

Review of Studies on the Pathogenesis of COVID-19 Virus

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Abstract:

As one of the serious infectious diseases, COVID-19 has brought serious harm to people's health and safety, and increased the burden of family and society. The COVID-19 pandemic continues to spread around the world. Based on this, we summarize the historical infectious diseases, classify infectious diseases, and introduce the pathogenesis of coronavirus and COVID-19 in detail in this paper. we hope it can provide help for people's understanding of the epidemic.

Key words: epidemic; COVID - 19; infectious diseases; pathogenesis

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1. Introduction

Since the emergence of human beings, infectious diseases have emerged. In human history, every major epidemic of infectious diseases not only directly affects people's health and life, but also may lead to the decline of state states and even the demise of some civilizations. In the past 250 years, there have been many outbreaks. For example, in 1772, the plague in Persia killed about 2 million people. The 1818 Tunisian plague epidemic killed about a quarter of the population; An outbreak of yellow fever in Barcelona, Spain in 1821 killed about a sixth of the population; In 1918, at the end of The First World War, an influenza pandemic[1] killed 50 million people. There have been eight outbreaks since 2000 alone[2], in which, COVID-19 outbreak in 2020 is the most severe and continuing worldwide. In this paper, we first classify infectious diseases and then specifically introduce the pathogenesis of coronavirus and COVID-19.

2. Classification of infectious diseases

Infectious diseases are divided into three categories: A, B and C. A class infectious diseases, also known as infectious diseases under compulsory management, are divided into plague and cholera. Plague is caused by plague bacillus, the harm and its serious infectious diseases, high mortality. Rodents, marmots and other rodents are the main source of infection of plague. The transmission channels include rat flea bites, respiratory tract infection, skin transmission and contact transmission. Clinical manifestations include high fever, enlarged lymph nodes and hemorrhage. Cholera is an acute diarrheal disease caused by infection with vibrio cholerae O1 or O139. The typical symptoms are severe and painless watery diarrhea, with severe diarrhea occurring more than ten times a day. Cholera causes severe dehydration and death within a short period of time. Vibrio bacteria can spread through water systems by drinking or eating water or food that has been infected with vibrio cholerae but has not been sterilized. There have been seven cholera pandemics in history, with the fifth and sixth being the most severe. One million more people died in the fifth cholera pandemic and 1.5 million in the sixth. Cholera causes an estimated 1.3 million to 4 million cases and 21, 000 to 143, 000 deaths worldwide each year, according to WHO estimates. It can be effectively controlled through isolation treatment, water and environmental disinfection, and public "keeping a good mouth shut".

Category B infectious diseases is also known as strict management of infectious diseases, including 26 kinds of disease: infectious atypical pneumonia, human infection with highly pathogenic avian influenza, viral hepatitis, bacterial, and amebic dysentery, typhoid and paratyphoid, AIDS, gonorrhea, syphilis, polio, measles, pertussis, diphtheria, tetanus neonatorum, epidemic cerebrospinal meningitis, scarlet fever, epidemic hemorrhagic fever, rabies, Leptospirosis, brucellosis, anthrax, Japanese encephalitis, tuberculosis, schistosomiasis, malaria, dengue fever, influenza A (H1N1).

Anthrax is a kind of bacteria called *Bacillus anthracis* caused by zoonotic infectious diseases, anthrax is divided into cutaneous anthrax, pulmonary anthrax and intestinal anthrax according to the symptoms, sometimes cause anthrax sepsis and meningitis. The death rate of pulmonary anthrax can be more than 90%. *Bacillus anthracis*

can generate spores in the external environment. Spores are dormant bodies formed by high concentration dehydration of bacteria. They can resist strong ultraviolet rays, high temperature and other harsh environments, and can survive for 10 years in suitable environments such as dry soil. At this stage, anthrax is still a threat to humans, and the key to preventing anthrax is to stay away from dead animals. Anthrax is also treatable with antibiotics.

Ebola hemorrhagic fever (EHF) caused by Ebola virus is the most deadly viral hemorrhagic fever in the world today. In the later stage of the disease, there will be liver and kidney function impairment, internal bleeding and external bleeding symptoms, and the fatality rate can reach about 50%, which is the highest risk level in the pathogen classification of all countries in the world. Ebola first entered the human population in 1976. There have been sporadic cases of Ebola in Africa, but it has not spread widely. The 2014-2016 Ebola outbreak in West Africa infected 26,000 people and killed 11,000. Since 2018, there has been another outbreak of Ebola in the Congo, with 3,340 cases and 2,210 deaths as of December 2019. The security situation in Congo also has a negative impact on the containment of the epidemic.

