Arunachalam G /J. Pharm. Sci. & Res. Vol. 12(12), 2020, 1552-1555

ISSN:0975-1459
Journal of Pharmaceutical Sciences and Research
www.jpsr.pharmainfo.in

Review on Coronavirus and its disease in mammals and birds.

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Abstract

Corona viruses are a group of related RNA viruses that cause diseases in mammals and birds. In humans, these viruses cause respiratory tract infections that can range from mild to lethal. Mild illnesses include some cases of the common cold (which is also caused by other viruses, predominantly rhinoviruses), while more lethal varieties can cause SARS, MERS, and COVID-19. Symptoms in other species vary: in chickens, they cause an upper respiratory tract disease, while in cows and pigs they cause diarrhea. There are as yet no vaccines or antiviral drugs to prevent or treat human coronavirus infections.

Keywords: Coronavirus, SARS, MERS and COVID-19

INTRODUCTION

Corona viruses are a group of related RNA viruses that cause diseases in mammals and birds. In humans, these viruses cause respiratory tract infections that can range from mild to lethal. Coronaviruses constitute the subfamily ***Orthocoronavirinae***, in the family *Coronaviridae*, order *Nidovirales*, and realm *Riboviria*. They are enveloped viruses with a positive-sense single-stranded RNA genome and a nucleocapsid of helical symmetry (1).

The genome size of coronaviruses ranges from approximately 26 to 32 kilobases, one of the largest among RNA viruses (2). 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 (3).

Etymology

The name "coronavirus" is derived from Latin *corona*, meaning "crown" or "wreath", itself a borrowing from Greek κορώνη *korṓnē*, "garland, wreath" (4 and 5). The name was coined by June Almeida and David Tyrrell who first observed and studied human coronaviruses (6). The word was first used in print in 1968 by an informal group of virologists in the journal *Nature* to designate the new family of viruses. 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 (3 and 6). This morphology is created by the viral spike peplomers, which are proteins on the surface of the virus (7).

History

Corona viruses were first discovered in the 1930s when an acute respiratory infection of domesticated chickens was shown to be caused by infectious bronchitis virus (IBV) (8). Arthur Schalk and M.C. Hawn described in 1931 a new respiratory infection of chickens in North Dakota. The infection of new-born chicks was characterized by gasping and listlessness. The chicks' mortality rate was 40–90% (9). Fred Beaudette and Charles Hudson six years later successfully isolated and cultivated the infectious bronchitis virus which caused the disease (10). In the 1940s, two more animal coronaviruses, mouse hepatitis virus (MHV) and transmissible gastroenteritis virus (TGEV), were isolated (11). It was not realized at the time that these three different viruses were related (12).

Human coronaviruses were discovered in the 1960s (13 and 14). They were isolated using two different methods in the United Kingdom and the United States (15). E.C. Kendall, Malcom Byone, and David Tyrrell working at the Common Cold Unit of the British Medical Research Council in 1960 isolated from a boy a novel common cold virus B814 (16, 17 and 18). The virus was not able to be cultivated using standard techniques which had successfully cultivated rhinoviruses, adenoviruses and other known common cold viruses. In 1965, Tyrrell and Byone successfully cultivated the novel virus by serially passing it through organ culture of human embryonic trachea (19). The new cultivating method was introduced to the lab by Bertil Hoorn (20). The isolated virus when intranasally inoculated into volunteers caused a cold and was inactivated by ether which indicated it had a lipid envelope (16 and 21). Around the same time, Dorothy Hamre (22) and John Procknow at the University of Chicago isolated a novel cold virus 229E from medical students, which they grew in kidney tissue culture. The novel virus 229E, like the virus strain B814, when inoculated into volunteers caused a cold and was inactivated by ether (23).

The two novel strains B814 and 229E were subsequently imaged by electron microscopy in 1967 by Scottish virologist June Almeida at St. Thomas Hospital in London (24 and 25). Almeida through electron microscopy was able to show that B814 and 229E were morphologically related by their distinctive club-like spikes. Not only were they related with each other, but they were morphologically related to infectious bronchitis virus (IBV) (26). A research group at the National Institute of

Health the same year was able to isolate another member of this new group of viruses using organ culture and named the virus strain OC43 (OC for organ culture) (27). Like B814, 229E, and IBV, the novel cold virus OC43 had distinctive club-like spikes when observed with the electron microscope (28 and 29).

