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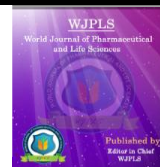
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A REVIEW ON CORONA VIRUS (COVID-19)

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Article Received on 11/02/2020

Article Revised on 01/03/2020

Article Accepted on 22/03/2020

ABSTRACT

Coronaviruses are a group of enveloped viruses with nonsegmented, single-stranded, and positive-sense RNA genomes. Apart from infecting a variety of economically important vertebrates (such as pigs and chickens), six coronaviruses have been known to infect human hosts and cause respiratory diseases. Among them, severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) are zoonotic and highly pathogenic coronaviruses that have resulted in regional and global outbreaks. Coronaviruses possess a distinctive morphology, the name being derived from the outer fringe, or “corona” of embedded envelope protein. Members of the family *Coronaviridae* cause a broad spectrum of animal and human diseases. Uniquely, replication of the RNA genome proceeds through the generation of a nested set of viral mRNA molecules. Human coronavirus (HCoV) infection causes respiratory diseases with mild to severe outcomes. In the last 15 years, we have witnessed the emergence of two zoonotic, highly pathogenic HCoVs: severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV). Replication of HCoV is regulated by a diversity of host factors and induces drastic alterations in cellular structure and physiology. In this review all (as we possible) information about Corona viruses are given.

KEYWORDS: Corona, respiratory, viruses, Hcov, host, RNA.

INTRODUCTION

A novel coronavirus, designated as 2019-nCoV, emerged in Wuhan, China, at the end of 2019. As of January 24, 2020, at least 830 cases had been diagnosed in nine countries: China, Thailand, Japan, South Korea, Singapore, Vietnam, Taiwan, Nepal, and the United States. Twenty-six fatalities occurred, mainly in patients who had serious underlying illness. Although many details of the emergence of this virus — such as its origin and its ability to spread among humans — remain unknown, an increasing number of cases appear to have resulted from human-to-human transmission. Given the severe acute respiratory syndrome coronavirus (SARS-CoV) outbreak in 2002 and the Middle East respiratory syndrome coronavirus (MERS-CoV) outbreak in 2012, 2019-nCoV is the third coronavirus to emerge in the human population in the past two decades — an emergence that has put global public health institutions on high alert.

China responded quickly by informing the World Health Organization (WHO) of the outbreak and sharing sequence information with the international community after discovery of the causative agent. The WHO responded rapidly by coordinating diagnostics

development; issuing guidance on patient monitoring, specimen collection, and treatment; and providing up-to-date information on the outbreak. Several countries in the region as well as the United States are screening travelers from Wuhan for fever, aiming to detect 2019-nCoV cases before the virus spreads further. Updates from China, Thailand, Korea, and Japan indicate that the disease associated with 2019-nCoV appears to be relatively mild as compared with SARS and MERS.

Coronaviruses make up a large family of viruses that can infect birds and mammals, including humans, according to world health organisation (WHO). These viruses have been responsible for several outbreaks around the world, including the severe acute respiratory syndrome (SARS) pandemic of 2002-2003 and the Middle East respiratory syndrome (MERS) outbreak in South Korea in 2015. Most recently, a novel coronavirus (SARS-CoV-2, also known as COVID-19) triggered an outbreak in China in December 2019, sparking international concern. While some coronaviruses have caused devastating epidemics, others cause mild to moderate respiratory infections, like the common cold.

Types

Coronaviruses belong to the subfamily Coronavirinae in the family Coronaviridae. Different types of human coronaviruses vary in how severe the resulting disease becomes, and how far they can spread. Doctors currently recognize seven types of coronavirus that can infect humans.

Common types

1. 229E (alpha coronavirus)
2. NL63 (alpha coronavirus)

3. OC43 (beta coronavirus)
4. HKU1 (beta coronavirus)

Rarer strains that cause more severe complications include MERS-CoV, which causes Middle East respiratory syndrome (MERS), and SARS-CoV, the virus responsible for severe acute respiratory syndrome (SARS). In 2019, a dangerous new strain called SARS-CoV-2 started circulating, causing the disease COVID-19.

