

Special Issue on

2019 New Coronavirus

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Part I

Introduction

1.1 What is 2019 New Coronavirus?

2019 new coronavirus was discovered due to emerging viral pneumonia cases in Wuhan; and the infectious disease was named "COVID-19" by the World Health Organization (WHO). It is the seventh coronavirus capable of infecting humans, which was named "SARS-CoV-2" by the International Committee on Taxonomy of Viruses (ICTV) (the others are HCoV-OC43, HCoV-HKU1, HCoV-NL63, HCoV-229E, SARS-CoV, MERS-CoV). The virus is about 100 nanometers in diameter (Figure 1).

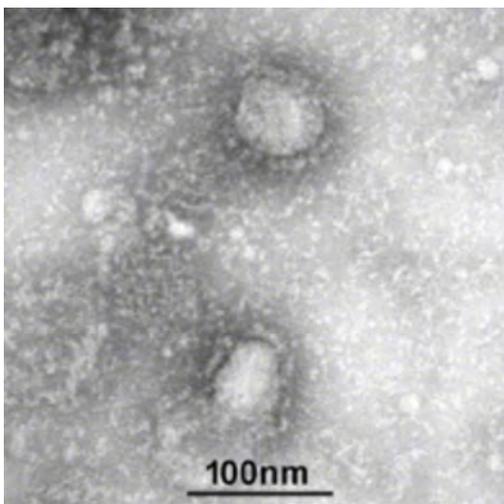


Figure 1. SARS-CoV-2 under the electron microscope

It has been discovered in recent years that bats are likely to be natural hosts for emerging coronaviruses, such as SARS-CoV. Infected by the low-pathogenicity coronaviruses (HCoV-OC43, HCoV-HKU1, HCoV-NL63, HCoV-229E), which are currently prevalent in the population, the patient expels toxic secretions from the respiratory tract through sneezing and coughing, then spreads it to other susceptible populations by droplet transmission or direct contact. Two



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high-pathogenicity members of the coronavirus family, SARS-CoV and MERS-CoV, caused epidemics and outbreaks in China in 2003 and in Middle East in 2012, respectively. Quickly, Chinese scientists have completed the whole genome sequencing of SARS-CoV-2 and the three-dimensional structures of key viral proteins have been analyzed by the structural virologists. Some old drugs such as Remdesivir, Favipiravir and Chloroquine, and also traditional Chinese medicines showed potential for the treatment of COVID-19.

1.2 Clinical Features

At present, the incubation period of the disease is generally 2-7 days, and the longest is no more than 41 days. The onset is hidden, and the progress is slow and/or followed by rapid-go-worse. The patient at incubation period is contagious. Median duration of viral shedding was 20 days in survivors, but SARS-CoV-2 was detectable until death in non-survivors. The longest observed duration of viral shedding in survivors was 37 days.

Main manifestations of infection include fever, fatigue, dry cough, headache, and diarrhea. Some mild patients do not have fever and obvious respiratory symptoms. Most of the patients have a good prognosis, and the symptoms of children are relatively mild. The patients with older age and comorbidities such as hypertension, diabetes and coronary heart disease, will have high risk of death.

1.3 How to Tell if You Are Infected with SARS-CoV-2?

First, do you have the journey history to the affected area?

Second, you need to judge whether you have contacted the infected person.

Third, distinguish between common cold, flu and new coronavirus pneumonia:

- The common symptoms of a common cold are sneezing, runny nose, and a lack of ventilation.

Part II

Diagnosis Test of SARS-CoV-2

2.1 Virus Features

SARS-CoV-2 are circular or oval in shape under an electron microscope, have a diameter of 60-140 nm. The genome of

■ Flu is often characterized by high fever, sore muscles, and sore throat.

■ In addition to the above-mentioned symptoms, the diagnosis of COVID-19 requires a professional institution for viral nucleic acid testing (China CDC or CDC-designated hospitals).

