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SARS-CoV-2 as Emerging Disease: Preventive Instructions and Review of Literature

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Abstract: In late December, 2019, a novel coronavirus was first reported in Wuhan, named as SARS-CoV-2 caused a series of acute atypical respiratory diseases. To date, virus has infected >9 million people and almost 630,193 death that is estimated about 6% it mainly transmitted through contaminated respiratory droplets between people. So far, many hypotheses have been put forward about how the virus originated but here on theory about the origin of the virus as a result of mutation and natural selection will be discussed. Right now there is not enough information to make sure that weather recovery from COVID-19 is safe or immunity does provide long-term protection against COVID-19. The persistence of the virus has been investigated at various surfaces. Many companies are trying to make a vaccine for this virus, so that, the Moderna American company has been able to get the approval of three phases of making the vaccine. In this review we tried to introduce the SARS-CoV-2 and review the preventive instructions and related literature.

INTRODUCTION

The COVID-19 virus was first reported in late December in Wuhan, China[1]. It is found that 41 patients were hospitalized with symptoms of fever, shortness of breath and cough were identified by laboratory tests as SARS-CoV-2 and approximately two-third of them were associated with the famous Huanan seafood market which is a major market for seafood and live animals[2, 3]. In this market, a variety of live animals daily were sold and among them bats with different species and Pangolins (anteaters) that were smuggled into China were recognized as the first and second hosts of this virus. First genome of the coronavirus was sequenced in January, 2020 and named COVID-19 at first, virus primarily was transmitted between people mostly through respiratory droplets and has spread across the world. To date, virus has infected >9 million people and almost 630,193 death that is estimated about 6%.

SARS-CoV-2 origin: So far, several articles have been published on the origin of the virus but here is a summary of an study in nature journal that generally describes how the virus originated through spontaneous mutations and the evolution of the virus[4].

Mutation in the Receptor-Binding Domain (RBD) from S protein structure: This site contains 6 amino acids through which the virus binds specifically to its receptor, Angiotensin 2 (ACE2), this study reported that mutations cause change of 5 amino acids in these 6 in COVID-19 as a result, the virus can be strongly attach to its receptors in

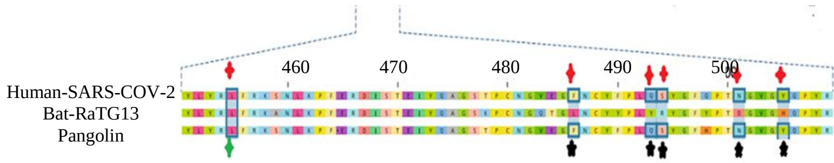

Fig. 1: Alignment of amino acids between 3 coronaviruses[4]. Red flags: Six similar amino acids between the coronavirus Pangolin and COVID-19; Black flags: Five different amino acids between corona bat virus (Bat RatG13) and COVID-19; Green flags: A similar amino acid between corona bat virus (Bat RatG13) and COVID-19

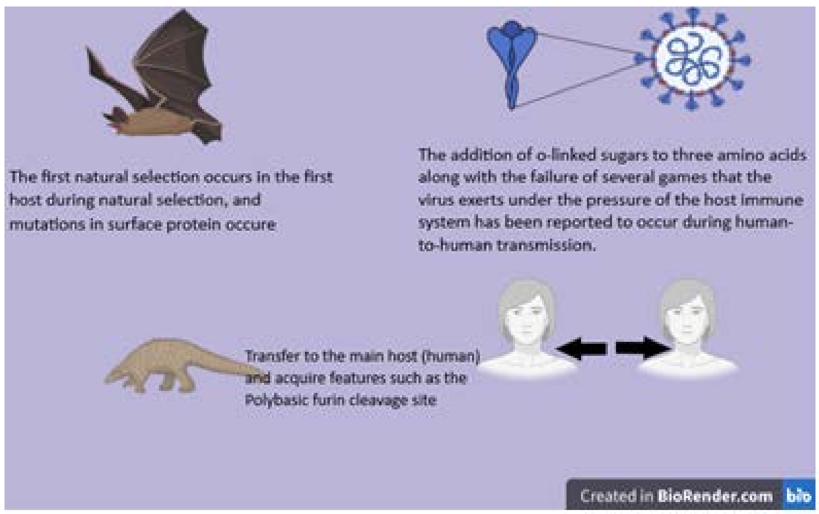

Fig. 2: The virus can change and acquires feature such as mutations from transfer between first, intermediate and second hosts[4]

humans. In fact, this mutation occurs as a result of natural selection which is related to the phenomenon of evolution (Fig. 1 and 2).

