WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 9, Issue 5, 1971-1994. Review Article ISSN 2277– 7105

PROTEIN DATA BANK OF CORONA VIRUS→A GLOBAL PANDEMIC→STAY SAFE→STAY TUNED

Arunava Chandra Chandra*, Dr. Dhrubo Jyoti Sen and Dr. Beduin Mahanti

Department of Pharmaceutical Chemistry, School of Pharmacy, Techno India University, Salt Lake City, Sector-V, EM-4, Kolkata-700091, West Bengal, India.

Article Received on
10 March 2020,

Revised on 31 March 2020,
Accepted on 20 April 2020,

DOI: 10.20959/wjpr20205-17479

***Corresponding Author**
Arunava Chandra Chandra
Department of Pharmaceutical Chemistry, School of Pharmacy, Techno India University, Salt Lake City, Sector-V, EM-4, Kolkata-700091, West Bengal, India.

ABSTRACT

Common human corona viruses, including types 229E, NL63, OC43 and HKU1, usually cause mild to moderate upper-respiratory tract illnesses, like the common cold. Most people get infected with one or more of these viruses at some point in their lives. Symptoms of common human coronaviruses: (1) runny nose (2) sore throat (3) headache (4) fever (5) cough (6) general feeling of being unwell. Human coronaviruses can sometimes cause lower-respiratory tract illnesses, such as pneumonia or bronchitis. This is more common in people with cardiopulmonary disease, people with weakened immune systems, infants, and older adults.

Common human coronaviruses usually spread from an infected person to others through: (1) the air by coughing and sneezing (2) close personal contact, like touching or shaking hands (3) touching an object or surface with the virus on it, then touching your mouth, nose, or eyes before washing your hands.

In the United States, people usually get infected with common human coronaviruses in the fall and winter, but you can get infected at any time of the year. Young children are most likely to get infected, but people can have multiple infections in their lifetime.

Protect yourself from getting sick: (1) wash your hands often with soap and water for at least 20 seconds (2) avoid touching your eyes, nose, or mouth with unwashed hands (3) avoid close contact with people who are sick.

Protect others when you are sick: (1) stay home while you are sick (2) avoid close contact with others (3) cover your mouth and nose when coughing or sneezing (3) clean and disinfect objects and surfaces.

There is no vaccine to protect you against human coronaviruses and there are no specific treatments for illnesses caused by human coronaviruses. Most people with common human coronavirus illness will recover on their own. However, to relieve your symptoms you can: (1) take pain and fever medications (Caution: do not give aspirin to children) (2) use a room humidifier or take a hot shower to help ease (3) a sore throat and cough (3) drink plenty of liquids (4) stay home and rest. If you are concerned about your symptoms, contact your healthcare provider.

Testing for common human coronaviruses:

Sometimes, respiratory secretions are tested to figure out which specific germ is causing your symptoms.

- *If you are found to be infected with a common coronavirus (229E, NL63, OC43, and HKU1), that does not mean you are infected with the 2019 novel coronavirus.*
- *There are different tests to determine if you are infected with 2019 novel coronavirus. Your healthcare provider can determine if you should be tested.*

KEYWORDS: Pandemic, PDB, Corona crown, Lockdown, Hotspot, Quarantine, Isolation, Social distancing, Death poll.

CORONA VIRUSES

INTRODUCTION

Corona virus is a global Pandemic. A pandemic is the global outbreak of a disease. There are many examples in history, the most recent being the COVID-19 pandemic, declared as such by the World Health Organization on March 12, 2020.

Pandemics are generally classified as epidemics first, which is the rapid spread of a disease across a particular region or regions. The Zika virus outbreak that began in Brazil in 2014 and made its way across the Caribbean and Latin America was an epidemic, as was the Ebola outbreak in West Africa in 2014-2016. The U.S. has been experiencing an opioid epidemic since 2017 because of the widespread misuse and high numbers of deaths caused by the drug, according to the U.S. Department of Health and Human Services. COVID-19 began as an epidemic in China, before making its way around the world in a matter of months and becoming a pandemic. But epidemics don't always become pandemics, and it's not always a fast or clear transition. For example, HIV was considered an epidemic in West Africa for decades before becoming a pandemic in the late 20th century. Now, thanks to advances in modern medicine, HIV is considered endemic, which means the rate of the

disease is stable and predictable among certain populations, according to the American Medical Association.

Latin corona, meaning **crown** or **wreath**. **Corona viruses** are a group of related viruses that cause diseases in mammals and birds. In humans, corona viruses cause respiratory tract infections that can range from mild to lethal. Mild illnesses include some cases of the common cold (which has other possible causes, predominantly rhinoviruses), while more lethal varieties can cause SARS, MERS, and COVID-19. Symptoms in other species vary: in chickens, they cause an upper respiratory tract disease, while in cows and pigs they cause diarrhea.[1]

Figure-1: Save world: Stay safe.

History: Corona viruses were first discovered in the 1930s when an acute respiratory infection of domesticated chickens was shown to be caused by infectious bronchitis virus (IBV). The history of human corona viruses began in 1965 when Tyrrell and Bynoe 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 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 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 cultures.[2]

Within the same time frame, Almeida and Tyrrell 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. Ongoing research using serologic techniques has resulted in a considerable amount of information regarding the epidemiology of the human respiratory corona viruses. It was found that in temperate climates, respiratory corona virus infections occur more often in the winter and spring than in the summer and fall. Data revealed that coronavirus infections contribute as much as 35% of the total respiratory viral activity during epidemics. Overall, the proportion of adult colds produced by corona viruses was estimated at 15%. In the three 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 two viruses demonstrated periodicity, with large epidemics occurring at 2- to 3-year intervals. Strain **229E** tended to be epidemic throughout the United States, whereas strain **OC43** was more predisposed to localized outbreaks. As with many other respiratory viruses, reinfection was common. Infection could occur at any age, but it was most common in children.

Despite the extensive focus placed exclusively on strains **OC43 and 229E**, it was clear that there were other corona virus strains as well. As shown by Bradburne, coronavirus strain B814 was not serologically identical with either OC43 or 229E. Contributing to the various

strain differences in the family of coronaviruses, McIntosh *et al* found that 3 of the 6 strains previously identified were only distantly related to OC43 or 229E.

