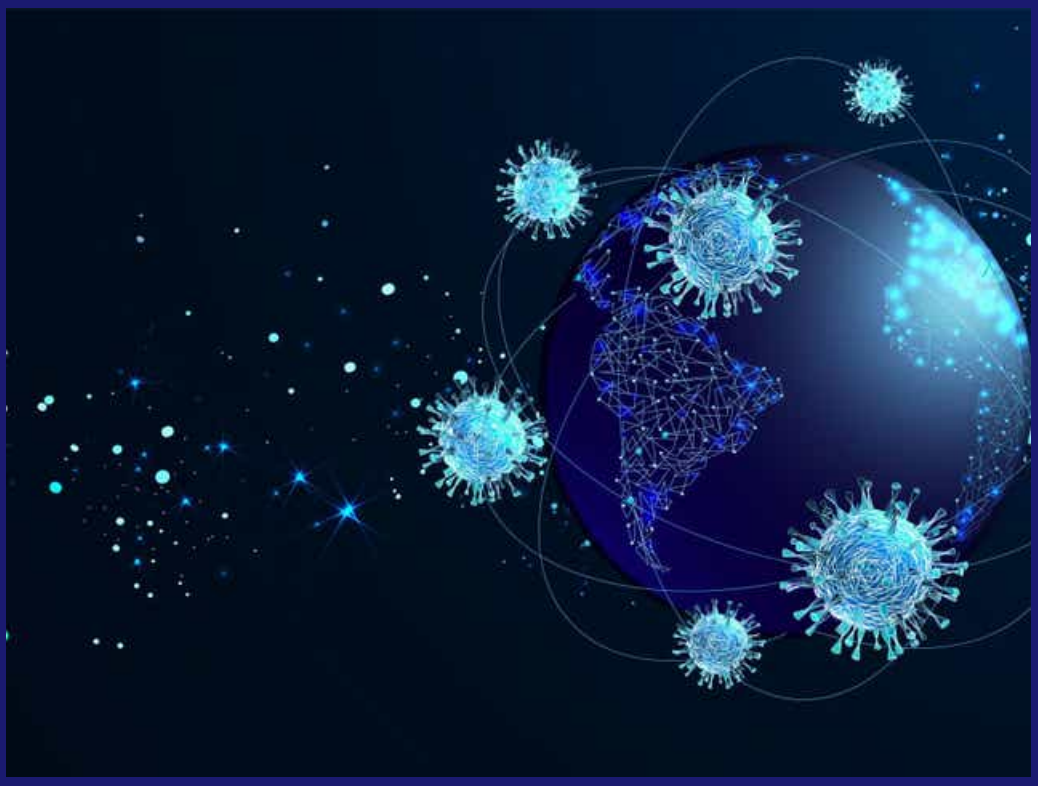
**SIR P. T. SARVAJANIK COLLEGE OF SCIENCE**
**DEPARTMENT OF PHYSICS**


Special Issue, April & August-2020

# COVID-19

## The Global Pandemic



# Editorial

***"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."***

***-Marie Curie***

On March 11, 2020, the novel coronavirus (SARS-CoV-2) was declared a 'Pandemic' by the World Health Organization (WHO) as the contagious respiratory illness swept across the globe at a galloping pace and altered the course of the history of the human race. Corona has impacted almost all aspects of human life and various prescient hypotheses have been put forward for the future of mankind.

This issue of SPECTRUM is dedicated to COVID-19. On the platter, we have a gamut of well curated articles highlighting different aspects of this dreaded pathogen and our dogged battle to tame it.

The first article is "Oscillations between aspiration and conspiration: The timeline of development of vaccines" by Dr. Nisha Patel. There are numbers of milestones in the history of vaccines. In this article, the history of development of vaccines from its inception to the modern vaccine techniques is elucidated.

Dr. Dhiraj Shah in his article, "Aarogya Setu: Digital contact tracing application developed by GOI" has given a lucid introduction to Aarogya setu application and provided all the technical details about the Aarogya Setu App.

Subtle differences between bacteria and viruses are highlighted by Mr. Vishal Unagar in the article "Difference between Bacteria and Virus." It includes basic differences in its structure, life, their types, mode of transmission, symptoms caused, and medicines.

Just a few months ago, the novel coronavirus (SARS-CoV-2) was alien to science. Six months down the lane, it seems as if hundreds of pathways appear to be open, however, there were no signposts on any of them. In spite of all the advances in science, we still have many unanswered questions about this virus and are grappling to figure out an answer. However, you will surely get the answer to a few questions in the articles "Why is Corona so menacingly successful?" and "Is it fair to blame bats for Covid-19?" by Dr. Pruthul Desai.

In the preceding article, Dr. Desai has discussed the anatomy of the virus, its modus operandi and the human body's response to the viral attack particularly in the case of SARS-CoV-2. The latter one gives a message that we should see COVID-19 as a grim reminder that human well-being requires responsible stewardship of nature - not just dominance.

It is said that when you choose hope, everything is possible. One of the potent weapons in our *repertoire* to fight COVID-19 is a vaccine. A global push is on to develop a vaccine to slow down the spread of COVID-19. In the article, "Approaches to the Elusive Vaccine for COVID-19," Dr. Desai explains how different research groups across the globe are using novel approaches in a bid to devise a vaccine in record breaking time. The method used by the virus to infect human cells and immune system's response is discussed. There is much more to contemplate in the changing world due to Covid-19! We hope you will enjoy this collection of articles. We look forward to hearing from you! Your valuable feedback can be sent on ptscsphy@gmail.com

**SPECTRUM**
Special Issue
April & August - 2020

**Published by**
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# Contents

# 1. Oscillations Between Aspiration and Consternation: The Timeline of Development of Vaccines

*-Dr. Nisha Patel*

**The corona pandemic is swapping out the entire world at an unprecedented pace. In the past, humanity had seen many pernicious disasters like floods, earthquakes, tsunami, volcanic eruptions and also epidemics due to infectious diseases but they have been more circumscribed and less deadly. Although all of these epidemics have their own stories of dread and obliteration, there had never been a catastrophe so abrupt and so universal. To combat the virus, entire mankind is yearning for the Covid-19 vaccine. In the bygone days, vaccines had helped to circumvent situation related to infectious disease. It is time to look back in the history for development of vaccines. In this article a detailed history of vaccine development since its inception to date has been presented.**

## 1.1 Introduction

A ubiquitous fact is that it will take only moment for the world to change and the way we perceive it. When we turn on the pages of history, they are replete with instances when major disease outbreaks have altered and upturned the ways in which civilizations and political structures functioned. The course of the history of the world have been transformed by major epidemics in the past. Each of these epidemics began as a biological phenomenon, but soon turned into economic, social or political ones. Loss of lives and livelihoods had followed distress and desolation experienced. Despite the scale of despoliation, the human race made peace with its surroundings and came out triumphant with message which resonates the same even in current situation – "There is hope!" "" In the current condition of pandemic, the entire world is placing hope on the scientists to develop a vaccine for COVID-19 with optimism. Development of Vaccine has entered in to its fourth century. It is therefore, time to look back and consider the history of the field, which is now long and illustrious.

## 1.2 The History of Vaccines

### 1.2.1 Origin of Vaccines

There are number of major milestones in the history of vaccines. According to the records, the origin of the vaccines goes as far back as 400 B.C., the time of Hippocrates who is also considered as the father of modern medicine. Hippocrates saved Athens from a plague epidemic and for that was revered by the Athenians. Hippocrates was the first to establish the

diagnostic methods of examination. According to Hippocrates, the physician had to examine a patient, observe symptoms carefully, make a diagnosis and then treat the patient. Therefore, Hippocrates established the basics of clinical medicine as it is practiced even today[2].

No records about the development in this field are available upto 1000 AD. Reports suggested that there was the ancient popular inoculation practice existed in China date back to about 1000 A.D. before the Jennerian vaccination. It was vriolation by means of human pox against smallpox. Son of a Chinese statesman was inoculated against smallpox by blowing powdered smallpox sores into his nostrils [8]. Another technique for inoculation was introduced in Turkey around 1672 which involved the removal of fluid from the pustules of an infected individual and subsequently rubbing it into a skin scratch of a healthy individual. After few decades, this technique also reached to Europe. The Great Britain got aware of variolation in 1721. These two words have Latin origin. In Latin word varus means "mark on the skin" and the word inoculare means "to graft."

### 1.2.2 The Time Period of Eighteenth Century

The eighteenth century witnessed few remarkable progresses as far as the field of vaccination is concerned, starting from dissemination of variolation from countries like China and Turkey to America and England. This was followed by triumph of Edward Janner in the late eighteenth century.