The IBV-like novel cold viruses were soon shown to be also morphologically related to the mouse hepatitis virus (11). This new group of IBV-like viruses came to be known as coronaviruses after their distinctive morphological appearance (15). Human corona virus 229E and human coronavirus OC43 continued to be studied in subsequent decades (30 and 31). The coronavirus strain B814 was lost. It is not known which present human corona virus it was (32). Other human coronaviruses have since been identified, including SARS-CoV in 2003, HCoV NL63 in 2004, HCoV HKU1 in 2005, MERS-CoV in 2012, and SARS-CoV-2 in 2019 (33 and 34). There have also been a large number of animal coronaviruses identified since the 1960s.

Structure

Coronaviruses are large, roughly spherical, particles with bulbous surface projections (350. The average diameter of the virus particles is around 125 nm (.125 μm). The diameter of the envelope is 85 nm and the spikes are 20 nm long. The envelope of the virus in electron micrographs appears as a distinct pair of electron-dense shells (shells that are relatively opaque to the electron beam used to scan the virus particle) (36 and 37).

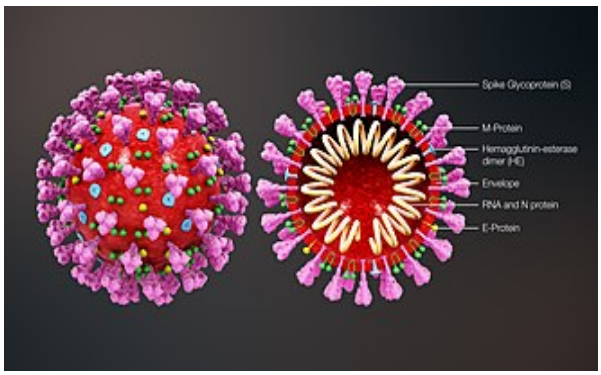

Figure 1. Cross-sectional model of a coronavirus

The viral envelope consists of a lipid bilayer, in which the membrane (M), envelope (E) and spike (S) structural proteins are anchored (38). The ratio of E:S:M in the lipid bilayer is approximately 1:20:300 (39). On average a corona virus particle has 74 surface spikes (40).

The coronavirus surface spikes are homotrimers of the S protein, which is composed of an S1 and S2 subunit. The homotrimeric S protein is a class I fusion protein which mediates the receptor binding and membrane fusion between the virus and host cell. The S1 subunit forms the head of the spike and has the receptor binding domain (RBD). The S2 subunit forms the stem which anchors the spike in the viral envelope and on protease activation enables fusion. The E and M protein are important in forming the viral envelope and maintaining its structural shape (37).

Inside the envelope, there is the nucleocapsid, which is formed from multiple copies of the nucleocapsid (N) protein, which are bound to the positive-sense single-stranded RNA genome in a continuous beads-on-a-string type conformation (37 and 41). The lipid bilayer envelope, membrane proteins, and nucleocapsid protect the virus when it is outside the host cell (42).

Genome

Coronaviruses contain a positive-sense, single-stranded RNA genome. The genome size for coronaviruses ranges from 26.4 to 31.7 kilobases (43). The genome size is one of the largest among RNA viruses. The genome has a 5′ methylated cap and a 3′ polyadenylated tail (44). The genome organization for a coronavirus is 5′-leader-UTR-replicase (ORF1ab)-spike (S)-envelope (E)-membrane (M)-nucleocapsid (N)-3′UTR-poly (A) tail. The open reading frames 1a and 1b, which occupy the first two-thirds of the genome, encode the replicase polyprotein (pp1ab). The replicase polyprotein self cleaves to form 16 nonstructural proteins (nsp1–nsp16) (44). The later reading frames encode the four major structural proteins: spike, envelope, membrane, and nucleocapsid (45). Interspersed between these reading frames are the reading frames for the accessory proteins. The number of accessory proteins and their function is unique depending on the specific coronavirus (44).

