CONOCIMIENTO
THE COVID CHRONICLES
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COVID-19: CAUSES AND CONSEQUENCES
PERSONAL ACCOUNTS OF THE PANDEMIC

From La Vida, Biology Club
IISER Berhampur
“Shield your existence from the fear that you can also fade away.”

In the midst of the current war against disease and death, we are gearing up to embrace the new normal. We are healing, we are praying, we are nurturing and growing. In this dynamic situation, change is the only constant. Let the mask be the sword as we, the warriors, paint the new world.

Cover Illustration by Vinayak Siv
Batch 2017
“The darkest hour has only sixty minutes”, so said Morris Mandel, an American educator and journalist. Although it is not just an hour or two, or days or even months, with death tolls rising over 3,00,000 and with nearly 4 million active infection of SARS-CoV2 worldwide, humanity is still fighting strong against the current pandemic of COVID-19. From the doctors in hospitals, scientists in labs, law protectors on roads, sanitation workers, administrative people to every responsible citizen following rules and regulations, the war is on!

As science students in one of the esteemed institutes of the country, there is responsibility on each one of us, to contribute to these efforts, to educate, to share the knowledge, and most importantly to dispel the rumours associated with the pandemic. In line with these thoughts, we bring to you this ‘Conocimiento’ or anthology of COVID-19, comprising of essays and review articles on the recent literature on SARS-CoV-2, contributed by the BS-MS students of all four batches. A motivation for publishing a second part prevails as there are numerous topics to be covered in one. The purpose will be served if this first COVID-19 issue of IISER Berhampur could help to reach out to one and all and convey the message in the words of Madame Marie Curie, “Nothing in life is to be feared, it is only to be understood. Now is the time to understand more, so that we may fear less.”

The ‘Conocimiento’ is dedicated to all the COVID-19 workers across the globe with a ray of hope that good days are not too far away.
One fine day...

After 3 days...“Shiver me timbers!!”

“Need to go...to the.hospital...”

“Get it over with!”
“Good grief!”

“This should do the trick!”

2 weeks later...

STAY HOME.
SAVE LIVES.
Help stop coronavirus
1  STAY home
2  KEEP a safe distance
3  WASH hands often
4  COVER your cough
5  SICK? Call the helpline

https://www.mohfw.gov.in
THE COVID-19 DICTIONARY

A layman’s guide to terminologies associated with the pandemic.

Prajwal Patil, Ankit Mohanty, Sanskriti Sinha
1. Corona Virus: Coronavirus is a family (taxonomic hierarchical unit) of viruses that cause respiratory diseases. Some of the members include Rhino virus (common cold), MERS-CoV (first reported in 2011), SARS-CoV-1 (first reported in 2002) and the newly emerged SARS-CoV-2. They are usually found in their natural reservoir hosts – Bats and civets, but can accidentally infect humans after evolving. The club-shaped viral spike peplomers present on the surface, (glycoproteins) create the look of a corona (Latin: crown) surrounding the virion when observed with an electron microscope.

2. COVID-19 (Coronavirus Disease): The disease caused by the virus named ‘SARS-CoV-2’. It is characterized by symptoms like fever, dry cough, fatigue, sore throat, headache among other signs.

3. Outbreak, Epidemic, Pandemic: Outbreak is a sudden rise in the localized incidence of a disease. An outbreak can turn into an epidemic if a disease spreads quickly and affects many individuals at the same time, over a broad area. A pandemic is an epidemic that has spread across a large region, multiple continents or worldwide. In a pandemic large proportion of a population is infected and number of newly infected individuals keep increasing exponentially. During such situations WHO recommends certain protocols to all the nations to take necessary precautions.

4. Contagious vs Infectious: The words are frequently used interchangeably which is not appropriate. As the name suggests, something that is “capable of causing infection” is infectious. Contagious refers to the ability of being “transmitted from one individual to another.” A contagious agent is automatically infectious, but vice versa is not necessary to be true.

5. Incubation time: Time taken from the moment of infection till the first symptoms are seen is denoted as incubation time. Ministry of Health and Family Welfare, Government of India says, the incubation period for SARS-CoV2 ranges from 1 to 12.5 days (with median estimates of 5 to 6 days), but can be as long as 14 days.

6. Index case: The first documented case of a person affected of a certain genetic or infectious disease. The patient is known as the “Patient zero.”

7. Droplet transmission: COVID-19 spreads mainly by droplets produced as a result of coughing or sneezing by an
infected person. One can get the infection either by being in close contact with COVID-19 patients (within 1 metre) or via the droplets that survive on surfaces and clothes for many days. Such objects are called fomites. Although there are various speculations of the virus particle being air borne this statement is not correct.

8. **R<sub>0</sub> – Basic reproductive number:**
The basic reproduction number of any infectious disease outbreak is the amount of new cases generated directly from one existing case in a population where everyone is susceptible to the disease (as in the current scenario). R<sub>0</sub> is not constant and it changes with time and environmental conditions. Currently R<sub>0</sub> for COVID-19 is around 1.4 to 3.9. If R<sub>0</sub> > 1, the disease is highly infectious and new cases increase exponentially. If R<sub>0</sub> < 1, the disease starts vanishing.

9. **Community spread:** Essentially, this implies “the spread of a contagious disease to individuals in a particular geographic location who have no known contact with other infected individuals or who have not recently traveled to an area where the disease has any documented cases.”

10. **Hotspots:** These are the most high-risk areas with maximum cases of COVID-19 within a locality. A lot of individuals in these areas are infected and there is a high chance that one might get infected if he/she enters the area. So, there is a strict monitoring of the movement in and out of these areas.

11. **Self-Isolation:** An infected person is isolated and treated by medical officers. Any kind of contact with patient is strictly prohibited. Doctors and nurses use protective wear while interacting with patients. Treatment of patients are carried out in isolation wards till he/she recovers.

12. **N-95 mask:** Health personnel, treating COVID-19 patients, are using N-95 respirator as it functions as a filter membrane not allowing the small SARS-
CoV2 (50-200nm) particles to enter through nose and mouth.

13. **PPE:** Personal protective equipment is used by the COVID-19 fighters who are working on field to prevent the risk of disease transmission. Safety helmets, gloves, eye protection, high-visibility clothing, safety footwear and safety harnesses are necessary component of a protective gear.

14. **Social distancing:** Citizens are recommended to maintain necessary physical distance while interacting with others. Social gathering, meetings or any other activities that might increase the risk of infections to masses are prohibited. People are encouraged to stay at home.

15. **Quarantine:** The act of staying at home, avoiding social contact as much as possible and maintaining a distance of 6 ft with everyone for 10-14 days. It is recommended by health care officials to the individuals suspected with COVID-19 infection as a precaution from spreading the infection. The patient is under constant medical observation for any symptoms during this time.

16. **Contact tracing:** The practice of identifying and monitoring individuals who may have had contact with an infectious person. It is used as a means of controlling the spread of an infectious disease.

17. **Breaking the chain:** SARS-CoV2 is highly contagious which keeps spreading in a community by forming a chain amongst individuals. If the chain is interrupted at a one point the virus won't transmit further. The feat can be achieved by imposing social distancing.

18. **Flattening the curve:** The curve we are talking about is the graph of the proportion of population getting infected with time which usually has a bell shape. Exponential growth occurs till it has infected most of the population (the peak). With recovery of patients, the curve starts to decline. Decreasing the spread, therefore, “flattens” the curve.

19. **WHO:** The World Health Organization is a specialized agency of the United Nations, responsible for international public health. It provides guidelines and formulates schemes for improving public health.

20. **ICMR:** Indian Council of Medical Research is currently leading the fight against COVID-19 in India via strategy formulation to prevent disease transmission and policy making for diagnosis & therapeutics.
COVID 19 : THE BASICS

A Small Virus and its Attack on Mankind

Akankshya Sahu
COVID-19 has emerged as a major challenge to humanity. Since, there are no specific vaccines or antivirals yet, and there is a rapid spread among healthy people, humanity is fighting against time to control and combat the pandemic.