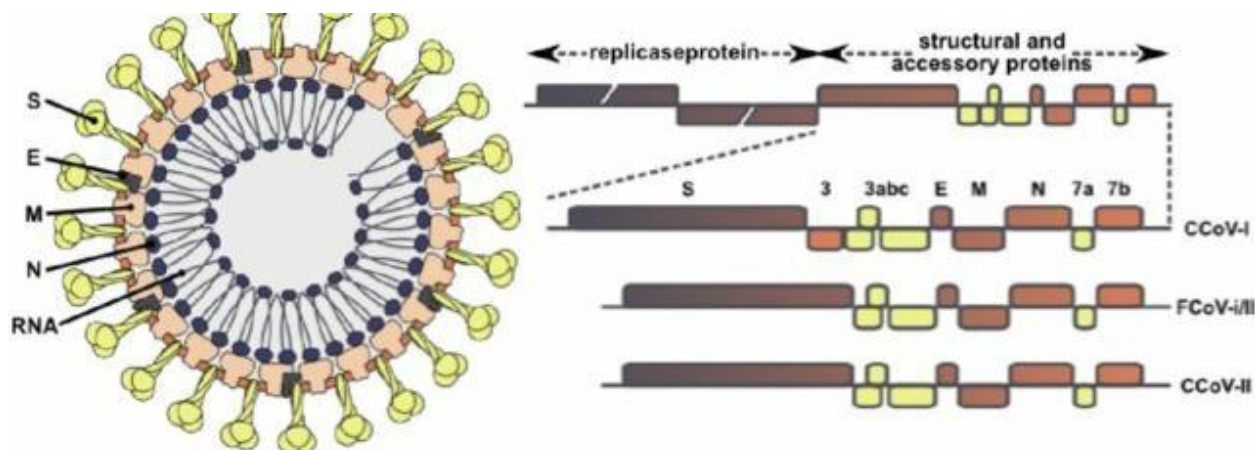


Fig. Coronavirus structure and comparison of CCoV and FCoV genome.

Transmission

Limited research is available on how HCoV spreads from one person to the next. However, researchers believe that the viruses transmit via fluids in the respiratory system, such as mucus.

Coronaviruses can spread in the following ways:

Coughing and sneezing without covering the mouth can disperse droplets into the air. Touching or shaking hands with a person who has the virus can pass the virus between individuals. Making contact with a surface or object that has the virus and then touching the nose, eyes, or mouth. Some animal coronaviruses, such as feline coronavirus (FCoV), may spread through contact with feces. However, it is unclear whether this also applies to human coronaviruses. The National Institutes of Health (NIH) suggest that several groups of people have the highest risk of developing complications due to COVID-19.

These groups include:

1. Young children
2. People aged 65 years or older
3. Women who are pregnant

Coronaviruses will infect most people at some time during their lifetime. Coronaviruses can mutate effectively, which makes them so contagious.

To prevent transmission, people should stay at home and rest while symptoms are active. They should also avoid close contact with other people. Covering the mouth and nose with a tissue or handkerchief while coughing or

sneezing can also help prevent transmission. It is important to dispose of any tissues after use and maintain hygiene around the home.

COVID-19

In 2019, the Centers for Disease Control and Prevention (CDC) started monitoring the outbreak of a new coronavirus, SARS-CoV-2, which causes the respiratory illness now known as COVID-19. Authorities first identified the virus in Wuhan, China.

More than 74,000 people have contracted the virus in China. Health authorities have identified many other people with COVID-19 around the world, including many in the United States. On January 31, 2020, the virus passed from one person to another in the U.S.

The World Health Organization (WHO) have declared a public health emergency relating to COVID-19.

Since then, this strain has been diagnosed in several U.S. residents. The CDC have advised that it is likely to spread to more people. COVID-19 has started causing disruption in at least 25 other countries.

The first people with COVID-19 had links to an animal and seafood market. This fact suggested that animals initially transmitted the virus to humans. However, people with a more recent diagnosis had no connections with or exposure to the market, confirming that humans can pass the virus to each other.

Information on the virus is scarce at present. In the past, respiratory conditions that develop from coronaviruses, such as SARS and MERS, have spread through close contacts.

On February 17, 2020, the Director-General of the WHO presented at a media briefing the following updates on how often the symptoms of COVID-19 are severe or fatal, using data from 44,000 people with a confirmed diagnosis:

Table 1: The Director-General also noted that the risk of serious complications increases with age. According to the WHO.

