AN INSIGHT OF COVID - 19

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ABSTRACT

Coronavirus disease 2019 (COVID-19) is a potentially severe acute respiratory infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The virus was identified as the cause of an outbreak of pneumonia of unknown cause in Wuhan City, Hubei Province, China, in December 2019. The clinical presentation is that of a respiratory infection with a symptom severity ranging from a mild common cold-like illness, to a severe viral pneumonia leading to acute respiratory distress syndrome that is potentially fatal. The novel coronavirus uses the same receptor, angiotensin-converting enzyme 2 (ACE2) as that for SARS-CoV, and mainly spreads through the respiratory tract. Importantly, increasingly evidence showed sustained human-to-human transmission, along with many exported cases across the globe. The clinical symptoms of COVID-19 patients include fever, cough, fatigue and a small population of patients appeared gastrointestinal infection symptoms. The elderly and people with underlying diseases are susceptible to infection and prone to serious outcomes, which may be associated with acute respiratory distress syndrome (ARDS) and cytokine storm. Currently, there are few specific antiviral strategies, but several potent candidates of antiviral's and repurposed drugs are under urgent investigation.

Index terms: COVID19, Coronavirus, treatment

INTRODUCTION

The history of human coronaviruses began in 1965 when Tyrrell and Bynoe[1] found that they could passage a virus named B814. It was found in human embryonic tracheal organ cultures obtained from the respiratory tract of an adult with a common cold. The presence of an infectious agent was demonstrated by inoculating the medium from these cultures intranasally in human volunteers; colds were produced in a significant proportion of subjects, but Tyrrell and Bynoe were unable to grow the agent in tissue culture at that time.

At about the same time, Hamre and Procknow[2] were able to grow a virus with unusual properties in tissue culture from samples obtained from medical students with colds. Both B814 and Hamre's virus, which she called 229E, were ether-sensitive and therefore presumably required a lipid-containing coat for infectivity, but these 2 viruses were not related to any known myxo- or paramyxoviruses. While working in the laboratory of Robert Chanock at the National Institutes of Health, McIntosh et al[3] reported the recovery of multiple strains of ether-sensitive agents from the human respiratory tract by using a technique similar to that of Tyrrell and Bynoe. These viruses were termed "OC" to designate that they were grown in organ culture.(de Wit *et al*.,2 016)

Within the same time frame, Almeida and Tyrrell[4] performed electron microscopy on fluids from organ cultures infected with B814 and found particles that resembled the infectious bronchitis virus of chickens. The particles were medium sized (80–150 nm), pleomorphic, membrane-coated, and covered with widely spaced club-shaped surface projections. The 229E agent identified by Hamre and Procknow and the previous OC viruses identified by McIntosh et al had a similar morphology.

In the late 1960s, Tyrrell was leading a group of virologists working with the human strains and a number of animal viruses. These included infectious bronchitis virus, mouse hepatitis virus and transmissible gastroenteritis virus of swine, all of which had been demonstrated to be morphologically the same as seen through electron microscopy. This new group of viruses was named coronavirus (*corona* denoting the crown-like appearance of the surface projections) and was later officially accepted as a new genus of viruses.

In the 3 decades after discovery, human strains OC43 and 229E were studied exclusively, largely because they were the easiest ones to work with. OC43, adapted to growth in suckling mouse brain and subsequently to tissue culture, was found to be closely related to mouse hepatitis virus. Strain 229E was grown in tissue culture directly from clinical samples. The 2 viruses demonstrated periodicity, with large epidemics occurring at 2- to 3-year intervals.

(Tortorici & Veesler, 3019)

GENOME AND STRUCTURE

In December 2019, a new type viral pneumonia cases occurred in Wuhan, Hubei Province; and then named "2019 novel coronavirus (2019-nCoV)" by the World Health Organization (WHO) on 12 January 2020.

Coronaviruses possess a distinctive morphology, the name being derived from the outer fringe, or "corona" of embedded envelope protein. Coronaviruses are animal and human pathogens that can cause lethal zoonotic infections like SARS and MERS. They have polycistronic plus-stranded RNA genomes and belong to the order *Nidovirales*, a diverse group of viruses for which common ancestry was inferred from the common principles underlying their genome organization and expression, and from the conservation of an array of core replicase domains, including key RNA-synthesizing enzymes (Paraskevis *et al*., 2020)

Coronaviruses are medium-sized RNA viruses with a very characteristic appearance in electron micrographs of negatively stained preparations (Fig. 1). The nucleic acid is about 30 kb long, positive in sense, single stranded and polyadenylated. The RNA is the largest known viral RNA and codes for a large polyprotein. This polyprotein is cleaved by viral-encoded proteases to form the following: an RNA-dependent RNA polymerase and an ATPase helicase; a surface hemagglutinin-esterase protein present on OC43 and several other group II coronaviruses; the large surface glycoprotein (S protein) that forms the petal-shaped surface projections; a small envelope protein (E protein); a membrane glycoprotein (M protein); and a nucleocapsid protein (N protein) that forms a complex with the RNA. The coding functions of several other ORFs are not clear. The strategy of replication of coronaviruses involves

a nested set of messenger RNAs with common polyadenylated 3-ends. Only the unique portion of the 5-end is translated.[21]

All coronaviruses develop in the cytoplasm of infected cells, budding into cytoplasmic vesicles from the endoplasmic reticulum. These vesicles are either extruded or released from the cell within the same time frame, and then the cell is destroyed (Zhu etal.,2020 & Chan *et al*., 2020).