**Coronavirus Disease 2019 (COVID-19)** is an acute infectious respiratory disease caused by the virus SARS-CoV-2. This virus is easily transmitted through respiratory droplets via human-to-human contact. The previous strains of coronaviruses, Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) and Middle East Respiratory Syndrome Coronavirus (MERS-CoV), both had their origins from wild and domesticated animals in South China and Saudi Arabia, respectively.\[^1\]\[^2\] Although there is a speculation that, like other coronaviruses, the natural host of n-CoV 19 is some species of bat, it needs stronger scientific evidence. A theory of existence of an intermediate host causing the jump of the virus in *Homo sapiens* also prevails.

Diseases caused by this strain of virus had most probably occurred in people handling animals in wet markets and farms in Wuhan city where the first case is documented. Soon the disease spread among healthy individuals who came in contact with the infected people. To complicate it further, a high percentage of cases, do not show any of the COVID-19 symptoms, known as “asymptomatic”! (Refer Article No. 2). Noticing the symptoms is possible only after the virus has completed its incubation (or presymptomatic) period in its host (Refer Article No. 4). Consequently, transmission control of this disease is very difficult which is the second biggest hurdle, the world is facing, following the challenge of finding a vaccine/antiviral for treatment of patients.

For an understanding about how this disease spreads, let us take the case study of the Diamond Cruise. \[^3\]
On 5 February 2020, in Yokohama, Japan, a cruise ship – the Diamond Cruise - hosting 3,711 people immediately underwent a 2-week quarantine after a former passenger was found with COVID-19 post-disembarking on 2 February. As on 20 February, 634 persons on board tested positive for the virus. In the case study, statistical estimation of asymptomatic proportion of infected people was done. Clearly, asymptomatic cases seem to be “DRIVERS” for COVID-19 transmission. Also, since the cruise ship was a confined area for the population considered in this study, it also explains the need for imposing strict restrictions like social distancing and lockdowns.

The current pandemic situation would have been avoided if early recognition and early intervention strategies were done when the first occurrence of the disease was reported. For early recognition, increased number of testing of potential COVID-19 patients and isolation of such people must be done. Intervention includes taking measures for containment of any disease which spreads rapidly.

Early intervention methods/ strategies can be taken with preparedness (social, medical as well as financial) for any such spread of a disease and emergency situations and thorough monitoring of visitors who come to a country from another country at international airports in case of an epidemic/a pandemic situation. Subsequently, intense preventive measures can be taken as necessary. We must also note that those countries which are following such intervention methods successfully have comparatively lower number of COVID-19 infected people than those countries which are not successful in following the intervention methods. With successful intervention methods, in an optimistic scenario where infected individuals are isolated from the healthy individuals we can “flatten the curve” (Refer Article No. 2) where we can notice delay by few days for a new infected case and also
number of new infection cases decreases. (Observe the graphs)

We can take into account the deadly Spanish flu \(^5\) pandemic which took lives of 17-50 million people in a timespan of around 3 years (January 1918 – December 1920). COVID-19 is still under control if we compare it with Spanish flu due to better intervention strategies and better medical facilities, but if we don’t control the spread of this disease today, we may get to see a situation which can be as deadly as Spanish flu. The chain of transmission should be broken to control the severity.

I would like to conclude with a list of unanswered yet urgent questions.

1. There are many R&D solutions coming up for testing of COVID-19, but we still don’t know which of them will give faster and accurate results.
2. Why are some patients recovering from the disease without any specific treatment and some are not?
3. Is immunity to COVID-19 possible? If so, how long does it last?
4. Is there any other way of transmission of disease other than its transmission through respiratory droplets and close contact with infected people? What
are the long term effects of the virus in our body?

5. Kids are not as much affected with COVID-19, even in affected cases they don't seem to get severely ill. Why is this happening? Why are some people at higher risk than others?

6. When will this pandemic end?

REFERENCES


[2] World Health Organization (WHO) - official website


[5] Wikipedia article for information on Spanish flu
HERD IMMUNITY AND PANDEMICS

Eshani Ganjoo, Pratyush Mishra, Tanishta Bhattacharya

It’s about breaking the chain
INTRODUCTION

In the middle of a global health crisis, that has brought the whole world to a standstill, suspending daily activities, daily wage labourers struggling to meet their needs and the whole society plunged into an economical depression, herd immunity is a relevant concept associated with disease outbreaks, a phenomenon which protected mankind in the past from other deadly viruses such as smallpox and polio.

HERD IMMUNITY

Herd immunity refers to the indirect protection from a contagious disease that happens when huge proportion of people in a population becomes immune to it. Whether this immunity is acquired through previous infection or obtained via vaccination, for diseases caused by human to human transmission, it turns out to be difficult to maintain a chain of infection. Vulnerable individuals who can’t be vaccinated because of weak immunity, for whom vaccine doesn’t induce immunity, infants, people with vaccine allergies and people suffering from an immune-suppressing disease like HIV or cancer, are benefitted in this process. Immune people around hinder them from being infected.

More infectious a disease, the threshold level of immunization required to protect a population increases. The infectivity is measured by the reproduction number, $R_0$ of the
virus. Reproduction number refers to the average number of secondary infections caused by the infectious disease at any point during the progression of the disease. For SARS-COV-2 with a \( R_0 \) of 1.4 to 3.9, nearly 60% of the population has to be immune for an effective herd immunity to develop.

**HERD IMMUNITY BY NATURAL INFECTION AND RECOVERY**

The approach to induce herd immunity through unchecked infection would lead to high rate of serious illness and deaths. The health systems will be overwhelmed well beyond their capacity even in developed countries like the USA, UK and Germany. In the present scenario, hospitals lack infrastructure including isolation centres, beds, protective gears as well as ventilators for such a magnitude of patients. If cases keep on soaring high, the lack of manpower will become another shortcoming.

Lack of data regarding an individual being immune to SARS-COV-2, once recovered from the infection, poses a question. One study by a Chinese research team suggested that in Rhesus monkeys infection was not observed upon re-exposure to the virus indicating development of immunity. However, there have been some cases of people testing positive even after they have recovered.

Another important question that arises is for how long the immune protection would last. For people infected with OC43 and HKU1, the coronaviruses that regularly circulate among humans causing common cold stay immune for less than a year whereas for those who were affected by SARS, the immunity protection is for a much longer duration.

For SARS-COV-2 there has been no confirmed report yet. Herd immunity will occur subsequently, but, at present with less information about the virus, allowing people to get infected will result in thousands of people dying.

Moreover, SARS-CoV2's genetic material being made of RNA, the threat of higher mutation rate to change morphology
and re-spread in the human population also persists which would make the effort to gain herd immunity through usual infection fruitless.

DEVELOPMENT OF VACCINE FOR SARS-COV-2

A vaccine for SARS-COV-2 is the best hope to develop herd immunity against COVID-19. However, there exists no specific vaccine for SARS-COV-2 as of now and it may take at least a couple of years to develop a safe and effective vaccine because to reach the market a vaccine must go through highly sophisticated protocol of six developmental steps including a three-phase clinical stage. (Refer : Article No. 7). On the other hand, as infection rates start to diminish due to other factors, research on the vaccine is likely to slow down and become neglected, something that happened with SARS-COV vaccine.

FUTURE

Human race faced pandemics in the past and had emerged out of them strongly. In the middle of COVID-19 pandemic where we are learning as we speak, realizing at each moment that what we knew yesterday or day before was not entirely correct and new information on this virus emerging constantly, the hope is to find one vaccine candidate that works out, so that immunity can be developed as a herd.

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COVID-19 ETIOLOGY

The Cause Behind The Cataclysm

Sukanya Chakraborty
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THE EVENTS AT A GLANCE

December, 2019. In the city of Wuhan, located in the Hubei province of Central China, a cluster of unaccountable pneumonia cases are reported.