#### 1.2.2.1 Variolation that Started from Turkey and Reached the England

The aforementioned technique of immunization which was introduced in Turkey was latterly known as Variolation or Inoculation. Despite the heavy toll in form of death of thousands of people due to smallpox in western and central Europe, leading minds were not particularly inclined to embrace what seemed to be a highly unhygienic practice. Indeed, the venerated Royal Society of London was inundated with reports from various sources of the Chinese and Ottoman (Turkish) practices by 1700, but chose not to act upon this information. On the other hand, individual acts of bravery and prudence allowed a handful of quite remarkable personalities to convey the lifesaving procedures that would save the lives of thousands. Prominent among these early promoters was the Lady Mary Wortley Montagu, wife of the British ambassador to the Ottoman Empire and a talented figure, who excelled as a writer and poet. She had been personally inflicted with an episode of smallpox, having lost a brother to smallpox, she herself got inflicted by it and suffered severe scaring from the infection in 1715. As a demonstration of her belief in the practice, Lady Montagu in 1718 volunteered her four year old son, Edward, for inoculation by an experienced and elderly Greek woman. Apparently, she strong-

armed the embassy surgeon, Dr. Charles Maitland, to witness and document the procedure. The doctor reluctantly agreed and watched with considerable discomfort as the old woman introduced the dried scabs into the child's arm with a rusty and dull needle. Lady Montagu had elected not to inform her husband, Ambassador Edward Wortley-Montagu, of the risky procedure that had been conducted upon his only male heir until at least a week had passed and the fear of the death of child mellowed out. Upon returning home, Lady Montagu broadly advocated for variolation and, as a person of considerable prominence, gained the attention of her friend Caroline of Anspach, the Princess of Wales and future queen to George II. Amidst a particularly obnoxious London epidemic in 1721, Lady Montagu demanded that Maitland inoculate her daughter, Mary, who was four years old at the time. Back home in Britain, Maitland initially resisted this request, since variolation was regarded to be an "eastern" or "Asian" practice, which could sully his reputation. Ever subservient to Lady Montagu, Maitland eventually agreed to do so but only if the procedure was witnessed by prominent members of the Royal College of Physicians. At least one of the witnesses, Dr. James Keith, was so impressed that he had Dr. Maitland variolate his only remaining son (all others had died from smallpox). Within weeks, the news of variolation spread through the London medical community and among the gentry[7]. Lady Montague became a great proponent of the procedure and worked thoroughly on advocating this process for its ability to protect against the spread of smallpox.

#### 1.2.2.2 Shake-out in the World

In spite of few deaths recorded due to variolation, the word inoculation continued to spread owing to the data revealing that variolation was still the safeguard against the spread of smallpox. Moreover, Benjamin Franklin- one of the Founding Fathers of the United States, a leading writer, painter, political philosopher, politician, scientist, inventor, humourist, civic activist, statesman, diplomat, a major figure in the American Enlightenment and the history of physics for his discoveries and theories in the realm of electricity - who lost his son in 1736, wrote:"I long regretted that I had not given it to him by inoculation, which I mention for the sake of parents who omit that operation on the supposition that they should never forgive themselves if a child died under it; my example showing that the regret may be the same either way, and that therefore the safer should be chosen."

In the year 1759, Dr. William Heberden, at his own disbursement and with the backing of Benjamin Franklin, published a pamphlet entitled "Some Account of the Success of Inoculation for the Small-Pox in England and America: together with plain instructions by which any person may be enabled to perform the operation and conduct the patient through the distemper."

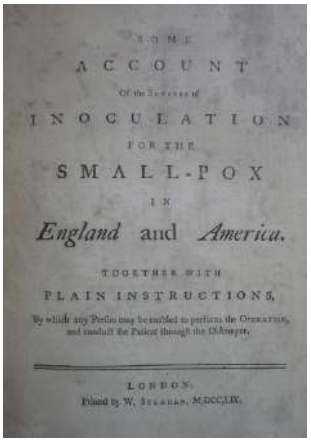


Figure 1: Front page of pamphlet published by Dr. William Heberden and Benjamin Franklin (Source:https://www.historyofvaccines.org/sites/default/files/inline-images/000092-224x300_0.png)

#### 1.2.2.3 Quantum Leap by Edward Jenner

Edward Jenner was a bird lover, whose first major contribution to science was observations on the Natural History of the Cuckoo - a letter he composed while practising as a physician in Berkeley. As a fourteen year old student, Jenner started his training in medicine in 1763 under the mentorship of Dr. Daniel Ludlow. Among his other studies, Jenner was instructed in the art of smallpox variolation. Seven years later, Jenner apprenticed in surgery and anatomy at St. George's Hospital in London and then returned to Gloucestershire.

Figure 2: Blossom's Horn: Jenner's Inspiration
(Source:
http://www.bbc.co.uk/staticarchive/28cadfd0d4020d203f0391679858d8545863c084)

The turning point in the story came at this stage or actual story of vaccine begins here with "Blossom." "Blossom", a mahogany brown old Gloucester cow, one of the oldest dairy breeds

in England and now is one of the rarest. Her portrait is in the Jenner Museum, Berkeley, Gloucestershire and her hide is on the wall of the library of St. George's Hospital, London. Blossom and her milkmaid, Sarah Nelmes were infected with cowpox. The key moment in this tale arises during a conversation between Jenner and milkmaid Sarah, who informed Janner that ladies of her profession were rarely, if ever, afflicted with smallpox. This revelation provided an epiphany moment for Jenner, who deduced that the milkmaids were prone to cowpox, a skin infection that caused minor lesions somewhat akin to smallpox. Jenner then connected the dots and he postulated that the transfer of material from a cow's or milkmaid's cowpox lesions might confer protection against smallpox. The idea was successfully tested on May 14, 1796 when Edward Jenner inoculated eight year old James Phipps, the son of Jenner's gardener. There was a mild illness between the 7th and 9th day. A vesicle formed and died away without giving the least trouble. A few days later, on 1st July, Jenner intentionally infected James Phipps with smallpox. The normal inflammatory signs of variolation (swelling and fever) were absent and the boy remained healthy without any signs of localized inflammation or infection which was the sign that the original inoculation had protected the child from smallpox. Jenner then performed similar inoculations and infection schema with a total of two dozen people and published his research in the year 1801 report to the Royal Society of London. The Royal Society remained cautious at first, likely based on their remembrance of the opposition targeted at Lady Montagu and Cotton Mather. However, soon they embraced Jenner's approach. This was the landmark achievement as the discovery of immunity in general and the smallpox vaccine in particular. Therefore, the medical community adopted the term vaccine which is based upon the Latin term "vacca" which means cow to honour Jenner (and Blossom)[8].

## 1.3 The Time Period of Nineteenth Century

The nineteenth century was a major landmark in the history of vaccines since it witnessed discoveries made by Louis Pasteur and Robert Koch- the scientist who discovered the germ responsible for tuberculosis.

### 1.3.1 With Louis Pasteur we Witnessed the Birth of Vaccines made in Laboratory

Pasteur was an outstanding scientist in advance of his contemporary colleagues in many respects. He moved from subject to subject from chicken cholera, anthrax, Swine erysipelas up to the rabies vaccine with an exceptional clairvoyance. On 30 October 1878, Pasteur received a strain of bacteria that caused chicken cholera from Henry Toussaint, a professor of the Veterinary School of Toulouse. He soon learned how to grow the chicken cholera microbe in chicken broth. In 1879, Pasteur observed by chance that 'old' cultures of chicken cholera