Severe Acute Respiratory Syndrome (SARS)

Severe acute respiratory syndrome (SARS) is a viral respiratory disease caused by a SARS-associated coronavirus. It was first identified at the end of February 2003 during an outbreak that emerged in China and spread to 4 other countries. WHO co-ordinated the international investigation with the assistance of the Global Outbreak Alert and Response Network (GOARN) and worked closely with health authorities in affected countries to provide epidemiological, clinical and logistical support and to bring the outbreak under control.

SARS is an airborne virus and can spread through small droplets of saliva in a similar way to the cold and influenza. It was the first severe and readily transmissible new disease to emerge in the 21st century and showed a clear capacity to spread along the routes of international air travel.

SARS can also be spread indirectly via surfaces that have been touched by someone who is infected with the virus.

Most patients identified with SARS were previously healthy adults aged 25-70 years. A few suspected cases of SARS have been reported among children under 15 years. The case fatality among persons with illness meeting the current WHO case definition for probable and suspected cases of SARS is around 3%.

Middle East Respiratory Syndrome (MERS)

Middle East Respiratory Syndrome (MERS) is a viral respiratory illness that is new to humans. It was first reported in Saudi Arabia in 2021 and has since spread to

several other countries, including the United States. Most people infected with MERS-CoV developed severe respiratory illness, including fever, cough and shortness of breath. Many of them have died.

Coronavirus disease (COVID-19)

Coronavirus disease (COVID-19) is an infectious disease caused by a newly discovered coronavirus. Most people infected with the COVID-19 virus will experience mild to moderate respiratory illness and recover without requiring special treatment. Older people, and those with underlying medical problems like cardiovascular disease, diabetes, chronic respiratory disease, and cancer are more likely to develop serious illness.

The best way to prevent and slow down transmission is to be well informed about the COVID-19 virus, the disease it causes and how it spreads. Protect yourself and others from infection by washing your hands or using an alcohol based rub frequently and not touching your face.

The COVID-19 virus spreads primarily through droplets of saliva or discharge from the nose when an infected person coughs or sneezes, so it's important that you also practice respiratory etiquette (for example, by coughing into a flexed elbow).

Prevention and Treatment

A number of vaccines using different methods have been developed against human coronavirus SARS-CoV-2. Antiviral targets against human coronaviruses have also been identified such as viral proteases, polymerases, and entry proteins. Drugs are in development which targets these proteins and the different steps of viral replication.

Vaccines are available for animal coronaviruses IBV, TGEV, and Canine CoV, although their effectiveness is limited. In the case of outbreaks of highly contagious animal coronaviruses, such as Porcine epidemic diarrhea virus (PEDV), a member of the genus Alphacoronavirus in the family Coronaviridae, causes acute diarrhea and/or vomiting, dehydration and high mortality in neonatal piglets, measures such as destruction of entire herds of pigs may be used to prevent transmission to other herds.

CONCLUSIONS

There are hundreds of coronaviruses, most of which circulate in animals. Only seven of these viruses infect humans and four of them cause symptoms of the common cold. But, three times in the last 20 years, a coronavirus has jumped from animals to humans to cause severe disease.

SARS, a beta coronavirus emerged in 2002 and was controlled mainly by aggressive public health measures. There have been no new cases since 2004. MERS emerged in 2012, still exists in camels, and can infect people who have close contact with them.

COVID-19, a new and sometimes deadly respiratory illness that is believed to have originated in a live animal market in China, has spread rapidly throughout that country and the world. The new coronavirus was first detected in Wuhan, China in December 2019. Tens of thousands of people were infected in China, with the virus spreading easily from person-to-person in many parts of that country.

The novel coronavirus infections were at first associated with travel from Wuhan, but the virus has now established itself in 177 countries and territories around the world in a rapidly expanding pandemic. Health officials in the United States and around the world are working to contain the spread of the virus through public health measures such as social distancing, contact tracing, testing, quarantines and travel restrictions. Scientists are working to find medications to treat the disease and to develop a vaccine.

The World Health Organization declared the novel coronavirus outbreak "a public health emergency of international concern" on January 30. On March 11, 2020 after sustained spread of the disease outside of China, the World Health Organization declared the COVID-19 epidemic a pandemic. Public health measures like ones implemented in China and now around the world, will hopefully blunt the spread of the virus while treatments and a vaccine are developed to stop it.

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