Epidemiologic and volunteer inoculation studies found that respiratory corona viruses were associated with a variety of respiratory illnesses; however, their pathogenicity was considered to be low. The predominant illness associated with infections was an upper respiratory infection with occasional cases of pneumonia in infants and young adults. These viruses were also shown to be able to produce asthma exacerbations in children as well as chronic bronchitis in adults and the elderly.[3]

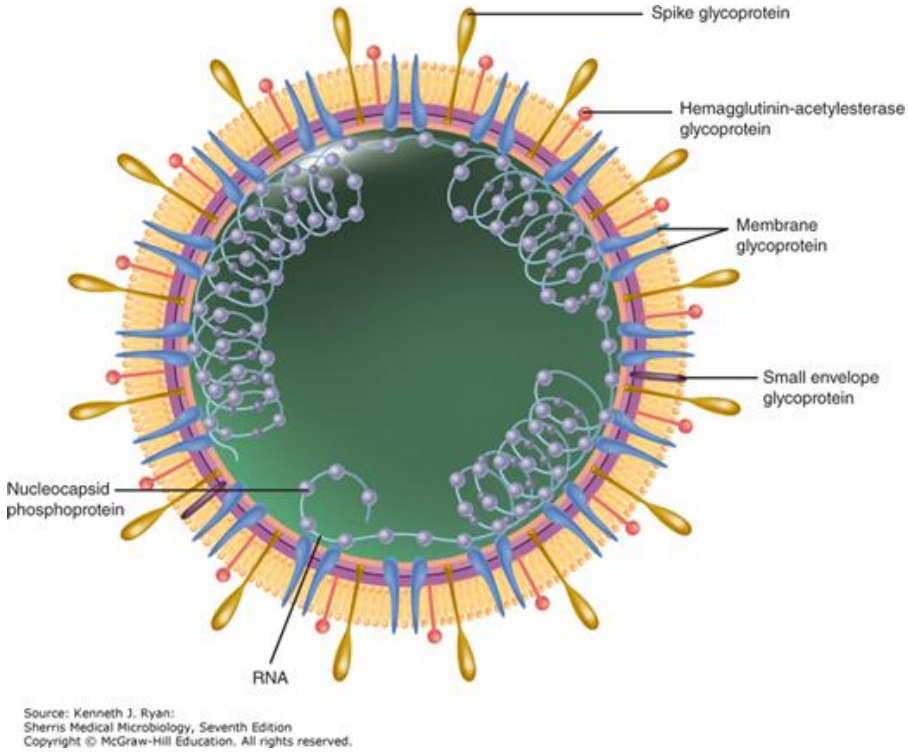

Figure-2: Corona crown.

While research was proceeding to explore the pathogenicity and epidemiology of the human corona viruses, the number and importance of animal corona viruses were growing rapidly. Corona viruses were described that caused disease in multiple animal species, including rats, mice, chickens, turkeys, calves, dogs, cats, rabbits and pigs. Animal studies included, but were not limited to, research that focused on respiratory disorders. Study focus included disorders such as gastroenteritis, hepatitis and encephalitis in mice; pneumonitis and sialodacryoadenitis in rats; and infectious peritonitis in cats. Interest peaked particularly regarding areas of encephalitis produced by mouse hepatitis virus and peritonitis produced by infectious peritonitis virus in cats. Pathogenesis of these disease states was various and

complex, demonstrating that the genus as a whole was capable of a wide variety of disease mechanisms. Human and animal corona viruses were segregated into 3 broad groups based on their antigenic and genetic makeup. Group I contained virus 229E and other viruses, group II contained virus OC43 and group III was made up of avian infectious bronchitis virus and a number of related avian viruses.[4]

Corona virus Disease: Corona viruses vary significantly in risk factor. Some can kill more than 30% of those infected, such as MERS-CoV, and some are relatively harmless, such as the common cold. Corona viruses can cause colds with major symptoms, such as fever, and a sore throat from swollen adenoids. Corona viruses can cause pneumonia (either direct viral pneumonia or secondary bacterial pneumonia) and bronchitis (either direct viral bronchitis or secondary bacterial bronchitis). The human corona virus discovered in 2003, SARS-CoV, which causes severe acute respiratory syndrome (SARS), has a unique pathogenesis because it causes both upper and lower respiratory tract infections.

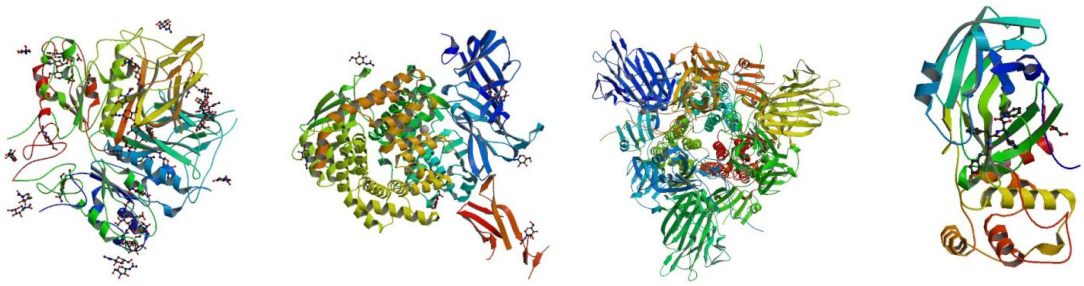

Figure-3: PDB of (1) Human coronavirus OC43 (HCoV-OC43), β-CoV (2) Human coronavirus HKU1 (HCoV-HKU1), β-CoV (3) Human coronavirus 229E (HCoV-229E), α-CoV (4) Human coronavirus NL63 (HCoV-NL63).

Symptoms: Four human corona viruses produce symptoms that are generally mild:

1. Human corona virus OC43 (HCoV-OC43), β-CoV
2. Human coronavirus HKU1 (HCoV-HKU1), β-CoV
3. Human coronavirus 229E (HCoV-229E), α-CoV
4. Human coronavirus NL63 (HCoV-NL63), α-CoV

Three human corona viruses produce symptoms that are potentially severe:

1. Middle East respiratory syndrome-related coronavirus (MERS-CoV), β-CoV
2. Severe acute respiratory syndrome coronavirus (SARS-CoV), β-CoV
3. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), β-CoV

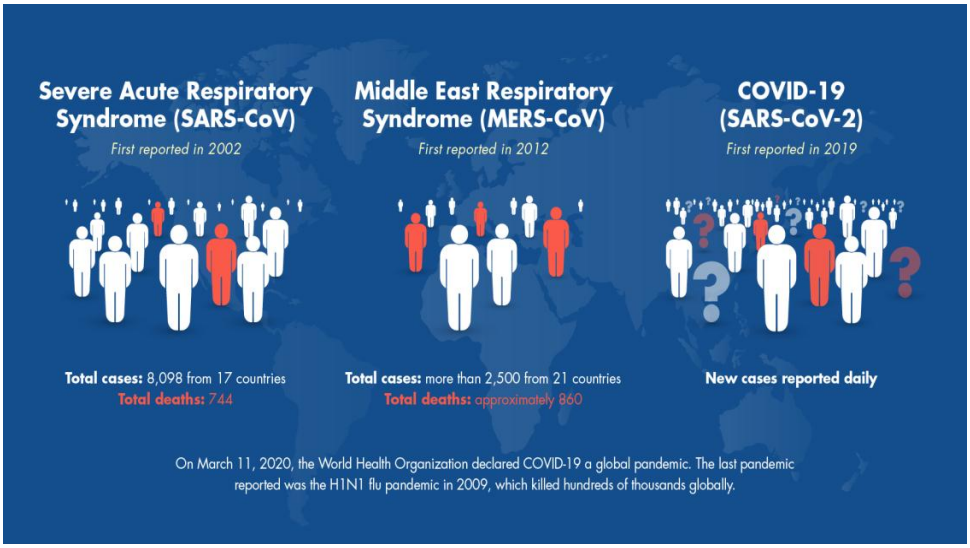

Figure-4: Death poll COVID.