AIDS, also known as acquired immune deficiency syndrome, is caused by the HIV virus. HIV attacks the human immune system, making infected people gradually lose their ability to fight various diseases. Infected people often die from infection with common pathogens, malignant tumors. HIV was only discovered in 1981. To date, HIV remains a major global public health problem, causing more than 32 million deaths to date. The main modes of transmission of AIDS are sexual transmission, blood transmission and mother-to-child transmission. AIDS is one of the most intractable medical problems of the moment. It is a retrovirus that inserts its own genome into the genome of a patient and is very difficult to eradicate. So far, AIDS has no effective vaccine, and there is no drug that can be eradicated. However, the antiretroviral drugs currently in use can effectively suppress the virus, and long-term use can effectively suppress the virus in an infected person's body for decades, in a sense turning AIDS into a contagious "chronic disease".

C class infectious diseases is also known as the monitoring and control of infectious diseases, including 11 kinds of diseases, epidemic and endemic typhus, kala-azar, filariasis, echinococcosis, leprosy, influenza, epidemic parotitis, rubella, acute hemorrhagic conjunctivitis, and than cholera, dysentery, typhoid and paratyphoid infectious diarrhea disease, hand, foot and mouth disease.

Influenza virus is called influenza virus. It is divided into A, B, C, and influenza viruses only discovered in recent years will be classified as D. Influenza virus can cause human, poultry, pigs, horses, bats and other animals infection and morbidity, is the pathogen of human influenza, avian influenza, swine influenza, equine influenza and other human and animal diseases. Approximately 500 million people were infected and 20 to 50 million died worldwide in Spanish flu in 1918-1920. Asian flu led to 1 to 2 million deaths worldwide in 1957-1958. Russian flu killed more than 1 million people in 1889-1890. Hong Kong flu in 1968 killed 1 million people worldwide and is still circulating today. It is considered seasonal.

3. Coronavirus

Coronaviruses[3-5] get their name from the obvious bulges of rod-like particles that can be seen under a microscope and resemble the crowns of medieval European emperors, it is seen in Figure 1.

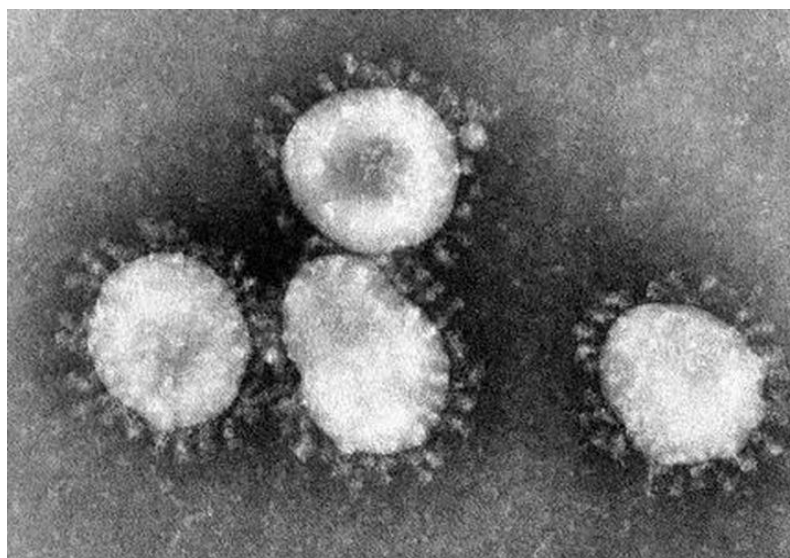


Figure1 Electron microscope image of coronavirus

Etiology of coronaviruses: single-stranded plus stranded RNA viruses with methylated "caps" at the 5' end of the RNA strand and PolyA "tails" at the 3' end. Coronaviruses have an enveloped structure with three proteins on it: Spike Protein (S), Envelope Protein (E) and Membrane Protein (M), and a few species include Haemagglutinin-esterase (HE). According to the characteristics of serotype and genome, it can be divided into four genera α , β , γ and δ . It can infect many animal species. Sensitive to heat, 56°C for 30 minutes, ether, 75% ethanol, chlorine-containing disinfectant, peracetic acid and chloroform and other lipid solvents can effectively inactivate the virus.

