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Advances and Challenges in the Detection and Prevention of COVID-19

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Abstract: At the moment when the COVID-19 pandemic has not completely ended, COVID-19 is still spreading worldwide, and the treatment and prevention measures of the virus are still very important. At present, research on COVID-19 mainly includes transmission mode and structure. Through this research, detection methods, drugs, and preventive measures for COVID-19 have also been developed. However, although all aspects are involved now, there are also many shortcomings. There is no means to completely prevent COVID-19. This paper mainly analyzed the research on the detection and prevention of COVID-19 and obtained the results of both aspects, such as PCR detection and RNA vaccine. The article provides a reference for the overall framework of future research, and the problem of whether there is a universal detection and vaccine type worldwide has not been solved. Future research can focus on the development of RNA vaccines, improve detection sensitivity, reduce detection costs, and achieve rapid detection.

Keywords: COVID-19, SARS-CoV-2 diagnosis, vaccine.

1. Introduction

The COVID-19 pandemic is an event with significant impact that causes millions of deaths and a world that is nearly shut down. Officially declared as a pandemic on March 11, 2020, COVID-19 has caused 13 million deaths in two years. By 2024, although the COVID-19 pandemic is gradually fading out of the world's view, the impact of this event remains. The outburst of COVID-19 creates an enormous impact on the world's economy, job market, health, and social life. COVID-19 eliminated a decade of progress in global level of life expectancy, a report released by the World Health Organization (WHO), states that this pandemic has wiped out nearly a decade of progress in improving life expectancy. Between 2019 and 2021, global life expectancy decreased by 1.8 years to 71.4 years, returning to the level of 2012 [1].

In 2020, the global economy experienced its most severe recession since World War II, with a 5.2% contraction in the global economic growth rate [2]. The impact of the epidemic on the global value chain is particularly significant, and disruptions in the global value chain may amplify the effect of the pandemic on trade, production, and financial markets. In addition, the epidemic has also led to a large number of job losses and income reductions, causing hundreds of millions of people to fall into extreme poverty. In 2021, the global labor market suffered a huge impact due to COVID-19 and lost the equivalent of 100 million full-time jobs. In addition, the global number of unemployed people in 2022 is 205 million, with an unemployment rate of 5.7%, which is a rate last seen in 2013 [3].

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Because of these huge impacts, it is still important to study COVID-19 and ways to reduce its effect on health and society.

The current study on COVID-19 focuses mostly on the structure and its transmission route, and how it spreads from animal to people and thus between people. However, there is less information about the detection methods for COVID-19 and the development of related vaccines. This information is important because it can teach people how to detect whether they have an infection and ways to prevent them from getting COVID-19. It is important to provide a broad overview of the whole aspect of COVID-19 to give people a clearer view of what it is and how people can deal with it on both social and personal levels. This paper will provide a broad view of COVID-19's biological properties, how it spreads, ways people can detect the infection, and vaccines that are developed to prevent getting the infection.

2. The structure, transmission mode, detection methods, and vaccine types of COVID-19

2.1. Introduction of COVID-19

Corona-virus, officially named SARS-CoV-2, has its name because it has a very similar structure to SARS-CoV. Coronavirus has a nearly 85% homology to the SARS-CoV [4]. SARS-CoV-2 contains single-stranded positive-sense RNA wrapped within a membrane envelope with an average diameter of 75-150 nm.