COVID-19: Public health experts around the globe are scrambling to understand, track, and contain a new virus that appeared in Wuhan, China, at the beginning of December 2019. The World Health Organization named the disease caused by the virus COVID-19.

Scientists think this new virus first became capable of jumping to humans at the beginning of December 2019. It originally seemed like the virus first infected people at a seafood market in Wuhan and spread from there. But one analysis of early cases of the illness, published January 24th 2020 found that the first patient to get sick did not have any contact with the market. Experts are still trying to trace the outbreak back to its source. The type of animal the virus originated from is not clear, although one analysis found that the genetic sequence of the new virus is 96 percent identical to one coronavirus found in bats. Both SARS and MERS originated in bats.

Figure-5: Stay tuned.

Spreading of COVID-19: The virus is now spreading all over the world. Although it originated in China, the country took aggressive action at the start of the outbreak, shutting down transportation in some cities and suspending public gatherings. Officials isolated sick people and aggressively tracked their contacts, and had a dedicated network of hospitals to test for the virus. Now, the epicenter of the pandemic is in the US, which has more cases than any country in the world. New York City has the highest number of cases in the country. Previous US hot spots included a nursing home in Washington state, New Rochelle, New York, and the Boston area, where disease spread at a conference. Countries and Territories around the world have reported a total of 2,345,476 confirmed cases of the corona virus COVID-19that originated from Wuhan, China.[5]

Figure-6: Global COVID-19 case.

Step forward against Corona Virus (Prevention):

- Lockdown Prevention against Community Spreading
- Locate hotspot area
- Home & hospital Quarantine
- Social Distancing

Lockdown Prevention against Community Spreading: A lockdown is an emergency protocol that prevents people from leaving a given area. A full lockdown will mean you must stay where you are and not exit or enter a building or the given area. This scenario usually allows for essential supplies, grocery stores, pharmacies and banks to continue to serve the people. All non-essential activities remain shut for the entire period.

Figure-7: Lockdown.

Essential activities: Essential activities include picking up groceries and medical supplies, going to doctor and going on a walk provided you are following social distancing. If you work for an essential service, you will not need to adhere to these restrictions.

Workplace: Most major cities in the country have ordered private companies to let employees work from home. All offices will remain shut or work with minimal staff till the end of the lockdown period. The central and several state governments have announced relief packages for daily-wage earners and other temporary workers.

Emergency Services: Emergency services, like hospitals and pharmacies, will continue to operate as usual.

Stock up: Grocery stores, as well as mall which have such stores within it, will remain open. Stocks might be low, since transport services will be heavily restricted.

Locate Hotspot Area: The government decision to divide all districts across the country into hotspots, non-hotspots and green zones will help in managing the COVID-19 pandemic as well as partial opening up of economic activities during the extended period of the nationwide lockdown. This would help in management of hotspots and spread of pandemic he health and family welfare ministry, which has come out with a new set of guidelines for the second phase of lockdown till 3rd May 2020, has identified 170 hotspot districts, 207 non-hotspot districts reporting cases and 359 green zone districts not reporting any cases across the country as of Wednesday. These numbers will increase or decrease based on fresh cases of novel coronavirus infection. This is an emerging situation. The numbers can increase if the cases increase. According to people aware of the development, the new guidelines would help the central and state governments in allowing some economic activities in select areas.

There would be limited activities, such as functioning of repair shops, in the green zone districts while red zones will continue to have the current lockdown measures.

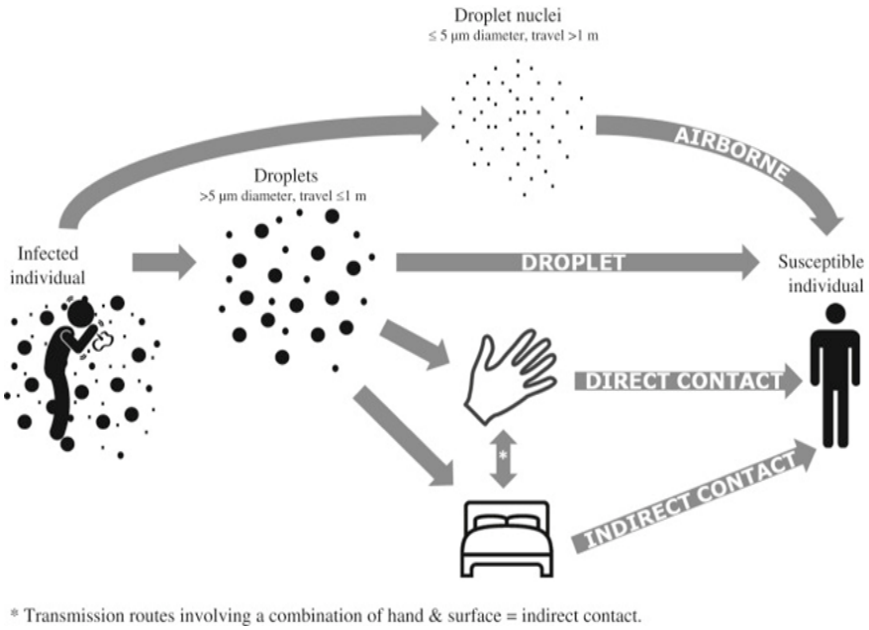

Figure-8: Transmission of COVID-19.

Home & hospital Quarantine: Quarantine is the separation and restriction of movement or activities of persons who are not ill but who are believed to have been exposed to infection, for the purpose of preventing transmission of diseases. Persons are usually quarantined in their homes, but they may also be quarantined in community-based facilities. Quarantine can be applied to an individual or to a group of persons who are exposed at a large public gathering or to persons believed exposed on a conveyance during international travel.[6]

A wider population- or geographic-level basis: Examples of this application include the closing of local or community borders or erection of a barrier around a geographic area (cordon sanitaire) with strict enforcement to prohibit movement into and out of the area. The purpose of this document is to provide guidelines for setting up of quarantine facilities during the current COVID-19 outbreak. The recommended duration of quarantine for COVID-19 based on available information is upto 14 days from the time of exposure. The purpose of quarantine during the current outbreak is to reduce transmission by:

- Separating contacts of COVID-19 patients from community
- Monitoring contacts for development of sign and symptoms of COVID-19, and
- Segregation of COVID-19 suspects, as early as possible from among other quarantined persons.

