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Review on Corona Virus (COVID-19): Pandemic Disease

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ABSTRACT

The coronavirus disease 19 (COVID-19) is highly transmittable and pathogenic viral infection caused by Severe Acute Respiratory Syndrome Corona Virus 2 (SARS-COV-2). Firstly, found in Wuhan, China and spread around the word. Genomic analysis revealed that SARS-COV-2 is Phyto genetically related To Severe Acute Respiratory Syndrome like (SARS like) bat viruses, therefore bats could be the possible primary reservoir. The intermediate source of origin and transfer to human is not known, however, the rapid human to human transfer has been confirmed widely. There is no clinically approved antiviral drug or vaccine available to be used against COVID-19. However, few broad-spectrum antiviral drugs have been evaluated against COVID-19 in clinical trials, resulted in clinical recovery. In current review, we summarize & pathogenicity of COVID-19 infection. We also discuss the mode of transmission, diagnosis, approaches for treatment, Drugs used in COVID-19, precautions, development of vaccine and recommendation for COVID-19.

INTRODUCTION

In late December 2019, a case of unidentified pneumonia was reported in Wuhan, Hubei Province, People's Republic of China (PRC). Its clinical characteristics were very similar to those of viral pneumonia. After analysis of respiratory samples, the experts at the PRC Centres for Disease Control declared that pneumonia, later known as Novel Coronavirus Pneumonia (NCP), was caused by a novel coronavirus [1].

The World Health Organization (WHO) officially named the disease 'COVID-19'. The International Committee on Taxonomy of Viruses named the virus 'Severe Acute Respiratory Syndrome Corona Virus 2' (SARS-CoV-2). Designation of a formal name for the novel coronavirus and the disease it caused is conducive to communication in clinical and scientific research. This virus belongs to the β-coronavirus family, a large class of viruses that are prevalent in nature. Similar to other viruses, SARS-CoV-2 has many potential natural hosts, intermediate hosts and final hosts. This poses major challenges for the prevention and treatment of viral infection. Compared with SARS and Middle East Respiratory Syndrome Corona Viruses (SARS-COV and MERS-COV, respectively), SARS-CoV-2 has high transmissibility and infectivity, and a low mortality rate.

Coronavirus is mostly infected to animals but new coronavirus is transfer from animal to people. On 29 February 2020, data published by WHO showed that since 12 December 2019 when the first case was reported, there had been 79 394 confirmed cases of SARS-CoV-2 infection and 2838 deaths [4]. In the meantime, 6009 cases had been confirmed and 86 patients had died in 53 countries and regions outside China [4]. COVID-19 poses a major threat to global public health.

In current review, we summarize & pathogenicity of COVID-19 infection. We also discuss the mode of transmission, diagnosis, approaches for treatment, Drugs used in COVID-19, precautions, development of vaccine and recommendation for COVID-19.

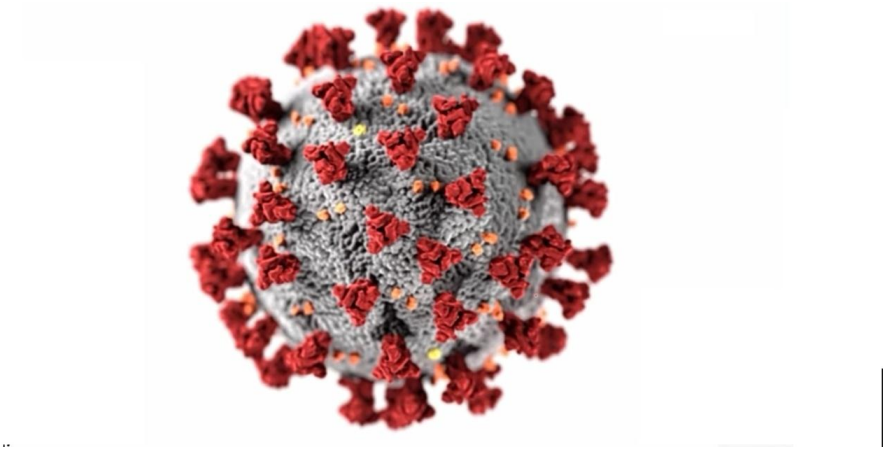

Figure No. 1: Structure of SARS-CoV-2

Morphology:

COVID-19 is caused by SARS –CoV-2 a β coronavirus who's named derives from Crown like structure in under electron microscope. It is composed of linear single stranded RNA molecule of positive (mRNA) polarity and from 28-32 kb in length. Genetic material is protected by lipid bilayer and membrane proteins (M-protein) also include surface protein S-protein (spike protein) E-protein (envelop protein) the S-protein has been a focus of pathogenesis studies in mice because it appears to be the critical determinant of cell tropism, species corona.