1.4 How to Prevent?

- Stop party; stay at home
- Avoid contact with wild animals
- Avoid close contact with people who have cold symptoms
- Wash hands (Soap or hand sanitizer)
- When you cough or sneeze, cover your nose and mouth with a tissue
- Wear a face mask when you go out
- Meat and eggs thoroughly cooked
- Appropriate exercise
- Don't be over panic, take precautions step by step.

1.5 Protective Measures Against SARS-CoV-2 by WHO

Source: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/advice-for-public>

Stay aware of the latest information on the COVID-19 outbreak, available on the WHO website and through your national and local public health authority. COVID-19 is still affecting the people in China but the situation is eventually contained. The COVID-19 outbreak has spread more than 100 countries as a global pandemic, and the situation is worst in Italy, Iran and South Korea. Most people who become infected experience mild illness and recover, but it can be more severe for others. Take care of your health and protect others.

SARS-CoV-2 is significantly different from those of SARS-CoV and MERS-CoV, with homology of 79% and 50%, respectively. As you know, the similarity between human and gorilla genome is 86-89% [1]. At present, from bats, scientists have found the coronavirus most close to SARS-CoV-2, with a genome homology of 96.2% [2].

2.2 Inactivation of SARS-CoV-2

The current understanding of the features of coronaviruses mainly comes from previous research on SARS-CoV and MERS-CoV [3]. Coronavirus is sensitive to ultraviolet and heat. At 30°C for 56 minutes, 75% ethanol, chlorine-containing disinfectant, peracetic acid and chloroform can inactivate the virus.

2.3 Principle of Diagnosis

Scientists develop detection methods for viral genetic material (DNA or RNA) or proteins. For example: a throat swab of a fever patient is often collected during the flu season. Then the genes of the flu virus are tested to determine if the patient is infected. Before the operation, the patients were routinely detected with four pathogens (HBV, HCV, HIV, Treponema pallidum). These detections are all based on cross-linking signal amplification of "antigen + antibody" complex; the detected antigen is the expression product of a certain gene of the virus, i.e., a certain protein.

2.4 Diagnosis Test

Currently, the National Health Committee's diagnosis test is based on nucleic acid detection [3]. The test samples come from: nasopharyngeal swabs, sputum, lower respiratory tract secretions, blood, feces, etc. There are two types of detection methods. The first type is RT-PCR: positive result of real-time fluorescent detection for SARS-CoV-2 nucleic acid in respiratory or blood specimens (Figure 1).

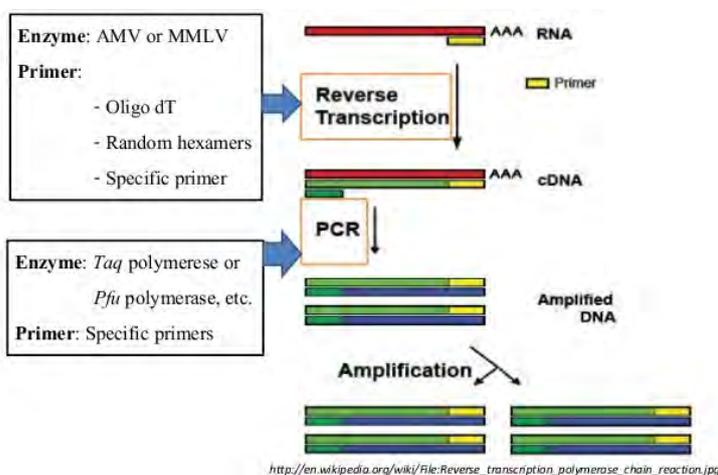


Figure 1. Flowchart of RT-PCR

The second type is sequencing: sequencing of viral genomes of respiratory or blood specimens, which highly homologous to SARS-CoV-2. In addition, in view of the special circumstances, clinical diagnosis cases were included when suspected cases had imaging characteristics of pneumonia.