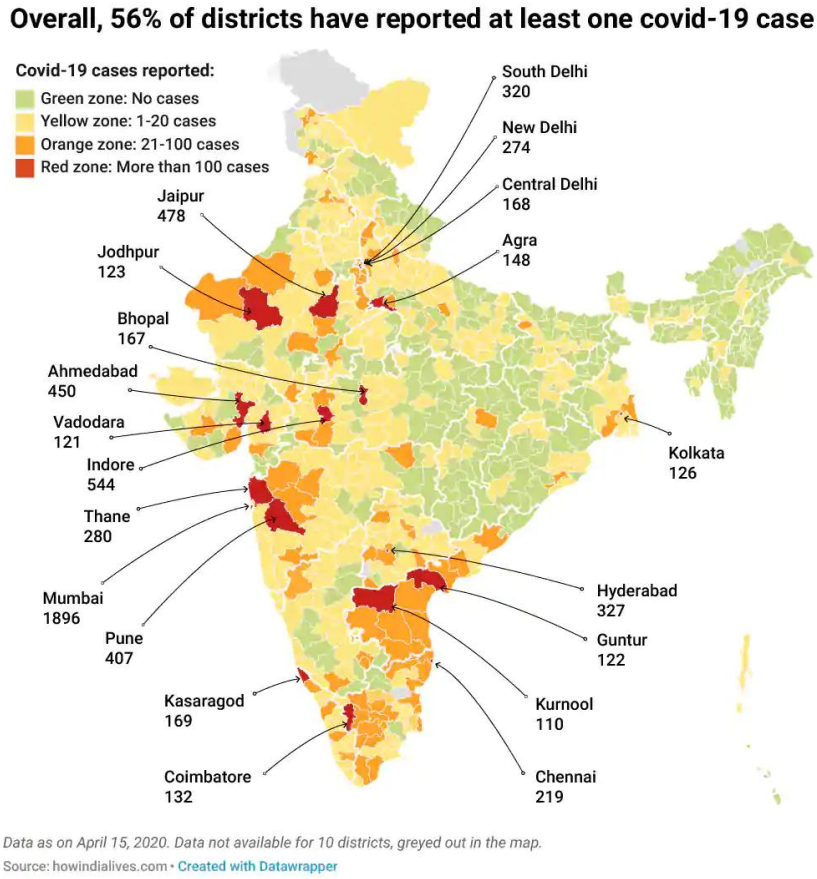

Figure-9: Hotspot zones.

The scope of this document is to cover the procedures required for:

- Physical infrastructure/Functional Services requirement at quarantine facilities.
- Procedure for medical monitoring of contacts, reporting formats.
- Protocol for referrals of suspects/Symptomatics and isolation of symptomatics if required temporarily.
- Infection control practices by medical personnel, supporting staffs and catering staffs etc.

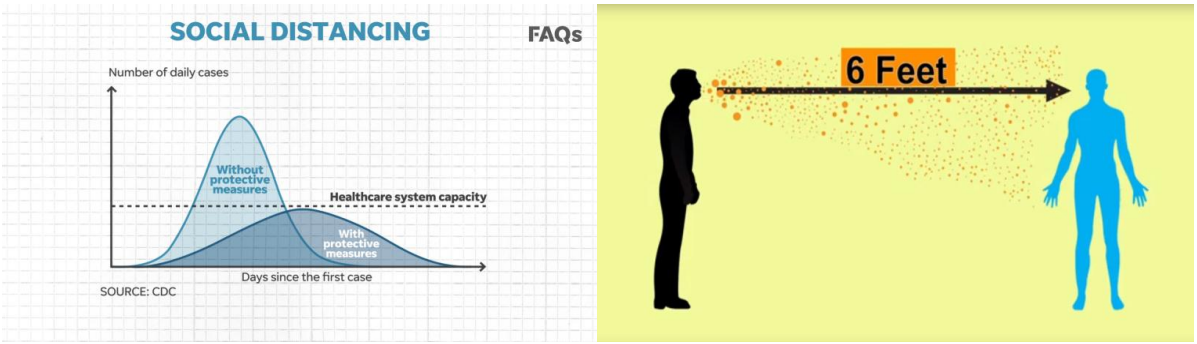

Figure-10: Social distancing.

Social Distancing: Social distancing, also called "physical distancing," means keeping space between yourself and other people outside of your home. To practice social or physical distancing:

- Stay at least 6 feet (2 meters) from other people
- Do not gather in groups
- Stay out of crowded places and avoid mass gatherings

In addition to everyday steps to prevent COVID-19, keeping space between you and others is one of the best tools we have to avoid being exposed to this virus and slowing its spread locally and across the country and world. When COVID-19 is spreading in your area, everyone should limit close contact with individuals outside your household in indoor and outdoor spaces. Since people can spread the virus before they know they are sick, it is important to stay away from others when possible, even if you have no symptoms.

Corona Virus survival Temperature: Currently, there are investigations conducted to evaluate the viability and survival time of SARS-CoV-2. In general, corona viruses are very stable in a frozen state according to studies of other corona viruses, which have shown survival for up to two years at –20°C. Studies conducted on SARS-CoV and MERS-CoV indicate that these viruses can persist on different surfaces for up to a few days depending on a combination of parameters such as temperature, humidity and light.

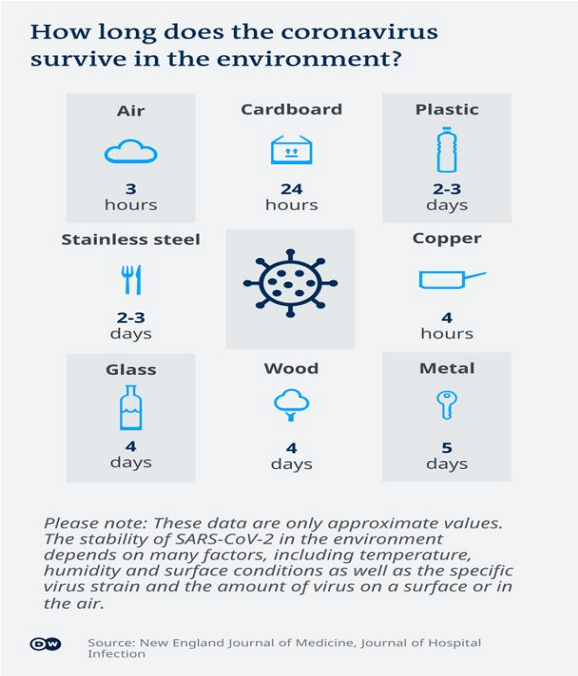

Figure-11: Surface Survival of COVID-19.

For example, at refrigeration temperature (4°C), MERS-CoV can remain viable for up to 72 hours. Current evidence on other coronavirus strains shows that while corona viruses appear to be stable at low and freezing temperatures for a certain period, food hygiene and good food safety practices can prevent their transmission through food.