Polybasic furin cleavage site and o-linked glycans: in fact, this feature which is related to the junction of two spike protein subunits, S1 and S2 gives the ability to Spike protein to be broken more effectively by Forin or other proteases and attach to its receptor and enter the cell. The effect of this site on the transmission and pathogenicity of the virus has been studied in animal models, another insertion mutation has been reported in this site which a leading proline amino acid is introduced between two subunits as a result o-linked glycans are added to the three amino acids along with the breakpoint of several bases. This feature is only seen in COVID-19. The main function of these glycans is not known but it may be inferred that they can form a quasi-mucinous protector on these amino acids to escape detection by the immune system.

Comparison of COVID-19 genome sequence and Bat RatGT13 gene sequence showed 96% genomic similarity between the two viruses but further studies on the structure of COVID-19 showed that RBD (Receptor Binding Domain) differs from Bat RatGT13 but exactly it is like the RBD in Pangolin coronavirus, a skin flush ant Eater that smuggles into the country.

Natural selection: There are two natural selection options: changing five amino acids of the six main amino acids or RBD which occurs in the receptor in the intermediate host or Pangolin.

Create a furin polybasic cleavage site and o-linked sugars that the virus exerts under the pressure of the host immune system which occurs during human-to-human transmission.

Figure 1 is shown part of S1 protein structure called ligand that bind to its receptor (in Bat RaTG13, COVID-19 and Pangolin). These 6 specific amino acids are exactly similar between two COVID-19 and Pangolin and COVID-19 and bat coronavirus similar in one amino acid.

Virus transmission: Available evidence suggests that the COVID-19 virus is transmitted as a result of close

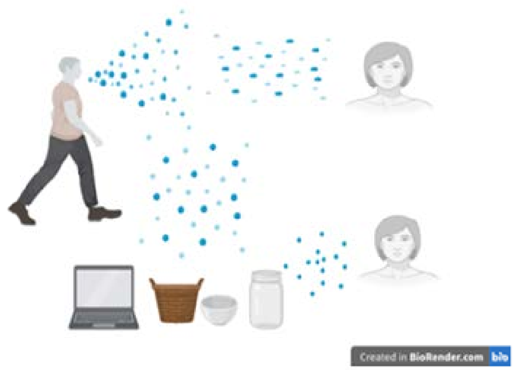

Fig. 3: The virus is transmitted through the respiratory droplets of infected people and contaminated surfaces

contact through respiratory droplets (such as coughs, Sneezing)[2, 5, 7] that reach the nose, mouth or eyes of infected person (Fig. 3). On the other hand, the droplets are too heavy, so, land on objects of the Earth's surface. People become infected with COVID-19 by touching these objects or surfaces and then touch their eyes, nose or mouth and inject the virus into their bodies. There are evidence that suggest small droplets (airborne droplets) could transmit the virus over distances longer than 40 inches through the air and is depended the aerosol production methods.

DETECTION METHODS

So far, at least 11 methods based on the identification the nucleic acid of the virus and eight antibody identification kits for the diagnosis of the virus have been approved by the National Medical Products Administration (NMPA). At present, serological tests are not usually performed as part of a screening or diagnosis because they will not be positive until the body makes an antibody to fight (against) the virus usually 5-10 days after infection. The use of serological tests may not be positive in patients with viral RNA, especially, in the early stages of the disease but retrospectively it has been shown to provide an immune response. Another importance of using serological tests is when rapid antigen testing and/or molecular tests are neither available nor stable, serology can be used as a complementary diagnostic tool[7].

RT-PCR is the standard method for detecting COVID-19. Samples from the lower respiratory tract are recommended for patients with whooping cough. The detectable viral load depends on the days after the onset of the disease. The overall protocol for molecular detection of the virus in the real-time PCR method includes a master mix containing non-nucleated water, forward and reverse primers, a fluorophore-quencher probe and a reaction compound (consisting of reverse transcription, polymerase, magnesium, nucleotides and additives). During RT-PCR, the fluorophore-quencher probe is detached and produces a fluorescent signal. This reaction takes approximately 45 min and can occur on a 96-well plate where each well contains a different sample or control. There must be both positive and negative controls for interpreting the final results correctly when running RT-PCR.

In the first 14 days after onset, SARS-CoV-2 was more reliable in sputum followed by nasal swabs while throat swabs were unreliable 8 days after the onset of symptoms, due to changes in Viral loads, a negative test does not rule out the results of respiratory samples. These negatives can be caused by incorrect sampling methods, low viral load in the sampling area or mutations in the viral genome[8].

