Anbar University

Science College

Biotechnology Department

RNA enveloped viruses

Lecturer.D.Al-Moghira Khairi Al-Qaysi

Virology, Stephen N.J. Korsman, Gert U. van Zyl, ... Wolfgang Preiser 2012

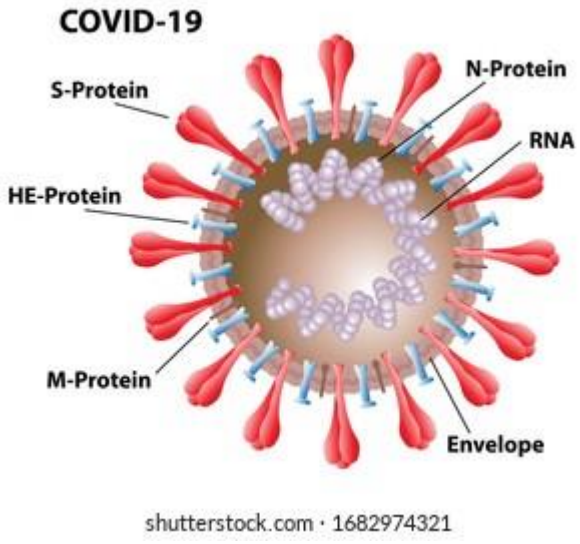
Jawetz Melnick & Adelbergs Medical Microbiology, Stefan Riedel (Author), Stephen Morse (Author), Timothy Mietzner (Author), Steve Miller.

Viruses, Pandemics, and Immunity, By Arup K. Chakraborty and Andrey S. Shaw

RNA-enveloped viruses

Coronaviruses

Coronaviruses are enveloped, 120- to 160-nm particles that contain an unsegmented genome of single-stranded positive sense RNA, the largest genome among RNA viruses**.**



Glycoprotein that serves as a matrix protein embedded in the envelope lipid bilayer and interacting with the nucleocapside, and the spike glycoprotein that makes up the petal-shaped. Some viruses (covid-19), contain a third glycoprotein that causes hemagglutination.

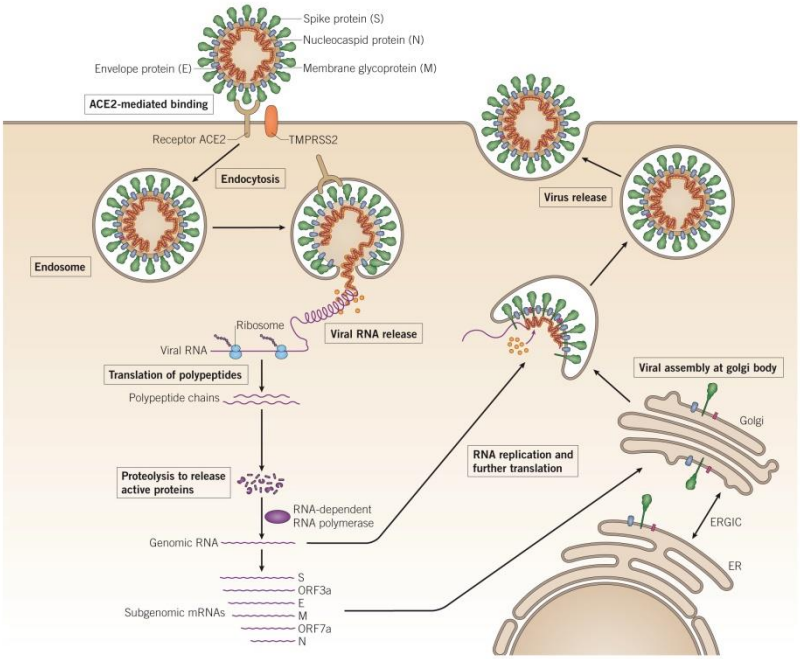
Classification

Family	Subfamily	Genus
Coronaviridae	Orthocoronavirinae	Deltacoronavirus

Coronavirus Replication

Because human coronaviruses do not grow well in cell culture, details of viral replication have come from studies with mouse hepatitis virus, which is closely related to human strain. The replication cycle takes place in the cytoplasm of cells.