January 30th, 2020. India reports its first case of the much dreaded Coronavirus Disease in Kerala. This marks the beginning of an arduous war against the epidemic.


April, 2020. Current estimates place the total number of confirmed cases worldwide to be more that four million and counting. In the wake of this unprecedented situation, the world today faces one of the biggest challenges to mankind in the recent past.
**THE BASICS**

Currently, we are navigating our way through a surreal crisis, with an accelerating death toll and a clouded future, all because of a virus. A good place to start therefore, would be by getting a clear picture of how this microscopic, yet powerful entity functions and what makes it such a formidable threat to humankind. A virus, an infectious agent much smaller than most bacteria, must invade a living cell to reproduce (replicate). The virus essentially attaches to a cell (called the host cell) by binding to a receptor, enters it, and releases its genetic material (DNA or RNA) inside the cell. The viral genetic material in turn exploits the host cell’s resources for its own proliferation. The infected cell usually dies because the virus prevents it from performing its normal functions. Upon dying, the cell releases new virus particles, which go on to infect other cells. An early determinant in the occurrence of viral infection is the extent to which body tissues and organs are accessible to the virus. This is in turn influenced by several host factors such as - physical barriers (such as mucus and tissue barriers), by the distance to be traversed within the body, and by natural defence mechanisms. As a group, viruses use all conceivable portals of entry, mechanisms of spread, target organs, and sites of excretion. This abundance of possibilities is not surprising considering the astonishing numbers of viruses and their variants.

If the virus reaches its target organ, infection occurs only if cells capable of supporting virus replication are present. Cellular susceptibility requires a cell surface attachment site (receptor) for the virions and also an intracellular environment that is conducive to virus replication and release. However, disease does not always follow successful virus replication in the target organ. Disease occurs only if the virus replicates sufficiently to damage essential cells, cause the release of toxic substances from infected tissues and damages cellular genes or organ
function indirectly as a result of the host immune response to the presence of virus antigens.

A PEEK INTO THE ARSENAL OF CORONAVIRUSES

The family of Coronaviruses, one of which is responsible for the current threat to humanity, have become the major pathogens of emerging respiratory disease outbreaks. A large family of positive sense single-stranded RNA viruses, these can be isolated in different animal species. Derived from the Latin word, “coronam”, essentially meaning crown, these viruses, true to their name, have a crown-like appearance in electron micrographs, due to their spike glycoproteins. The different CoVs display a diverse host range and tissue tropism, spanning birds, fish and mammals.

![Fig. 1 Replication Cycle of SARS-CoV-2, a Schematic Representation. Stages shown include attachment and endocytosis, uncoating and release of genetic material, biosynthesis within host cell and exocytosis of mature virions. Credit: Rohan Bir Singh, MD. (http://creativecommons.org/licenses/by/4.0/)](image-url)
The current COVID-19 pandemic, is believed to be due to the SARS-CoV-2 strain, belonging to the category of beta CoVs, (the other genera being alpha, gamma and delta) and can cause lower respiratory tract infections, though symptoms appear to be milder than SARS or MERS (belonging to the alpha and beta CoVs category). As with other respiratory pathogens, including flu and rhinovirus, the transmission is believed to occur through respiratory droplets from coughing and sneezing. Based on data from the initial cases in Wuhan and other investigations, the incubation time varies between 3 to 7 days and up to 2 weeks. This data also showed that this novel epidemic doubled about every seven days, whereas the basic reproduction number (R₀) is 1.4 to 3.9. In other words, on average, each patient transmits the infection to an additional 1.4 to 3.9 individuals.

Etiology is the study of the cause and origin of a disease or a condition. This article aims to shed light on these
aspects and for addressing the etiological mechanisms of SARS-CoV-2, insights into its viral structure, and genome must be unraveled. In addition, research will be needed to determine the structural characteristics of SARS-CoV-2 that underlie the pathogenic mechanisms. The genome of CoVs is a single-stranded positive-sense RNA with a 5'−cap and 3' poly-A tail (resembling mRNA which can be directly transcribed). The size of their genome is about 30 kilo bases, the largest among RNA viruses. Fundamentally, all viruses after infecting host cells, produce two classes of viral proteins - non-structural and structural, synthesised in that respective order. The genomic RNA is used as template to directly translate a poly-protein, which encodes viral non-structural proteins (nsps) to form the replication-transcription complex. In contrast, the four main structural proteins include the spike (S), envelope (E), membrane (M) and Nucleocapsid (N). Spike helps in docking to the host cell.

Fig. 3  Simulation of the SARS-CoV-2 structure. Cross sectional model showing components of the viral envelope causing infectivity. Credit : https://www.scientificanimations.com, image sourced from https://creativecommons.org/licenses/by-sa/4.0/deed.en
surface. It has two subunits S1 and S2 with S1 comprising the minimal Receptor Binding Domain and S2 helping in membrane fusion. Membrane establishes curvature of the membrane and stability. Envelope is fundamental in assembly of the mature virus, release and pathogenesis and nucleocapsid represses RNA interference, helping viral replication.

Since SARS-CoV-2 belongs to the same family of viruses as SARS and MERS CoVs, several studies have concentrated on the similarity between these strains. Although the evolutionary proximity of SARS-CoV-2 with the SARS and MERS CoVs does not seem to be overwhelming, studies have reported that they use the same receptor to access their target cells. A noticeable and unsettling difference, however, is the greater binding affinity of SARS-CoV-2 for the receptor compared to the previous strains. The receptor in question, the Angiotensin-Converting Enzyme 2 (ACE2; has the physiological functions of regulating heart and kidney function and controlling blood pressure),

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**Clinical presentation of patients with CoVID-19**

- Fever/Headache
- Hemoptysis
- Cough
- Myalgia
- Shortness of breath
- Pneumonia
- Septic shock
- Renal failure
- Diarrhea

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**Fig. 4 Clinical Presentation of COVID-19.** Systems getting affected other than respiratory tract are also shown based on receptor distribution and viral tropism.

Credit: Rohan Bir Singh, MD. (http://creativecommons.org/licenses/by/4.0/)
is expressed significantly in the face and tongue, which explains the ease of viral entry into the host through this route. Upon reaching the lungs, the virus binds to the said receptor by the interaction of the spike glycoprotein on its envelope and ACE2 on the alveolar surface. As a result of this attachment, this complex undergoes fusion and endocytosis into the host cell. The virus, once inside, hijacks the host cell transcriptional machinery to replicate and spread throughout the lung. As a result, with the disruption of the normal functioning of the ciliated alveolar cells, the airways cannot be cleared, leading to the accumulation of debris and fluids in the lungs, and culminating in acute respiratory distress syndrome. The kidney, heart and gut also express ACE2 receptors and the co-morbidities of COVID-19 are in fact most frequently reported in acute disorders of these organs. However, whether the virus replicates in the cells of these tissues is still under speculation.

In addition, the pathogenic mechanism that produces pneumonia following disease progression seems to be particularly complex. Although trends suggest that most cases are mildly symptomatic, some may process to develop severe complications. For the elderly and people with a history of chronic respiratory disorders, this could prove fatal. The data so far available seem to indicate that the viral infection is capable of producing an excessive immune reaction in the host. In some cases, a reaction characterized by the release of an overwhelming quantity of circulating immunomodulatory protein factors, or cytokines, takes place, addressed popularly as a 'cytokine storm'. The effect: extensive tissue damage. IL-6 (Interleukin-6), one of the key players, is produced by activated WBCs and acts on a large number of cells and tissues, having diverse effects on other immune system cells. It is thus implicated in the pathogenesis of the cytokine release syndrome (CRS), is an acute systemic inflammatory syndrome characterized by fever and multiple organ dysfunction. These mechanisms support evidence of this family of
viruses affecting the nervous, respiratory, gastrointestinal and livers of humans, livestock, bats, rodents and other wild animals.

