

ETIOLOGY AND PRECAUTIONS OF CORONA VIRUS

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ABSTRACT

The Coronaviruses (CoV) belong to the genus Coronavirus with its high mutation rate in the Coronaviridae. The objective of this manuscript is to have a preliminary opinion about the disease and prevention in this early stage of COVID-19 outbreak.

KEYWORDS: COVID-19, Coronaviruses, outbreak.

INTRODUCTION

Severe acute respiratory syndrome (SARS) coronavirus (SARS-CoV) is a novel virus that caused the first major pandemic of the new millennium.^[1,2,3] The rapid economic growth in southern China has led to an increasing demand for animal proteins including those from exotic game food animals such as civets. Large numbers and varieties of these wild game mammals in overcrowded cages and the lack of biosecurity measures in wet markets allowed the jumping of this novel virus from animals to human.^[4,5] Its capacity for human-to-human transmission, the lack of awareness in hospital infection control, and international air travel facilitated the rapid global dissemination of this agent. Over 8,000 people were affected, with a crude fatality rate of 10%. The acute and dramatic impact on health care systems, economies, and societies of affected countries within just a few months of early 2003 was unparalleled since the last plague. The small reemergence of SARS in late 2003 after the resumption of the wildlife market in southern China and the recent discovery of a very similar virus in horseshoe bats, bat SARS-CoV, suggested that SARS can return if conditions are fit for the introduction, mutation, amplification, and transmission of this dangerous virus.^[6,7,8,9] Here, we review the biology of the virus in relation to the epidemiology, clinical presentation, pathogenesis, laboratory diagnosis, animal models or hosts, and options for treatment, immunization, and infection control.

Viral Life Cycle

Trimers of the S protein form the peplomers that radiate from the lipid envelope and give the virus a characteristic corona solids-like appearance under an electron microscope. S is a class I fusion protein that consists of the amino-terminal S1 and carboxyl-terminal S2 subunits

connected by a fusion peptide. The two subunits are indispensable for receptor binding and membrane fusion, respectively. The receptor binding domain of S1 has been mapped to residues 318 to 510.^[10,11]

The binding of S1 to the cellular receptor will trigger conformational changes, which collocate the fusion peptide upstream of the two heptad repeats of S2 to the transmembrane domain, and, finally, fusion of the viral and cellular lipid envelopes.

Moreover, this process could be facilitated by the infected cell membrane-associated protease, such as factor Xa, which can cleave S into S1 and S2. This proteolytic cleavage is specifically inhibited by a protease inhibitor, Ben-HCl.^[12]

The key receptor of the host cell attached by S is angiotensin-converting enzyme 2 (ACE2), which is a metalloprotease expressed in the cells of the lung, intestine, liver, heart, vascular endothelium, testis, and kidney.^[13] Since ACE2 was shown to protect against acute lung injury in a mouse model and since the binding of the S protein to host cells results in the Down regulation of ACE2, this mechanism may contribute to the severity of lung damage in SARS.^[14] Cells expressing some lectins, including DC-SIGN, L-SIGN, and LSECtin, have been shown to augment the cellular entry of pseudo type virus expressing S but only in the concomitant presence of ACE2.^[15,16,17,18] Nonsusceptible cells expressing these lectins in the absence of ACE2, such as dendritic cells, were able to promote the cell-mediated transfer of SARS-CoV to susceptible cells.^[15] Although lysosomotropic agents can block viral entry, which indicates that endosomal acidification is required for entry, the activation of the S protein by protease can

bypass this inhibition and result in cell-to-cell fusion. Despite the role of the pH-sensitive endosomal protease cathepsin L in the entry pathway^[19,20], viral culture does not require pretreatment with trypsin. However, this pH-sensitive cathepsin L may be a target for agents such as chloroquine, which elevates endosomal pH.^[21,22] The process of viral disassembly in the cytoplasm for the release of viral RNA for translation and replication remains elusive. Translation starts with two large polyproteins from *Orf1a* and *Orf1ab*, which are post translationally cleaved by the two viral proteases into nsp1 to nsp16. These cleavage products form the replication-transcription complex, which replicates the viral genome and transcribes a 3'-coterminal nested set of eight subgenomic RNAs. It is therefore conceivable that infected cells contain a higher number of transcripts containing genes towards the 3' terminus of the viral genome. On this basis, reverse transcriptase PCR (RT-PCR) using the N gene may have a better sensitivity than those using the other genes.