2.5 False Negative?

False negative means that test report shows negative, but it is actually positive, which is a wrong judgment and equivalent to missed diagnosis. Why are nucleic acid tests false negative? In summary, there are the following factors [4]:

- **Sample Sites:** compared with upper respiratory tract samples (such as nasopharyngeal swabs), lower respiratory tract samples (such as alveolar lavage fluid) are easier to detect. However, collecting alveolar lavage fluid has technical difficulties, a high risk of infection, and a low patient acceptance.
- **Sampling Quality:** Different professionals have different sampling methods, resulting in uneven sampling quality. At the same time, the expelling time of virus at the collecting sites also affects the effectiveness.
- **Virus Characteristics:** The SARS-CoV-2 is a single-stranded RNA virus. The ubiquitous RNase in the environment easily degrades the virus.
- **Kit Sensitivity:** The SARS-CoV-2 can only be detected when the amount of virus in the sample is \geq threshold. There are differences in the quality of kits from different manufacturers, which have a certain impact on the test results.

How to tackle the false negative? It is reported that increasing the detection of the lower respiratory tract, stool, and blood samples, will increase accuracy. Additionally, the kits for detecting SARS-CoV-2-specific IgG/IgM antibodies from blood of patients are almost available. Many assays of research institutions and companies are under clinical trials. We hope that it can be applied to the detection as soon as possible, to make up for the shortcomings of the existing detection [4].

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3.1 What is Quarantine?

Plague flourished in Europe in the 14th century, when one third of Europe's population (about 25 million) died directly or indirectly from plague. As an important trade port, how did Venice respond? The local government issued a bill ordering all foreign merchant ships to stay in nearby islands for "forty days" [Latin words 'quarantagioni' original means "forty days"] to ensure that crews and cargo were free from plague before landing (Figure1). Thereafter, 'quarantagioni' was subjected to the meanings "quarantine period/quarantine"[1]. In contrast, the original meaning of "forty days" has gradually subsided. The word "quarantagioni" is the root of qua-, meaning "four." Common words include quarter, square, and so on.

3.2 What is Communicable Disease?

Communicable disease refers to a large group of diseases caused by various pathogenic microorganisms or parasites, which can be transmitted from person to person, person to animal, animal to animal. According to the degree of harm, there are 39 types of legal infectious diseases in China: Class A (Plague, Cholera), Class B (26 types), Class C (11 types)[2].



Figure 1 Origin of quarantine

3.3 Basic of Communicable Disease

- **Infection Source:** refers to humans or animals that carry pathogens in the body and continuously excrete them to the outside, such as bats carrying the SARS virus in 2003; patients of COVID-19 infected with SARS-CoV-2.
- **Transmission Route:** refers to the process in which the pathogen is excreted from the source of infection and reaches a new susceptible person or animal through a

certain mode of transmission. The common transmission routes contain ① air / droplet transmission, ② water/gut transmission, ③ close contact/sex transmission, ④ vertical transmission (mother-to-child), et al.

- **Susceptible Person:** refers to a state in which the person lacks immune protection against a pathogen of an infectious disease and is susceptible to infection. For example, elderly people with underlying diseases (diabetes/hypertension) have low immunity and are more susceptible to infection.

3.4 How to Prevent and Control Communicable Disease?

■ **Control the source of infection:** quarantines both the oldest and best way to control communicable diseases. Why the quarantine period is 14 days? Because the majority of observed latency for COVID-19 is 14 days.

■ **Cut off transmission:** a number of measures can be applied, such as environmental disinfection, washing hands, etc. ① To avoid air/droplet transmission: wear masks/goggles/protective clothing. ② To avoid water/intestinal transmission: heat and cook all foods.

■ **Protect Susceptible People:** science popularization, avoid going to places with crowd people, exercise, and psychological counseling are frequently used. In the old story, personnel/items of the Venetian merchant ship must be isolated for a 40-day to avoid spread to local residents.

3.5 See also--1 Malaria & 3 Nobel Prizes

It is estimated by WHO that the number of malaria cases in 2010 was 239 million (95% confidence interval: 219 million to 285 million), and in 2016 was 217 million (95% CI: 200 million to 259 million). In 2017, a total of 219 million cases of malaria occurred (95% CI: 203 million to 262 million). Most cases of malaria in 2017 occurred in the Africa region (200 million cases, 92%), the Southeast Asia region (5%) and the Eastern Mediterranean region (2%)[3]. Here is the list of three malaria-related Nobel Prizes (Figure 2)[4].