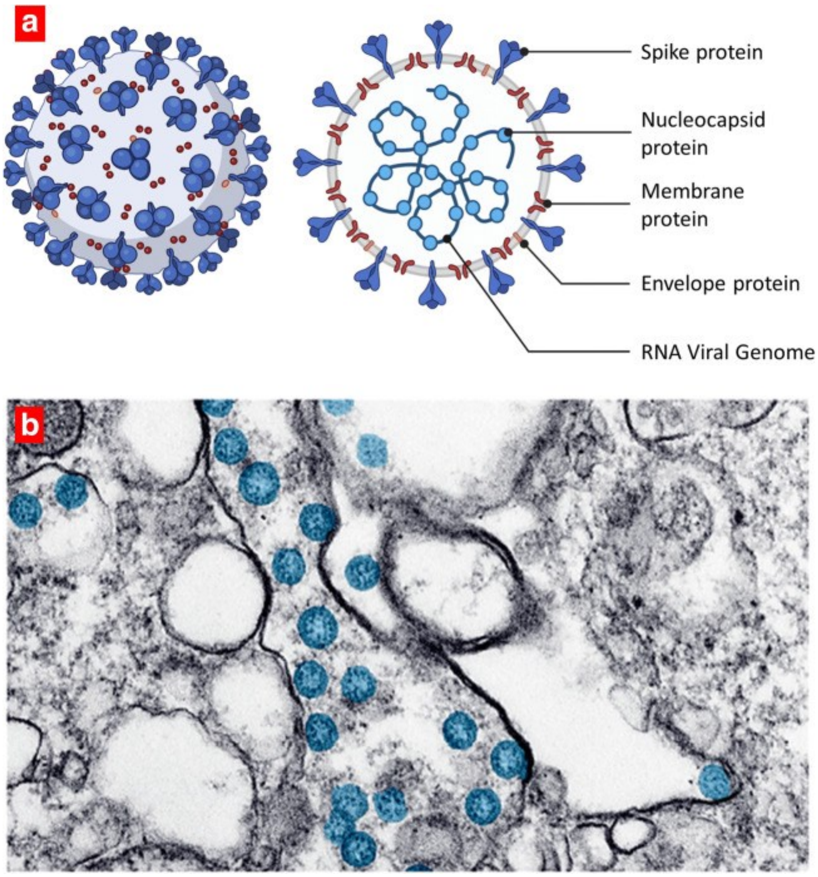

Figure 1: Human coronavirus. a Schematic structure of SARS-CoV-2 virus. b A transmission electron microscope image of SARS-CoV-2 spherical viral particles in a cell. The virus is colorized in blue [4].

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As shown in Figure 1, the envelope is covered with glycoprotein spikes which gave corona viruses their crown-like appearance. Four main structural proteins on the SARS-CoV-2's membrane envelope include spike (S) surface glycoprotein, membrane (M) protein, envelope (E) protein, and nucleocapsid (N) protein. Several other nonstructural proteins are also encoded by the viral genome [4]. Spike surface glycoprotein is responsible for recognizing the host cell receptors, which is the ACE2 receptor protein located on the host cell plasma membrane. Membrane protein help the virus to have its spherical shape. Envelope protein is in charge of virions assembly and release. Nucleocapsid protein helps packaging RNA genome in virions to form nucleocapsid, it also plays a role in pathogenicity as an interferon (IFN) inhibitor.

2.2. Transmission mode and symptoms of COVID-19

Coronavirus is widespread among birds and mammals. It obtains its diversity from cemented bats because bats are hosts to many different kinds of viruses and they live in an environment where there are any viruses and bacteria present. Initial cases reported in Wuhan, China, are considered to be an acquired infection from a zoonotic source from the Huanan wholesale seafood market which sold wild-life animals as well as domestic fowl. To determine the exact source of the virus, a comprehensive genetic sequence analysis was undertaken among different species of animals to isolate the possible virus reservoir. The results suggested that 2019-nCov is a recombinant virus between the bat CoV and an unknown-origin CoV. A study revealed, based on relative synonymous codon usage (RSCU) on a variety of animal species that bats are the most probable wildlife reservoir of 2019-nCov [5]. Human-to-human transmission can happen when one person contacts an infected person’s body tissue by inhaling the spray, touching the case’s oral, nasal, and eye mucous membranes, or even during medical treatment.

Symptoms of COVID-19 include fever, shortness of breath, coughing and extra. People who have a weaker immune system such as children or elders might show more severe symptoms and even lead to death. Symptoms of SARS-CoV-2 may take several days to reveal so people who are infected can spread the virus to others without being aware. This could lead to a sudden outburst of infected cases without the health care system being prepared. Because of that, scientists have developed ways to detect COVID-19 to make sure they found all the cases. Such detection methods follow three main categories: RNA detection and antibody detection.

2.3. Detection methods of COVID-19

RNA detection amplifies the RNA strand of COVID-19 to provide a verdict on whether the person taking the detection is infected by COVID-19. It can be used to detect infection at an early stage because viremia is usually seen early in the course of the disease [6]. RNA detection is the most sensitive detection method and is generally preferred because of that reason. However, this test needs high-quality RNA strands of the virus because they have to undergo multiple times of RNA replication and a poor quality might degrade during that process. One of the most common types of RNA detection of COVID-19 is reverse transcriptase real-time PCR (RT-qPCR).