As in other coronaviruses, SARS-CoV may attach by the hydrophobic domains of their replication machinery to the limiting membrane of autophagosomes and form double-membrane vesicles. Once sufficient viral genomic RNA and structural proteins are accumulated, viral assembly by budding of the helical nucleocapsid at the endoplasmic reticulum to the Golgi intermediate compartment occurs. Here, the triplemembrane-spanning M protein interacts with the N protein and viral RNA to generate the basic structure. It also interacts with the E and S proteins to induce viral budding and release.

Unlike other coronaviruses, the M protein of SARS-CoV also incorporates another triple-membrane-spanning protein of *Orf3a* into the virion.^[23] The N protein is the most abundantly expressed viral protein in infected cells in which the mRNA levels were amplified 3 to 10 times higher at 12 h postinfection than other structural genes^[24] and is therefore an important target for immunohistochemistry and antigen detection in clinical specimens. Various diagnostic tests, antiviral agents, and vaccines are designed on the basis of our understanding of the structure and function of the various viral proteins involved in the life cycle of this virus.

Precautions

➤ Wash your hands frequently

Regularly and thoroughly clean your hands with an alcohol-based hand rub or wash them with soap and water.

Why? Washing your hands with soap and water or using alcohol-based hand rub kills viruses that may be on your hands.

➤ Maintain social distancing

Maintain at least 1 meter (3 feet) distance between yourself and anyone who is coughing or sneezing.

Why? When someone coughs or sneezes they spray small liquid droplets from their nose or mouth which may contain virus. If you are too close, you can breathe in the droplets, including the COVID-19 virus if the person coughing has the disease.

➤ Avoid touching eyes, nose and mouth

Why? Hands touch many surfaces and can pick up viruses. Once contaminated, hands can transfer the virus to your eyes, nose or mouth. From there, the virus can enter your body and can make you sick.

➤ Practice respiratory hygiene

Make sure you, and the people around you, follow good respiratory hygiene. This means covering your mouth and nose with your bent elbow or tissue when you cough or sneeze. Then dispose of the used tissue immediately.

Why? Droplets spread virus. By following good respiratory hygiene you protect the people around you from viruses such as cold, flu and COVID-19.

➤ If you have fever, cough and difficulty breathing, seek medical care early

Stay home if you feel unwell. If you have a fever, cough and difficulty breathing, seek medical attention and call in advance. Follow the directions of your local health authority.

Why? National and local authorities will have the most up to date information on the situation in your area. Calling in advance will allow your health care provider to quickly direct you to the right health facility. This will also protect you and help prevent spread of viruses and other infections.

➤ Stay informed and follow advice given by your healthcare provider

Stay informed on the latest developments about COVID-19. Follow advice given by your healthcare provider, your national and local public health authority or your employer on how to protect yourself and others from COVID-19.

Why? National and local authorities will have the most up to date information on whether COVID-19 is spreading in your area. They are best placed to advise on what people in your area should be doing to protect themselves.

- Protection measures for persons who are in or have recently visited (past 14 days) areas where COVID-19 is spreading
- Stay at home if you begin to feel unwell, even with mild symptoms such as headache and slight runny nose, until you recover.

Why? Avoiding contact with others and visits to medical facilities will allow these facilities to operate more

effectively and help protect you and others from possible COVID-19 and other viruses.

- If you develop fever, cough and difficulty breathing, seek medical advice promptly as this may be due to a respiratory infection or other serious condition. Call in advance and tell your provider of any recent travel or contact with travelers.

Why? Calling in advance will allow your health care provider to quickly direct you to the right health facility. This will also help to prevent possible spread of COVID-19 and other viruses.

➤ **What are the symptoms this coronavirus causes?**

The virus can cause pneumonia. Those who have fallen ill are reported to suffer coughs, fever and breathing difficulties. In severe cases there can be organ failure. As this is viral pneumonia, antibiotics are of no use. The antiviral drugs we have against flu will not work. Recovery depends on the strength of the immune system. Many of those who have died were already in poor health.

➤ **Should I go to the doctor if I have a cough?**

In the UK, the medical advice is that if you have recently travelled from areas affected by coronavirus, you should:

- stay indoors and avoid contact with other people as you would with the flu
- call NHS 111 to inform them of your recent travel to the area

➤ **Is the virus being transmitted from one person to another?**

China's national health commission confirmed human-to-human transmission in January, and there have been such transmissions elsewhere.

➤ **How many people have been affected?**

As of 12 March, more than 125,000 people have been infected in more than 180 countries, according to the Johns Hopkins University Center for Systems Science and Engineering.

There have over 11,951 deaths globally.