In cases where the patient's molecular test results are negative and the patient still has specific symptoms of the virus, a combination of repeated swab and CT-scan of the lung may be useful in people with COVID-19-RTPCR negative test[9]. A study of 51 patients with COVID-19 diagnosed with CT scan of the chest and RT-PCRCT in 3 days concluded that CT sensitivity was 98% for COVID-19 infection and 71% sensitivity for RT-PCR[9].

Immunity: In a study published in the journal Cell, TenOever and colleagues found that SARS-CoV-2 could block the interferon signal. So, the first thing to do-call for boosting the immune system-works very well but the lung cells do not enter the Defensive mode and therefore, remain vulnerable to viral infection. Right now there is not enough information to make sure that weather recovery from COVID-19 is safe or immunity does provide long-term protection against COVID-19.

Now there are concerns about community immunity and whether initial infection could produce protective immunity against the virus. There is evidence of reinfection with the virus. It seems that COVID-19 like other corona viruses induces immunity but it has a short term period[10].

A research team at the University of Medical Sciences in China has exposed four macaque Rhesus monkeys to the virus. About 1 week later, all four monkeys had symptoms COVID 19 infection and had a high viral load. About 2 weeks later, the macaques recovered and were confirmed to have antiviral antibodies in their blood. two weeks later, the virus entered the body again but the monkeys did not become infected and became immune to the virus. this finding suggests that it is possible to provide protection against the virus. To ensure this result, protective antibodies should be measured in their blood for at least 6 months. The results of this study do not mean long-term immunity because immunity to other coronaviruses is not long-term.

According to a study of the University of Amsterdam, immunity to human coronavirus infection may takes only 6 months, in this study 10 men over the age of 35 to determine the amount of antibodies to the infection for each of the four types of human seasonal coronavirus were examined. The men were tested between the ages of 27 and 40, 3 or 6 months apart[11].

The researchers found that protective immunity against corona viruses is short-lived and recurrence occurs 12 months after infection and reduction of antibodies occurs 6 months after infection. It was also found the four corona strains of human viruses are biologically different and have nothing in common other than colds. However, they all appear to provide short-term immunity with rapid loss of antibodies. If the SARS-CoV-2 behaves like a seasonal corona virus in the future, a similar pattern may be predicted[12]. Because the virus is so, new, more research is needed into the safety of it.

What is herd immunity? Does it have an effectiveness in safety against COVID-19? Herd immunity means that in a large population where a contagious infectious agent is circulating, a large group of the population is immune against the virus or infectious agent. Group immunity occurs when people in a population are protected from a virus and the disease that results from it, so that, people who are not safe are protected because of the high population safety. In fact, group immunity can decrease the rate of transmission among people and in the case of COVID-19 it is achieved when the right vaccine or vaccines are available or discovered drugs prevent the disease from progressing and increase immunity of the community or increase group immunity.

Vaccine: Several large companies are currently trying to compete for produce, one of these is well-known company Moderna[13]. The Moderna Pharmaceutical Institute an American biotechnology company has partnered with NIH to design a COVID-19 vaccine with a fast response platform based on the introduction of naked nucleic acid (mRNA). Unlike the traditional method of vaccine production and instead of producing antibodies in the laboratory in this method the own cells of body make it (antibodies). In this way, the mRNA of the corona virus enters the cells and the antigen of the virus appears on the surface of the cell. The immune system is then stimulated and produces antibodies against the virus quickly.

In the initial study, the first dose of the vaccine was administered to a 45-years-old woman with mRNA-1273 on March, 16 and the experiment was performed on 45 healthy people by the National Institute of Allergy and Infectious Diseases by the National Institutes of Health (NIH). In this study are given two doses within 28 days. If the vaccine is successful, it is expected that the vaccine will be ready at least until next year, it will be first available to healthcare workers and then will be available to the market by February. Ever, since, the company started producing mRNA vaccine for COVID-19, it has been able to enter the second phase of clinical trials and it can be said that it is a turning point to bring this drug closer to the public and commercial markets because it has passed its initial safety tests.

In the second phase of the study, 600 people from ten different states and 8 states registered and entered the vaccination phase after performing physical screening. Theoretically, this would allow scientists to complete vaccinations more quickly. These vaccines are suitable for mutant-resistant viruses such as coronavirus, influenza and HIV. Margaret Liu, chairman of the International Vaccine Association, says such vaccines could lead to a global vaccine working against different types of viruses[14].

Virus survival: At different surfaces the virus could remain infected (Table 1). Surface disinfections with 0.1% sodium hypochlorite (diluted bleach) or 62-71% ethanol is effective within 1 min[15, 16].