Coronaviruses use the host cell's synthetic system to replicate and assemble their progeny. Specifically, receptor-mediated binding internalization; induce signal transduction (including DNA integration, protein changes); pathological changes (reactions of the immune system, etc); treatment and evolutionary selection in host populations.

4. COVID - 19 viruses

A novel Coronavirus[6-7] distinct from the SARS-Co V epidemic in 2003 and the MerS-Co V epidemic in Saudi Arabia in 2012 was detected in January 2020 and the full genome sequence was obtained. 11 February 2020 Severe Acute respiratory syndrome coronavirus 2(SARS-CO V-2) is named by the International Committee on Classification of Viruses. At the same day: WHO named COVID-19 as the pneumonia contracted by the Novel Coronavirus. Sars-cov2 is a single plus-stranded RNA virus belonging to β , which is round or oval in shape with envelope and 60-140nm in diameter. The genome length is 29903 bp, and the sequence of the genome is 5'-ORF1AB-S-ORF3a-e-m-ORF6-ORF7a-ORF8-n-ORF10. About 2/3 of the 5' terminal region encodes viral RNA polymerase protein, and the last 1/3 region encodes four structural proteins, including spike protein (S), envelope protein (E), membrane protein (M), nucleocapsid protein (N), as well as some non-structural proteins and helper proteins. Sars-cov2 was 96% similar to betaCOV RaTG13 of BATS and 82% similar to SARS.

This was followed by novel Coronavirus variants, defined as those with genetic mutations that are predicted or proven to affect infectivity, disease severity, immune escape, etc. With significant community transmission or multiple concentrated outbreak points, the number of associated cases and the proportion of all infections is increasing in multiple countries. The characteristics of the mutant include increased infectivity of mutant strains or other harmful epidemiological mutations, increased toxicity or changes in clinical manifestations, reducing the effectiveness of public health measures or vaccines or diagnostics.

The current epidemic variants are Omicron (Omicron BA.1, BA.2, A.3) and Deltacron. The omicron mutant also has important amino acid mutation sites of Alpha, Beta, Gamma and Delta spike proteins of the first four VOC variants, including mutations that enhance cell receptor affinity and viral replication. Novel coronavirusS protein mutations in K417N, E484A or N501Y suggested enhanced immune escape ability. The omicron mutant also had a triple mutation of K417N+E484A+N501Y.

5. Pathogenesis of COVID-19 virus

Cytokine storm refers to the rapid and massive production of cytokines such as IL-1, IL-6 and IL-12 in body fluids caused by infection with microorganisms. Cytokine storm is an important cause of acute respiratory distress syndrome and multiple organ failure. The cytokine storm mechanism of COVID-19 refers to the accumulation of a large number of immune cells and cytokines at the inflammatory site, increasing endothelial cell permeability, resulting in tissue congestion, edema, damage, and ultimately acute respiratory distress syndrome and multiple organ failure. The pathogenesis of COVID-19: First, immune cells become overactivated. The cytostructural basis of cytokine storm is immune cells such as neutrophils and lymphocytes. Neutrophils inactivate and kill pathogens by chemotaxis and phagocytosis. There are three main mechanisms of neutrophil sterilization: phagocytosis, degranulation and formation of neutrophil external trapping NETs. Neutrophil elastase, one of the key enzymes in the formation of NETs, is a destructive elastase that attacks the extracellular matrix, promotes inflammatory responses and induces cytokine storms. Cytokines are then released in large quantities. Interleukin-6 (IL-6) is a key cytokine in the cytokine storm caused by COVID-19, which can enhance vascular permeability and seriously damage organ function. Cytokine storm can be controlled by blocking the IL-6 signaling pathway. Interferon is the body's natural immune defense against virus, but the delay of IFN effect can cause the virus to replicate rapidly and induce deadly cytokine storm. Chemokines play an important role in the immunopathological damage of viral diseases. TNF - α is recognized as a typical proinflammatory cytokine induced by virus cytokine storm, which promotes the differentiation and secretion of immune cells[8-9].

6. Conclusion

In this paper, we mainly introduce the relevant content of coronavirus. Specifically, we classify infectious diseases and expound the pathogenesis of coronavirus and novel coronavirus, which is more conducive to understanding and mastering infectious diseases.

7. References

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