

Understanding the Covid – 19: Microbiology and Pathogenesis

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Abstract: Recently the world is facing a new viral pandemic which is known to many as Corona virus, few call it Covid 19, some literatures have named it as SARS-CoV-2. One disease many names, though various modes of information entire globe is updated with one or all of its name, about the sign and symptoms and mortality of the disease. This article is a genuine attempt by the authors to review the literature and data available to us with a purpose to understand the pathogenesis of this viral infection.

Key Word: Coronavirus, Covid-19, SARS, SARS-CoV-2, Plasma therapy

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I. Introduction

A virus is almost like a microscopic parasite due to their inability to survive and multiply outside of a host body. Where as a virus contain all the key elements that aid in replication like any other living organism for e.g. DNA, RNA but at the same time they lack the capacity to independently read and act upon the information contained within these nucleic acids.

Coronaviruses are group of one such structure that infects mammals and birds predominantly. Among humans it primarily attacks the Respiratory tract. Disease symptoms vary greatly ranging from mild flu to severe acute respiratory illness.

Coronaviruses constitute the subfamily *Orthocoronavirinae*, in the family *Coronaviridae*, order *Nidovirales*, and realm *Riboviria*. (1,2) They are enveloped viruses with a positive-sense single-stranded RNA genome and a nucleocapsid of helical symmetry. The genome size of coronaviruses ranges from approximately 26 to 32 kilobases, one of the largest among RNA viruses.(3) They have characteristic club-shaped spikes that project from their surface, which in electron micrographs create an image reminiscent of the solar corona, from which their name derives.(4) The name refers to the characteristic appearance of virions (the infective form of the virus) by electron microscopy, which have a fringe of large, bulbous surface projections creating an image reminiscent of the solar corona or halo.(5) This morphology is created by the viral spike peplomers, which are proteins on the surface of the virus.(6)








Types	Genera	Disease
 SARS-CoV-2 (2019-nCoV)	Betacoronavirus	Coronavirus disease 2019 (COVID-19). As of 3rd Apr, >1,010,000 infected, >53,000 death
 SARS-CoV	Betacoronavirus	Severe acute respiratory syndrome(SARS), mortality rate 9%
 MERS-CoV	Betacoronavirus	Middle East respiratory syndrome(MERS), mortality rate >30%
 HCoV-HKU1	Betacoronavirus	Upper and lower respiratory tract disease
 HCoV-NL63	Alphacoronavirus	Common cold
 HCoV-OC43	Betacoronavirus	Common cold
 HCoV-229E	Alphacoronavirus	Common cold

Table courtesy : YUDONG YIN AND RICHARD G. WUNDERINK. MERS, SARS and other coronaviruses as causes of pneumonia. Asian Pacific Society of Respirology. 2017

As the world is struggling with this pandemic the scientific associations world wide is struggling at the same time to develop a cure for the same. To understand the complexity of this disease and its effect on human body it is very important to understand the microbiology and pathogenesis involved.

Nomenclature

In October 2019 outbreak of respiratory infection was noted in Wuhan Province of China, it was found to be because of a new strain of Coronavirus thus giving it its first and most accepted global name “ Novel Corona Virus” , World Health Organisation later renamed it as 2019-nCoV which depicts its year of outbreak followed by novel strain of Coronavirus. The International Committee on Taxonomy of Viruses later renamed it to SARS-CoV-, taking account its affect of human body, where it primarily causes severe acute respiratory Stress (SARS) ; another popular name for the disease is COVID-19 which stands for corona virus disease of 2019. (7,8)

Microbiology of SARS-CoV-2

More than two decades ago David Tyrrell and Steven Myint have provided record of corona viruses in their contribution to the text book of medical microbiology. (10) They described these virions as spherical to pleomorphic enveloped in electron microscopic imaging. (10)

Image 1 : Structure of Coronavirus virion 11

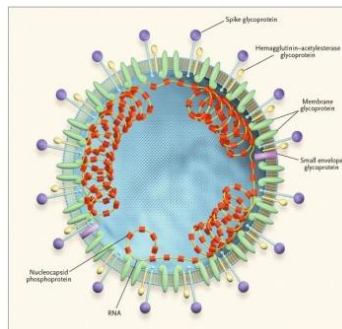
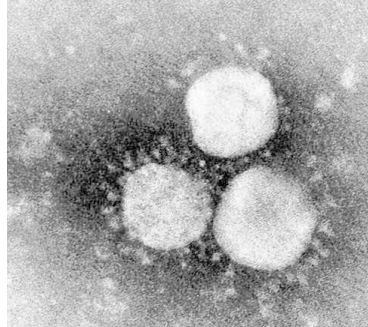


Image 2 : EM image of Corona virion 12



(Courtesy S.Sikotra, Leicester Royal Infirmary, Leicester, England.)

The outer envelope presents glycoprotein projections on outer surface. Enclosed within the envelope is the core which contains a single strand of positive-sense RNA ($Mr 6 \times 10^6$) associated with nucleoprotein enclosed within the matrix protein. The function of outer glycoprotein projections is to facilitate attachment to the host cell and also carry the main antigenic epitopes, particularly the epitopes recognized by neutralizing antibodies. Once virus gains entry into the host cell, and uncoats, the genome is transcribed and then translated. A unique feature of replication is that all the mRNAs form a “nested set” with common 3’ ends; only the unique portions of the 5’ ends are translated. There are 7 mRNAs produced. The shortest mRNA codes for the nucleoprotein, and the others each direct the synthesis of a further segment of the genome. The proteins are assembled at the cell membrane and genomic RNA is incorporated as the mature particle forms by budding from internal cell membranes.