Specifically, corona viruses are thermolabile, which means that they are susceptible to normal cooking temperatures (70°C). Therefore, as a general rule, the consumption of raw or undercooked animal products should be avoided. Raw meat, raw milk or raw animal organs should be handled with care to avoid cross-contamination with uncooked foods. We and others have reported that infectivity of SARS CoV (SARS coronavirus) was lost after heating at 56°C for 15 minutes but that it was stable for at least 2 days following drying on plastic. It was completely inactivated by common fixatives used in laboratory. Another study showed that it was inactivated by ultraviolet light, alkaline (>pH: 7), or acidic (<pH: 7) conditions. Human corona viruses have been shown to survive in PBS [Phosphate Buffered Saline] or culture medium with 5–10% FCS [Fetal Calf Serum] for several days but they only survive a few hours after drying. There have been some studies reporting an association between the SARS outbreak, metrological factors, and air pollution. Thus, information on the survival of the SARS coronavirus (SCoV) in the environment at different temperature and humidity conditions is of significant interest to understanding virus transmission. A recent study using surrogate corona viruses (transmissible gastroenteritis virus (TGEV) and mouse hepatitis virus (MHC)) has investigated the effect of air temperature and relative humidity on coronavirus survival on surface. The survival effects of these environmental factors on SARS coronavirus remain unclear. In the present study, we report the stability of the SARS coronavirus at different temperatures and relative humidity.[7]

STRUCTURE & REPLICATION OF CORONA VIRUS

1. Clinical specimens and RNA extraction: Nasopharyngeal and oropharyngeal swab and sputum samples were collected from symptomatic patients to detect SARS-CoV-2 by real-time reverse transcriptase (RT)-PCR. RNA was extracted from clinical samples with a QIAamp viral RNA mini kit (QIAGEN, Hilden, Germany) following the manufacturer's instructions. All specimens were handled under a biosafety cabinet according to laboratory biosafety guidelines of Korea Centers for Disease Control and Prevention for COVID-19.

2. Real-time RT-PCR: The optimal concentration of primers and probes, which were synthesized using a published sequence, was determined with the RNA transcripts of SARS-

CoV. The primer and probe sequences used for RNA-dependent RNA polymerase gene detection were: 5′-GTGARATGGTCATGTGTGGCGG-3′ (Forward), 5′-CARATGTTAAASACACTATTAGCATA-3′ (Reverse) and 5′-CAGGTGGAACCTCATCAGGAGATGC-3′ (Probe in 5-FAM/3′-BHQ format) and the primer and probe sequences used for E gene detection were: 5′-ACAGGTACGTTAATAGTTAATAGCGT-3′ (Forward), 5′-ATATTGCAGCAGTACGCACACA-3′ (Reverse) and 5′-ACACTAGCCATCCTTACTGCGCTTCG-3′ (Probe in 5-FAM/3′-BHQ format). A 25-µL reaction was setup that contained 5 µL of RNA, 12.5 µL of 2×reaction buffer provided with the Agpath IDTM 1 step RT-PCR system (Thermo Fisher Scientific, Waltham, USA), 1 µL of 25 × enzyme mixture, 1 µL of forward and reverse primers at 10 pM, and 0.5 µL of each probe at 10 pM. Reverse transcription was performed at 50°C for 30 minutes, followed by inactivation of the reverse transcriptase at 95°C for 10 minutes. PCR amplification was performed with 40 cycles at 95°C for 15 seconds and 60°C for 1 minute using an ABI 7500 Fast instrument (Thermo Fisher Scientific).

3. Virus isolation: The virus was isolated from nasopharyngeal and oropharyngeal samples from putative COVID-19 patients. Oropharyngeal samples were diluted with viral transfer medium containing nasopharyngeal swabs and antibiotics (Nystatin, penicillin-streptomycin 1:1 dilution) at 1:4 ratio and incubated for 1 hour at 4°C, before being inoculated onto Vero cells. Inoculated Vero cells were cultured at 37°C, 5% CO_2 in 1× Dulbecco's modified Eagle's medium (DMEM) supplemented with 2% fetal bovine serum and penicillin-streptomycin. Virus replication and isolation were confirmed through cytopathic effects, gene detection, and electron microscopy. Viral culture of SARS-CoV-2 was conducted in a biosafety Level-3 facility according to laboratory biosafety guidelines of Korea Centers for Disease Control and Prevention.

4. Factors effecting Virus Pathogenesis: Co-morbidities are cardiovascular and cerebrovascular disease as well as diabetes. Several abnormalities also have been observed including cellular immune deficiency, coagulation activation, myocardia injury, hepatic and kidney injury, and secondary bacterial infection. In the majority of cases of severe disease and death, lymphopenia and sustained inflammation have been recorded. Notably, these observations in COVID-19 patients are similar to those who suffered from severe acute respiratory syndrome (SARS) during the 2003 epidemic. There may be a biological

mechanism behind this epidemiological anomaly. Several kinds of vaccines and antiviral drugs that are based on S protein have been previously evaluated, showed vaccines can be based on the S protein include full-length S protein, viral vector, DNA, recombinant S protein and recombinant RBD protein. Considering that, in the *in-vitro* study, antiviral therapies are design based on S protein include RBD–ACE_2 blockers, S cleavage inhibitors, fusion core blockers, neutralizing antibodies, protease inhibitors, S protein inhibitors, and small interfering RNAs. There are some recombinant compounds such as IFN with **Ribavirin** [CAS No: 36791-04-5; IUPAC: 1-[(2*R*,3*R*,4*S*,5*R*)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-1*H*-1,2,4-triazole-3-carboxamide]which has only limited effects against COVID-19 infection. The receptor-binding domain of SARS-CoV-2 has a higher affinity for ACE_2, while it is a lower affinity for SARS-CoV. Angiotensin-converting enzyme (ACE) and its homologue ACE_2, belongs to the ACE family of dipeptidylcarboxy dipeptidase. However, their physiological functions are varied. On the other hand, ACE_2 serves as the binding site for COVID-19. Based on this information, Gurwitz suggested using available angiotensin receptor 1 (AT1R) blockers, such as losartan, as therapeutics for reducing the severity of COVID-19 infections. At present therapy is based on identifying and developing monoclonal antibodies that are specific and effective against COVID-19 combines with remdesivir as a novel nucleotide analog prodrug that was used for the treatment of the Ebola virus disease. To understand the rate of virus spread among people, it is crucial to figure out whether COVID-19 is mutating to improve its binding to human receptors for infection considering its high mutation rate. Any adaptation in the COVID-19 sequence that might make it more efficient at transmitting among people might also boost its virulence. The COVID-19 is expected to become less virulent through human to human transmissions due to genetic bottlenecks for RNA viruses often occur during respiratory droplet transmissions.[8]

Treatment

Symptomatic treatment and supportive therapy: Currently, symptomatic treatment and supportive therapy are mainly adopted for patients with COVID-19, and these include the treatment of basic diseases, symptom relief, effective protection and supportive treatment of internal organs, active prevention and treatment of complications, and respiratory support if necessary. More attention should be paid for maintaining the balance of water and electrolytes and maintaining the stability of the internal environment. Glucocorticoids can be used for a short time according to the degree of dyspnea and the progress of chest imaging.

Antiviral therapy: Currently, there are no specific anti-SARS-CoV-2 drugs in the clinic. The most efficient research strategy is "old drug, new use." **Remdesivir** (GS-5734) [CAS No: 1809249-37-3; IUPAC: (2*S*)-2-{(2*R*,3*S*,4*R*,5*R*)-[5-(4-Aminopyrrolo[2,1-f][1,2,4]triazin-7-yl)-5-cyano-3,4-dihydroxy-tetrahydro-furan-2-ylmethoxy]phenoxy-(*S*)-phosphorylamino}propionic acid 2-ethyl-butyl ester], a drug under development by Gilead Sciences in the United States, is a nucleoside analog prodrug that can inhibit Ebola virus, thereby playing an antiviral role. *In-vitro* and *in-vivo* experiments confirmed that a low dose of remdesivir can inhibit SARS-CoV and MERS-CoV.