The initial steps of coronavirus infection involve the specific binding of the coronavirus spike (S) protein to the cellular entry receptors, The virus attaches to receptors on target cells by the glycoprotein spikes on the viral envelope (either by S or HE). The receptor for human coronavirus 229E is aminopeptidase N. The particle is then internalized, probably by absorptive endocytosis. The S glycoprotein may cause fusion of the viral envelope with the cell membrane. The first event after uncoating is translation of the viral genomic RNA to produce a virus-specific RNA-dependent RNA polymerase. The viral polymerase transcribes a complementary (-strand) RNA. Newly synthesized genomic RNA molecules interact in the cytoplasm with the nucleocapsid protein to form helical nucleocapsids. There is a preferred binding site for N protein within the leader RNA. The nucleocapsids bud through membranes of the rough endoplasmic reticulum and the Golgi apparatus in areas that contain the viral glycoproteins. Mature virions may then be transported in vesicles to the cell periphery for exit or may be released upon cell lysis.



Virions are apparently not formed by budding at the plasma membrane. Large numbers of particles may be seen on the exterior of infected cells and are presumably adsorbed to it after virion release. Certain coronaviruses induce cell fusion; this is mediated by the S glycoprotein. Coronaviruses exhibit a high frequency of mutation during each round of replication, including the generation of a high incidence of deletion mutations. Coronaviruses undergo a high frequency of recombination during replication; this is unusual for an RNA virus with a nonsegmented genome and may contribute to the evolution of new virus strains.

Pathogenesis

Following viral transmission, the virus attaches to the surface of the epithelial membrane of the oral cavity, the mucosal membranes of the conjunctiva or the otic canal. ACE 2 protein, which is highly expressed on multiple human cells including type II alveolar cells, oral, esophageal, ileal epithelial cells, myocardial cells, proximal tubule cells of the kidneys as well as urothelial cells of the bladder is believed to

mediate the internalization of the virus**.** The spike (S) protein is cleaved by a cellular enzyme named furin. This cleavage is essential for viral entry to the lung cells. Finally attaches ACE 2 receptors to enter the host cells.

Stage 1:

Asymptomatic state (initial 1–2 days of infection)

The inhaled virus likely binds to epithelial cells in the nasal cavity and starts replicating. ACE2 is the main receptor. The ciliated cells are primary cells infected in the conducting airways. There is local propagation of the virus but a limited innate immune response. At this stage the virus can be detected by nasal swabs. Although the viral burden may be low, these individuals are infectious. The RT-PCR for the viral RNA might be useful to predict the viral load. For the RT-PCR cycle number to be useful, the sample collection procedure would have to be standardized. Nasal swabs might be more sensitive than throat swabs.

Stage 2: Upper airway and conducting airway response (next few days)

The virus propagates and migrates down the respiratory tract along the conducting airways, and a more robust innate immune response is triggered. Nasal swabs or sputum should yield the virus as well as early markers of the innate immune response. At this time, the disease COVID-19 is clinically manifest.

For about 80% of the infected patients, the disease will be mild and mostly restricted to the upper and conducting airways. These individuals may be monitored at home with conservative symptomatic therapy.

Stage 3: Hypoxia, ground glass infiltrates, and progression to ARDS

Unfortunately, about 20% of the infected patients will progress to stage 3 disease and will develop pulmonary infiltrates and some of these will develop very severe disease. The virus now reaches the gas exchange units of the lung and infects alveolar cells. large number of viral particles are released, and the cells undergo apoptosis and die. The end result is likely a self-replicating pulmonary toxin as the released viral particles infect cells in adjacent units. I suspect areas of the lung will likely lose most of their cells. Elderly individuals are particularly at risk because of their diminished immune response and reduced ability to repair the damaged epithelium. The elderly also have reduced mucociliary clearance, and this may allow the virus to spread to the gas exchange units of the lung more readily.

Complications

-Respiratory system involvement

-Cardiovascular involvement

Heart failure and coronary artery disease are the most particular comorbidities that have been identified in COVID-19 patients

-Kidney involvement

Acute kidney injury is one of the major contributing factors of COVID-19-related death. The kidneys are potential targets for COVID-19

Hematologic involvement

Thrombocytopenia associated with COVID-19 reflects the severity of the disease. Coronavirus may invade the hematopoietic cells or cause abnormal hematopoiesis secondary to immune system response. In addition, virus-induced alveolar damage affects the resident megakaryocytes in the lungs (decrease platelet production).

GI tract involvement

GI symptoms infrequently accompany COVID-19 pneumonia. About 2–10% of patients with COVID-19 had GI symptoms such as diarrhea, abdominal pain and vomiting.