THE MYSTERY OF THE SPIKE PROTEIN

Most of the current research has focused on elucidating the exact sequence of amino acids in the receptor binding domain of the virus spike glycoprotein. This will facilitate understanding of the nature of interaction with ACE2 and the resulting binding affinity, which is the major concern in SARS-CoV-2 infectivity.

Experimental techniques include high-throughput sequencing of the receptor binding domain in the spike glycoprotein and mammalian ACE2, followed by alignment and in silico analysis of the ACE2-RBD complex. The interaction interfaces are simulated by modern bioinformatic software tools to isolate and identify the key amino acid sites. Animal models are an indispensable tool in the study of infectious diseases. Since the ACE2 receptor in mice cannot interact with SARS-CoV-2, it is unsuitable to be used as a model directly. Transgenic mice expressing human ACE2 have been developed to facilitate this study. Mutations in ACE2 to alter the binding affinity may be a feasible approach to uncover new findings. Testing these in cell culture and animal models would be the future goals.

Fig. 5 Three dimensional simulations of the spike glycoprotein. Structure of the SARS-CoV-2 spike glycoprotein reveals the architecture of the key player of viral entry into host cells. Credit: Alexandra C. Walls, Young-Jun Park, David Veesler
Owing to the importance of the S glycoprotein which anchors the virus to the host cell and fusing with the membrane to get internalized, it becomes a focal aspect to study for our better understanding of the SARS-CoV-2 virus. A recent study that used electron microscopy to study the spike glycoprotein of SARS-CoV-2 interestingly found that the Receptor Binding Domain is flexible, hence can be approached by receptors to bind and guarantee virus entry. This implies that blocking the viral entry is crucial. Due to the large genetic diversity of Coronaviridae family and also the fact that these viruses undergo frequent recombination events recent efforts have focussed on trying to trace the rise of SARS-CoV-2 from the existing coronaviruses through RNA.
recombination. Since the surface glycoproteins in an enveloped virus are one of the major determinants of its pathogenicity, the S protein was used for sequence alignment and phylogenetic tracing. The minimal RBD (S1) of SARS-CoV-2 differs significantly from the previous strain of SARS as it expresses many novel glycosylation sites, which would alter the binding capacity to the host cell receptor and help viral entry. Cytotoxic T-lymphocytes’ epitopes recognize specific viral peptides and are the most effective control of viral replication and spread. Viruses may escape this recognition through mutations in CTL. An antigenic analysis showed that most of the CTL epitopes in 2019-nCoV are novel but some of the epitopes were similar to the ones found in SARS-CoV, a promising result for future applications in vaccine development.

In other news, a team of researchers at the Indian Institute of Technology, Kanpur, has been employing specialised real-time imaging techniques to visualize the mechanisms of viral entry better. Using an elegant technique known as smFRET (Single-Molecule Fluorescence Resonance Energy Transfer), the S glycoprotein is tagged with a ‘donor’ fluorescent dye and the ACE2 with an ‘acceptor’ dye counterpart. Once the two get closely opposed, excitation by a laser, causes the donor to transfer some energy to the acceptor, altering the spectral output of both the tags, and this is in turn, dictated by the degree of separation between the two components. Such insights into the dynamics of membrane fusion might give us strategies to counter the disease.

WHERE DO WE GO FROM HERE?

Etiology, science that deals understanding factors which cause a disease is one of the many aspects that need to be dealt with in our battle against this pandemic. It is always easier to understand a problem better or devise solutions if we know the cause of the same. Similarly, when dealing with any disease, comprehending the cause
of the disease and trying to eliminate it is a more reliable way rather than treating merely the symptoms. What we aimed for in this article, was to amalgamate the research findings concerning the cause of the disease currently plaguing the world. This would help to bring us a step closer in discerning the ways to develop vaccines and potential treatments, and in general be informed and responsible citizens in this struggle. Needless to mention, all research aimed at alleviating the current situation will take time to yield revolutionary results. The admirable camaraderie of the entire scientific world may achieve feats never seen before.

REFERENCES


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Myth: Mosquito bite can spread the virus

Fact: There is no accounted fact. The virus attacks the respiratory tract and not the blood. So, it is impossible for a mosquito to spread this disease. Mosquitoes are vectors for diseases such as dengue and chikungunya, also caused by viruses.


Myth: Blood test is required to determine the presence of the virus.

Fact: There is no test now that needs blood to test the presence of the virus. Currently this is done by "swab test." It involves taking a sample of mucous from the nostril or mouth. Avoid giving blood to any people asking for such.
CHARTING THE PANDEMIC

COVID-19 EPIDEMIOLOGY

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INTRODUCTION

The emergence and rapid spread of Corona Virus Disease-19 (COVID-19) has so far been an epidemiological storm to behold. The first reports of novel pneumonia (which was COVID-19) popped up as December 2019 was ending, in Hubei province, Wuhan city, China although retrospective analyses find a carrier to be symptomatic on December 1st. Studying how the virus has jumped species, as well as species it can infect, may turn out to be crucial to find out where the virus came from, a question that has been long speculated now but not accurately answered.

ABOUT THE VIRUS

Coronaviruses are a group of related viruses that causes ailments in mammals and birds. In humans, they have been seen to cause respiratory tract infections ranging from mild illnesses like common cold to lethal ones like Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS). The virus family has an unusual knack of jumping species boundaries, although symptoms in other species vary.

Earlier two more viruses of this family are known to cause severe disease outbreaks in humans- SARS in 2003 and MERS in 2012 having significant Case Fatality Rates (CFR) with 14 percent and 34 percent respectively. (Refer Article No. 4) The virus SARS Coronavirus 2 (SARS-CoV-2) of this family, is responsible for COVID-19. Initially, it was known as 2019 novel Coronavirus (2019-nCoV) but later the name was changed to SARS-CoV-2 due to close resemblance of the virus to that of the SARS virus.
SPECTRUM OF SEVERITY

SYMPTOMS
The most common symptoms of COVID-19 are fever, tiredness, and dry cough. Some patients may have aches and pains, nasal congestion, runny nose, sore throat, or diarrhoea. These symptoms are usually mild and begin gradually. Some people become infected but don't develop any symptoms and don't feel unwell. The average incubation period of the virus inside the host ranges from 2-14 days and they remain infectious during this period even if they don't show any symptoms. So technically, a suspected patient should be isolated for 14 days. But there have been reports of people showing symptoms after 20 days of viral exposure.

COVID-19 starts once the virus gets access to the mucous membrane in the throat through our eyes, nose, or mouth. The immune system then may respond with early symptoms like a sore throat, a fever, or a dry cough, within 14 days. The virus then begins its journey down the respiratory tract and since it has been shown that our lower airways have more ACE2 receptors that bind to the virus, it is more likely to go deeper than viruses like the common cold. SARS CoV-2 infects ciliated cells in the alveoli, these cells stop carrying out their normal activity like clearing the airways with consequent accumulation of debris and fluids in lungs and acute respiratory distress syndrome (ARDS). About 5 to 8 days after symptoms begin, shortness of breath is seen. ARDS starts a few days later. ARDS can result in rapid breathing, a fast heart rate, dizziness, and sweating. Many people who get ARDS need a ventilator to facilitate breathing.

PEOPLE AT MORE RISK
For most people as stated earlier, the symptoms end with a cough and a fever. More than 8 in 10 cases are mild and do not need special treatment. But for some, the infection gets more severe. The median age of infected subjects has been found to be 59 years and the median age of death 75 years with the
median time from early symptoms to death especially for the people belonging to above 70 age group being 11.5 days (20 days in case of below 70 years). This clearly shows the faster and more severe disease progression in the elderly. ACE2 binding affinity by the receptor-binding domain (RBD of the virus) is a major determinant in the infectivity of the virus. Hence, we can conclude that the ACE2 gene expression in individuals based on their sex, age, race, smoking status, and other parameters can give us an idea about their susceptibility to COVID19. Relatively few cases of COVID-19 infection have been reported in children. Currently, it is unknown if differences reported in the number is because of the difference in exposures (e.g., children are less likely to care for sick contacts), disease severity, testing, or surveillance. \cite{CDC}

The severity of the infection depends mainly on the immune system of the host. If the person has a well-functioning immune system, he/she would be less affected by the virus. Older people and those with underlying medical problems like lung diseases and asthma, high blood pressure, heart problems, diabetes, people taking immune-suppressive drugs, HIV patients, pregnant women are more susceptible to the virus as they have a weakened immune system.