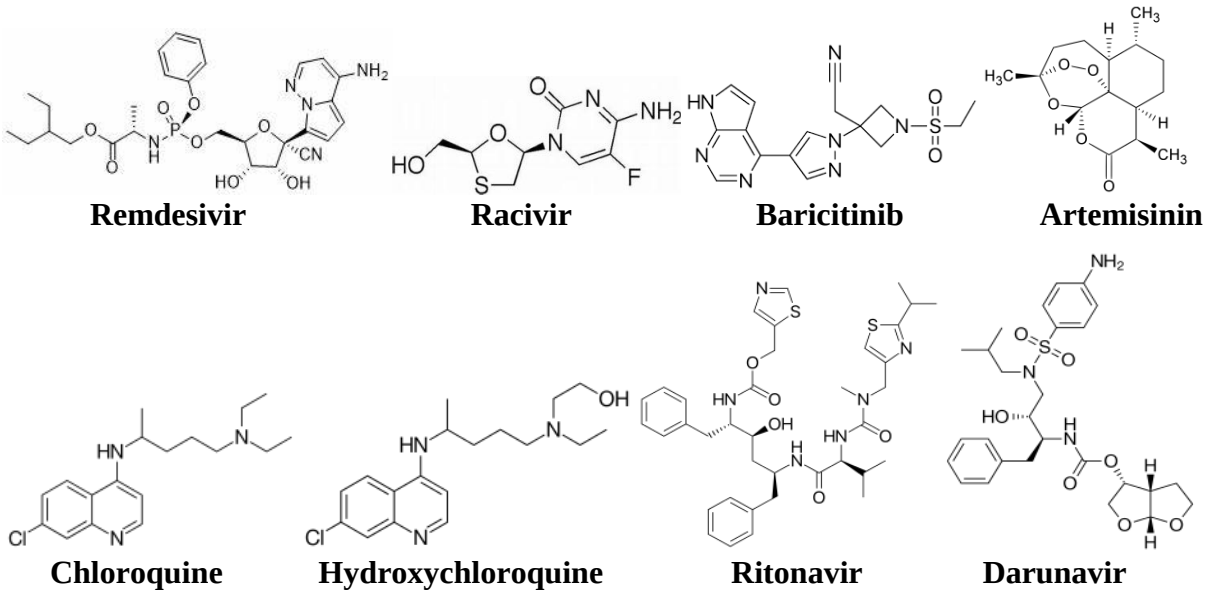

Figure-12: Drugs.

It has a good inhibitory effect. Remdesivir, with complete pharmacokinetic results and good safety, may be one of the most promising drugs against SARS-CoV-2 pneumonia. Currently, under the leadership of China Japan Friendship Hospital, a phase III clinical trial of racivir for the treatment of COVID-19 has been officially launched in Wuhan Jinyintan Hospital on February 5, 2020, and its efficacy will be determined using a strict clinical double-blind test validation. Recent studies have shown that **Racivir** [CAS No: 137530-41-7; IUPAC: 4-amino-5-fluoro-1-[(2*S*,5*R*)-2-(hydroxymethyl)-1,3-oxathiolan-5-yl]-1,2-dihydropyrimidin-2-one] and **Chloroquine** [CAS No:54-05-7; IUPAC: (*RS*)-*N'*-(7-chloroquinolin-4-yl)-*N*,*N*-diethyl-pentane-1,4-diamine] exhibit good inhibitory effects on SARS-CoV-2 *in-vitro*. In addition, according to the novel coronavirus pneumonia diagnosis and treatment plan (trial version sixth), inhalation of alpha interferon inhalation and **Ralproveravir** and **Ritonavir**[CAS No: 155213-67-5; IUPAC:1,3-thiazol-5-ylmethyl *N*-[(2*S*,3*S*,5*S*)-3-hydroxy-5-[(2*S*)-3-methyl-2-{[methyl({[2-(propan-2-yl)-1,3-thiazol-4-yl]methyl})carbamoyl]

amino}butanamido]-1,6-diphenylhexan-2-yl]carbamate] or intravenous injection of ribavirin can also be administered.

Chinese medicine treatment: COVID-19 belongs to the category of Chinese medicine for epidemic diseases. The cause of the disease is viral infection. Different people can be treated based on the syndrome differentiation: the early stage (cold dampness and stagnant lung), the middle stage (pestilence and toxin closing lung), the severe stage (internal closure and external removal), and the recovery stage (deficiency of lung, spleen, and qi). To date, at least 54 preventive, observational, and interventional drug studies have been registered in the national clinical trial registration center, involving a variety of traditional Chinese and Western medicines, and these include Lianhua Qingwen capsule, chloroquine, **Darunavir** and **Corbistar** etc. **Darunavir** [CAS No: 206361-99-1; IUPAC: [(1*R*,5*S*,6*R*)-2,8-dioxabicyclo[3.3.0]oct-6-yl] *N*-[(2*S*,3*R*)-4-[(4-aminophenyl)sulfonyl-(2-methylpropyl)amino]-3-hydroxy-1-phenyl- butan-2-yl] carbamate].

SARS-CoV-2 is now turning into a major challenge in China. The sudden outbreak of COVID-19 once again proves that biosafety is an indispensable part of human security. Bats are only the natural hosts of SARS-CoV-2. There should be one or two intermediate hosts of wild animals between the natural host and humans. If wild animals are not treated well, humans may be punished by nature. Currently, the number of cases of COVID-19 infection is still increasing. To further eliminate the source of infection, prevent the route of transmission, protect the susceptible population, and achieve early detection, early isolation and treatment must depend on the joint efforts of clinical and medical treatment, public health, and basic research. To fight this disease, we need to be well prepared at the frontline to stay ahead of this epidemic.

Antimalarial drugs: These drugs also fall under three categories based on their mode of action aryl amino-alcohol compound, antifolate compound and **Artemisinin** [CAS No: 63968-64-9; IUPAC: (3*R*,5a*S*,6*R*,8a*S*,9*R*,12*S*,12a*R*)-Octahydro-3,6,9-trimethyl-3,12-epoxy-12*H*-pyrano[4,3-*j*]-1,2-benzodioxepin-10(3*H*)-one]. Most of these drugs are eliminated gradually from the body remaining for long periods of time after intake. A disadvantage of this drug is that antimalarial drug resistance develops for any drugs under this category**. Hydroxychloroquine** [CAS No: 118-42-3; IUPAC: (RS)-2-[{4-[(7-chloroquinolin-4-yl)amino]pentyl}(ethyl)amino]ethanol] is also being studied as a treatment for coronavirus disease 2019 (COVID-19)**.**

Anti-HIV drugs: These drugs are classified into different categories based on their targets reverse transcription, retro-transcription, proteolytic processing, viral-cell fusion, co-receptors interactions and incorporation of proviral DNA into the host genome. Drugs that fall in these categories have been approved by the FDA (Food and Drug Administration) and are now officially used for the treatment of HIV.