➤ **Why is this worse than normal influenza, and how worried are the experts?**

We don't yet know how dangerous the new coronavirus is, and we won't know until more data comes in. Seasonal flu typically has a mortality rate below 1% and is thought to cause about 400,000 deaths each year globally. Sars had a death rate of more than 10%. Another key unknown is how contagious the coronavirus is. A crucial difference is that unlike flu, there is no vaccine for the new coronavirus, which means it is more difficult for vulnerable members of the population – elderly people or those with existing respiratory or immune problems – to protect themselves. Hand-washing and avoiding other people if you feel unwell are important. One sensible step is to get the flu vaccine,

which will reduce the burden on health services if the outbreak turns into a wider epidemic.

➤ **Have there been other coronaviruses?**

Severe acute respiratory syndrome (Sars) and Middle Eastern respiratory syndrome (Mers) are both caused by coronaviruses that came from animals. In 2002, Sars spread virtually unchecked to 37 countries, causing global panic, infecting more than 8,000 people and killing more than 750. Mers appears to be less easily passed from human to human, but has greater lethality, killing 35% of about 2,500 people who have been infected.

So far, most of those infected with the virus have been in China, and most of the deaths have occurred there, as well. But now South Korea, Iran and Italy are coping with significant outbreaks. Italy has imposed restrictions throughout the country. The United States has seen more than 800 cases and about 30 deaths. Many do not seem linked to international travel, which suggests that the virus is spreading in communities. The coronavirus may have infected up to 1,500 people in the Seattle area alone, hints a model produced by infectious disease experts. The number of infections may be doubling every six days, according to another model, but the nation's capacity to test for the infection has lagged.

Much remains unknown about the virus, including how many people may have very mild or asymptomatic infections, and whether they can transmit the virus. The precise dimensions of the outbreak are hard to know.

➤ **What is a coronavirus?**

Coronaviruses are named for the spikes that protrude from their surfaces, resembling a crown or the sun's corona. They can infect both animals and people, and can cause illnesses of the respiratory tract.

At least four types of coronaviruses cause very mild infections every year, like the common cold. Most people get infected with one or more of these viruses at some point in their lives.

Another coronavirus that circulated in China in 2003 caused a more dangerous condition known as Severe Acute Respiratory Syndrome, or SARS. The virus was contained after it had sickened 8,098 people and killed 774.

Middle East Respiratory Syndrome, or MERS, first reported in Saudi Arabia in 2012, is also caused by a coronavirus.

The new virus has been named SARS-CoV-2. The disease it causes is called Covid-19.

➤ **How dangerous is it?**

It is hard to accurately assess the lethality of a new virus. It appears to be less often fatal than the coronaviruses

that caused SARS or MERS, but significantly more so than the seasonal flu. The fatality rate was over 2 percent, in one study. But government scientists have estimated that the real figure could be below 1 percent, roughly the rate occurring in a severe flu season.

About 5 percent of the patients who were hospitalized in China had critical illnesses.

Children seem less likely to be infected with the new coronavirus, while middle-aged and older adults are disproportionately infected.

Men are more likely to die from an infection compared to women, possibly because they produce weaker immune responses and have higher rates of tobacco consumption, Type 2 diabetes and high blood pressure than women, which may increase the risk of complications following an infection.

“This is a pattern we’ve seen with many viral infections of the respiratory tract — men can have worse outcomes,” said Sabra Klein, a scientist who studies sex differences in viral infections and vaccination responses at the Johns Hopkins Bloomberg School of Public Health.

➤ **How is the new coronavirus transmitted?**

Experts believe that an infected animal may have first transmitted the virus to humans at a market that sold live fish, animals and birds in Wuhan. The market was later shut down and disinfected, making it nearly impossible to investigate which animal may have been the exact origin.

Bats are considered a possible source, because they have evolved to coexist with many viruses, and they were found to be the starting point for SARS. It is also possible that bats transmitted the virus to an intermediate animal, such as pangolins, which are consumed as a delicacy in parts of China, and may have then passed on the virus to humans. The outbreak grew because of human-to-human transmission.

People infected with the virus produce tiny respiratory droplets when they breathe, talk, cough or sneeze, allowing the virus to travel through the air. Most respiratory droplets fall to the ground within a few feet. People, who are in close contact with those infected, particularly family members and health care workers, may catch the virus this way.

Scientists don’t know how long the new coronavirus can live on surfaces, and preliminary research suggests that hot and humid environments may not slow down the pathogen’s spread. Warm weather does tend to inhibit influenza and milder coronaviruses.