**OTHER ORGANS AFFECTED**

Presence of ACE-2 in heart, liver, testis, kidney, intestine and other tissue, make them more susceptible to fall prey to SARS-CoV-2. The SARS-CoV-2 enters the cell of these organs with the help of ACE-2. ACE-2 is involved in the function of regulating the heart and kidney and maintaining blood pressure, so any interruption or modification of ACE-2 can cause serious illness. This simply leads us to the inference that if an individual has some pre-existing disease, that affects the above-mentioned organs, it is more likely to be severely affected by this virus. Also, as fluid collects in the lungs, they carry less oxygen to the blood. Blood, therefore,
may not supply the organs with enough oxygen to survive. This can cause improper functioning of kidneys, lungs, and liver.

Sometimes the body's response to infection can go into overdrive. For example, when SARS-CoV-2 enters the lungs, it triggers an immune response, attracting immune cells to the region to attack the virus, resulting in localized inflammation. But in some cases, excessive or uncontrolled levels of cytokines are released which then activate more immune cells, resulting in hyperinflammation. This is associated with multiple organ dysfunction and can seriously harm the patient. (Refer Article No. 4)

Some people who have COVID-19 report symptoms involving their:

**EYES, NOSE, AND MOUTH**

Some people with the novel coronavirus have been diagnosed with pinkeye. There have been reports of loss of smell or taste.

**HEART AND BLOOD VESSELS**

The virus may cause heart problems and fatal blood clots.

**STOMACH, LIVER, INTESTINES, AND KIDNEY**

The virus has been stated to cause a loss of appetite, nausea, diarrhoea, and indigestion. Reports also say one may have these symptoms even before fever or any respiratory problems. It has been found that in severe cases, COVID-19 might lead to liver damage and kidney problems.
THE FATALITY RATE

The case fatality rate (CFR) for COVID-19, the ratio of the number of deaths to the total number of infected people for COVID-19 which gives an estimate of the probability of dying if infected by the virus, is higher than that of seasonal influenza and lower than that of SARS-CoV. CFRs will also vary geographically, between age groups and temporally. The CFR was found to be around for China 4.00% (March 16). However, the true number of cases will be greater than reported because very mild or asymptomatic infections will often be excluded from the actual counts, which means that the CFR associated with COVID-will be lower than that currently reported.

TRANSMISSION, TREATMENT AND PREVENTING THE SPREAD

INFECTIVITY AND REPRODUCTION NUMBER

Although SARS-CoV and MERS-CoV are both closely related to SARS-CoV-2, the biological differences between these viruses are prominent and account for the greater infectivity of SARS-CoV-2 and its very different epidemiological dynamics. The exceptional local and global spread of SARS-CoV-2 came as a surprise. The effective reproduction number (R) is an estimate of the number of secondary cases generated by the presence of one infected individual over the course of his infectious period. Different studies of COVID-19 estimate a basic reproduction range to be from around 1.4 to 3.9 which is much more than the reported effective reproduction
number for SARS (1.77) or seasonal influenza (0.9-2.1).

Based on a study on 103 publicly available SARS CoV-2 genomes, it was identified that 101 of them exhibited two linked SNPs defining two strains, L being a major strain (~ 70%) and S being a minor strain. (Xiaolu Tang et al., 2020)

Genomic alignment with other closely related viruses showed that regardless of being the less prevalent, S strain is the ancestral strain of SARS-CoV-2. The L strain was derived from the S strain. The fact that L strain is more prevalent suggests that L has a higher transmission rate compared to the S strain. This deems the L strain to be more aggressive than the S strain because of the potential higher transmission and/or replication rates.

The analysis also suggests that human interference may have shifted the relative abundance of S and L types soon after the outbreak. The study was only on 103 genomes which just represents a drop in the ocean. A recovered person cannot get infected unless the virus mutates so that it can overcome the host immune system. This selection pressure can lead to the emergence of multiple new strains.

**SPREAD**

The virus is reported to spread mainly through person-to-person contact via respiratory droplets generated by coughing and sneezing, or possibly through surface contaminated by people coughing or sneezing on them. Contaminated fomites can transmit it among animate and inanimate objects. The virus material gets deposited on fomites by direct contact with body secretions or fluids, or contact with soiled hands, or through aerosolized virus generated while talking or sneezing.

Airborne transmission refers to the presence of viral matter within droplet nuclei, which are generally considered to be particles <5μm in diameter and can remain suspended in the air for long periods and be transmitted over distances greater than 1m. In the context of COVID-19, the airborne
transmission may be possible in specific circumstances and settings in which procedures or support treatments that generate aerosols are performed, mainly in clinical procedures. These times and distances will vary under real-world conditions, depending on factors including temperature, humidity, ventilation, and the amount of virus deposited.

There is some evidence that COVID-19 infection may be present in faeces. However, only one study has been able to culture the virus from stool specimens. There have been no cases involving faecal-oral transmission of the COVID-19 virus to date. (WHO)

There is also evidence of animals and pets of COVID-19 patients being infected with the disease, the ones who come in close contact with infected humans. Further evidence is needed to understand if they can spread the disease. As of now, human to human transmission plays the main role in the spread of the disease. (WHO)

**ASYMPTOMATIC CASES**

More alarming are the cases of asymptomatic infections, suggesting that a symptom-based screening process may not be sufficient. These cases suggest the possibility of the virus getting transmitted even before a virus-carrying person shows any symptoms. The risk of catching COVID-19 from someone with no symptoms at all is low since the main way the disease spreads is through the expulsion of respiratory droplets while coughing or sneezing. However, it is possible to catch COVID-19 from someone who has a mild cough and does not feel ill. Although SARS CoV-2 is a new virus that humans are being affected with, studies have shown that for few people the symptoms might not be prominent due to anti-body cross-reaction and partial immunity because of pre-existing common seasonal coronaviruses that have been circulating in the human population.
STAGES OF TRANSMISSION

The novel coronavirus has four stages of transmission — the same as that for other infectious diseases.

Stage 1 is the first onset of the disease in people with travel history. Quarantining them at this stage and allowing no local spread from them can help contain the transmission and prevent it from going to the next stage.

Stage 2 is when those who acquired the infection through travel spread the virus to their close friends or family. Tracing everyone who came in close contact with the infected provides a significant aid in preventing further spread.

Stage 3 is when infections happen in the community and a source for the virus cannot be traced. At this stage of community transmission, large geographical lockdowns are crucial.

Stage 4 is when the disease becomes an epidemic in a country, with an increasing number of cases and a growing number of fatalities, with no one knowing when everything would come back to normal or whether it would, at all.

FLATTENING THE CURVE

On several news and media websites, experts have said that to put up a fight against the novel COVID-19 outbreak, we have to "flatten the curve" (Refer the COVID dictionary in this collection). At the same time, reports are saying the state of Kerala has "flattened the curve", which is very impressive, but might not sound that amazing without context. What is "the curve", and why would one want to flatten it? Do we keep flattening it till it becomes a straight line? Why hasn't everyone just flattened their curve?

The ominous curve is a graph that characterizes the impact of COVID-19 over a fixed area. It is a plot of time since the first reported COVID-19 case in the area (on the x-axis) against the number of cases. (on the y-axis) (refer to Fig. 1.) The predicate form of the graph, based
on previous outbreaks, seems to be a curve that peaks and then drops. Accompanying the curve is a straight dotted line parallel to the x-axis, representing the number of cases that place is equipped to deal with. Why would that be significant, though?