Figure-13: Antiviral Vaccine Therapy.

Anti-inflammatory drugs: Huge inflammatory response is observed in COVID-19. Anti-inflammatory drugs especially JAK-STAT inhibitors, used against rheumatoid arthritis, may be effective against elevated levels of cytokines and useful in inhibiting viral infection. According to recent study, an inflammatory drug, **Baricitinib** [CAS No: 1187594-09-7; IUPAC: 2-[1-Ethylsulfonyl-3-[4-(7*H*-pyrrolo[2,3-d]pyrimidin-4-yl)pyrazol-1-yl]azetidin-3-yl]acetonitrile]when used in combination with anti-viral drugs like **Remdesivir** increases the potential of the drug to reduce viral infection.

Monoclonal antibodies: The virus is known to enter the host cells by binding the S protein to ACE_2 receptors. By developing neutralizing antibodies against the receptors, there is a high possibility for reducing the severity of the disease. Currently, only a handful of drugs have been approved for use against SARS-CoV-2. The majority of currently marketed or clinical therapeutic monoclonal antibodies (MAbs) and Fc fusion proteins (FcFPs) are used for indications in oncology or immunology, although in recent years a broader array of disease indications is being targeted by MAbs and FcFPs. The 396 currently known monoclonal antibodies and Fc fusion proteins on the market or in clinical trials are known to bind at least 185 different targets. Of these MAbs and FcFPs, 133 bind the top 16 targets (e.g. CD20, VEGF/VEGF receptor, TNF-α, IL-6/IL-6 receptor, amyloid beta) alone,

generating significant competition on those “hot” targets, while the remaining 263 bind 169 different targets. Binding of a therapeutic MAb or FcFP to its cognate target can result in many different potential mechanisms of action (MOAs). Known MOAs include antagonism of a soluble ligand or receptor, blockage of cell–cell interaction, agonism of a receptor, antibody-dependent cellular cytotoxicity (ADCC), antibody-dependent cellular phagocytosis (ADCP), complement-dependent cytotoxicity (CDC), apoptosis, and non-apoptotic programmed cell death. Some MAbs confer multiple MOAs on a target, as exemplified by anti-CD20 MAbs.

Ongoing clinical trials: Currently, there are numerous companies that have applied for clinical trials to repurpose existing drugs as well as to develop vaccines and drugs to fight against the fast spreading COVID–19. In the case of repurposing the existing drugs, randomized controlled treatment (RCT) are being carried out by various biotechnological companies as well as research organizations such as National Institutes of Health (NIH), USA to identify disease specific drugs. The major drugs undergoing clinical trials that have the potential to treat this viral infection. More research may be required in traditional medicine to utilize them in the treatment of COVID-19.

Self-care: If you feel sick you should rest, drink plenty of fluid, and eat nutritious food. Stay in a separate room from other family members, and use a dedicated bathroom if possible. Clean and disinfect frequently touched surfaces. Everyone should keep a healthy lifestyle at home. Maintain a healthy diet, sleep, stay active, and make social contact with loved ones through the phone or internet. Children need extra love and attention from adults during difficult times. Keep to regular routines and schedules as much as possible. It is normal to feel sad, stressed, or confused during a crisis. Talking to people you trust, such as friends and family, can help. If you feel overwhelmed, talk to a health worker or counsellor. Schools shut down, shopping malls closure, workplaces closed with people working from home, airlines grounding fleet, markets in mess, even some countries in a lockdown – this is the global impact caused by the COVID-19 corona virus. When corona virus affects a person, symptoms can be: Fever, flu-like symptoms such as coughing, sore throat and fatigue, shortness of breath. Symptoms of corona virus can range from mild illness to pneumonia. Some people will recover easily, and others, especially old people and those with immunodeficiencies may get sick very quickly.

Through coughing or sneezing, or by contact with hands, surfaces or objects contaminated with the virus, people can get infected. If an infected person's saliva touches a surface, then that surface an become a virus zone for some time. Any person who touches that surface, eg, a doorknob, or button of a lift, has a possibility to contract this virus. The main thing we need to do is to enhance immunity, especially for the lungs and respiratory system. Strong immunity is necessary to fight any kind of foreign body or disease. As we can't control external situations, we work on increasing our capacity to resist any disease. These tips below are in addition to the common sense things eg washing hands etc, that are already being recommended through many media channels and blogs.

Guduchi (*Tinospora cordifolia*). In Sanskrit, guduchi is also called as 'Amrita', which translates to 'the root of immortality'. This herb, Guduchi is known for its many medicinal properties for all kind of disease, and as an immunity booster.

Amalaki (*Phyllanthus emblica* also one of the ingredients of triphala, another well-known ancient formula) is an antioxidant and, a heat stable and rich source of Vitamin C, fruit, and an immunity booster.

Tulsi (*Ocimum sanctum*) or sacred basil is another plant known for enhancing immunity and is traditionally used for all kind of cold, cough and flus. Tulsi herb is very effective in treating upper respiratory and lower respiratory diseases such as cough, cold, and dyspnea. Tulsi is strong anti-viral, and strengthens respiratory system. It has antibacterial and antiviral properties. You can have tulsi leaves directly or consume it in the form of herbal tea.

Figure-14: Holistic source to combat COVID-19.

Turmeric (*Curcuma longa*) takes care of allergy and immunity. Known anti-viral, anti-bacterial and anti-fungal spice. It has anti-inflammatory properties and gives a massive boost to your immune system.

Neem (*Azadirachta indica*) can be added to turmeric as well if taking as powder. Neem is good for fever and boosts immunity.

Traditional herb mix called trikatu is part of first aid kit for all cold, and flus. It is useful as preventative for them. Trikatu promotes digestive strength, and is good for respiratory system. Trikatu is an Ayurvedic blend of equal parts of the fruits of Black Pepper (*Piper nigrum*), Long Pepper (*Piper longum*) and the rhizomes of Ginger (*Zingiber officinale*). It is used to support normal gastric function and normal circulation.

An ayurvedic supplement called Chyawanprash. This ancient recipe has been used for thousands of years for immunity enhancement amongst other things.

A drop or two of ghee or cold pressed sesame oil inside your nostrils and sniffing it in will lubricate the nasal passage and throat, and strengthen the inner mucus membrane to keep away foreign bodies.

Another tip is to reduce your sugar intake as sugar reduces your body's immunity levels.

Pranayama or breathing exercise are good for strengthening respiratory system. Prana is the life force in our body. Pranayama means the exercise of increasing the life force in our body. *Anulom-Vilom* and *Bhramari* pranayama are good and easy start.

According to the World Health Organization (WHO), the most effective way to protect yourself against corona virus is by frequently cleaning of your hands with alcohol-based hand rub or washing them with soap and water.

Stress and fear can reduce immunity, so stay calm – meditation can be useful.