Probe-based RT-qPCR has been considered to be the gold standard method for SARS-CoV-2 detection and is currently one of the most widely used tests in many countries for screening the populations as recommended by WHO and CDC [6]. The mechanism of RT-qPCR is to convert the collected COVID-19 RNA into complementary DNA. Then, using cDNA as a template, PCR amplification was performed using gene-specific primers and DNA templates under the action of DNA polymerase to obtain the target fragment. During the PCR process, fluorescent probes bind to DNA. When the DNA polymerase breaks the probe, the fluorescent group and quenching group separate, emitting a fluorescent signal. RT-qPCR can target many different types of genes of COVID-

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19, including RNA-dependent RNA polymerase (RdRp) gene, nucleocapsid (N) gene, envelope (E) gene, spike (S) gene, and ORF1b or ORF8 regions of the SARS-CoV-2 genome [6]. Targeting two or more genes during RT-qPCR tests can reduce the likelihood of false positives but would take a lot of time and effort, which can cause problems when the infected cases are rising in society. Although RT-qPCR is recommended for its accuracy, it also has many drawbacks. Doing RT-qPCR tests requires expensive equipment and skilled researchers so it isn't very available in countries that have scarce medical resources, the testing of RT-qPCR only takes 4-6 hours but sending the RNA into the lab might take around 24 hours which causes a delay in reporting [6]. This makes the detection not very convenient and unable to produce results quickly.

Antibody detection detects the presence of antibodies in one's blood/serum/plasma samples to see if the body is infected by the pathogen. One antigen can only bind to one type of antigen, so the detection result will not be affected by another pathogen that might exist in the Body. The antigen is secreted as an immune response from the body to bind and inactivate pathogens. There are totally five classes of antibodies: IgM, IgD, IgG, IgA, and IgE, which are classified by their difference in C-terminus regions. IgM is the first antibody produced during an infection, while IgG is the most common and abundant one in serum [5]. This makes these two classes of antibodies the most optimal target to find in an antibody test. Antibodies remain present in the body for a longer period than the virus' RNA, causing antibody detection's detection efficiency to be higher than that of RT-qPCR after 5.5 days of symptom onset [6]. The antibody test can provide information on both active and past infections based on the different classes of antibodies present in the body, which helps the health-care system to track the flow for transmission in the community.

Enzyme-linked immunosorbent type assays (ELISA) are the most common antibody detection used to detect Coronavirus. In the ELISA test, the recombination COVID-19 antigen is coated on a microtiter plate to serve as the target for the antibody. The test subject's serum, which may contain COVID-19 antibodies, is then added to the plate. The antibody in the serum will bind to the antigen and stay on the plate, while the other antibodies that did not bind with the COVID-19 antigen will be washed away [7]. This step makes sure that the result is not affected by the antibody unrelated to the detection. Then, another antibody that is labeled with an enzyme is added to the plate. These secondary antibodies bind with the antibody that binds to the COVID-19 antigen, making the number of enzymes proportional to the amount of the test substance in the specimen. The substrate required for enzyme reaction is added and becomes a colored product because of the reaction. Scientists can detect the amount of color change which tells them the concentration of antibodies in the serum [7]. Enzyme reaction happens relatively quickly and is highly sensitive because of its high catalytic efficiency. However ELISA detection contains many processes and the material can be easily polluted, which may cause errors in the results. In addition to virus testing, another significant aspect of cutting off the transmission route of the virus is to establish an immune barrier to make the population less susceptible to infection. A vaccine is a medication that prepares the body's immune system for diseases that it has never been exposed to before. In this way, people's bodies can act more quickly to the real virus compared to the body that does not eject a vaccine. The vaccine is mostly made up of parts of the virus to set the immune system to alarm and other substances that preserve the vaccine's effectiveness. The WHO classifies COVID-19 vaccines that have been analyzed or approved for clinical trials into the following categories: inactivated vaccine, live attenuated, vector, RNA, DNA, protein subunit, and virus-like particle (VLP) vaccines [8].