lost their virulence. Chickens inoculated with old cultures became protected against a virulent wild strain and survived. Interestingly, the few chickens surviving the disease still excreted virulent bacteria, so indicating the existence of healthy carriers, an important concept to explain the mysterious spread of germs during epidemics. In February 1880, Pasteur presented his results to the French Academy of Sciences. Pasteur also developed the anthrax vaccine in his laboratory, not long after performing his studies on chicken cholera. In 1881, Pasteur used his own anthrax vaccine, which contained attenuated live bacterial cultures in addition to carbolic acid, and demonstrated that all vaccinated animals survived while the control group died. Vaccination against rabies in 1885 was the last discovery by Louis Pasteur that immortalized him. Pasteur was 63 years old, handicapped by a permanent paralysis of his left arm as the sequel of a cerebral haemorrhage. In 1879, Pierre Galtier, a French veterinarian working in Lyon, demonstrated that rabies could be transmitted to rabbits by dog saliva. In 1880, Pasteur started studying rabies and succeeded in transmitting the disease to rabbits by intra-cerebral inoculation of brain extracts. The disease occurred after 1–2 weeks, instead of several weeks or months following bites. He found that virulence was exacerbated through iterative passages on rabbit brains shortening the incubation time to 6 days, with a rapidly fatal disease in dogs. This virulent strain was called 'fixed virus.' In 1884, Pasteur successfully attenuated the virulence of fixed virus by passages from dogs to monkeys, so increasing the incubation time for dogs, rabbits and Guinea pigs. Animals receiving the monkey virus were protected against the highly virulent fixed virus. Taking advantage of the long period of incubation of rabies, he then thought to use the attenuated vaccine as a therapy to stimulate the resistance of patients, i.e. the immune response. In 1885, with Emile Roux, Pasteur designed a new process to attenuate the fixed virus. Rabbit spinal cords infected with the fixed virus were desiccated and long-exposed to air in glass flasks. In these conditions, the virus lost its virulence in 15 days. By daily injections of rabbit spinal cord emulsions, progressively less and less attenuated, he could protect dogs against the highly virulent virus, including those inoculated by the intracerebral route. Then, fate knocked at Pasteur's door. On 6 July 1885, Joseph Meister, a 9 year old boy, came from Alsace to consult Dr Joseph Grancher at the hospital in Paris. He had been severely bitten by a rabid dog at the hands, legs and hips. The physician convinced a reluctant Pasteur to vaccinate the boy because he was inevitably going to die: it was the only way for him to stand a chance of survival! The treatment started on 7 July, 60 hours after the accident. The boy received 12 consecutive injections of extracts of rabbit spinal cords attenuated by a 14 days desiccation procedure. On 16 July 1885, he was inoculated with a spinal cord extract from a rabbit dead of infection induced by the fixed virus. Joseph Meister survived; Pasteur had performed the first therapeutic vaccination to cure a universally lethal disease. In October 1885, Jean Baptiste Jupille, a 15 year old shepherd from the Jura, in the east of France, was severely bitten by a rabid dog. He too was successfully protected by vaccination. In October

1886, more than 2490 patients were vaccinated at the Pasteur laboratory, in Paris. In the same time, statistics revealed mortality of about 40% among 320 unvaccinated patients bitten by rabid animals. After vaccination, mortality fell to 0.5%. This universal triumph of antirabies vaccination contributed to the creation of the Pasteur Institute in 1888. Louis Pasteur set three objectives for the new Institute: 'It must be a public dispensary to treat rabies, a research centre for infectious diseases and a teaching centre for studies on microbiology'. This exceptional scientist, observer, skilful experimenter, and imaginative philosopher died in 1895, after opening a new era in medicine and biology[3].

## 1.4 The Time Period of Late Nineteenth and Twentieth Century

During this period, vaccine production was taken over by factory-type laboratories, which formed the precursors of the biological products supply houses. Many types of vaccines were produced. Following is the brief time-line for development of vaccines.

**Cholera and Typhoid:** At the end of the nineteenth century, particularly in 1896 and 1897, the cholera and typhoid vaccines were developed and which was followed by the introduction of the plague vaccine. Further, the plague vaccine was led by the preparation of anti-plague horse serum at the Pasteur Institute by Alexandre Yersin.

**Tetanus:** In 1884, German scientist, Arthur Nicolaier was able to correlated tetanus with an anaerobic soil bacterium found in wounds. After few years, the Japanese investigator Shibasaburo Kitasato was able to isolate this bacterium. At the beginning of World War I in 1914, the tetanus toxoid was introduced following the development of an effective therapeutic serum against tetanus by Emil Von Behring and Shibasaburo Kitasato.

**Diphtheria:** Emile Roux from France had discovered diphtheria toxin in the year 1888. In France, during the year 1888, Emile Roux discovered the diphtheria toxin. This discovery through the scientific contributions of many others led to the development of passive serum therapies.

**Tuberculosis and BCG:** Tuberculosis which is commonly known as the"Great White Plague" is another disease that started spreading as an epidemic as soon as the industrialization began. This disease caused approximately 15% of deaths in the eighteenth and nineteenth centuries across the world.

In 1908, Albert Calmette and Camile Guerin (two bacteriologists from the Pasteur Institute) announced discovery of Mycobacterium bovis, which is a strain of tubercle bacilli that could be used to create a vaccine against tuberculosis. This strain had an attenuated virulence while maintaining its antigenicity and became widely known as BCG.

**DTP:** Global recommendations continue to entail for routine immunization of children against diphtheria, tetanus and pertussis with the combined DTP vaccine to sustain immunity in childhood and adolescence. Therefore, DTP has become one of the most widely used vaccines to achieve widespread immunity across age groups. DTP was licensed in 1949.

**Yellow Fever:** In 1937, live-attenuated vaccine for yellow fever was successfully developed by Max Theiler and other scientist from Rockefeller foundation

**Influenza:** Influenza has proved to be very difficult to trace back in history owing to its non-specific symptoms and features. In the year of 1918, the "Spanish flu" influenza pandemic had become responsible for 25–50 million deaths worldwide and more than one-half million in the U.S. The first person to isolate influenza virus was Richard E. Shope, a physician who conducted his research in the Department of Animal Pathology at The Rockefeller Institute in Princeton, in 1931. Isolated virus was a member of the orthomyxovirus family, from a mammalian host. He was also able to induce the syndrome of swine influenza in pigs by applying respiratory secretions intranasally.

The successful isolation and transmission of the influenza virus from humans was made possible by scientists Christopher Andrews, Wilson Smith and Patrick Laidlaw from the British National Institute for Medical Research in 1933. The contracts to develop vaccine against the H5N1 avian influenza virus were awarded to Aventis Pasteur and to Chiron in 2004. Unfortunately, one of the difficulties in dealing with influenza is the continuous mutability of the viral genome necessitating annual reassessments and reformulations of the vaccine. This has led to a suboptimal effectiveness of influenza vaccines, which are only successful against strains included in the vaccine formulation or strains of homogeneous subtype.

Several pandemics were caused by the influenza virus: during the years 1957–1958, The"Asia" influenza pandemic caused by H2N2 influenza virus and in the years 1968–1969, the "Hong Kong" influenza pandemic caused by an H3N2 influenza virus resulted in death of thousands of lives. Future studies should focus on producing vaccines protective against variant strains and creating surveillance systems to detect novel strains in time to formulate the proper vaccines.

**Poliomyelitis:** Poliomyelitis commonly known as Polio, is an intestinal infection spread between humans through the fecal–oral route. It is a disease of the developed nations striking younger individuals most frequently in warmer weather.

John Enders, Thomas Weller, and Fredrick Robbins had proved the ability of poliomyelitis viruses to grow in tissue cultures. For their discovery they received Nobel Prize in Physiology or Medicine 1954.

**Measles, Mumps, and Rubella:** After the successful development of polio vaccine, soon the

attention was shifted to vaccines for other three common viral diseases of childhood: measles, mumps and rubella. John Enders who known as the "Father of Modern Vaccines" had a particular interest in revealing the virus responsible for measles. John Enders and Thomas Peebles isolated the measles virus in cell culture in the year 1954. In the same year, trials of formalin-inactivated mumps vaccine in humans began by Joseph Stokes and his colleagues. In 1964, a rubella epidemic swept the U.S. resulting in 12.5 million cases of rubella infection, with an estimated 20,000 newborns having congenital rubella syndrome (CRS), along with foetal and neonatal deaths in the thousands. Paul Parkman and Harry Meyer Jr. developed the first live-attenuated rubella vaccine at the NIH Division of Biological Standards in 1966.

**Varicella Zoster - Herpes Virus:** Varicella (chickenpox) is caused by the varicella zoster virus (VZV). Michiaki Takahashi, Professor of Virology at the Research Institute for Microbial Diseases at Osaka University, successfully produced the Oka vaccine strain of live, attenuated varicella vaccine in the 1970s.

**Rotavirus:** Rotavirus is the leading cause of severe acute gastroenteritis among infants and children worldwide. Dr. Ruth Bishop and colleagues were the first to describe rotavirus in humans in 1973. The development of live, attenuated, oral, safe, and effective rotavirus vaccines was then attempted starting in the mid-1970s. Dr. Albert Kapikian and colleagues, at the NIH (National Institute of Health, U.S.) developed the RRV strain that was afterwards used to develop the RRV-TV or the RotaShield. Live oral, and tetravalent vaccine for rota virus licensed in 1998 to be used in infants at 2, 4, and 6 months of age.

**Hepatitis:** The etiological agent of clinical hepatitis, identified by its distinguishing yellow jaundice, was found to be infectious in the early 1900s. The different hepatitis strains, A and B, were first differentiated in 1942. In 1986, a killed hepatitis A vaccine was prepared by Provost et al. which was proved safe and highly effective in extensive clinical trials. In 1968, a killed hepatitis B vaccine was prepared and clinical trials for it began in 1975 proving the safety and efficacy of the vaccine. Later in 1981, Merck and Pasteur Institute independently licensed the plasma-derived vaccine. In 2001, at the beginning of the new millennium, A combined hepatitis A inactivated and hepatitis B (recombinant) vaccine (Twinrix by SmithKline Beecham) was licensed. In the year 2002, a vaccine that combined diphtheria, tetanus, acellular pertussis, inactivated polio, and hepatitis B antigens (Pediarix by GlaxoSmithKline) was licensed.