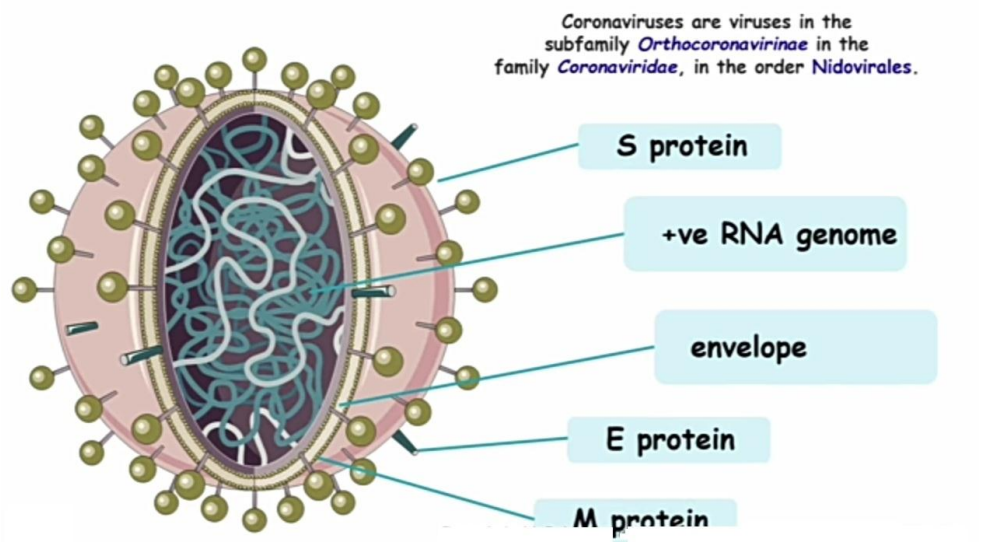

Figure No. 2: Morphology of SARS-CoV-2

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 (α- coronavirus)
2. NL63 (α- coronavirus)
3. OC43 (β- coronavirus)
4. HKU1 (β- coronavirus)

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

Life Cycle:

The life cycle of SARS-CoV-2 in host cells; begins its life cycle when S protein binds to the cellular receptor ACE2. After receptor binding, the conformation change in the S protein facilitates viral envelope fusion with the cell membrane through the endosomal pathway. Then SARS-CoV-2 releases RNA into the host cell. Genome RNA is translated into viral replicase polyproteins pp1a and 1ab, which are then cleaved into small products by viral proteinases. The polymerase produces a series of subgenomic mRNAs by discontinuous transcription and finally translated into relevant viral proteins. Viral proteins and genome RNA are subsequently assembled into virions in the ER and Golgi and then transported *via* vesicles and released out of the cell.