Stage of severity	Rough percentage of people with COVID-19
Mild disease from which a person can recover	More than 80%
Severe disease, causing breathlessness and pneumonia	Around 14%
Critical disease, including septic shock, respiratory failure, and the failure of more than one organ	About 5%
Fatal disease	2%

Few children get COVID-19, although they are still investigating the reasons for this. However, while some viruses are highly contagious, it is less clear how rapidly coronaviruses will spread.

Symptoms vary from person-to-person with COVID-19. It may produce few or no symptoms. However, it can also lead to severe illness and may be fatal.

Common symptoms include

1. Fever

2. Breathlessness

3. Cough

4. It may take 2–14 days for a person to notice symptoms after infection.

Corona virus life cycle

Steps

1. Attachment and entry
2. Replicase protein expression
3. Replication and transcription
4. Assembly and release.

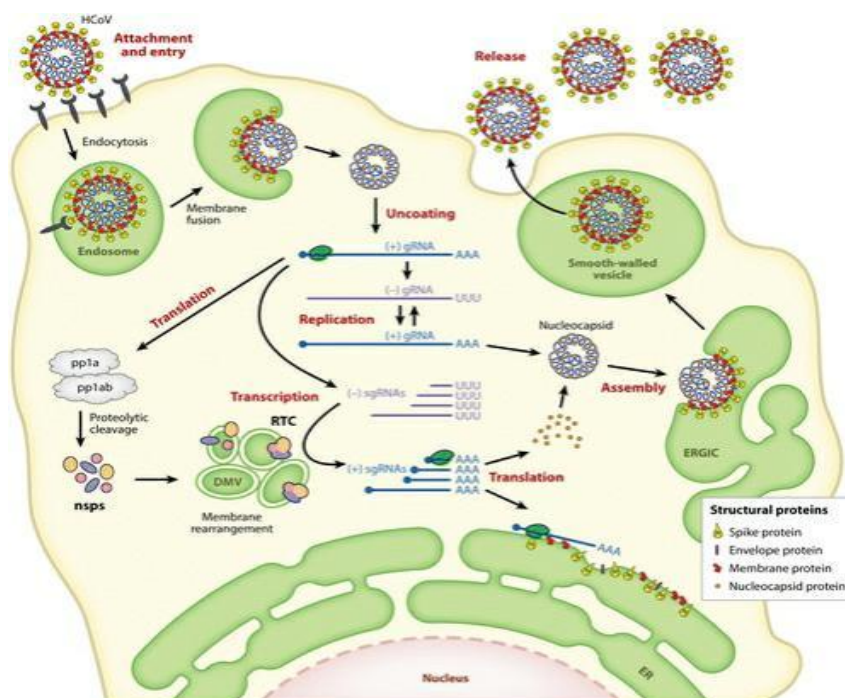


Fig. Life cycle of Corona virus.

Epidemiology

In December 2019, many pneumonia cases that were clustered in Wuhan city were reported and searches for the source have shown Huanan Seafood Market as the origin. The first case of the COVID-19 epidemic was discovered with unexplained pneumonia on December 12, 2019, and 27 viral pneumonia cases with seven being severe, were officially announced on December 31,

2019. Etiologic investigations have been performed in patients who applied to the hospital due to similar viral histories of these patients has strengthened the likelihood of an infection transmitted from animals to humans. On January 22, 2020, novel CoV has been declared to be originated from wild bats and belonged to Group 2 of beta-coronavirus that contains Severe Acute Respiratory Syndrome Associated Coronavirus (SARS-CoV).

Although COVID-19 and SARS-CoV belong to the same beta corona virus subgroup, similarity at genome level is only 70%, and the novel group has been found to show genetic differences from SARS-CoV. Similar to the SARS epidemic, this outbreak has occurred during the Spring Festival in China, which is the most famous traditional festival in China, during which nearly 3 billion people travel countrywide. These conditions caused favorable conditions for the transmission of this highly contagious disease and severe difficulties in prevention and control of the epidemic. The period of the Spring Festival of China was between January 17 and

February 23 in 2003, when the SARS epidemic peaked, while the period of the festival was between January 10 and February 18 in 2020. Similarly, there was a rapid increase in COVID-19 cases between January 10-22. Wuhan, the center of the epidemic with 10 million population, is also an important center in the spring festival transportation network. The estimated number of travelers during the 2020 spring festival has risen 1.7 folds when compared with the number traveled in 2003 and reached to 3.11 billion from 1.82 billion. This large-scale travel traffic has also created favorable conditions for the spread of this difficult-to-control disease.