**AIDS:** In the year 1996, the International AIDS Vaccine Initiative (IAVI) was launched, calling for the speedy development of a human immunodeficiency virus (HIV) vaccine for use worldwide. The initiative created the Scientific Blueprint for AIDS Vaccine Development.

**Cervical Cancer:** In 2006, the first vaccine developed to prevent cervical cancer had been licensed.

## 1.5 Challenges Due to Newly Emerging Diseases

During past two decades of the twenty-first century, improvements in health sector has provided tremendous help to vector control diseases. Nevertheless, there still remain challenges to deal with the newly emerging diseases like, ebola and marburg hemorrhagic fevers, human monkeypox, bovine spongiform encephalopathy, severe acute respiratory syndrome (SARS), west nile virus, avian influenza, middle east respiratory syndrome (MERS-CoV), Covid-19 and many more other viral, bacterial and protozoal disease.

With newly emerging diseases, the need of augmentation of vaccine development has been multiplied. In fact, the importance of inducing protective immunity through vaccination turns out to be the most powerful tool and effective approach to prevent the spread of emerging viruses among populaces, specifically, among people who are immunologically naive and prone hosts.

## 1.6 Nobel Prizes

### 1.6.1 Details about Nobel Prizes for Discoveries in the Field of Immunology.

**1901:** The inaugural Nobel Prize in Physiology or Medicine was awarded to the German physiologist Emil Adolf von Behring in 1901 for the concept developed by him about passive transfer in addition to serum therapy. The discovery proved that serum could be acquired from immune animal and transferred to others as a protection which later on helped in the development of vaccines for diphtheria and tetanus.

**1908:** After studies of starfish larvae, in 1882 Ilya Mechnikov pointed to phagocytosis as one of the immune system's ways of operating. By this he meant that certain cells in the blood, white blood cells, work by encapsulating and destroying harmful bacteria and other micro-organisms. Paul Ehrlich contributed to the field of immunology by his study of the transfer of blood serum with antibodies to treat and counteract diphtheria. For these jointly they received Nobel Prize for the year 1908.

**1919:** Jules Bardet received Nobel Prize in 1919. He performed studies about cholera in 1896, which showed that as our immune system protects us from attacks by micro-organisms and poisonous substances. The blood includes factors or bodies that destroy bacteria. This depends on the collaboration of two types of factors in the blood: antibodies formed by immunization against specific bacteria and complement proteins that also exist in blood that is not immunized. Antibodies and complement proteins are bound to one another, which can be used to detect certain diseases, including syphilis.

**1945:** The Nobel Prize in Physiology or Medicine 1945 was awarded jointly to Sir Alexander Fleming, Ernst Boris Chain and Sir Howard Walter Florey for the discovery of penicillin and its curative effect in various infectious diseases.

**1951:** In 1951, the immunologists trio – Bruce Beutler, Jules Hoffmann and Ralph Steinman won Nobel Prize for developing vaccines and therapies against infections, cancer and inflammatory diseases.

**1961:** Our immune system protects us against attacks by micro-organisms and rejects foreign tissue. Part of our immunity has a hereditary basis, but part of it is acquired and is not present in the foetus. In 1949 Macfarlane Burnet theorized that the ability to distinguish between one's own and foreign tissue is not hereditary but is acquired during the foetus stage. For that he received Nobel Prize in 1961.

**1996:** Peter Doherty and Rolf Zinkernagel received Nobel Prize in 1996. They proved how the immune system recognizes virus-ridden cells. A kind of white blood cell, T-cells, kills the virus-ridden cells, but only if they recognize both the foreign substances, viruses and certain substances from the body's own cells. The discovery has provided an important basis for vaccines and medicines for infectious diseases, but also for inflammatory diseases and cancer.

**2008:** The Nobel Prize 2008 was awarded to Francoise Barre-sinoussi and Luc Montagnier for their discovery of human immune deficiency virus.

**2011:** The Nobel Prize in Physiology or Medicine 2011 was divided one half jointly to Bruce A. Beutler and Jules A. Hoffmann and another half to Ralf M. Steinman "for their discoveries concerning the activation of innate immunity" and "for his discovery of the dendritic cell and its role in adaptive immunity."

### 1.6.2 New Horizon in the Field of Immunology

Every year cancer kills millions of people and it has presented greatest health challenges to humans. James P. Allison and Tasuku Honjo have separately uncovered mechanisms that block key proteins and allow the immune system to attack cancer, creating an entirely new way to fight the disease. They had been awarded the 2018 Nobel Prize 2018 in the Physiology or Medicine. James P. Allison studied a known protein that functions as a brake on the immune system. His breakthrough idea was about the potential of releasing the brake and thereby unleashing our immune cells to attack tumours. Further, he paved the way for novel approach for treating cancer patients. In parallel, Tasuku Honjo discovered a protein on immune cells and after careful exploration of its function, ultimately revealed that it also operates as a brake, but with a different mechanism of action. Therapies based on his discovery proved to be strikingly

effective in the fight against cancer. These two discoveries can be considered as landmark in fight against cancer.

## 1.7 Conclusion

Vaccination has been of inordinate importance throughout centuries. It started with inoculation techniques in 1000 A.D. in china, Turkey and many other Asian countries. As the pages of new century and scientists added to the history, these vaccination techniques were improved step by step giving rise to more advanced vaccination techniques by people like Edward Jenner and later on, Louis Pasteur and others. Howbeit, there is still plenty of room for furtherance with the presence of ongoing pandemics and the spread of newly emerging viruses. An important goal is to strengthen our base of science - vaccine development, disease prevention. (scientist were over confidence) It was commonly believed during middle of the 20th century that epidemics and pandemics were effectively decimated, new and re-emerging infectious diseases are appearing in the past two decades in the various parts of the world and further entire mankind is completed threatened with the fact that this type of incidences will increase in the near future, due to changes in human demographics and behaviour, immigration, and speed of travel in foreign countries along with other facts. The importance of vaccine safety continues to grow throughout the 21st century. Scientists also perfected new ways of administering immunizations including edible vaccines and needle-less injections. Needless to say that however formulated or delivered, vaccines will remain the most effective tool we tend to possess for preventing disease and improving public health in the future.

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## 2. The Difference Between Bacteria and Virus
*-Mr. Vishal Unagar*

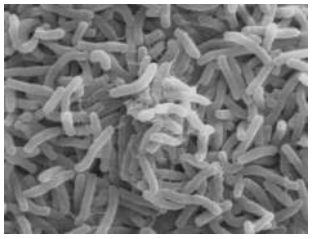

Figure 1: Vibrio cholerae bacteria
(Source: https://images.app.goo.gl/xADYFWwGRstf6sXEA)

Bacteria are microscopic, single-celled organisms that thrive in diverse environments. These organisms can live in soil, the ocean and inside the human body[1]. An image of a Vibrio cholerae bacteria is shown in the fig.(1).

Figure 2: Corona virus
(Source: https://images.app.goo.gl/ff4VGoLvmv4MRqsT9)

A virus is a submicroscopic infectious agent that replicates only inside the living cells of an organism. They are 10 to 100 times smaller than the smallest bacteria[2]. An image of the corona virus is shown in the fig.(2).

### 2.1 The Difference in their Structure

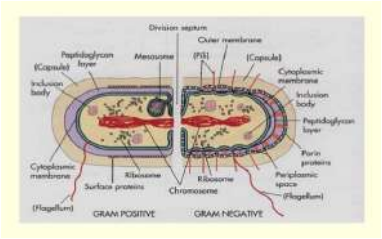


Figure 3: Structure of bacteria
(Source: https://images.app.goo.gl/eHAwLvF3vnrtLrRU9)

Bacteria are simple, single celled organisms, called prokaryotes, which means their DNA is contained within a certain area of the cell called the nucleoid, but not enclosed. Bacteria are one of the oldest living things on earth, having been in existence for at least 3.5 billion years[3] as shown in the above figure.

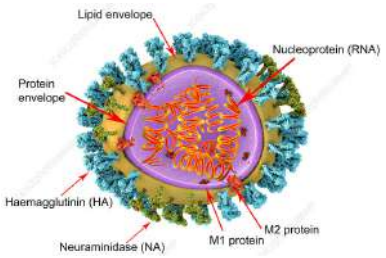


Figure 4: Structure of influenza virus
(Source: https://images.app.goo.gl/VJDzCqTPLYxTk7JA7)

Viruses consist of a piece of genetic material, such as DNA or RNA surrounded by a protein shell called a capsid. Sometimes this shell is surrounded by an envelope of fat and protein molecules, and out of this envelope may project glycoprotein protrusions, called Peplomers[4] as shown in the above figure.