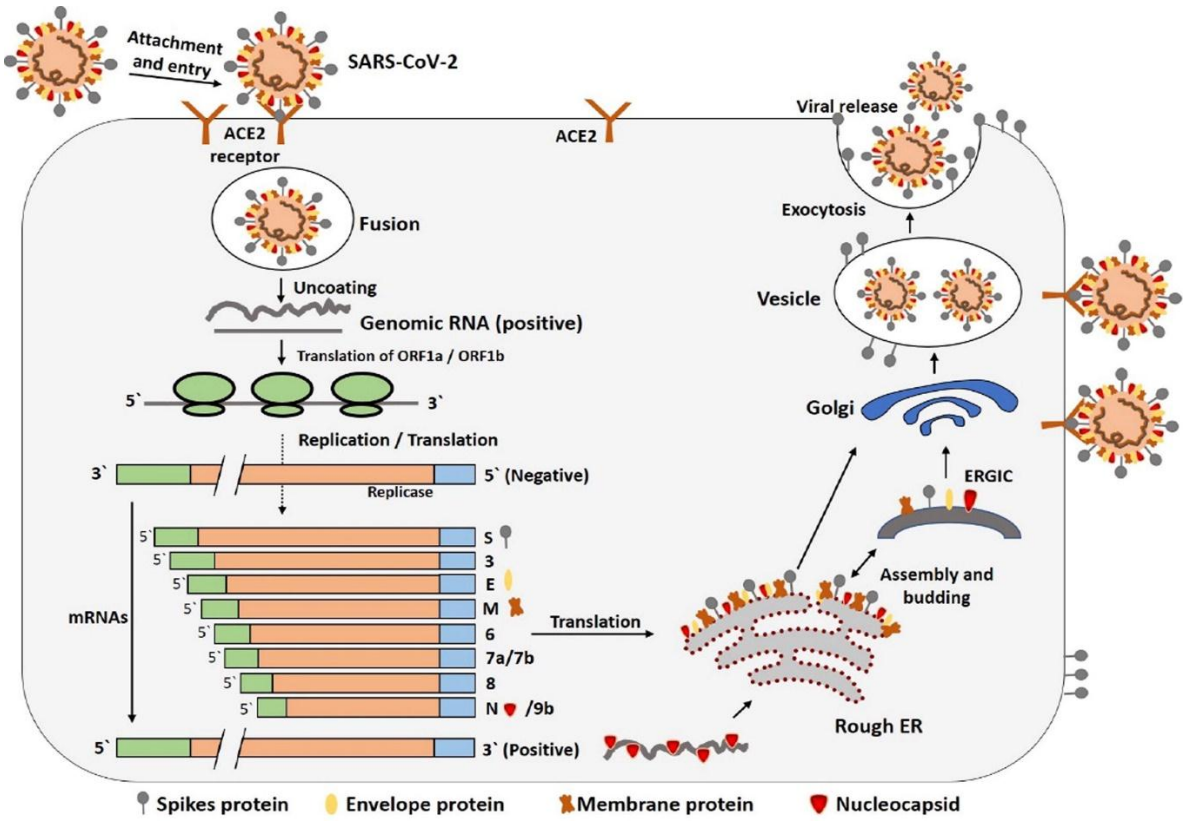

Figure No. 3: Life cycle of SARS-CoV-2

Transmission:

The novel coronavirus is spread in various ways; *via*

1. Person to person
2. Contact with an infected surface
3. Zoonotic

1. Person to person:

Human to human transmission of SARS-CoV-2 occurs mainly between family members, including relatives and friends who intimately contacted with patients or incubation carriers.

It is reported that 31.3% of patients travelled to Wuhan and 72.3% of patients contacting with people from Wuhan.

However, researchers believe that the viruses transmit *via* fluids in the respiratory system, such as mucus.

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.

2. Contact with an infected surface:

It may be possible to get infected by touching the infected surface or object and then touching the mouth, nose or eyes through which virus can pass.

3. Zoonotic:

Direct contact with intermediate host animals or consumption of wild animals was suspected to be the main route of SARS-CoV-2 transmission.

Symptoms:

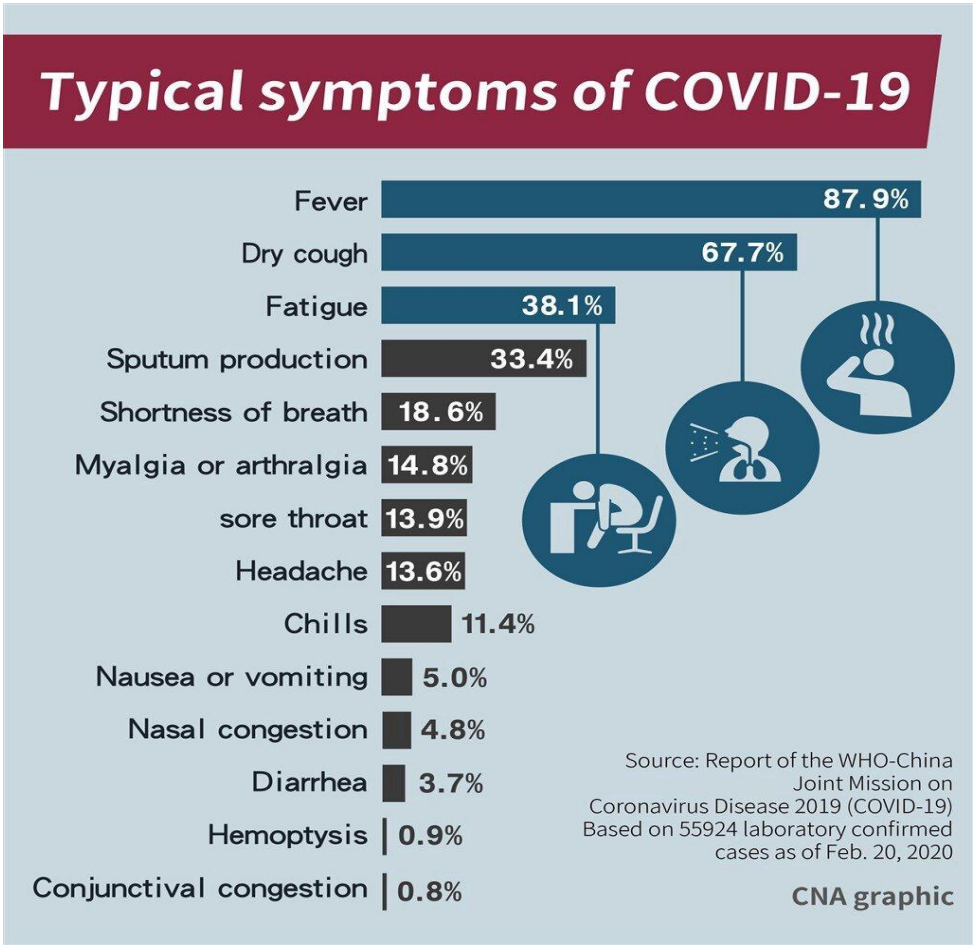

Figure No. 4: Typical Symptoms of COVID-19

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 diarrhoea
5. Fever in rare cases
6. Sore Throat
7. Exacerbated asthma

Other symptoms include

I. Tiredness
II. Aches
III. Chills
IV. Loss of smell
V. Loss of taste
VI. Headache
VII. Muscle pain
VIII. Corid toes

Nowadays, Pink eyes is recognised as atypical symptoms.

Diagnosis:

COVID-19 testing can identify the SARS-CoV-2 virus. Method – Detect the presence of virus itself may include RT-PCR, isothermal nucleic acid amplification and those detect antibodies produced in response to infection.

Detection of antibodies (serology) can be used for diagnosis.

Figure No. 5: Testing Kit

1. RT-PCR :

- Using real time reverse transcription polymerase chain reaction {rRT-PCR} the test can be done on respiratory samples obtained by various methods, including a nasopharyngeal swab or sputum sample.

- Identify any person who infected by SARS-CoV-2 by using RT-PCR, because name itself indicate that reverse transcriptase i.e viral RNA is single stranded, which must be converted into double stranded.

- Reason behind for this procedure is PCR only amplify DNA not RNA in amplification process use fluoresce dye which attach to DNA known to be CYBER GREEN probe which is expensive.

- After doing all these procedure we conclude that patient either positive or negative by increasing fluoresce value graph as compare with cycle number.

- If graph increase with respect to cycle no. then respective patient suffering from COVID-19 as positive patient and vice-versa.

- According to various research, every country has their own gene targets in this technique. Ex- China-ORFI ab and N; Germany-RdRP, E, N ;

Japan – Pancorona and multiple targets, spike protein;

Thailand – N:

US – There targets in N gene;

France – Two targets in RdRP.

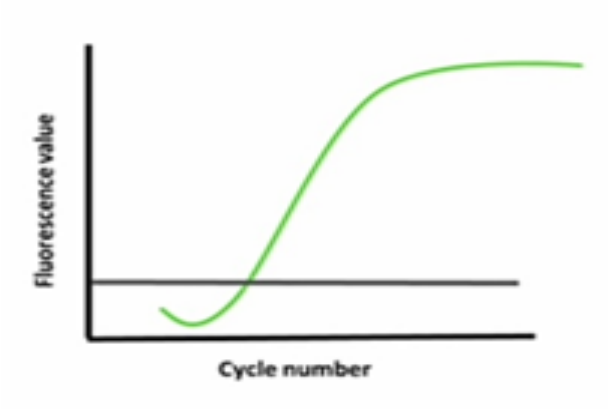

Figure No. 6: RT-PCR test graph which indicate positive test as graph increases with respective to Cycle number.