COVID-19 is not the first, and it is likely not the last one to cause an epidemic worldwide. Living in a global village, "we" may seem far apart, but can also be very closely connected. As human beings, we should understand, learn and respect nature!

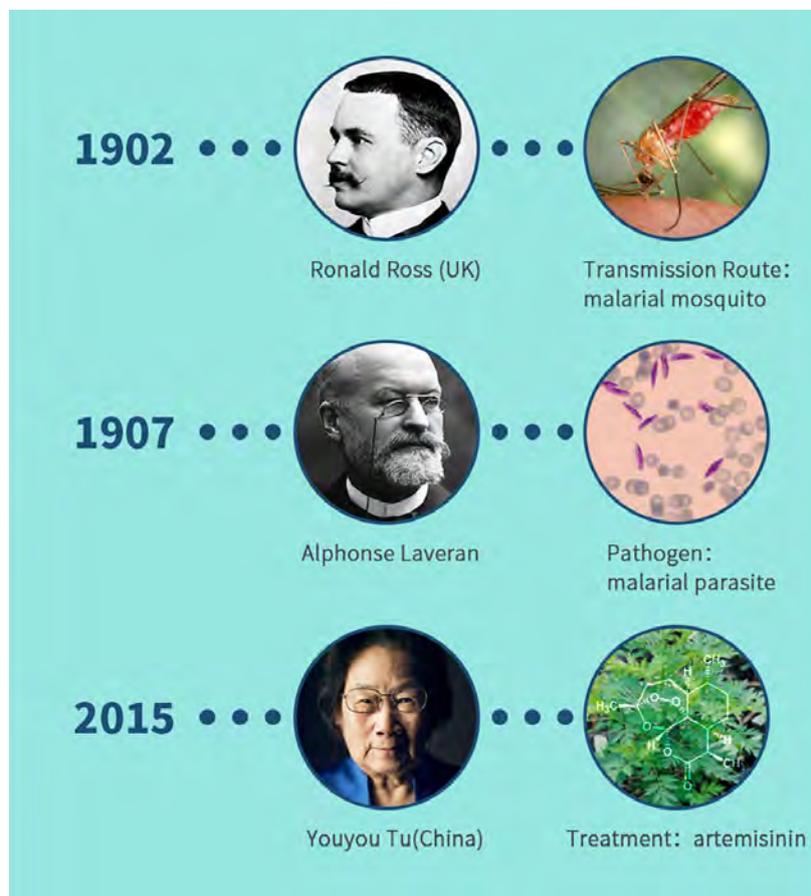


Figure 2. Nobel Prizes for malaria

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4. <https://www.nobelprize.org/medicine>

4.1 What's the Vaccine?

Vaccine refers to the prophylactic biological products used for human immunization to prevent and control the occurrence and prevalence of diseases. The earliest vaccine practice was recorded in Tang Dynasty of China. Sun Simiao collected pus from patients with smallpox and painted on health people to obtain immunity against smallpox. Hundreds of years later, a British doctor, Edward Jenner, developed the modern vaccinology. He injected children with pustule collections from hands of milkmaids, who infected with attenuated cowpox virus, to protect children against smallpox infection.

In the following centuries, vaccines have been developed to prevent various infectious diseases, such as hepatitis B, rabies, measles and tetanus, contributed greatly to public health safety.

4.2 How Long can We Develop a Successful Vaccine?

Vaccine is still the most effective way to prevent the infectious diseases. Therefore, upon the outbreak of pneumonia caused by SARS-CoV-2 infection, a focus of attention is that: when we will have available vaccine. Three months? Three years? Five to ten years? To answer this question, we might refer to the vaccine development against pathogens that cause "international public health emergencies" in recent years.

In 2014, the Ebola epidemic occurred in Africa. Ebola virus is a severe pathogen, with infection mortality of more than 70%. The disease outbreak promoted the global vaccine development by academies and pharmaceutical companies worldwide. Finally, the first Ebola vaccine (Figure 1) was approved at the end of 2019, which is more than five years from the beginning of the epidemic outbreak.