Joy and enthusiasm can raise immunity. Stay joyful. One of the ways to increase joy is by increasing gratitude. See what good is coming through to you in this situation that whole world is in. Were you craving for some time out, or time to spend with children or family? Here it is now, use it.

There is no country, skin colour, community or religion that is immune to a virus. Maintain your humanity. Remain compassionate and graceful.

Carrots, kale and apricots for beta carotene: Beta carotene gets converted to vitamin A, which is essential for a strong immune system. It works by helping antibodies respond to toxins and foreign substances. Good sources of beta carotene include sweet potatoes, carrots, mangoes, apricots, spinach, kale, broccoli, squash and cantaloupe.

Oranges, strawberries and broccoli for Vitamin C: Vitamin C increases blood levels of antibodies and helps to differentiate lymphocytes (white blood cells), which helps the body determine what kind of protection is needed. Some research has suggested that higher levels of vitamin C (at least 200 milligrams) may slightly reduce the duration of cold symptoms. You can easily consume 200 milligrams of vitamin C from a combination of foods such as oranges, grapefruit, kiwi, strawberries, Brussels sprouts, red and green peppers, broccoli, cooked cabbage and cauliflower.

Eggs, cheese, tofu and mushrooms for Vitamin D: Vitamin D regulates the production of a protein that selectively kills infectious agents, including bacteria and viruses. Vitamin D also alters the activity and number of white blood cells, known as T 2 killer lymphocytes, which can reduce the spread of bacteria and viruses. Winter-associated vitamin D deficiency -- from a lack of sun-induced vitamin D production -- can weaken the immune system, increasing the risk of developing viral infections that cause upper respiratory tract infections. Inversely, research suggests that vitamin D supplements may help to protect against acute respiratory tract infections. Good food sources of vitamin D include fatty fish, including canned fish like salmon and sardines; eggs, fortified milk and plant milk products; cheese, fortified juice, tofu and mushrooms. And while there is no evidence to prove that vitamin D supplements will protect you from corona virus, it's wise to consider a D supplement if you feel you are not getting enough of this important vitamin, which can be measured by a blood test.

Beans, nuts, cereal and seafood for zinc: Zinc helps cells in your immune system grow and differentiate. One meta-analysis revealed that zinc supplements may shorten the duration of symptoms of the common cold. However, it concluded that "large high-quality trials are needed" before definitive recommendations can be made. Sources of zinc include beans, chickpeas, lentils, tofu, fortified cereals, nuts, seeds, wheat germ, oysters (including canned), crab, lobster, beef, pork chop, dark meat poultry and yogurt.

Milk, eggs, nuts and more for protein: Protein is a key building block for immune cells and antibodies and plays a crucial role in helping our immune system do its job. Protein comes from both animal and plant-based sources and includes fish, poultry, beef, milk, yogurt, eggs and cottage cheese, as well as nuts, seeds, beans and lentils, protein-rich snacks, such as roasted chickpeas, which can be eaten in place of snacks devoid of protein, such as animal crackers, for example.

Bananas, beans and more for prebiotics: Probiotics and prebiotics help boost the health of the microbiome, which in turn supports our immune system. Sources of probiotics include fermented dairy foods such as yogurt and kefir, and aged cheeses, as well as fermented foods such as kimchi, sauerkraut, miso, tempeh and sourdough bread. Sources of prebiotics include whole grains, bananas, onions, garlic, leeks, asparagus, artichokes and beans.

Though not dietary staples, some herbs may be helpful when looking for natural alternatives for viral symptoms. One of the more convincing studies found that supplementation with elderberry substantially reduced upper respiratory symptoms when taken for the cold and flu.

Water, fruit, soup and more for hydration: Finally, stay hydrated. Mild dehydration can be a physical stressor to the body. Person should aim to consume 2.7 liters or 91 ounces of fluids daily, and men, 3.7 liters or 125 ounces; an amount that includes all fluids and water-rich foods, such as fruits, vegetables and soups.

Medical treatments: If you have mild symptoms and are otherwise healthy, self-isolate and contact your medical provider or a COVID-19 information line for advice.

CONCLUSION: C-O-R-O-N-A

C: Clean your hands, O: Off from gatherings, R: Raise your immunity, O: Only think to wear mask, N: No to hand shake, A: Avoid large crowds.

Coronavirus is a large family of viruses which contains some enveloped, positive-sense, single-stranded RNA virus. The name “Coronavirus” came from the Latin word Corona and the Greek word *korone*, which means crown. There are four types of corona viruses (CoV) such as alpha coronavirus, beta coronavirus, gamma coronavirus and delta coronavirus. Severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East Respiratory Syndrome-related Coronavirus (MERS-CoV) are under the beta coronavirus, which enters into the host cells and binds to the specific receptor such as ACE2 and DPP4 receptor

respectively. COVID-19is a novel coronavirus which first came in Wuhan, China, in December 2019 and now it is pandemic in worldwide. Actually corona viruses are zoonotic, that means they are transmitted through animals to people. SARS-CoV spread through civet cats to humans and MERS-CoV transmitted from dromedary camels to humans. But in case of COVID-19, the mechanism of action is unknown because this is a mutated gene of coronavirus. COVID-19 produced by much-more number of mutations into host. Vaccines and antiviral drugs are not approved till now for the treatment of COVID-19. World Health Organization (WHO) authorized 15 laboratories to provide reference testing support for COVID-19.

REFERENCES

1. Dr. Dhrubo Jyoti Sen, Dr. Sudip Kumar Mandal, Arpita Biswas, Dipra Dastider and Dr. Beduin Mahanti; Corona is culprit of ridiculous offensive nonsense air: World Journal of Pharmaceutical Research: 2020; 9(4): 503-518.
2. McIntosh K. Corona viruses: a comparative review.Curr Top Microbiol Immunol, 1974; 63: 85–129.
3. Prof. Dr. Dhrubo Jyoti Sen; Zika virus outbreak: the global endemic to pandemic: European Journal of Pharmaceutical and Medical Research: 2017; 4(3): 01-07.
4. Jalpa Soni, Avani Patel, Khushboo Patel, Dhiren Chaudhary, Tejas Chaudhari and Prof. Dr. Dhrubo Jyoti Sen; Global threat of nipah virus and treatment: European Journal of Pharmaceutical and Medical Research: 2018; 5(6): 703-712.
5. Ravi Patel, Ishan Panchal, Dilip Chavda, Priya Modiya, Hiren Marvaniya, Kaumil Modi and Dhrubo Jyoti Sen; H1N1/09 influenza: 20th century flu pandemics: Journal of Chemical and Pharmaceutical Research: 2010; 2(3): 605-619.
6. Heymann, David L; Shindo, Nahoko (2020). "COVID-19: what is next for public health?". The Lancet, 395(10224): 542–545.
7. Chan, Jasper Fuk-Woo; Yuan, Shuofeng; Kok, Kin-Hang; To, Kelvin Kai-Wang; Chu, Hin; Yang, Jin; et al. (2020). "A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster". The Lancet, 2020; 395(10223): 514–523.
8. https://www.who.int/emergencies/diseases/novel-coronavirus-2019.