According to research, the survival of COVID-19 in the air depends on factors such as heat and humidity[17]. Health officials recommend that medical staff use so-called N95 masks because they filter about 95% of all liquid or air particles[17].

When the virus is in droplets <5 μ (known as airborne particles or aerosols), researchers say it can stay in the air for about half an hour before falling to the surface which can last for hours. Experts believe that the virus is not spread by air but in fact, it can travel through the air and be suspended for about half an hour. The virus does not stay in the air for long time and it is not dangerous for most people who are not physically close to an infected person. But the condition of healthcare centers and hospitals is different and hospital staff have to be very careful because the amount of viral load in those half hours in these places is higher than in normal places and also that health care workers may collect smaller and larger droplets on their protective equipment as a result of exposing with infected patients. A particle suspended in the air at a height of about 1.8 m is released and falls to the ground in 34 min. Therefore, most viral particles contain the virus in the first half hour. According to the study, the virus can be detected in airborne particles for up to 3 h but it cannot be said that it can be transmitted for up to 3 h. Apoorva Mandavilli, How Long Will Coronavirus Live on Surfaces or in the Air Around You? 2020. Transmission capacity is the same in the first half hour and gradually the number of suspended particles is reduced to 3 h and it is important to note that the risk of transmission through the air in normal and secluded places as well as outdoors is very low and more about indoor spaces The air conditioning is low and the load on

Table 1: Virus survival at different surface[15, 16]

Surfaces	Examples	Time
Plastics	Milk containers and detergent bottles, subway and bus seats, backpacks, elevator buttons	5 days
Stainless steel	Refrigerators, pots and pans, sinks, some water bottles	2 days
Cardboard	Shipping boxes	1 days
Glass	Drinking glasses, measuring cups, mirrors, windows	4 days
Paper	Mail, newspaper	4-5 days
Wood	Furniture, decoration, shelves	4 days
Gloves	Surgical gloves	4-5 days
Ceramics	Dishes, pottery, mugs	5 days
Copper	Pennies, teakettles, cookware	4 h

Table 2: sterilization guide of N95 mask

	Melt blown filtration media		Static-charged cotton		*E. coli*
Samples	Filtration efficiency (%)	Pressure drop (Pa)	Filtration efficiency (%)	Pressure drop (Pa)	disinfected efficiency (%)
70Ċ hot air in oven, 30 min	96.60	8.00	70.16	4.67	>99
UV light, 30 min	95.50	7.00	77.72	6.00	>99
75% alcohol, soaking and drying	56.33	7.67	29.24	5.33	>99
Chlorin-based disinfection, 5 min	73.11	9.00	57.33	7.00	>99
Hot water vapor from boilling water, 10 min	94.74	8.00	77.65	7.00	>99
Initial samples before treatment	96.79	8.33	78.01	5.33	

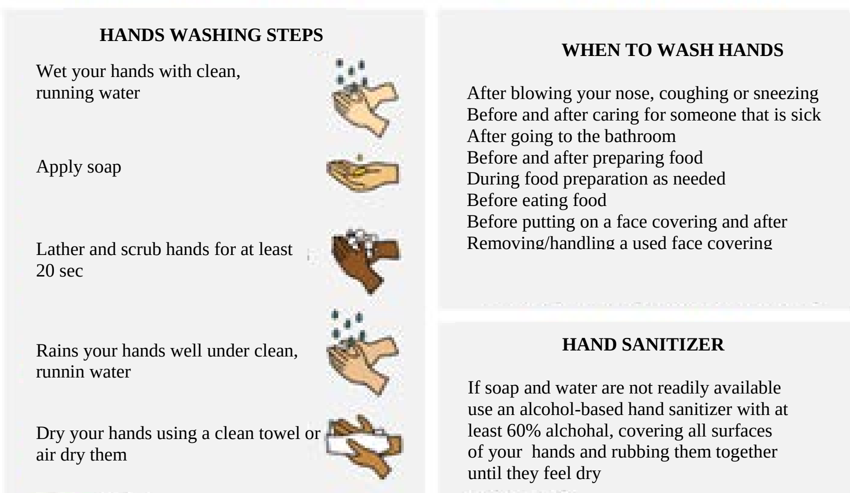

Fig. 4: The standard method for hand washing to remove microorganisms

the virus is very high such as in a hospital setting. Sterilization guide and reuse of N95 mask is shown in Table 2.

There are some notices about using disinfection which are not using alcohol and chlorine-based disinfection methods on N95 masks. Those will remove the static change in the microfibers in N95 facial masks, reducing filtration efficiency. In addition, chlorine also retains gas after de-contamination and these fumes may be harmful.