Zika vaccine is another example. At the end of 2015, Zika epidemic spilled over to more than 80 countries and regions from Brazil. Since infection of Zika virus during pregnancy can lead to severe congenital microcephaly, the development of vaccine is an urgent demanded. Although many vaccines showed good protective effect on animal models, the most advanced vaccines are still in clinical trials four years later. Therefore, the fact is that vaccine development takes quite a long time, even for the most urgent infectious diseases.

So why does it take so long to develop a vaccine? Firstly, it needs to design and determine the effective components as antigen, such as inactivated or attenuated virus, or subunit of virus. Manufacturing processes and quality control have to be established. Secondly, experiments are required to obtain enough data for application of clinical trials, including evaluations of effectiveness and toxicology for vaccine candidates in animal models. This process usually takes months or years. Finally, further validations in humans are required in phase I, II and III clinical trials as the basis for vaccine approval, which usually takes years. Therefore, the vaccine against SARS-CoV-2 may not be applied to the current epidemic in a short time. However, given the disease emergency, the development and drug-approval process may be greatly accelerated, shortening significantly the development cycle.

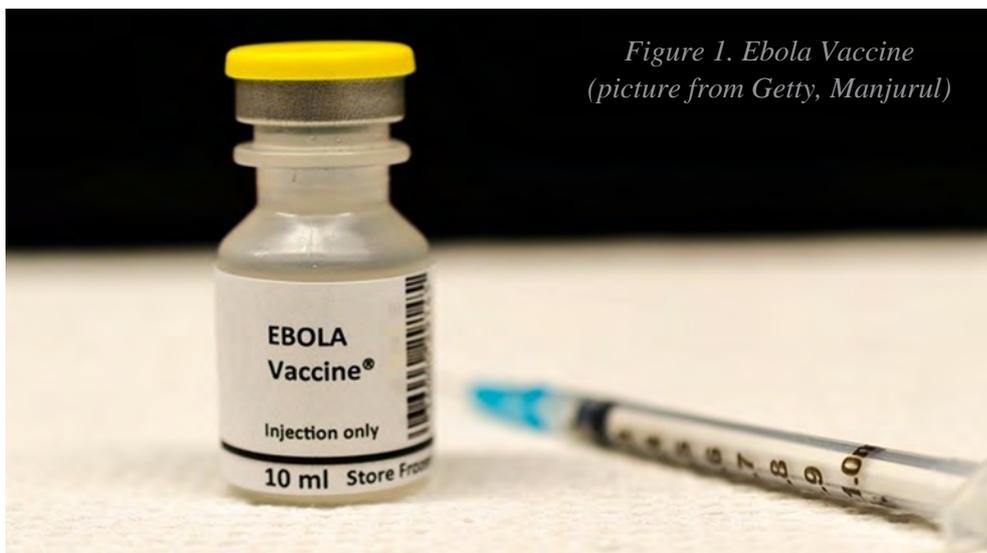


Figure 1. Ebola Vaccine
(picture from Getty, Manjurul)

4.3 Status & Prospect of SARS-CoV-2 Vaccine

Nowadays, the global development of SARS-CoV-2 vaccines are booming. Although the SARS-CoV-2 is a new virus for us, we have substantial knowledge of its

brother viruses, such as SARS coronavirus and MERS coronavirus. Based on the experience in vaccine development against SARS/MERS-CoV, we will reduce the risk of vaccine development against SARS-CoV-2. We hope the vaccine will be available as soon as possible to control the current epidemics. It can also serve as the stockpile to prevent possible re-emergence of such diseases in the future.



Figure 2. Stages for vaccine development

Part V

How to Protect Kids from SARS-CoV-2?

With the prevalence of the COVID-19, the number of cases in children infected has gradually increased, including infant infections, which make parents feel anxious. How can we protect our children from the COVID-19?