The ideal goal of fighting an epidemic or pandemic is to completely halt the spread. We say we've beaten a pandemic if we cut off its spread entirely. Of course, we would like that win, but it would be appreciated if we could do it with the least amount of deaths along the way. If the peak of the curve is below the hospital's capacity, then the hospitals have adequate resources to sustain and hopefully cure all the infected people. It reduces the number of cases that are active at any given time, which in turn gives doctors, hospitals, police, schools, and vaccine-manufacturers time to prepare and respond, without becoming overwhelmed. It would also stop the spread of the disease since infected people can be contained. Both the red and blue curves add up the number of new cases over time, the slope of the curve indicating how the virus is spreading. Keeping the curve down —

**Fig 1.** A plot of time since the first reported COVID-19 case in the area (on the x-axis) against the number of cases. (on the y-axis). The dotted line parallel to the x-axis represents the number of cases that place is equipped to deal with. Adapted from CDC / The Economist.
decreasing the rate of increase of new cases prevents overwhelming of the finite resources available for curbing the spread and treating the infected.

**MODELS**

Regions, where social-distancing measures have been implemented, deserve the assurance that the decision to enact these measures is well informed. For a novel pathogen like SARS-CoV-2, mathematical modeling of transmission under differing scenarios is a crucial method to generate accurate strategies. Many models have been made to predict the spread and fatality of COVID-19. Most models are made based on the states of individuals. There are three main states of an individual, susceptible(S), infected(I), and recovered(R). These models are called SIR models and are made on the assumption that a person once recovered from the disease will not be infected again. Certain studies also used another state – Exposed but not yet infected (E) giving some more clarity to their model. Here we presume that all individuals are equally likely to be infected and the patients are equally likely to infect others unless they die or recover. Other advanced studies divide the population into different subgroups based on age, gender, who meets who, and so on. Most of the models are made from the data obtained during the early stages of the outbreak which is incomplete. Modelers carry out hundreds of simulations to make sure that a change in a single input has a minimal impact.

In a study, Koo and colleagues assessed the potential of such social distancing interventions to curb the spread of COVID-19 in Singapore. The study is worth noting, since Singapore was among the first to report imported cases, and has succeeded in preventing community spread so far. They adapted an existing epidemic simulation model for influenza and used data on the composition and behavior of the population of Singapore to assess the potential consequences of specific social-distancing strategies, based on the assumption that between 7.5% and
50% of infections were asymptomatic. The interventions were quarantine with or without school closure and workplace distancing. The combined intervention, in which quarantine, school closure, and workplace distancing were implemented, was the most effective: compared with the baseline scenario of no interventions, the combined intervention reduced the estimated median number of infections by 99·3% (IQR 92·6–99·9) when R was 1·5, by 93·0% (81·5–99·7) when R was 2·0, and by 78·2% (59·0–94·4) when R was 2·5. (J.R. Koo et al., 2020)

Another study investigated the consequence of the most common social distancing measures that have been initiated to contain the epidemic in India: workplace non-attendance, school closure, and workplace distancing. The interventions were quarantine with or without school closure and workplace distancing. The combined intervention, in which quarantine, school closure, and workplace distancing were implemented, was the most effective: compared with the baseline scenario of no interventions, the combined intervention reduced the estimated median number of infections by 99·3% (IQR 92·6–99·9) when R was 1·5, by 93·0% (81·5–99·7) when R was 2·0, and by 78·2% (59·0–94·4) when R was 2·5. (J.R. Koo et al., 2020)

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Fig. 3. Forecast of the COVID-19 epidemic in India when social distancing is implemented. Each of the four panels shows the progress of the pandemic under lockdowns of various durations. The three-week lockdown starting 25th March was insufficient and a resurgence would have been observed, as shown in panel (a). A further lockdown of 28 days spaced by a 5-day suspension would have been futile, as shown in panel (b). The protocols in panels (c) and (d), which involve three lockdowns with 5-day relaxations and a single 49-day lockdown respectively, reduce the number of infections significantly. This forecast is based on all cases being symptomatic. Adapted from R. Singh & R. Adhikari (2020)
closure, “Janata curfew” and lockdown. (R. Singh & R. Adhikari, 2020) Since social contacts are influenced by age, the efficacy of these measures is dependent on both the age structure of the population and the frequency of contacts between age groups across the population. As this data is geographically specific, the same measures can have different outcomes when applied to regions with significantly different age and social contact structures. Taking all this into account, the various predictions suggested by the model are shown in Fig. 2 and Fig. 3. The estimates of the potential of these measures allows further planning. Clearly, such approaches will cause disruption of the society which makes it crucial to understand the extent of such interventions needed. The global economy is crashing. Most industries are on the verge of bankruptcy. Millions, both rich and poor, are losing their sources of livelihood. In this scenario, the government must enact policies that are socially and economically just since the effectiveness of quarantine and social distancing measures will be ultimately influenced by how much people find public health authorities and political institutions reliable.

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[8] [www.who.int](http://www.who.int)

[9] [www.cdc.gov](http://www.cdc.gov)

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**Myth:** Eating eggs and meat related products can cause the disease.

**Fact:** So far, no cases have been registered regarding the consumption of meat and the occurrence of the disease. Thoroughly cooked products are safe to consume. The viral route of entry is through the respiratory tract, not the gut. But avoid taking any animal meat that has died mysteriously of a disease. Vegetarians are probably on a safer side.
CORONAVIRUS: Therapeutics & Diagnostics

Somya Satpathy
Asutosh Behera
Deepti Ranjan Pradhan
Uttam Das
Gyanaranjan Parida
INTRODUCTION

The coronavirus outbreak has been labeled as a *pandemic* by WHO. To date there are no specific vaccines or medicine for it. Treatments are under investigation and are yet to be tested by clinical trials. Learning about therapeutics and diagnostics is equally important as the measures of social distancing and containing the disease. The therapeutics and diagnosis of COVID-19 or SARS-CoV-2 revolves around the understanding of the structure, proteins in and on the cell and the genetic material of the virus. There will be many universal theories for both, based on the symptoms and the response of the immune system, to the viral entities.

Time is of essence, as the virus has infected over 4 million people and caused over 3 lakh deaths, with numbers still going up. The feasibility and the certainty of the theories are of utmost importance, even though it is a temporary remedy. Search for potential vaccines has been initiated, but, still a long way to go. So, we prefer to the drugs that could slow down the symptoms and viral replication.

DIAGNOSIS

Diagnostic testing for COVID-19 is critical for tracking the virus, understanding epidemiology, informing case management and for suppressing transmission.

Spike protein (S-protein) performs two primary tasks that aid in host infection:

1. Mediating the attachment between the virus and host cell surface receptors;
2. Facilitating viral entry into the host cell by assisting in the fusion of the viral and host cell membranes. *ACE2* (Angiotensin converting enzyme2) is an endogenous membrane protein that enables COVID-19 infection.

During infection the extracellular peptidase domain of ACE2 [3] binds to the receptor binding domain (RBD) of spike protein (check grammar of this...
sentence). Change in several residues at RBD and ACE2 interface stabilizes the interaction.

These entities are the major targets for diagnosis of SARS-CoV2. Different countries have adopted similar approaches by targeting various segments from this region. Some of the important diagnostic tests, playing a major role in detection of coronavirus are enlisted here:

**RT-PCR TESTS**

WHO recommends collecting samples from both the upper and lower respiratory tracts. This can be performed through expectorated sputum, bronco-alveolar lavage, or endotracheal aspirate. These samples are assessed for viral RNA using RT-PCR \[^4\]. If a positive test result is achieved, it is recommended to repeat the test for re-
verification purposes. A negative test with a strong clinical suspicion also warrants repeat testing. RT-PCR is currently the widely used technique for detection purposes for its accuracy. In this procedure, the RNA of the virus is first reverse transcribed, to create cDNA. The cDNA is then amplified by PCR. The PCR products are aligned with the reference SARS-CoV2 genome with the purpose of looking for its abundance in the sample.