## 2.2 Are They Living or Non-living?

Bacteria are living organisms. They have a cell wall and all the components necessary to survive and reproduce, although some may derive energy from other sources[3]. Viruses are not considered to be "living" because they require a host cell to survive long-term for energy and to reproduce, so they like a parasite[4].

## 2.3 The Difference in their Types

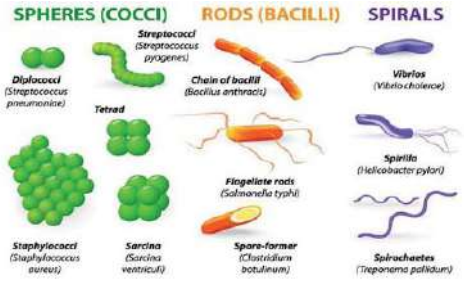


Figure 5: Types of Bacteria
(Source: https://images.app.goo.gl/raNKw2Y4MHFMCUSy9)

The three basic bacterial shapes are: coccus (spherical), bacillus (rod-shaped), and spiral (twisted), however pleomorphic bacteria can assume several shapes[5] as shown in the above figure.

- **Cocci**: They are round cells, sometimes slightly flattened when they are adjacent to one another.
- **Bacilli**: They are rod-shaped bacteria.
- **Spirilla**: They are curved bacteria which can range from a gently curved shape to a corkscrew-like spiral. Many spirilla are rigid and capable of movement. A special group of spirilla known as spirochetes are slender, long and flexible.

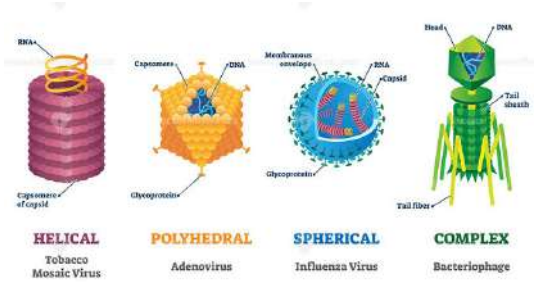


Figure 6: Types of virus
(Source: https://images.app.goo.gl/EZ2uT7Kd1WSvakqt6)

Viruses are classified into four groups based on shape: Helical viruses, Polyhedral viruses, Enveloped viruses and Complex viruses as shown in the fig.(6)[6].

- **Helical**: They are consist of nucleic acid surrounded by a hollow protein cylinder or capsid and possessing a helical structure.
- **Polyhedral**: They are consist of nucleic acid surrounded by a polyhedral shell or capsid.
- **Enveloped**: viruses consist of nucleic acid surrounded by either a helical or polyhedral core and covered by an envelope.
- **complex (Head and Tail)**: They have a irregular shapes, or have complex structures.

## 2.4 The Difference in Symptoms

The major difference between bacteria and virus are in symptoms. Symptoms usually reflect the area of the body infected and the infecting organism. For example, a bacterial infection of

the skin may cause a discharge, swelling, pain and redness in a certain area, whereas a viral infection, such as hepatitis-C may cause abdominal pain, joint pain, nausea or vomiting, and yellowing of the skin or eyes.

### 2.5 Transmission of Bacteria and Virus

Bacteria and viruses can be transmit in similar ways, such as[7]:

- Being exposed to droplets expelled when a person coughs or sneezes in your vicinity.
- Close contact with an infectious person.
- Contact with contaminated food or water.
- Contact with infected surfaces and then touching your nose, mouth or eyes.
- Contact with infected body fluids through urine, feces or physical relationship.
- Contact with infected animals or insects such as fleas, ticks or mosquitoes.
- Transmission from mother to child during birth.

### 2.6 The Difference in Medicine

Antibiotics may be used to treat some bacterial infections, but they do not work against viruses. Some severe bacterial infections may be prevented by vaccination. Antivirals have been engineered that can treat some viral infections, such as H1N1 or HIV. They are not effective against all bacteria[8].

## References


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**[8] Available online: https://www.healthline.com/health/bacterial-vs-viral-infections (accessed on 24 May, 2020).**

## 3. Aarogya Setu: Digital Contact Tracing Application Developed by GOI

*-Dr. Dhiraj Shah*

Contact tracing is an important factor in infectious disease control as it is the process of identifying persons ("contacts") who may have been in contact with an infected individual. Contact tracing is more effective at earlier stages of an outbreak than at later stages where most of the community is self-isolating anyway. COVID-19 applications are mobile software applications designed to aid contact tracing in response to the COVID-19 pandemic.

COVID-19 applications make use of Bluetooth signals to log a user's proximity to other smart phones. On 10 April 2020, Google and Apple jointly announced that they would integrate functionality to support such Bluetooth-based apps directly into their Android and iOS operating systems.

Digital contact tracing, especially if widely deployed, may be more effective than traditional methods of contact tracing. A model study was carried out by Oxford University of a corona virus outbreak in a city of one million people; the outbreak is halted if 80% of all smart phone users use a tracking system [1]. In the model, the elderly are still expected to self-isolate, but individuals who are neither symptomatic nor elderly are exempt from isolation unless they receive an alert that they are at risk of carrying the disease.

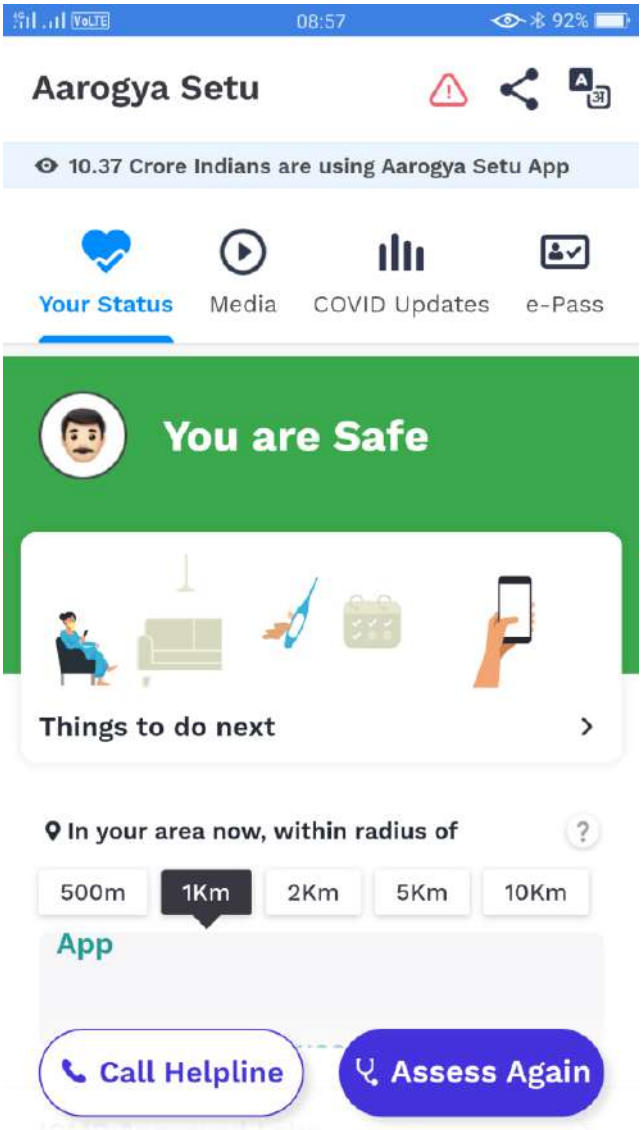
Aarogya Setu (literally, bridge for freeness from disease) is Indian COVID-19 tracking mobile application developed by the National Informatics Centre and that comes under the government Ministry of Electronics and Information Technology.

The stated purpose of this app is to spread awareness of COVID-19 and to connect essential COVID-19 - related health services to the people of India [3]. This app augments the initiatives of the Department of Health to contain COVID-19 and shares best practices and advisories. It is a tracking app which uses the smart phone's GPS and Bluetooth features to track the corona virus infection. The app is available for Android and iOS mobile operating systems. With Bluetooth, it tries to determine the risk if one has been near (within six feet of) a COVID-19 - infected person, by scanning through a database of known cases across India. Using location information, it determines whether the location one is in belongs to one of the infected areas based on the data available This app is an updated version of an earlier app called Corona Kavach (now discontinued) which was released earlier by the Government of India [4].