II. Transmission

As per the recent evidences reproduced in work of Liu J et al, Burke RM et al and Li Q COVID-19 virus undergoes human transmission primarily via respiratory droplets (Particle size > 5-10U μ m) contact routes. (11, 12, 13) There are different theories about it being an airborne disease where as Ong SW et al could not find evidence for airborne spread. (14)

Droplet transmission occurs when a person is in close contact (1 m) with some one who has respiratory symptoms and therefore is at risk of having mucosa or conjunctive exposed to potentially infective respiratory droplets .Another mode of transmission is through fomites in the immediate environment

III. Pathogenesis

Robert J Mason, described the pathogenesis of virus in three stages. According to him, first two days of infection are asymptomatic (described as Stage 1) followed by sudden exacerbation of respiratory symptoms. (15) In stage 3 there is hypoxia, ground glass infiltrates and progression of Acute Respiratory Distress syndrome. Patients with COVID-19 present with clinical manifestations including fever, nonproductive cough, dyspnea, myalgia, fatigue, normal or decreased leukocyte counts, and radiographic evidence of pneumonia , which are similar to the symptoms of SARS-CoV and MERS-CoV infections. (16,17)

A more detailed description of the pathogenesis is given in work of Xiaowei et al they have mentioned that although the pathogenesis of COVID-19 is poorly understood the generalised mechanism of Coronaviruses can give us a lot of information. (18)

Belouzard et al. discovered an important proteolytic cleavage event occurring at SARS-CoV S protein at position (S2') to be the propogating factor behind membrane fusion and viral infectivity. (19) Apart from this, Viral Entry into host cell is also mediated via the clathrin-dependent and -independent endocytosis. (18) Upon entry, the viral RNA genome is released into the cytoplasm. Thereafter it is translated into two polyproteins and structural proteins, leading to onset of viral replication process.(21) The newly formed envelope glycoproteins are inserted into the membrane of the endoplasmic reticulum or Golgi, and the nucleocapsid is formed by the combination of genomic RNA and nucleocapsid protein. Then, viral particles germinate into the endoplasmic reticulum-Golgi intermediate compartment (ERGIC). At last, the vesicles containing the virus particles then fuse with the plasma membrane to release the virus (22)

While the virus enters host cells, the antigen presentation cells(APC) present in host defense system recognize the viral antigens and kickstart an immune response. Antigenic peptides are presented by major histocompatibility complex (MHC; or human leukocyte antigen (HLA) in humans) and then recognized by virus-specific cytotoxic T lymphocytes (CTLs). Hence, the understanding of antigen presentation of SARS-CoV-2 will help our comprehension of COVID-19 pathogenesis. (23)

Antigen presentation subsequently stimulates the body's humoral and cellular immunity, which are mediated by virus-specific B and T cells. Similar to common acute viral infections, the antibody profile against SARS-CoV virus has a typical pattern of IgM and IgG production. The SARS-specific IgM antibodies disappear at the end of week 12, while the IgG antibody can last for a long time, which indicates IgG antibody may mainly play a protective role, and the SARS-specific IgG antibodies primarily are S-specific and N-specific antibodies. The recent reports show that the number of CD4+ and CD8+ T cells in the peripheral blood of SARS-CoV-2-infected patients is significantly reduced, whereas its status is excessive activation, as evidenced by high proportions of HLA-DR (CD4 3.47%) and CD38 (CD8 39.4%) double-positive fractions. Similarly, the acute phase response in patients with SARS-CoV is associated with severe decrease of CD4+ T and CD8+ T cells. (24,25)

ARDS is the common immunopathological event for SARS-CoV-2 infections. (21) One of the main factor responsible for ARDS is the cytokine storm, the deadly uncontrolled systemic inflammatory response resulting from the release of large amounts of pro-inflammatory cytokines and chemokines by immune effector cells in SARS-CoV infection. (26,27). Similar to those with SARS-CoV, individuals with severe MERS-CoV infection show increased levels of IL-6, IFN- α , and CCL5, CXCL8, CXCL-10 in serum compared to those with the mild-moderate disease . The cytokine storm will trigger a violent attack by the immune system to the body, cause ARDS and multiple organ failure, and finally lead to death in severe cases of SARS-CoV-2 infection, just like what occurs in SARS-CoV and MERS-CoV infection. (28)

IV. Conclusion

There are seven types of coronaviruses known to infect humans. Patients infected with these viruses develop respiratory symptoms of various severity. HCoV-229E and HCoV-OC43, the two coronaviruses discovered in early years, cause common cold. The other five coronaviruses lead to more severe respiratory tract infection, which can potentially be lethal. Since 2000, there have been three major world-wide health crisis caused by coronaviruses, the 2003 SARS outbreak, the 2012 MERS outbreak, and the 2019 COVID-19 outbreak. Thousands of people died during these epidemics, while surprisingly no vaccine, treatment, or diagnostic has been established. The outbreak of COVID-19 is yet another wake-up call for the biomedical community to make serious efforts to understand the biology of these viruses, and find ways to prevent and treat the infections.

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