Table 2: The number of cases and death of COVID – 19 outbreak according to WHO situation reports 22 on February 11, 2020.

Country	Cases	Deaths	Region
China	42,708	1,017	Asia
Singapore	45	0	Asia
Hong Kong	42	1	Asia
Thailand	33	0	Asia
South Korea	28	0	Asia
Japan	26	0	Asia
Malaysia	18	0	Asia
Germany	16	0	Europe
Australia	15	0	Australia
Vietnam	15	0	Australia
United State	13	0	North America
France	11	0	Europe
Macao	10	0	Asia
United Kingdom	8	0	Europe
United Arab Emirates	8	0	Asia

Table 3: State/UT wise list of COVID confirmed cases. (As on 14.03.2020 at 04:55 PM).

S. No.	Name of State / UT	Total Confirmed cases (Indian National)	Total Confirmed cases (Foreign National)	Cured/ Discharged	Death
1	Delhi	7	0	1	1
2	Haryana	0	14	0	0
3	Kerala	19	0	3	0
4	Rajasthan	1	2	1	0
5	Telangana	1	0	0	0
6	Uttar Pradesh	11	1	5	0
7	Union Territory of Ladakh	3	0	0	0
8	Tamil Nadu	1	0	0	0
9	Union Territory of Jammu and Kashmir	2	0	0	0
10	Punjab	1	0	0	0
11	Karnataka	6	0	0	1
12	Maharashtra	14	0	0	0
13	Andhra Pradesh	1	0	0	0
Total number of confirmed cases in India		67	17	10	2

Diagnosis, Treatment, and Prevention

In most cases of self-limited infection, diagnosis of coronaviruses is unnecessary, as the disease will naturally run its course. However, it may be important in certain clinical and veterinary settings or in epidemiological studies to identify an etiological agent.

Diagnosis is also important in locations where a severe CoV outbreak is occurring, such as, at present, in the Middle East, where MERS-CoV continues to circulate. The identification of cases will guide the development, of public health measures to control outbreaks. It is also important to diagnose cases of severe veterinary CoV-

induced disease, such as PEDV and IBV, to control these pathogens and protect food supplies. RT-PCR has become the method of choice for diagnosis of human CoV, as multiplex real-time RT-PCR assays have been developed, are able to detect all four respiratory HCoV and could be further adapted to novel CoVs. Serologic assays are important in cases where RNA may be difficult to isolate, is no longer present, and for epidemiological studies.

To date, there are no anti-viral therapeutics that specifically target human coronaviruses, so treatments are only supportive. In vitro, interferons (IFNs) are only partially effective against coronaviruses. IFNs in combination with ribavirin may have increased activity in vitro when compared to IFNs alone against some coronaviruses; however, the effectiveness of this combination in vivo requires further evaluation [coronavirus] The SARS and MERS outbreaks have stimulated research on these viruses and this research has identified a large number of suitable anti-viral targets, such as viral proteases, polymerases, and entry proteins. Significant work remains, however, to develop drugs that target these processes and are able to inhibit viral replication.

Only limited options are available to prevent coronavirus infections. Vaccines have only been approved for IBV, TGEV, and Canine CoV, but these vaccines are not always used because they are either not very effective, or in some cases have been reported to be involved in the selection of novel pathogenic CoVs via recombination of circulating strains. Vaccines for veterinary pathogens, such as PEDV, may be useful in such cases where spread of the virus to a new location could lead to severe losses of veterinary animals. In the case of SARS-CoV, several potential vaccines have been developed but none are yet approved for use. These vaccines include recombinant attenuated viruses, live virus vectors, or individual viral proteins expressed from DNA plasmids. Therapeutic SARS-CoV neutralizing antibodies have been generated and could be retrieved and used again in the event of another SARS-CoV outbreak. Such antibodies would be most useful for protecting healthcare workers. In general, it is thought that live attenuated vaccines would be the most efficacious in targeting coronaviruses. This was illustrated in the case of TGEV, where an attenuated variant, PRCV, appeared in Europe in the 1980s. This variant only caused mild disease and completely protected swine from TGEV. Thus, this attenuated virus has naturally prevented the reoccurrence of severe TGEV in Europe and the U.S. over the past 30 years. Despite this success, vaccine development for coronaviruses faces many challenges. First, for mucosal infections, natural infection does not prevent subsequent infection, and so vaccines must either induce better immunity than the original virus or must at least lessen the disease incurred during a secondary infection. Second, the propensity of the viruses to recombine may pose a problem by rendering the vaccine useless and potentially

