**MLS 406 – VIROLOGY ASSINGMENT**

**QUESTION: DISCUSS THE ETIOLOGY, ORIGIN, STRUCTURE AND PATHOPHYSIOLOGYOF COVID-19.**

 In the last twenty years, several viral epidemics such as the severe acute respiratory syndrome coronavirus (SARS-CoV) in 2002 to 2003, H1N1 influenza in 2009, have been recorded. Coronaviruses are a large family of zoonotic viruses that cause illness ranging from the common cold to severe respiratory diseases. A novel coronavirus outbreak was first documented in Wuhan, Hubei Province, China in December 2019.

**ETIOLOGY**

Corona viruses are positive-stranded RNA viruses with a crown-like appearance under an electron microscope 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, Betacoronavirus, Deltacoronavirus, and Gammacoronavirus. Genomic characterization has shown that probably bats and rodents are the gene sources of alphaCoVs and betaCoVs. On the contrary, avian species seem to represent the gene sources of deltaCoVs and gammaCoVs.

**STRUCTURE**

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

* Spike protein 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.
* Nucleocapsid protein 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 replicate-transcriptase complex (RTC), and subsequently package the encapsulated genome into viral particles.RNA is the genome of the virus.
* Envelope proteinis 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 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 is present in a subset of beta coronaviruses. 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.

**PATHOPHYSIOLOGY**

CoVs are enveloped, positive-stranded RNA viruses with nucleocapsid. In Corona viruses, the genomic structure is organized in a +ssRNA of approximately 30 kb in length and with a 5′-cap structure and 3′-poly-A tail. The transcription works through the replication-transcription complex organized in double-membrane vesicles and via the synthesis of subgenomic RNAs (sgRNAs) sequences. Transcription termination occurs at transcription regulatory sequences, located between the open reading frames (ORFs) that work as templates for the production of subgenomic mRNAs. In the atypical CoV genome, at least six open reading frames can be present. Among these, a frame shift between ORF1a and ORF1b guides the production of both pp1a and pp1ab polypeptides that are processed by virally encoded chymotrypsin-like protease (3CLpro) or main protease, as well as one or two papain-like proteases for producing 16 non-structural proteins. Apart from ORF1a and ORF1b, other ORFs encode for structural proteins, including spike, membrane, envelope, and nucleocapsid proteins and accessory protein chains. Different CoVs present special structural and accessory proteins translated by dedicated sgRNAs.

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**REFRENCES**

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By Ninja Nerd science-march 15th 2020-cited from WHO, CDC