## 3.1 Technical details of Aarogya Setu

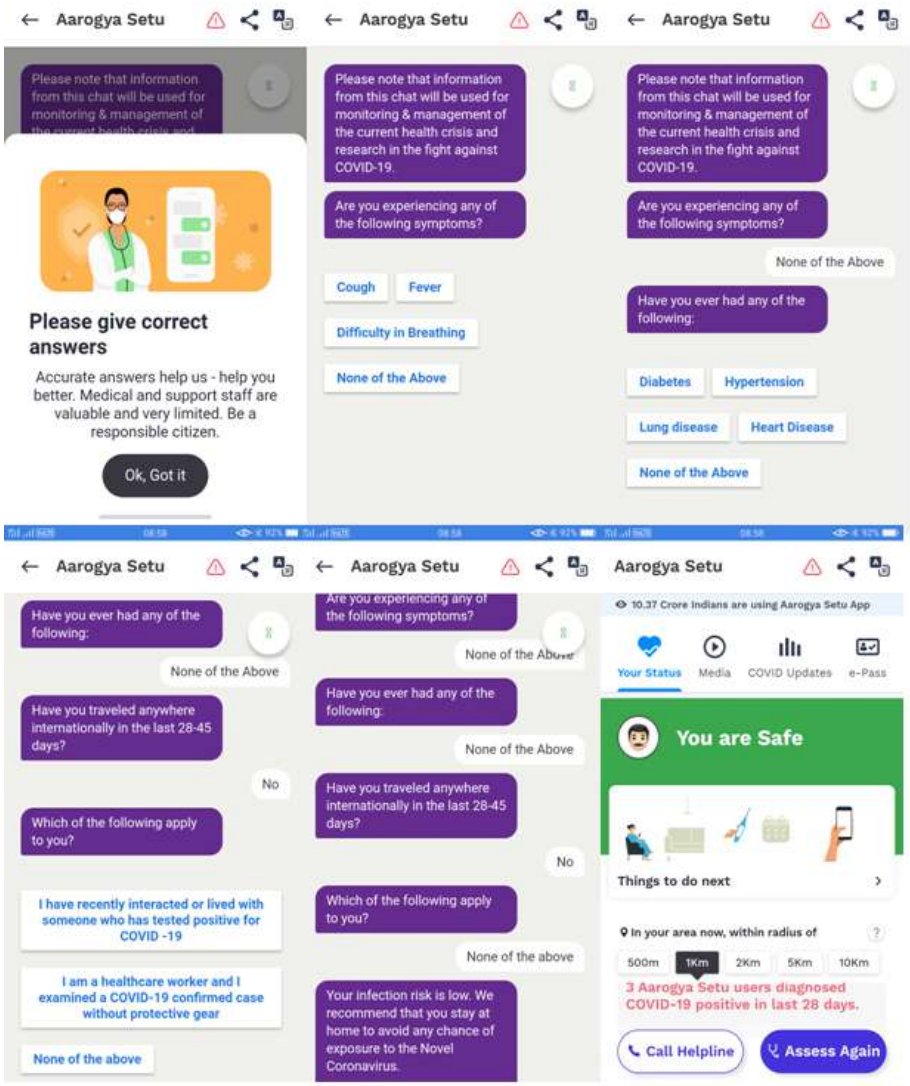
Aarogya Setu has five sections:

1. Your Status (tells the risk of getting COVID-19 for the user) The image given below shows the status of risk of getting Covid-19 for the individual person. Tells how many COVID-19 positive cases are likely in a radius of 500m, 1km, 2km, 5km and 10km from the user.



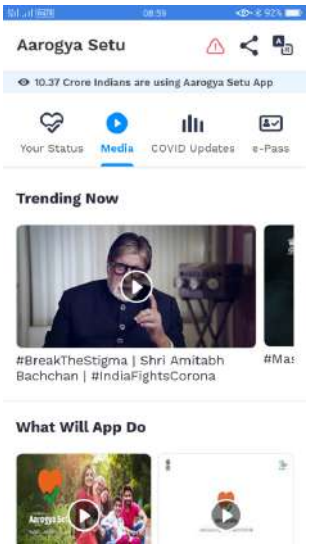
2. Self Assess (lets the user know the risk of being infected)

   In the self assess test, as shown in the images below, it will ask basic question related to your health like, weather you have cough, fever, difficulty in breathing which are the basic symptoms of people affected from COVID-19, then weather you have any of the following like diabetes, hypertension or any heart diseases. The reason behind this question is that people having these symptoms are more at risk rather than normal persons.



3. Media

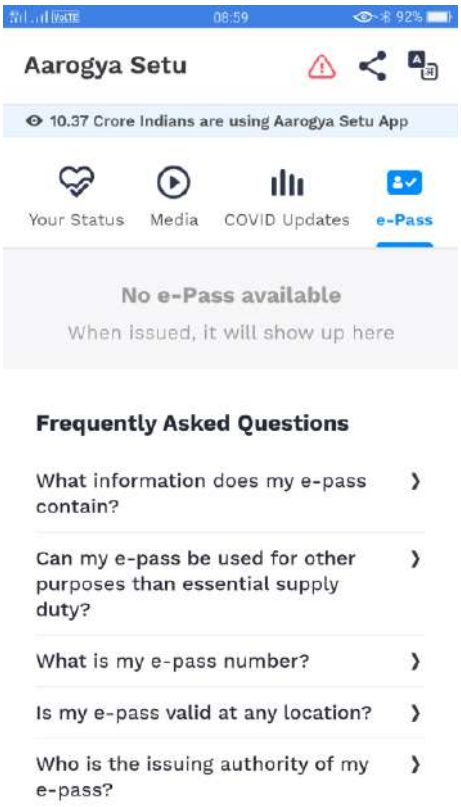
   In this application, awareness videos related to COVID-19 from renowned persons is given.




4. COVID-19 Update

   In this application, awareness videos related to COVID-19 from renowned persons is given.

5. E-pass (yet not issued through Application).




The app is built on a platform that can provide an Application Programming Interface (API) so that other computer programs, mobile applications and web services can make use of the features and data available in Aarogya setu.

## 3.2 Response

arogya Setu crossed five million downloads within three days of its launch, making it one of the most popular government apps in India [5]. It became the world's fastest-growing mobile app beating Pokemon Go, with more than 50 million installs, 13 days after launching in India on 2 April 2020[3]. Till 16th May 2020, there were more than 103 million installs in India. In an order on 29 April 2020, the central government made it mandatory for all employees to download the app and use it - "Before starting for office, they must review their status on Aarogya Setu and commute only when the app shows safe or low risk" [6]. The Union Home ministry also said that the application is mandatory for all living in the COVID-19 contaminant zone.

# References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# 4. Why is Corona So Menacingly Successful?

*-Dr. Pruthul Desai*

**The new coronavirus SARS-CoV-2 continues to challenge the wisdom of healthcare specialists and biologists. As Covid-19 is painfully demonstrating, our interconnected global economy helps spread new infectious diseases. It is an *aide-memoire* of the season that infectious diseases haven't finished yet. Rarely has the threat of disease occupied so much of our thinking. Research to develop a vaccine for SARS-CoV-2 is underway at an unprecedented scale. In this article the anatomy of the virus and its *modus operandi* is discussed. In the end, human body's response to the viral attack particularly in the case of SARS-CoV-2 is also presented.**

## 4.1 Introduction

With much of the globe in the throes of the COVID-19 pandemic, most of the human population is facing one of the greatest challenges ever. What started as an epidemic mainly limited to China in December 2019, has now become a truly global pandemic. On March 11 the The World Health Organization (WHO) officially declared the Covid-19 outbreak a pandemic. The virus is indiscriminate and ruthless in its efficiency. It does not spare rich nor the poor, neither the religious nor the atheist, inflicting greater damage to the older people. Although the mortality rate of COVID-19 is less than 3%, its rapid spread across the world has brought economic activities around the world to a grinding halt. The poor countries have to bear the biggest brunt leaving millions of people across globe without work and money. Even after more than three months the crisis continues to grip the world in its stranglehold with no signs of abating.

The newly identified coronavirus, SARS-CoV-2, was first reported in Wuhan, China on December 31, 2019. In one month, reported cases outnumber those from the Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) epidemic which occurred in 2003 and was dubbed as "the first pandemic of the 21st century."

Why did the SARS-CoV-2 more infectious? Why has it gone berserk and bizarre? This question is still shrouded in mystery, and scientists are scrambling to find an answer to it. Today coronavirus is the subject of study at an unprecedented scale, though a vaccine is an *ignus fatuus*. We take a look at some of the latest evidence that helps answer this question.

## 4.2 What is Novel Corona Virus 2019?

The novel coronavirus was named after the family of viruses - coronavirus family. Coronaviruses have been causing problems for humanity for a long time. Four members of this family of coronaviruses (OC43, HKU1, NL63, and 229E) have been irritating human beings with a common cold, which is routinely overcome by the body's immune system and therefore do not pose any threat. Other two others (SARS-CoV-2002, MERS-2013) caused far more severe diseases but were either restricted mainly to their country of origin or didn't become a pandemic.