increasing the evolution and diversity of the virus in the wild. Finally, it has been shown in FIPV that vaccination with S protein leads to enhanced disease. Despite this, several strategies are being developed for vaccine development to reduce the likelihood of recombination, for instance by making large deletions in the nspl or E proteins, rearranging the 3' end of the genome, modifying the TRS sequences, mutant viruses with abnormally high mutation rates that significantly attenuate the virus.

Owing to the lack of effective therapeutics or vaccines, the best measures to control human coronaviruses remain a strong public health surveillance system coupled with rapid diagnostic testing and quarantine when necessary. For international outbreaks, cooperation of governmental entities, public health authorities and health care providers is critical. During veterinary outbreaks that are readily transmitted, such as PEDV, more drastic measures such as destruction of entire herds of pigs may be necessary to prevent transmission of these deadly viruses.

Symptoms

Cold- or flu-like symptoms usually set in from 2–4 days after a coronavirus infection and are typically mild. However, symptoms vary from person-to-person, and some forms of the virus can be fatal.

Symptoms include:

1. Sneezing
2. Runny nose
3. Cough
4. Watery diarrhea
5. Fever in rare cases
6. Sore Throat
7. Exacerbated asthma

Scientists cannot easily cultivate human coronaviruses in the laboratory unlike the rhinovirus, which is another cause of the common cold. This makes it difficult to gauge the impact of the coronavirus on national economies and public health. There is no cure, so treatments include self-care and over-the-counter (OTC) medication. People can take several steps, including:

1. Resting and avoiding overexertion
2. Drinking enough water
3. avoiding smoking and smoky areas
4. Taking acetaminophen, ibuprofen, or naproxen for pain and fever
5. Using a clean humidifier or cool mist vaporizer
6. A doctor can diagnose the virus responsible by taking a sample of respiratory fluids, such as mucus from the nose, or blood.
7. Standard recommendations to prevent infection spread

Its include regular hand washing, covering mouth and nose when coughing and sneezing, thoroughly cooking meat and eggs. Avoid close contact with anyone showing

symptoms of respiratory illness such as coughing and sneezing.

CONCLUSION

Over the past 50 years the emergence of many different coronaviruses that cause a wide variety of human and veterinary diseases has occurred. It is likely that these viruses will continue to emerge and to evolve and cause both human and veterinary outbreaks owing to their ability to recombine, mutate, and infect multiple species and cell types.

Future research on coronaviruses will continue to investigate many aspects of viral replication and pathogenesis. First, understanding the propensity of these viruses to jump between species, to establish infection in a new host, and to identify significant reservoirs of coronaviruses will dramatically aid in our ability to predict when and where potential epidemics may occur. As bats seem to be a significant reservoir for these viruses, it will be interesting to determine how they seem to avoid clinically evident disease and become persistently infected. Second, many of the non-structural and accessory proteins encoded by these viruses remain uncharacterized with no known function, and it will be important to identify mechanisms of action for these proteins as well as defining their role in viral replication and pathogenesis. These studies should lead to a large increase in the number of suitable therapeutic targets to combat infections. Furthermore, many of the unique enzymes encoded by coronaviruses, such as ADP-ribose-1''-phosphatase, are also present in higher eukaryotes, making their study relevant to understanding general aspects of molecular biology and biochemistry. Third, gaining a complete picture of the intricacies of the RTC will provide a framework for understanding the unique RNA replication process used by these viruses. Finally, defining the mechanism of how coronaviruses cause disease and understanding the host immunopathological response will significantly improve our ability to design vaccines and reduce disease burden.

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