TRANSMISSION

Host and reservoir

Based on virus genome sequencing results and evolutionary analysis, bat has been suspected as natural host of virus origin, and SARS-CoV-2 might be transmitted from bats via unknown intermediate hosts to infect humans. It is clear now that SARS-CoV-2 could use angiotensin-converting enzyme 2 (ACE2), the same receptor as SARS-CoV [8], to infect humans. The epidemic of unknown acute respiratory tract infection broke out first in Wuhan, China, since 12 December 2019, possibly related to a seafood market. Several studies suggested that bat may be the potential reservoir of SARS-CoV-2 (Hamming et al., 2004).

Incubation and contagious period

Based on currently epidemiological survey, the latency period is generally from 3 to 7 days, with a maximum of 14 days. Unlike SARSr-CoV, 2019-nCoV is contagious during the latency period (de Wilde *et al*., 2018

REPLICATION

The virion S-glycoprotein on the surface of coronavirus can attach to the receptor, ACE2 on the surface of human cells. After membrane fusion, the viral genome RNA is released into the cytoplasm, and the uncoated RNA translates two polyproteins, pp1a and pp1ab, which encode non-structural proteins, and form replication-transcription complex (RTC) in double-membrane vesicle. Continuously RTC replicate and synthesize a nested set of subgenomic RNAs, which encode accessory proteins and structural proteins. Mediating endoplasmic reticulum (ER) and Golgi, newly formed genomic RNA, nucleocapsid proteins and envelope glycoproteins assemble and form viral particle buds (Millet & Whittaker, 2015).

SYMPTOMS

In January 2020, coronavirus SARS-CoV-2 was identified as the cause of an outbreak of severe pneumonia, now known to be a complication of the coronavirus disease 2019 (covid-19). Since then, the spread of covid-19 has increased exponentially, with the World Health Organization declaring a pandemic on 11 March. By 15 April, more than 1 900 000 cases and 123 000 deaths had been reported worldwide (Chowell *et al*., 2015)

HEMATOLOGY EXAMINATION

In the early stage of the disease, the total number of leukocytes decreased or keeps normal, with decreased lymphocyte count or increased or normal monocytes. High attention should be paid on the situation where the

absolute value of lymphocyte is less than 0.8×10^9/L, or the numbers of CD4 and CD8 T cells are significantly decreased, which generally recommend rechecking the blood routine changes after 3 days (Wang *et al*., 2020).

TREATMENT

Vaccine

Making vaccines usually takes a decade or more between development, safety testing and manufacturing,**.** Antiviral drugs and systemic corticosteroid treatment commonly used in clinical practice previously, including neuraminidase inhibitors (oseltamivir, peramivir, zanamivir, etc), ganciclovir, acyclovir, and ribavirin, as well as methylprednisolone for influenza virus, are invalid for COVID-19 and not recommended. Remdesivir (GS-5734) is a 1′-cyano-substituted adenosine nucleotide analog prodrug and shows broad-spectrum antiviral activity against several RNA viruses **(Omrani *et al*., 2014).**

The α-interferon atomization inhalation can be considered (5 million U per time for adults in sterile injection water, twice a day). (Falzarano et al., 2013).

Corticosteriod therapy

Methylprednisolone can be used as appropriate for patients with rapid disease progression or severe illness. According to the severity of the disease, 40 to 80 mg of methylprednisolone per day can be considered, and the total daily dose should not exceed 2 mg/kg

Other medications

1. Symptomatic treatment of fever. When the temperature is higher than 38.5 ℃, ibuprofen can be used for antipyretic.
2. Nutrition support treatment. Inpatients are screened for nutrition risk based on the NRS2002 score when they are admitted to the hospital. it is recommended to eat protein-rich foods (such as eggs, fish, lean meat, dairy products) and carbohydrate-containing diets. The supposed ideal energy intake is 25–30 kcal / (kg·d) and the protein mass are 1.5 g / (kg·d) (Legault *et al*., 2018)
3. Reduce the incidence of stress ulcers and gastrointestinal bleeding. Use H_2 receptor antagonists or proton pump inhibitors in patients with gastrointestinal bleeding risk factors.
4. Reduce the secretion of lung glands and improve the respiratory function, it is recommended to use selective (M1, M3) receptor anticholinergic drugs to reduce the secretion, relax the smooth muscle in airway, relieve airway spasm and improve the pulmonary ventilation (Lai, 2005)

PREVENTION

Persons with close contacts and suspicious exposure should be advised to have a 14-day health observation period, which starts from the last day of contact with the 2019-nCoV infected patients or suspicious environmental exposure. Once they display any symptoms, especially fever, respiratory symptoms such as coughing, shortness of breath, or diarrhea, they should reach out for medical attention immediately

Patients with suspected 2019-nCoV infection

Patients with a suspected infection should be isolated, monitored, and diagnosed in hospital as soon as possible. Patients with mild symptoms and suspected infection may consider in-home isolation and home care.

CONCLUSION

The outbreak of COVID-19 swept across China rapidly and has spread to 85 countries/territories/areas outside of China as of 5 March 2020. Scientists have made progress in the characterization of the novel coronavirus and are working extensively on the therapies and vaccines against the virus.

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