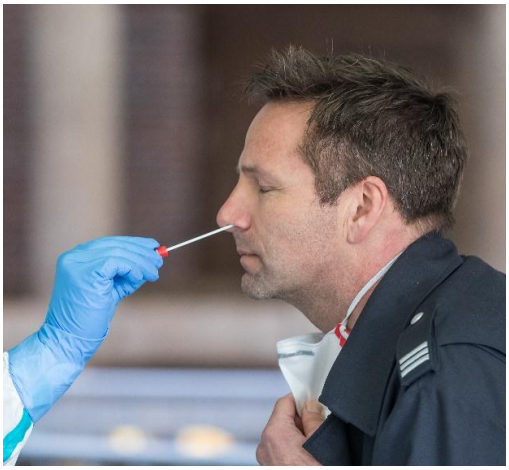

Figure No. 7: Demonstration of a Nasopharyngeal swab for COVID-19 testing

Figure No. 8: Demonstration of a Throat swab for COVID-19 testing

2. Rapid Antibody Test (Blood Test) :

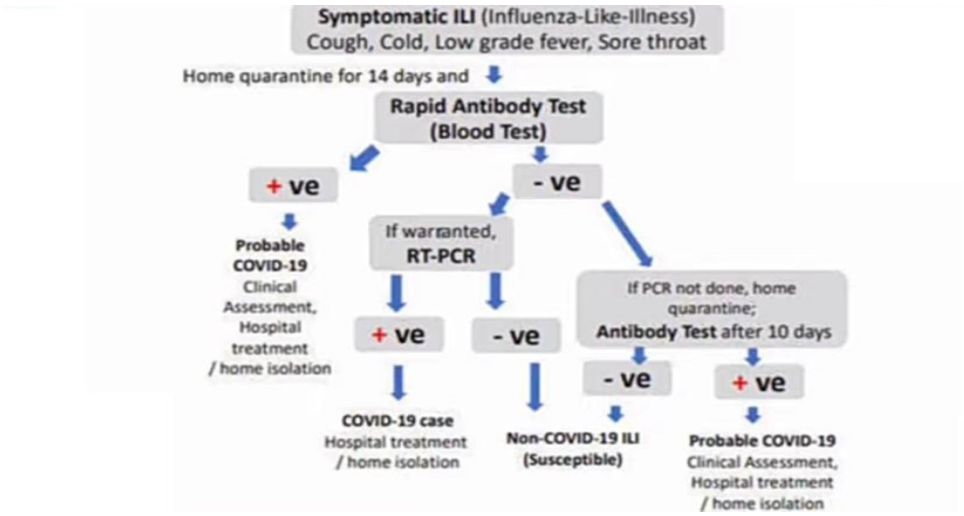

Figure No. 9: Rapid antibody test

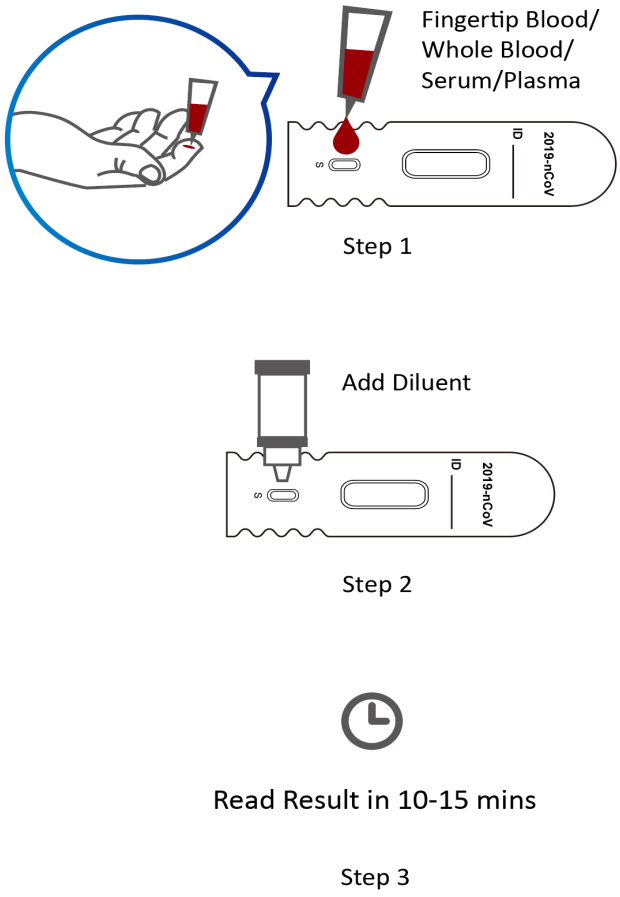

Figure No. 10: Procedure for Rapid antibody test

3. Isothermal Amplification Assays :

On 27 March 2020, the FDA approved an "Automated Assay" from Abbott Diagnostics, called ID Now, that uses an isothermal nucleic acid amplification method.