SEROLOGICAL TESTS

The fastest RT-PCR tests take at least a few hours. In contrast, rapid test kits, based on antibody detection, can give results in less than an hour, but, they are far less from being accurate (30 to 70%) than RT-PCR. In these tests, whole blood, serum, or plasma may be used for testing.

Some of the test kits are as follows (Ray biotech):

- 10 Minutes Rapid Detection of SARS-CoV-2 N-Protein Antibodies: Lateral flow devices are available for the detection of IgG and IgM antibodies to the coronavirus N-protein in serum, plasma, and peripheral blood.

- ELISA kits are available such as N-Protein ELISA kit, human IgG Indirect ELISA kit and human ACE2 ELISA kit.

Fig. 3 Lateral Flow Detection
(Source: https://www.raybiotech.com/)

- COVID19 Spike protein Array: Semi-quantitative detection of IgM and IgG antibodies in serum or plasma to the spike (S) protein.

- Polyclonal rabbit antibodies against N-protein, Spike Protein S1 Receptor Binding Domain, Spike Protein Subunit 2 (S2) Protein.

- Quantbody is an array-based multiplex ELISA system for simultaneous quantitative measurement of multiple cytokines, which have been reported during infection of the coronavirus.
CRISPR BASED TESTS

Recent reports about the gene-editing tool CRISPR being used by some companies to detect SARS-Cov2 are in the news. Scientists have demonstrated a CRISPR-Cas12 based assay, for detection of SARS-CoV-2 from extracted patient sample RNA [5], called SARS-CoV-2 DNA Endonuclease-Targeted CRISPR Trans Reporter (DETECTR). Since CRISPR can be modified to target any genetic sequence, the test kit’s developers “programmed” it to home on two target regions in the genome of the novel coronavirus. One of these sequences is common to all SARS-like coronaviruses, while the other is unique to SARS-CoV-2. Testing for the presence of both sequences ensures that the new DETECTR tool can distinguish between SARS-CoV-2 and closely related viruses. This assay performs simultaneous reverse transcription and isothermal amplification using loop-mediated amplification (RT–LAMP) [6] for RNA extracted from nasopharyngeal or oropharyngeal swabs in universal transport medium (UTM), followed by Cas12 detection of predefined coronavirus sequences. Cleavage of a reporter molecule associated with the Cas12 confirms the detection of the virus.

CT - IMAGING TESTS

Patient's lungs are imaged and looked upon for symptoms like ground-glass opacity, consolidation [7]. Though the symptoms are not confirmatory for...
covid-19 it can aid in screening or accelerate the speed of diagnosis, especially with shortages of RT-PCR. The assay has high specificity, but low sensitivity making the chest computed tomography a critical diagnostic tool for COVID-19, used in close combination with clinical manifestations and epidemiological evidence for disease confirmation.

**THERAPEUTICS**

Drug discovery and clinical research activities in COVID-19 prevention and treatment is increasing in pace. While no specifically approved treatments currently exist, stakeholders are looking to repurpose approved drugs that have worked against similar coronaviruses or other infectious diseases in the past or are hypothesized to attack or immobilize SARS-CoV-2 based on the mechanism of action. For the in vitro study, antiviral therapies, designed based on S protein, include RBD (Receptor Binding Domain)-ACE2 blockers, S cleavage inhibitors, fusion core blockers, neutralizing antibodies, protease inhibitors, S protein inhibitors, and small interfering RNAs. Plasma and stem cells from patients who have recovered from COVID-19 are also being investigated. Several other studies are now being carried out actively for therapeutic purposes. Progress achieved so far:

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**Myth:** The most common myth circulating is that heat can kill the virus.

**Fact:** Viruses like influenza cannot sustain hot temperatures. SARS-CoV-2 however, has not been characterised in this aspect. Once this virus enters the body there is no way one can eliminate it by drinking warm water (body temperature remains constant until someone is severely ill). The body must fight the virus with its own defences.

*All Myths and Facts compiled by Ankit Mohanty*
## REPURPOSED DRUGS

Following are the lists of repurposed drugs and their previous uses:

<table>
<thead>
<tr>
<th>Drug name</th>
<th>Conventional use</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flavilavir (favipiravir)</td>
<td>Antiviral against Influenza</td>
<td>Yousuke Furuta, Takashi Komeno, and Takaaki Nakamura. Favipiravir (T-705), a broad-spectrum inhibitor of viral RNA polymerase 2017 Aug 2</td>
</tr>
<tr>
<td>Remdesivir</td>
<td>Viral replication inhibitor</td>
<td>Yu-chen Cao, Qi-xin Deng, and Shi-xue Daib. Remdesivir for SARS-Cov2 causing COVID-19: An evaluation of the evidence</td>
</tr>
<tr>
<td>chloroquine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ivermectin</td>
<td>Anti-Parasitic drug</td>
<td>Calya, Druce et al. The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 in vitro, June 2020</td>
</tr>
<tr>
<td>CD24Fc</td>
<td>Biological Immunomodulator</td>
<td>CD24Fc as a Non-antiviral Immunomodulator in COVID-19 Treatment - ClinicalTrials.gov (NIH)</td>
</tr>
<tr>
<td>Leronlimab</td>
<td>Anti-CCR5 receptor antibody</td>
<td>Leronlimab Continues to Improve Health in Patients with Novel Coronavirus - Targeted Oncology</td>
</tr>
<tr>
<td>Nitazoxanide (NTZx)</td>
<td>Antiviral against influenza,</td>
<td>Nitazoxanide, a new drug candidate for the treatment of MERS coronavirus - François Rossignol</td>
</tr>
<tr>
<td></td>
<td>MERS</td>
<td></td>
</tr>
<tr>
<td>Camostat Mesilate</td>
<td>Serine protease inhibitor</td>
<td>Camostat mesilate therapy for COVID-19- Yoshikaru Uno 2020 Apr 29</td>
</tr>
</tbody>
</table>
CONVALESCENT PLASMA THERAPY

Researchers have theorized that convalescent plasma could be used as passive immunotherapy in other coronaviruses such as MERS and in SARS-CoV-2 to neutralize the virion particle \(^8\). In this therapy, neutralizing antibodies are selected, using B cells from the infected but recovered patients through single cell sorting and antibody cloning techniques. A case series of ten patients in China with COVID-19 and acute respiratory distress syndrome treated with convalescent plasma showed the therapy improved their clinical status. (Kai Duan et.al., 2020)

However, CP infusion still has its latent risk such as aggravating hyper immune issue...
attacks based on the foundation that CP therapy is passive immunity with administering pathogen-specific antibodies to patients. This implies that CP therapy is more effective in earlier stages of disease and researches have confirmed it. (Qian Zhao, Yong He, 2020) Therefore, the optimal timing of administering CP on COVID-19 needs to be carefully considered.

VACCINE DEVELOPMENT

A vaccine should stimulate the human immune system, to prepare it against a future attack. The idea is to pre-expose individuals with attenuated or killed virus or some of its structural part, against which the body can mount an immune response.

For the development of a vaccine against SARS-CoV-2, a similar approach is under consideration by Serum Institute of India and Sanofi Pasteur, France. An alternative strategy is also to generate antibodies against the spike proteins of the virus, which is being followed by Moderna Inc., MA, in USA. A German Enterprise, CureVac, aims to design an RNA-based vaccine against the virus. In this approach, RNA that codes for some of the viral proteins is introduced into the body. This RNA can be used to produce viral proteins, against which the body can synthesize antibodies, thus preparing for the virus’s attack. Other current investigational vaccines being tested in humans include a replicative-defective adenovirus type 5 (Ad5)-nCoV that expresses COVID-19 viral proteins and a lentiviral vector system to express viral proteins and immunomodulatory genes to modify antigen-presenting cells.

All these studies are under different phases of clinical trials. These vaccines may become available in near future, but the time it will take for these to reach the market depends on the efficacy and success in all three phases of clinical trials.