First, we should know the source and transmission routes of childhood infections. One source of infection of children is the infected people of COVID-19, like adults. Three major routes of infection are through droplet, contact and conjunctiva transmission. Since the immunologic function of children is not as good as adults, respiratory infections are more likely to occur in children. Therefore, parents should pay more attention to cutting off the source and transmission routes of children from the COVID-19.



5.1 What Should Parents Do in the Daily Life?

- **Staying Home.**

If not necessary, parents should not take your children out, especially in confined spaces and places with a dense crowd. If necessary, parents should not try to use public transportation, and stay as far away from others as possible, such as keeping a distance of more than 1 m from others.

■ Wearing a Face Mask.

Parents should help children to wear masks when they go out. Please instruct them correctly use masks and help them adjust the position of the masks to ensure the protective effect. If the protective effect is reduced, it may contaminate the inside of the mask and cause infection. Repeated use of disposable masks is not recommended. Since newborns and small babies cannot wear masks, protection for infants should be passive. Parents should wear masks when taking care of them, please do not kiss them, do not cough, sneeze or exhale to them. When you cough or sneeze, please cover your mouth and nose completely with paper towels and wash your hands carefully with running water.

■ Washing Hands Frequently.

Parents should urge children to develop good habits as follows: 1) do not touch the surface of objects in public areas (especially frequently touched surfaces such as elevator buttons), do not touch or rub the mouth, nose, eyes and other parts with unclean hands; 2) Washing hands use soap or hand sanitizer before eating or after touching unclean objects (Figure 1); 3) Be sure to rinse hands with running water and carefully rub each part of your hands according to the seven-step washing method.



Figure 1. Washing hands is a good way to prevent SARS-CoV-2

■ Cleaning & Ventilating the Room.

It is important to clean the room by air purifier or ultraviolet radiation and ventilate the room regularly every day. Keeping the children warm and prevent the child from getting cold during the ventilation. At the same time, please wipe the surface of the object with alcohol disinfection daily to keep the home environment clean.

■ Enhancing Immunologic Function.

Balanced nutrition, proper exercise, and adequate sleep can boost children's immunity. Children should have a balanced diet with protein, vegetarian, and fruits in daily life. Properly arrangement of doing exercise and sleep on time is also important.

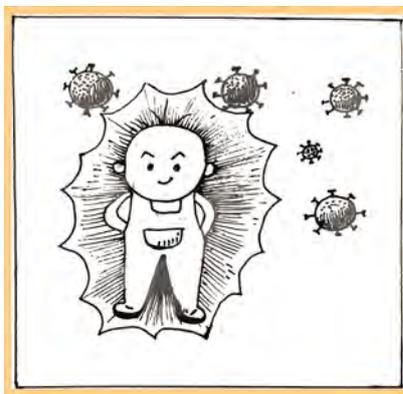


Figure 2. Enhance immunity for child

5.2 What Should We Do if Children Get Fever?

Children with any age that have fever for more than 3 days should go to the hospital.

- Newborns and infants within 3 months should go to the hospital whenever they have fever.
- Infants aged 3-6 months that have a temperature exceeding 38°C or fever for more than 24 hours should go to the hospital.
- Infants aged 6 months to 2 years old who have fever over 24 hours should go to the hospital for treatment.
- If your children have a weak mental reaction, headache, chills, cough, dyspnea, reduced convulsions, vomiting, diarrhea, or oliguria, they should be taken to the hospital as soon as possible.
- If the children or parents have a history of travel or residence in the affected area within 14 days before the onset, or contacting with infected people, the medical institution should be truthfully notified.

5.3 What Should Parents Do after Returning to Work?

When parents return to work after the holiday, the opportunities for contact with others will be increased with the increased risk of contracting the COVID-19. In this case, parents must strengthen their own protection, try to avoid going to crowded public places, and wear masks correctly when going out. Furthermore, parents should change clothes and shoes immediately when you go home, handle face masks properly, and do not touch your children until clean your entire body, from hair to toe.

Let us understand the knowledge of prevention, cut off the source of infection and transmission routes for children, and build a protective wall of COVID-19 for our children.