Viruses have ancient origin dating back to over a billion year. In fact, viruses may be responsible for significant episodes of evolutionary change, especially in more complex types of organisms. One such compelling change took place for the worse during last two decades. The SARS (Severe Acute Respiratory Syndrome) outbreak in China in 2003 was found to be caused by a particular strain of coronavirus - SARS-CoV-2002. What baffled the scientists was, "how did the strain of the virus jump over from animals to humans?" The answer probably lies in the fact that wildlife acts as the pre-emergence niches of many pathogens. Increased environmental changes and greater human contact with wildlife is believed to be responsible for this "spillover" from animals to humans.

"Everybody in the field was shocked," says microbiologist Susan Weiss of the University of Pennsylvania. "People started really caring about this group of viruses." Findings revealed that the coronavirus crossed over from animals - most likely civet bats- to humans and resulted in a disease named zoonosis. The propensity of this virus to cross over was revealed when in 2012, it unusually crossed over from camel to humans to cause MERS (Middle East Respiratory Syndrome) epidemic in the middle east. The purported virus has taken lives of 858 people to date, primarily in Saudi Arabia, representing approximately 34 percent of those infected.

The aftermath of these outbreaks had been moderate compared to the havoc unleashed by SARS-CoV-2 that is causing the Covid-19 pandemic. In the span of few months it has infected nearly 2.75 million people across the globe and claimed more than 200,000 lives. The numbers are changing at breathtaking speed. These staggeringly large numbers are an extraordinary achievement for a spiky ball of genetic material coated in fatty chemicals called lipids, and which measures 80 billionths of a metre in diameter. Humanity has been brought to its knees by a very humble assailant.

## 4.3 How Did it Start?

SARS, MERS and the new coronavirus almost certainly all originated in bats. The most recent analysis of the SARS-CoV-2 genome found that 96 percent of its RNA matches with that of the coronavirus previously identified in a specific bat species in China. Its origin remains the subject of not only scientific debate, but a politically charged dispute in the international community. "These viruses have been floating around in bats for a long time" without sickening the animals, says microbiologist Stanley Perlman of the University of Iowa.

Bats were not part of the Wuhan market where animals were sold for human consumption. This raises a question, "how did the virus spread from bats to humans?" It led many to believe that there must be an 'intermediary species' such as pangolins, in the chain connecting bats to humans. These purported species must have provided fertile dens for the virus to increase its diversity by facilitating more or different mutations.

"This virus probably jumped from a bat into another animal, and that other animal was probably near a human, maybe in a market," says virologist Professor Edward Holmes of Sydney University. "And so if that wildlife animal has a virus it's picked up from a bat and we're interacting with it, there's a good chance that the virus will then spread to the person handling the animal. Then that person will go home and spread it to someone else and we have an outbreak."

## 4.4 What Exactly is Covid-19?

Viruses as we all know don't have their own biochemistry because they borrow ours. Viruses are weird microscopic particles consisting of a tiny piece of genetic information (about 10,000 times less than that contained in the human genome) and a protein or lipid (fatty molecule) shell. Whether these particles are living things is the subject of much debate, as they don't meet many of the usual criteria for life.

Coronaviruses are enveloped, single-stranded RNA viruses, which means that their genome consists of a strand of RNA (rather than DNA) and that each viral particle is wrapped in a protein "envelope." But RNA replication typically lacks the error-correction mechanism, so RNA viruses make mistakes during replication. Coronaviruses have the longest genomes of any RNA virus - consisting of 30,000 letters, or bases - and the more material a pathogen copies, the more opportunity there is for mistakes. While this may sound to be in our favour, the downside is that these viruses mutate very rapidly. Some of these mutations may confer new properties, such as the ability to infect new cell types - or even new species [1].

A coronavirus particle consists of four structural proteins: the nucleocapsid, envelope, membrane and spike. The nucleocapsid forms the genetic core, encapsulated in a ball formed by the

envelope and membrane proteins. The spike protein forms club-shaped protrusions that stick out all over the ball, resembling a crown or the sun's corona - hence the name. The fig.(1). shown a possible structure of the SARS-CoV-2 virus. These protrusions bind to receptors on host cells, determining the cell types - and thus the range of species - that the virus can infect [1].

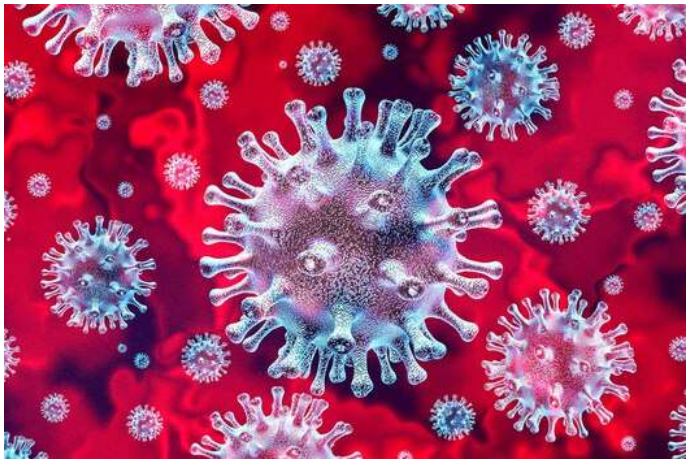

Figure 1: Spike protein conformation of SARS-CoV-2
(Source: https://www.webmd.com/lung/coronavirus)

The unique feature of the SARS-CoV-2 is that its spike protein contains a site that recognizes and becomes activated by a host-cell enzyme called furin which is present in various human organs, such as the liver, the lungs, and the small intestines. The fact that this enzyme resides in all of these human tissues means that the virus can potentially attack several organs at once. "[The furin activation site] sets the virus up very differently to SARS-CoV, in terms of its entry into cells, and possibly affects virus stability and hence transmission" says Prof. Gary Whittaker, a virologist at Cornell University, in Ithaca, New York.

Spike proteins and furin activation sites are not the whole story, however: The human cell also contains elements that make it vulnerable to the novel coronavirus. The spike protein needs to bind to a receptor on human cells called ACE2 (Cell receptors play a key role in passing chemicals into cells and in triggering signals between cells). Research has shown that ACE2 allows SARS-CoV-2 to infect human cells. "If we think of the human body as a house and SARS-CoV-2 as a robber, then ACE2 would be the doorknob of the house's door. Once the S-protein grabs it, the virus can enter the house," says Liang Tao, a researcher at Westlake University.

While coronaviruses that cause common cold infect the upper respiratory tract (the nose and

throat), those like SARS-CoV that cause severe illness, infect the lower respiratory tract (the lungs) leading to acute respiratory problems. The SARS virus binds to a receptor called ACE2, and MERS binds to one called DPP4 - both are found in lung cells, among other places. Since the distribution of receptors in human cells is different for ACE2 and DPP4, the impact of these viruses on human body is altogether different. MERS is found to be deadlier than SARS but is less infectious.

"DPP4 is expressed [highly] in the lower bronchi [airways leading into the lungs], so you have to have a large number of viruses coming in, because our airways are very good at filtering out pathogens," says virologist Christine Tait-Burkard of the University of Edinburgh. "You need prolonged, intense exposure [to reach the lungs], which is why we see people who work closely with camels getting sick." Analysis of SARS-CoV-2 strongly suggests the new virus, like SARS, uses ACE2 to gain entry to cells. This observation would fit with the fact that it appears, so far, to be less deadly than MERS (the current estimated mortality rate for the new coronavirus appears to be about 2 percent.)

## 4.5 How Does it Spread?

According to the WHO, the novel coronavirus is primarily spread by droplets from someone who is coughing, sneezing or even talking within a few feet away. But much remains unknown about what amount of virus one needs to be exposed to in order to become sick, known as the minimal infectious dose. If someone inhales virus-ridden particles than he catches the infection. The inhaled particles come into contact with the cells lining the throat and larynx. These cells have large numbers of ACE2 receptors on their surfaces.

Once inside, that RNA penetrates itself into the cell's own replication machinery and makes multiple copies of the virus. These burst out of the cell, and the infection spreads. To survive and thrive, a virus must operate like a spy in enemy territory, skilled at passing its genetic material from cell to cell without alerting the host's immune response. If this process causes tissue damage that leads to organ failure, the virus risks perishing along with its host. That's why the viruses with very high mortality rate are not successful in spreading. In contrast, those viruses whose mortality rate is low, such as SARS-CoV-2, get longer time to multiply in the infected patient's body and therefore have greater chance of proliferating.

"A Covid-19 infection is generally mild, and that really is the secret of the virus's success," says Professor Jonathan Ball of Nottingham University. "Many people don't even notice they have got an infection and so go around their work, homes and supermarkets infecting others."