REFERENCES


LIFE IN LOCKDOWN

Deeksha Mittal
The havoc wreaked by the COVID-19 outbreak in the whole world has forced a situation where commoners cannot step out of their houses, thus, creating a lockdown situation. While the scientists are constantly working for a cure and tireless efforts are being made by the government and the doctors to handle the situation and minimise the casualties, the life during lockdown for civilians remains challenged.

Belonging to the better-off part, for us, life during lockdown is not very difficult or challenging owing to the amenities we have, and hence people like us are engaging themselves in recreational activities at home itself. “I have time to read all those books I bought and never opened, watch all the movies on my list, write all the books I have been playing in my head” – says Giulia Grimaldi, a journalist in Italy. [2] Also, a survey conducted by Hammerkopf Consumer Survey in New Delhi, Mumbai, Chennai and Bengaluru, found out that the internet browsing increased by 71% during the first week of lockdown, where the primetime for streaming turned out to be 7pm. [3] With colleges and schools all closed, students are receiving online lectures so that their studies don’t get hampered. “For students who are going to classes 10 and 12, our teachers have been taking classes on Zoom.” said Asha Nathan, principal, Chennai Public School, Anna Nagar. [5] A rather non ignorable fact came when a local television channel in China reported the increase in divorce application during isolation which indicates intensified altercations between quarantined couples. However, if we ignore the brighter side of our story and move a little further, living in lockdown has not been easy for those earning on a daily basis and belonging to the middle class in the society. “Economically, it’s a disaster. All my friends and colleagues are self-employed or have small businesses and they’re all broke”- says Justin Davidson, Rome. [4] Middle class gets hit hard most of the time maybe because in crises as such, government is mainly focused towards the vulnerable (BPL citizen) to provide the aid.
Days in lockdown have not been easy if we consider those who were exposed to it first and were totally unaware of the coming up situation. “On new year's eve, Jan. 24, I watched the glorious performances from a gala aired on CCTV, Chinese television. But our celebratory meal was sparse, pieced together from the few ingredients I'd been able to buy in that last-minute shopping trip.”- says a Wuhan resident [1], where a lockdown was imposed all of a sudden, without making the public mentally aware. Coming down, the most vulnerable group during the lockdown remains the one of daily wage workers, which is now struggling for food and shelter. Despite relief measures taken by the authorities, the panic didn’t get calmed and the situation only got worsened when a group of people started marching off to their hometown on foot.

Overall, going through a few personal accounts regarding life in lockdown primarily suggests it being difficult mainly for small-businessmen and daily wage workers. The situation right now definitely requires everyone’s efforts or the doomsday would be near. We need to think critically and act accordingly.

REFERENCES
Team La Vida wanted to get an idea of how people form different disciplines perceive the current pandemic. So we asked this question to all our faculty.

"If you had access to all the resources you wanted, be it inexhaustible finances or a limitless workforce, how would you intend to solve the predicament the world is currently facing?"

Here is what some of them had to say...
Equipped with inexhaustible finances, I would have donated money to all the needy so that they can buy essentials and stay at home. With limitless work force I would have taken every Corona suspect and infected patient to a remote island and treated them with the best possible Medicos. I will also engage mental health workers for awareness about Coronavirus and for caring about the mental health of public.

~ Itimayee Panda, Student Counsellor

Considering the potential threat of a pandemic caused by the SARS-CoV-2 virus, researchers and doctors have been racing to understand this new virus and the pathophysiology of this disease to discover the best possible effective therapeutic agents and vaccines. Drug repurposing is one of the methods in which we have several existing promising small molecule drug candidates. For instance, remdesivir a nucleotide analogue that may block viral nucleotide synthesis to stop viral replication which was originally discovered for Ebola virus infection. Given a chance, we would like to synthesize a range of such novel small molecules against the SARS-CoV-2 to find out the potential lead compound. We wish to work on the synthesis of additional drug candidates for treating the SARS-CoV-2 that by following target based screening of new compounds.

~ Dr. Thirupathi Barla, Department of Chemical Sciences

COVID-19 infection is real problem for the entire world. We know very little about this virus. To tackle the problem one needs to adopt two pronged strategies, (1) Prevent (2) Cure. To prevent, we need to know how it spreads and detect infected cases. Accurate data collection is important. In the absence of any particular method, the best way is to avoid contact with infected person. We need to establish more testing centres that is rapid and cost effective. IISER BERHAMPUR has taken the right step in this direction. In our lab. we will be able to test a large number of samples to map the spread. While observing the prevention through social distancing, care has to be taken about the socio-economic conditions of people arising out of lockdown to force social distancing. Towards cure, there has to concentrated effort to find a vaccine or possible therapeutic treatment. At this moment it is difficult to say when we will get a cure, but our effort in this direction is in accelerated mode. All I can say is have faith and stay safe by following the simple rules of good hygiene.

~ Prof. S.N. Mishra, Dean, Academic Affairs

The hack: PPE for all for 40 days. An ‘after’thought: The way the horrors of the twin nuclear blasts has kept at bay further escalation, I hope the pandemic does the same to the world’s fantasy with bio warfare. May better sense prevail!

~ Dr. Sandeep Chatterjee, Department of Physical Sciences
“A developed India by 2020 is not a dream but a mission that we all Indians can take up and succeed” - Dr. APJ Abdul Kalam.

When our former president said these words in his book “India 2020 a vision for the new millennium” coauthored by Dr. Y.S. Rajan, a precedent was set to transform the dream into reality. We did succeed to a large extent in this mission but no one would have imagined during this course that a pandemic awaits at the finish line. The global COVID19 pandemic is a test for all nations of the world, a test of healthcare, economy and welfare of citizens. India, the second most populous nation has done remarkably well till now with the early implementation of the biggest lockdown the world has ever seen.

But the real test begins now.

We have to first accept the current situation as a challenge that we can overcome. Mankind faced pandemics in the past and have emerged out of them. This needs to conveyed effectively to the general public by media through various forms. Pandemics do end and a new normalcy will ensue. The health care workers have been phenomenal in their efforts but they need new strategies for their protection and well being. Production of PPE is being ramped up and needs to be increased more. In the Aarogya Setu app which is a good success till now, a feature can be added where people can sign up to assist in the production process. These people can be screened, trained and used for the production process with the help of local centres close to their homes. There are lot of people who want to contribute but are not sure where to start. Every academic institute in the country should be encouraged to participate in the testing process. The risks associated with testing are minimal and significantly outweigh the benefits. Without testing there is no way that quarantine centres can separate infected from healthy people. The biggest challenge for our nation now is management of our migrant workforce who are not so privileged. In addition to the efforts by government, NGOs who already have experience in organising donation camps need to be empowered here for reaching out and extending the help. One of the biggest lessons learnt in this pandemic is that we as a nation have abundant natural resources and food produce but we need to be reliant on indigenous technologies. Testing kits for example are still being imported from outside and testing therefore is subject to availability of these kits. With abundant skilled workforce, we need to encourage more biotechnology startups dedicated for developing such technologies. Dr. Abdul Kalam might not have envisaged the current 2020 in his vision but he definitely had a mission for us. We must reunite as a nation rising above communal, social and economic disparities and once again carry his mission forward.

~ Dr. Vinay Bulusu, Department of Biological Sciences

Stay tuned for our next issue soon!
CONOCIMIENTO

From La Vida, Biology Club
IISER Berhampur

STUDENT TEAM

Anish Koner (Batch 16)
Sukanya Chakraborty (Batch 17)
Anuska Mohapatra (Batch 17)
Vinayak Siv (Batch 17)
Rabi Sankar Pal (Ph.D Student)
Pratyay Seth (Ph.D Student)
Sourav Dey (Ph.D Student)

FACULTY ADVISORS

Ruthrotha Selvi Bharathavikru
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ADDITIONAL RESOURCES (LINKS)

MyGov (COVID-19)
Ministry of Health and Family Welfare (Govt. of India)
Indian Council of Medical Research
World Health Organization
COVIDINDIA
COVID gyan