsid protein (N) binds to RNA in vitro and is heavily phosphorylated. N proteins binds the viral genome in a beads on a string type conformation. This protein likely helps tether the viral genome to replicase-transcriptase complex (RTC), and subsequently package the encapsulated genome into viral particles.
4. Envelope protein (E) is found in small quantities in within the virus. It is most likely a transmembrane protein and with ion channel activity. The protein facilitates assembly and release of the virus and has other functions such as ion channel activity. It is not necessary for viral replication but it is for pathogenesis.
5. Membrane protein (M) is the most abundant structural protein. It does not contain signal sequence and exists as a dimer in the virion. It may have two different conformations to enable it to promote membrane curvature as well as bind to nucleocapsid.

6.) Hemagglutinin-esterase dimer protein (HE) is present in a subset of betacoronaviruses. The protein binds sialic acids on surface glycoproteins. The protein activities are thought to enhance S protein-mediated cell entry and virus spread through the mucosa.

References:

<https://www.sciencedirect.com/science/article/pii/S0896841120300469>

<https://www.prosci-inc.com/covid-19/>

<https://www.mayoclinic.org/diseases-conditions/coronavirus/symptoms-causes/syc-20479963>

<https://www.sciencedaily.com/releases/2020/03/200317175442.htm>

<http://www.nature.com/articles/d41586-020-00154>

<https://www.cdc.gov/media/releases/2020/p0130>

<https://idpjournal.biomedcentral.com/articles/10.1186/s40249-020-00646-x>

<https://en.m.wikipedia.org/wiki/Coronavirus_disease_2019>

World Health Organization "WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020" <https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020>

Fehr AR, Perlman S. Coronaviruses: an overview of their replication and pathogenesis. Methods Mol Biol. 2015;1282:1–23. <https://doi.org/10.1007/978-1-4939-2438-7_1>

<https://youtu.be/PWzbArPgo-o>