4. Medical Imaging :

Chest CT scans are not recommended for routine screening. Radiologic findings in COVID-19 are not specific. Typical features on CT initially include bilateral multilobar ground glass opacities with a peripheral or posterior distribution. Subpleural dominance, crazy paving and consolidation may develop as the disease evolves.

Treatment:

Status	Drugs	Action mode	Anti-infective mechanism	Target diseases
Approved	Lopinavir/Ritonavir	Protease inhibitors	Inhibiting HIV-1 protease for protein cleavage, resulting in non-infectious, immature viral particles	HIV/AIDS, SARS, MERS
Approved, Investigational, Vet approved	Chloroquine	9-aminoquinolin	Increasing endosomal pH, immunomodulating, autophagy inhibitors	Malaria, autoimmune disease
Experimental	Remdesivir (GS-5734)	Nucleotide analogue prodrug	Interfering with virus post-entry	Ebola, SARS, MERS (A wide array of RNA viruses)
Investigational	Nafamostat	Synthetic serine protease inhibitor	Prevents membrane fusion by reducing the release of cathepsin B; anticoagulant activities	Influenza, MERS, Ebola
Approved	Ribavirin	Synthetic guanosine nucleoside	Interfering with the synthesis of viral mRNA (a broad-spectrum activity against several RNA and DNA viruses)	HCV, SARS, MERS
Approved	Oseltamivir	Neuraminidase inhibitor	Inhibiting the activity of the viral neuraminidase enzyme, preventing budding from the host cell, viral replication, and infectivity	Influenza viruses A
Approved	Penciclovir/ Acyclovir	Nucleoside analog	A synthetic acyclic guanine derivative, resulting in chain	HSV, VZV

Status	Drugs	Action mode	Anti-infective mechanism	Target diseases
			termination	
Approved, Investigational	Ganciclovir	Nucleoside analog	Potent inhibitor of the Herpesvirus family including cytomegalovirus	AIDS-associated cytomegalovirus infections
Investigational	Favipiravir (T-705)	Nucleoside analog: Viral RNA polymerase inhibitor	Acting on viral genetic copying to prevent its reproduction, without affecting host cellular RNA or DNA synthesis	Ebola, influenza A(H1N1)
Approved, Investigational, Vet approved	Nitazoxanide	Antiprotozoal agent	Modulating the survival, growth, and proliferation of a range of extracellular and intracellular protozoa, helminths, anaerobic and microaerophilic bacteria, viruses	A wide range of viruses including human/animal coronaviruses

Prevention:

No specific vaccine is developed for the prevention of the novel coronavirus. There are various ways for the prevention of the novel coronavirus.

1. Wear cloth face mask :

Protect yourself and others in public with a cloth face mask, particularly where it is difficult to maintain a 6 foot distance from others.

2. Wash your hands :

Stop the spread of disease causing germs by washing your hands often. Use hand sanitizer if soap and water is not available.

3. Cover your mouth and nose :

When you cough or sneeze, cover your mouth and nose with a tissue or your sleeve, rather than your hands. Try to avoid touching your face.

4. Avoid care facilities :

Do not visit nursing homes, long term care facilities or retirement communities, unless you are providing critical assistance.

5. Practise social distancing :

Work from home(if possible), engage in social distancing, maintain a 6-foot distance from other people and avoid crowded places and gathering in groups.

6. Clean and disinfect :

Use a virus-killing disinfectant to clean frequently used surfaces such as doorknobs.

7. Stay home when sick :

Avoid leaving the house if you are sick. Connect with healthcare providers by phone or through virtual visits.

8. Maintain healthy habits :

Get enough sleep, eat healthy foods, drink plenty of liquids and exercise, if you are able, to help keep your immune system strong.

Development of Vaccine:

The vaccine is designed to prevent symptoms and complications of the novel coronavirus. At the date there is no vaccine or antiviral drug is available on 2019-nCoV. There are going on in various countries.

Six Indian companies are working on a vaccine for COVID-19. Zydus Cadila is working on two vaccines, Serum Institute, Biological E, Bharat Biotech, Indian Immunologicals, and Mynvax are developing one vaccine each.

According to the WHO, three vaccine candidates are in the clinical testing phase, meaning they are able to be tested on humans, while nearly 70 are in the preclinical phase -- either in lab testing, or animal studies.

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 immunopoathological response will significantly improve our ability to design vaccines and reduce disease burden.

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