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ASSIGNMENT

Discuss the etiology, origin, structure and pathophysiology of covid-19

THE ETIOLOGY OF COVID -19

Etiology is the study of causation or origination, it can also be the cause of a disease or abnormal condition. CoVs are positive-stranded RNA viruses with a crown-like appearance under an electron microscope (coronam is the Latin term for crown) due to the presence of spike glycoproteins on the envelope. The subfamily Orthocoronavirinae of the coronaviridae family (order Nidovirales) classifies into four genera of CoVs: Alphacoronavirus(alphaCoV), Betacoronavirus (betaCoV), Deltacoronavirus(deltaCoV), and Gammacoronavirus (gammaCoV). Futhermore, the betaCoV genus divides into five sub-genera or lineages. Genomic chsracterization has shown that probabaly bats and rodents are the gene source of the alphaCoVs and betaCoVs. On the contrary, avian species seem to represent the gene sources of deltaCoVs and gammaCoVs.

Members of this large family of viruses can cause respiratory, enteric, hepatic and neurological diseases in different animal species, including camels, cattle, cats and bats. To date, seven humans have been identified. Some of HCoVs were identified in the mid-1960s, while others were only detected in the new millennium. Common human CoVs: HCoV- OO43, and HCoV-HKU1 (betaCoVs of the A lineage); HCoV-229E, and HCoV-NL63(alphaCoVs). They can cause common colds and self –limiting upper respiratory infections in immunocompetent individuals. In immunocompromised subjects and the elderly, lower respiratory tract infections can occur, Other human CoVs:SARS-CoV, SARS-CoV-2, and MERS-CoV(betaCoVs of the B and C lineage, respectively). These cause epidemics with variable clinical severity featuring respiratory and extra-respiratory manifestations. Although its origins are not entirely understood, these genomic analyses suggest that SARS-CoV-2 probably evolved from a strain found in bats, Since the mutation in the original strain could have directly triggered virulence towards humans, it is not certain that this intermediary exists.

THE ORIGIN OF COVID-19

The coronavirus disease 19 (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. 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. Covid -19 is a respiratory illness and is largely spread via droplets in the air. These are typically expelled when an infected person coughs or sneezes. Once symptoms develop, a person’s viral load declines steadily, and they become increasingly less infectious. However, people appear to keep shedding the virus for around two weeks after they recover covid-19, both in the saliva and stools. People with mild or no symptoms can have a very high viral load in their upper respiratory tracts, meaning they can shed the virus through spitting, touching their mouths or noses and then a surface, or possibly talking. The new coronavirus has also been found to persist for days on surfaces, though that doesn’t necessarily mean these virus particles could still infect other people. That could be diminished by ultraviolet light heat or humidity.

THE STURCTURE OF COVID-19

The covid-19 virus has several features we may be able to target with drugs to break it down and stop it entering cells. The covid-19 virus is humanity’s newest foe, with the potential to prematurely end millions of lives. In addition, covid-19 has a similar receptor- binding domain structure as SARS-CoV which suggests COVID-19(SARS-CoV-2) uses ACE2 receptor in humans for infection. 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 enclosed in protein

A spike protein(s): It 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.

RNA is the genome of the virus.

Nucleocapsid protein(N): It 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(RTS), and subsequently package the encapsulated genome into viral particles.

Envelope protein(E): It 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.

Membrane protein(M): It 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.

Hemagglutinin-esterase dimer protein(HE): It 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.

THE PATHOPHYSIOLOGY OF COVID-19

CoVs are enveloped, positive- stranded RNA viruses with nucleocapsid. For addressing pathogenetic mechanisms of SARS-CoV-2, its viral structure, and genome must be consideration. In CoVs, the genomic structure is organized in a +ssRNA of approximately 30kb in length- the largest known RNA viruses – and with a 5’-cap structure and 3’-poly-A tail. Pathophysiology and virulence mechanisms of CoVs, and therefore also of SARS-CoV-2 have links to the function of th nsps and structural proteins. Among functions of structural proteins, the envelope has a crucial role in virus pathogenicity as it promotes viral assembly and release. However, many of these features (e.g those of nsp2, and 11) have not been described yet. Among the structural elements of CoVs, there are spike glycoproteins composed the spikes on the viral surface, guiding the link to host receptors. SARS-CoV-2, the S2 subunit – containing a fusion peptide, a transmembrane domain, and cytoplasmic domain- is highly conserved. Thus, it could be a target for antiviral (anti-S2) compounds. Other structural elements on which research must necessarily focus are the ORF3b that has no homology with of SARS-CoVs and a secreted protein (encoded by ORF8) which is structurally different from the those of SARS-CoV. The pathogenic mechanism that produces pneumonia seems to be particularly complex, the viral infection is capable of producing immune reaction in the host. In some cases, a reaction takes place which as a whole is labeled a ‘cytokine storm’. The effect is extensive tissue damage. The protagonist of this storm is interleukin 6(IL-6) .IL-6 is produced by activated leukocytes and acts on a large number of cells and tissues. It is able to promote the differentiation of B lymphocytes, promotes the growth of some categories of cells, and inhibits the growth of others. It also stimulates the production of acute phase proteins and plays an important role in thermoregulation, in bone maintenance and in the functionality of the central nervous system. Although the main role played by IL-6 is pro inflammatory, effects. In turn, IL-6 increases during inflammatory diseases, infections, autoimmune disorders, cardiovascular diseases and some some types of cancer. It is also implicated into the pathogenesis of the cytokine release syndrome(CRS) that is an acute systemic inflammatory syndrome characterized by fever and multiple organ dysfunction.…

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