Inactivated vaccines and live attenuated vaccines are the most traditional types of vaccine used. Inactivated vaccine is produced by using chemical substances to inactive viruses cultured in the laboratory, this process causes the structure of the virus to be intact. One benefit of this is that the immune system can produce a more complex set of antibodies based on the different surface structures of the virus [8]. Compared to vaccines containing only some virus fragments, people

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ejected with the inactivated virus have a stronger immune defense for the real virus. The drawback for inactivated viruses, however, is that these vaccines must be manufactured in high-level laboratories under strict regulation, making it very hard to suddenly increase in production amount. Live attenuated vaccine is to use a weaker virus or one with low virulence which is produced by reverse genetics or adaption. Today, the main way of producing these live attenuated viruses is by including codon pair deoptimization (CPD) or virulence gene knockout. [8] The live attenuated vaccine can remain most of the amino acid sequence, causing more responses to happen in the immune system. It can be inhaled through mucosal, which helps to increase the immune defense of the upper respiratory tract. Through this vaccine helps to warn a larger area of the immune system, the virus's virulence can be restored during its replication and proliferation in the host so this could cause some possibility of causing serious reactions to the people ejected with the virus.

RNA vaccines, in contrast to the inactivated vaccine and live attenuated vaccine, is a relatively new technology. This vaccine uses a sequenced viral genome instead of a live virus to cause immune alarm, which makes the production of RNA vaccine faster to complete. This makes laboratories capable of producing a large amount of this type of vaccine in a short amount of time, providing essential medical tools in time during times of pandemic [9]. The basic mechanism of RNA vaccine is to deliver the nucleic acid molecule that contains the information about the chosen antigen into the host's targeted cells [10]. This can let the host cell transcribe the nucleic acid molecule into a targeted protein which serves as an antigen to trigger an immune response in the host's body. RNA vaccine is a new technology because the study of mRNA and its properties was previously blocked by a lack of technology about mRNA's minimum cellular uptake, making scientists obtain mRNA from cells. It was not until the year 1984, when in vitro mRNA transcription (IVT) was published, that it was possible to select a required mRNA strand from a DNA template. mRNA was first used as an ingredient for vaccines in the year 1993, which is relatively very brief in the entire history of medicine. It was not until 20 years later was mRNA vaccines investigated as a medical tool against infectious diseases [10]. Before the COVID-19 pandemic appears, mRNA vaccines are typically used for developing new cancer drugs. But now it has become a promising technology platform because the mRNA can be adjusted to deal with new mutations of the virus, it also needs less time to produce because it does not need cell culture. However, very strict storage and transportation requirements like ultra-low temperature conditions are needed to maintain mRNA's stability. This can cause trouble in vaccination in remote areas [10]. This means that mRNA vaccines have still defects and problems that need to be solved.

2.4. COVID-19's vaccine type

In addition to virus testing, another significant aspect of cutting off the transmission route of the virus is to establish an immune barrier to make the population less susceptible to infection. A vaccine is a medication that prepares the body's immune system for diseases that it has never been exposed to before. In this way, people's bodies can act more quickly to the real virus compared to the body that does not eject a vaccine. The vaccine is mostly made up of parts of the virus to set the immune system to alarm and other substances that preserve the vaccine's effectiveness. The WHO classifies COVID-19 vaccines that have been analyzed or approved for clinical trials into the following categories: inactivated vaccine, live attenuated, vector, RNA, DNA, protein subunit, and virus-like particle (VLP) vaccines [8].

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3. Conclusion

In this paper, the structure, transmission mode, detection methods, and vaccine types of COVID-19 are mainly discussed. This provides readers with a general understanding of this virus. After the COVID-19 epidemic, the world has realized that new prevention and treatment measures should be taken in the face of new viruses, such as the mRNA vaccine, which has received widespread attention in this epidemic. Only continuous innovation can ensure that society can safely and orderly overcome the epidemic and minimize the number of infections and deaths as much as possible. This can encourage scientists to explore immature fields as it may lead to favorable discoveries. This article does not mention all the detection methods of COVID-19 and all the vaccine types used to prevent it, and cannot provide readers with a comprehensive knowledge explanation. It is hoped that future research will not only bring about the discovery and development of mRNA vaccines but also all aspects of COVID-19.

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