Infected people may be able to pass on the new coronavirus even if they have few obvious symptoms, a

study in Germany has found. That’s “bad news,” said Dr. William Schaffner, an expert in infectious diseases at Vanderbilt University Medical Center in Nashville.

When people don’t know they are infected, “they’re up and about, going to work or the gym or to religious services, and breathing on or near other people,” he said. Still, a report by the World Health Organization suggests that asymptomatic cases are rare.

What symptoms should I look out for?

Symptoms of this infection include fever, cough and difficulty breathing or shortness of breath. The illness causes lung lesions and pneumonia. But milder cases may resemble the flu or a bad cold, making detection difficult.

Patients may exhibit other symptoms, too, such as gastrointestinal problems or diarrhea. Current estimates suggest that symptoms may appear in as few as two days or as long as 14 days after being exposed to the virus.

If you have a fever or a cough and recently visited China, South Korea, Italy or another place with a known coronavirus outbreak, or spent time with someone who did, see your health care provider. Call first, so the office can prepare for your visit and take steps to protect other patients and staff from potential exposure.

➤ **Is there a test for the virus? What is the treatment?**

There is a diagnostic test that can determine if you are infected. It was developed by the Centers for Disease Control and Prevention, based on genetic information about the virus provided by the Chinese authorities.

In early February, the C.D.C. sent diagnostic test kits to 200 state laboratories, but some of the kits were flawed and recalled. Now other laboratories are making their own tests. Other countries are using test kits manufactured locally or sent out by the W.H.O.

The C.D.C. announced That anyone who wanted to be tested could, if a doctor approves the request. Private companies, such as Lab Corp and Quest Diagnostics, are also rushing to provide tests at various labs across the country, but the supply has yet to meet public demand. Many patients complain that they still cannot get tested.

Once a coronavirus infection is confirmed, the treatment is mainly supportive, making sure the patient is getting enough oxygen, managing his or her fever and using a ventilator to push air into the lungs if necessary, said Dr. Julie Vaishampayan, chairwoman of the public health committee at the Infectious Diseases Society of America.

Patients with mild cases are told to rest and drink plenty of fluids —while the immune system does its job and heals itself,” she said. Most people with mild infections

recover in about two weeks. More than half of those who have been infected globally have already recovered.

A number of drugs are currently being tested as potential treatments, including an antiviral medication called remdesivir, which appears to be effective in animals and was used to treat the first American patient in Washington State. The National Institutes of Health is testing the drug on infected patient in a clinical trial in Nebraska. The drug's maker, Gilead, has also begun trials at various sites in Asia.

➤ **How long will it take to develop a vaccine?**

A coronavirus vaccine is still months away — and perhaps years. While new technology, advancements in genomics and improved global coordination have allowed researchers to act quickly, vaccine development remains an expensive and risky process.

After the SARS outbreak in 2003, it took researchers about 20 months to get a vaccine ready for human trials. (The vaccine was never needed, because the disease was eventually contained.)

By the time of the Zika outbreak in 2015, researchers had brought the vaccine development timeline down to six months.

Now, they hope that work from past outbreaks will help cut the timeline further. Scientists at the National Institutes of Health and several companies are working on vaccine candidates.

Dr. Anthony S. Fauci, director of the National Institute of Allergy and Infectious Diseases, said a preliminary clinical trial might get off the ground in as little as three months. But researchers would still need to conduct extensive testing to prove a vaccine was safe and effective.

➤ **How can I protect myself?**

The best thing you can do to avoid getting infected is to follow the same general guidelines that experts recommend during flu season, because the coronavirus spreads in much the same way. Wash your hands frequently throughout the day. Avoid touching your face, and maintain a distance — at least six feet — from anyone who is coughing or sneezing.

The risk of infection with the new coronavirus in the United States “is way too low for the general public to start wearing a face mask,” said Dr. Peter Rabinowitz, co-director of the University of Washington Meta Center for Pandemic Preparedness and Global Health Security.

But, he added, “If you have symptoms of a respiratory illness, wearing a mask reduces the risk of infecting others.”

Should I cancel my international travel plans?

The C.D.C. has warned Americans not to travel to China, Italy, Iran or South Korea unless it is absolutely essential. The State Department on Sunday warned Americans not to travel on cruise ships at all.

Older adults and people with chronic medical conditions should also consider postponing travel anywhere, particularly by air, federal officials warned.

Many countries have also enacted travel restrictions and bans, closing their doors to people from countries with sustained transmission of the virus. Governments around the world have been screening incoming passengers for signs of illness. Thailand and Malaysia have turned away yet another cruise ship, this one carrying a large number of Italians.