Table 2 guide is published by Stanford University. The main focus of the guide is on clearing the mask of coronavirus. The best recommended temperature is 70°C for 30 min. Proposed for 30 min in Owen or for 10 min with water steam that has reached boiling point can be a suggested way. In addition to eliminating viruses, this method retains the effectiveness of the mask in filtering up to 96.6%. Also, transmitting ultraviolet light for 30 min can sterilize the mask. The retention capacity of the mask filter in this method will be 95.5%. Other methods of sterilization have also been studied but damage the ability to filter the mask. An important caveat in this guide is not to disinfect the mask with alcohol or Vitex, these methods reduce the effectiveness of the mask in filtering to half. There are different ways to prevent the virus, however, washing hand protocol is important (Fig. 4).

CONCLUSION

The world's medical system against emerged and re-emerged diseases and pubic efforts to control this viral disease is necessary. More accurate understanding is depending on wide scientific studies. Experience of Covid can be a serious warning to rise emerged and re-emerged diseases in near future and this issue shows the necessity of greater preparedness and awareness to prevent and control these diseases.

REFERENCES

01. Zhu, N., D. Zhang, W. Wang, X. Li and B. Yang *et al*., 2020. A novel coronavirus from patients with pneumonia in China, 2019. N. Engl. J. Med., 382: 727-733.
02. Huang, C., Y. Wang, X. Li, L. Ren and J. Zhao *et al*., 2020. Clinical features of patients infected with 2019 novel Coronavirus in Wuhan, China. Lancet, 395: 497-506.
03. Hui, D.S., E.I. Azhar, T.A. Madani, F. Ntoumi and R. Kock *et al*., 2020. The continuing 2019-nCoV epidemic threat of novel coronaviruses to global health-the latest 2019 novel coronavirus outbreak in Wuhan, China. Int. J. Infect. Dis., 91: 264-266.
04. Andersen, K.G., A. Rambaut, W.I. Lipkin, E.C. Holmes and R.F. Garry, 2020. The proximal origin of SARS-CoV-2. Nature Med., 26: 450-452.
05. Burke, R.M., 2020. Active monitoring of persons exposed to patients with confirmed COVID-19-United States, January-February 2020. Morbidity and Mortality Weekly Report, Centers for Disease Control and Prevention, Atlanta, Georgia.
06. Li, Q., X. Guan, P. Wu, X. Wang and L. Zhou *et al*., 2020. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N. Engl. J. Med., 382: 1199-1207.
07. Haveri, A., T. Smura, S. Kuivanen, P. Osterlund and J. Hepojoki *et al*., 2020. Serological and molecular findings during SARS-CoV-2 infection: The first case study in Finland, January to February 2020. Eurosurveillance, Vol. 25.
08. Winichakoon, P., R. Chaiwarith, C. Liwsrisakun, P. Salee, A. Goonna, A. Limsukon and Q. Kaewpoowat, 2020. Negative nasopharyngeal and oropharyngeal swabs do not rule out COVID-19. J. Clin. Microbiol., Vol. 58, No. 5.
09. Paraskevis D., Kostaki E. G., Magiorkinis G., Panayiotakopoulos G., Sourvinos G. and Tsiodras S. 2020. Full-genome evolutionary analysis of the novel corona virus (2019-nCoV) rejects the hypothesis of emergence as a result of a recent recombination event. Infect, Genet., Evol., 79: 104212-104212.
10. Pappas, S., 2020. After recovering from COVID-19, are you immune?. Live Sci. Contributor, Vol. 1,
11. Lanese, N., 2020. Macaque monkeys can't become reinfected with COVID-19, small study suggests. Live Science Contributor, Future US, Inc., San Francisco, California.
12. Tidey, A., 2020. COVID-19: Immunity to coronaviruses may last just six months, says new study. Euronews, Lyon, France.
13. Kuchler, S.N.H., 2020. Coronavirus and the $2bn race to find a vaccine. The Financial Times, London, UK.
14. Akpan, N.A., 2020. COVID-19 vaccine has passed its first human trial. But is it the frontrunner?. National Geographic Society, Washington, USA.
15. Nazario, B., 2020. How long does the coronavirus live on surfaces?. Guardian News & Media Limited, UK.
16. WHO., 2020. Coronavirus disease 2019 (COVID-19). The World Health Organization, Geneva, Switzerland.
17. Lovelace Jr. B., N.H. Dunn and W. Feuer, 2020. WHO considers airborne precautions for medical staff after study shows coronavirus can survive in air. CNBC LLC, New Jersey, USA.