Airlines and cruise lines have canceled service to destinations affected by the outbreak, with others, including United Airlines, cutting back on domestic service and international service.

Is it too late to contain the virus?

W.H.O. officials have credited lockdown measures China imposed in late January for averting the spread of more cases from Wuhan. China sealed off cities, shut down businesses and schools, and ordered residents to remain in their homes. Officials use cellphone data to track and intercept those who have been to Hubei Province.

In recent weeks, government workers have gone door-to-door to round up people who are infected, placing them in stadiums and other buildings that have been converted to makeshift hospitals. Now, official reports suggest that new cases in China are waning.

But there is growing fear that containment may no longer be possible.

Clarence Tam, an assistant professor of infectious diseases at the School of Public Health at the National University of Singapore, said the surge of cases in multiple countries was “concerning because we know the transmissions are spreading at a fast rate.”

“We’ve learned some things of this new virus for the past couple of weeks that make it seem unlikely that containment will be a strategy that will completely stop this virus,” he added.

There is benefit to delaying its spread as long as possible. Containing the virus may buy health officials more time to stock hospitals with test kits and respirators, and for local governments, companies and schools to enact strategies — telecommuting and online classes, for instance — that may reduce the spread.

But the ability of nations to prepare for the arrival of coronavirus cases will depend largely on the strength of their health systems, capacity to conduct tests and effectiveness in communicating updates to the public.

“We have been dealing with flu for decades, and even now it seems some countries don’t even have a policy for influenza preparedness,” said Leo Poon, head of the University of Hong Kong’s public health laboratory sciences division. —Not to mention something which is new to them. That’s a problem.”

Children are just as likely to become infected with the new coronavirus as adults, finds one of the most detailed studies yet published on the spread of the virus, known as SARS-CoV-2. The analysis “based on data from Shenzhen in China — provides a partial answer to one of the most pressing questions surrounding the outbreak: the role of children.

Previous studies have suggested that kids are much less likely than other age groups to develop severe symptoms when infected by the coronavirus. But it was not clear whether this was because they weren’t getting infected or because they were fighting off the infection more effectively.

“Kids are just as likely to get infected and they’re not getting sick,” says Justin Lessler, an infectious-disease epidemiologist at Johns Hopkins Bloomberg School of Public Health in Baltimore, Maryland. He co-led the study with three other epidemiologists “Qifang Bi, also at Johns Hopkins, Ting Ma at the Harbin Institute of Technology in Shenzhen and Tiejian Feng at the Shenzhen Center for Disease Control and Prevention. They posted the analysis to the medRxiv preprint server on 4 March.

The study is unique in that it looked at not only people who were infected with the virus, but also large numbers of their close contacts, some of whom were infected and many of whom were not. The researchers followed 391 people who were diagnosed on the basis of their symptoms, and 1,286 of their close contacts to see whether these contacts tested positive for the virus even if they didn’t show symptoms. Overall, the team found that children under 10 who had potentially been exposed to the virus were just as likely to become infected as other age groups, with between 7% and 8% of contacts of known cases later testing positive.

The authors also found that people who lived in the same household as someone infected with the virus were about six times more likely get infected than those who made contact with an infected person in other settings.

“This may be the first clear evidence that children are as susceptible as adults to SARS-CoV-2 infection,” says Ben Cowling, an infectious-disease epidemiologist at the University of Hong Kong. He wonders whether the fact

that outbreaks haven’t been observed in schools could be down to the fact that children’s symptoms are mild.

Lessler says it’s still not clear whether children are important in transmitting the virus, as they are for influenza; children routinely develop flu symptoms and are common hubs in chains of transmission. “That’s one of the current critical remaining questions and we’re trying to figure out how to answer it,” he says. “I have a 7-month-old and a 6-year-old and I can’t imagine that, if they have any virus at all, they’re not getting it on somebody.”

The study could have important implications for slowing the spread of the virus through measures such as school closures. “Once we say containment is not an option, we can’t ignore the kids,” says Lessler.

CONCLUSION

The Real-time training during global emergencies is critical for effective preparedness and response. The outbreak was declared a Public Health Emergency, The international community has asked for US\$675 million to help protect states with weaker health systems as part of its Strategic Preparedness and Response Plan. The manuscript is got conclusion that still we don’t have any specific treatment for COVID 19, so we have to take more care like, Wash your hand often with soap and water for 20 seconds, Avoid touching your eyes, nose and mouth with unwashed hands, Stay at home when you are sick and Cover your cough or sneeze with a tissue or cloth.

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