By contrast, SARS-CoV – which is also caused by a coronavirus – makes patients much sicker

and kills about one in 10 of those infected. In most cases, these patients are hospitalised and that stops them infecting others – by cutting the transmission chain. Milder Covid-19 avoids that issue.

## 4.6 Body's Response to the Virus Attack

Our body has its own built-in mechanism to tackle threat posed by viruses. When a foreign microbe intrudes, the immune system usually makes proteins called antibodies that help to fight off the invader. The exact mechanism is described below.

When a virus attacks the first cell in the body, that cell has two jobs to do before it dies. The infected cell needs to issue a call for reinforcements, sending out a cascade of chemical signals that will activate an army of immune cells to come battle the invading virus. And it needs to issue a warning to other cells around it to fortify themselves, something it does by releasing proteins called interferons. When interferons land on neighbouring cells, they trigger those cells to enter defensive mode. The cells slow down their metabolism, stop the transport of proteins and other molecules around their interiors, and shutting down transcription, the process by which genetic instructions become proteins and other molecules and then dies [2]. (Transcription is the process that viruses hijack to make more of themselves). Unfortunately, most of these processes are also bad for the host.

In a study, Benjamin tenOever, a Professor of Biology at the Mount Sinai Icahn School of Medicine and his colleagues found that SARS-CoV-2 appears to block this interferon signal, meaning it messes with the cell's second job. So the first job - the call for immune system reinforcement - works just fine, but the cells in the lungs don't enter defensive mode and so remain vulnerable to viral infection.

"It just keeps replicating in your lungs, and replicating in your lungs and all the while you keep calling in for more reinforcements," said tenOever. As the virus keeps replicating, the immune army that arrives to battle it starts doing its job: attacking infected cells, digesting debris and chemicals spewed out by dying cells, even killing nearby cells in an attempt to staunch the damage. Unfortunately, if the virus continues to penetrate lung cells, this army may do more damage than good. The lung tissue becomes hopelessly inflamed; the blood vessels begin to leak fluids into the lung; and the patient begins to drown on dry land. This is known as a cytokine storm [8]. (In Greek, "cyto" means cell and "kino" means movement.) This seems to be the reason that some people become severely ill a couple of weeks after their initial infections and the unfortunate one die.

"A lot of the disease that's caused is actually the immune reaction - inflammation - and destruc-

tive things induced by viruses," Weiss says. "That will also determine how virulent a virus is: How much of a destructive immune response does it induce, as opposed to just a protective one?" Most of the people who have died from the new coronavirus to date "had comorbidities, like autoimmune diseases, or secondary infections, which can become much more prevalent once our innate immune systems are busy fighting a virus," Tait-Burkard says. "That's why the important thing is to treat people for comorbidities and give them antibiotics to stop bacterial infections taking hold."

Stealth is critical for these pathogens. A successful spy must be a master of disguise, and so it is with viruses: if they want to evade recognition by immune cells, they must change their protein coat frequently. This is achieved via tiny alterations in their genetic material called mutations [3]. This is especially true for the SARS-CoV-2 virus which has adopted itself to bypass body's defence mechanism.

Some researchers think bats harbor coronaviruses because they do not mount the intense immune response that humans do [1]. "A lot of the signalling molecules that alert our immune system are suppressed in bats, so they don't get sick," Tait-Burkard says. Rather than reacting, bats maintain a constant low-level response, which may contribute to the viruses' evolution. "[Bats] have a constant expression of interferons, which selects for viruses that are good at evading that response," Tait-Burkard says. "So bats are very good selection vessels for viruses that are very good at hiding."

## 4.7 How Long does the Immune Response Work?

The most important question that arises is will the immunity developed by the recovered patient last for his life time? How long will the antibodies developed against the virus work? Because the virus is so new, the answer isn't fully understood. But so far, by studying the patients who have recovered researchers have found large number of antibodies against the virus in them. These antibodies are generates by the immune system, and they coat an invading virus at specific points, blocking its ability to break into cells. That means that the human body will probably retain a memory of the virus for at least a few years and should be protected from reinfection, at least in the short-term.

"It is clear that immune responses are being mounted against Covid-19 in infected people," says virologist Mike Skinner of Imperial College London. "And the antibodies created by that response will provide protection against future infections – but we should note that it is unlikely this protection will be for life."

Instead, most virologists believe that immunity against Covid-19 will last only a year or two.

"That is in line with other coronaviruses that infect humans," says Skinner. "That means that even if most people do eventually become exposed to the virus, it is still likely to become endemic – which means we would see seasonal peaks of infection of this disease. We will have reached a steady state with regard to Covid-19."

The virus will be with us for some time, in short. But could it change its virulence? Some researchers have suggested that it could become less deadly. Others have argued that it could mutate to become more lethal. Skinner is doubtful. "We have got to consider this pandemic from the virus's position," he says. "It is spreading round the world very nicely. It is doing OK. Change brings it no benefit."

In the end, it will be the development and roll-out of an effective vaccine that will free us from the threat of Covid-19, says Skinner [8].

### 4.8 Conclusion

Fascinating, how a tiny piece of genetic information wrapped in a protein coat can cause such devastation. Compared to other viruses of its ilk, SARS-CoV-2 is more infectious and is far more of a menace. The lack of preparedness of the world in tackling a pandemic even after great development in the medical science has become evident. Covid-19 shows how vulnerable we remain. We have to adopt ourselves to start living with SARS-CoV-2 just the way we have done with influenza virus. Only a vaccine will be able to halt the galloping virus and eradicate it completely much the same as expulsion of the small pox. Is a brand new pernicious virus lurking round the corner? Only time will tell.

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# 5. Is it Fair to Blame Bats for COVID-19?

*-Dr. Pruthul Desai*

**It is believed that the three zoonotic diseases - SARS-CoV, MERS and Sars-Cov-2 which have caused havoc across the world have all been originated by bats. Widespread media coverage has served as catalyst which accelerated the demonizing of bats amongst the population at large. But bats are an important part of the regulatory mechanism of the ecosystem. Instead of blaming the bats, the senseless and indiscriminate exploitation of the available resources by humans has triggered the "spillover" of pathogens from animals to humans. A detailed discussion on the importance of bat on the ecosystem, the role played by humans in damaging it which has exacerbated the spread of COVID-19 is presented.**

## 5.1 Introduction

The emergence of zoonotic diseases came as no surprise to many scientists as around 60% of emerging infectious diseases in humans can be traced back to human interactions with animals, with more than 300 emerging infectious diseases having been identified since 1940.

COVID-19 - a zoonotic disease, which started as an epidemic mainly limited to China in December 2019, has engulfed the entire globe in its fold at a breathtaking speed. The pandemic has touched the shores of nearly all the continents and has thrown the entire global economy into a tizzy.

No one yet knows exactly who gifted us the new coronavirus - Sars-Cov-2. Wildlife, domestic animals and humans all host viruses, but cross-species transmission is sporadic. For the current pandemic hogging all the limelight and its two previous milder cousins, SARS-CoV-2002 and MERS-2013, the needle of suspicion is pointed at one animal species: bats - the only flying mammal on the Earth.

Suddenly, this reclusive and nocturnal mammal, is in limelight, owing to the widespread attention-grabbing media headlines. The unwanted spotlight lead to the demonization, eviction, and slaughtering of bats even when they are most needed. Since the outbreak, there has been alarming upsurge in the incidents of the panicked residents calling the authorities or taking upon themselves to destroying bat roosts and smoking them out, fearing them to be carriers of the dreaded COVID-19.

Wildlife campaigners say such action not only runs the risk of concentrating pathogens in remaining animal populations, but is also replicating the disastrous behaviour that created coro-

naviruses in the first place. For example, vampire bats were culled in Peru during the 1970s to control the transmission of rabies- an act driven by fear and a lack of knowledge about the disease but findings have shown that these desultory actions did not at all mitigate the disease may have disproportionately killed the bats that were least likely to spread the infection. In Uganda, an attempt to wipe out a large colony of Egyptian fruit bats led to a far higher incidence of Marburg virus when the site was recolonized by more susceptible individuals [1].

There is now a looming danger that frightened people and misguided officials may resort to indiscriminate culling which may eventually lead to their extinction. It is axiomatic to say that there is no greater threat than the intolerance and eradication that results from misguided fear.

"In recent decades there has been a great increase in the number of human infections associated with bat viruses," said Robert Siegel, professor of microbiology and immunology at Stanford University. It also exposes the deeply ingrained problems of speciesism, creating the perception that bats are spreading diseases to humans instead of humans catching diseases from bats - a minor, but important, nuance [2].

## 5.2 Why are Bats a Reservoir for Viruses?

The winged nocturnal mammals as shown in the fig. (1), have never really enjoyed good press, except for, say Batman. However, COVID-19 is bringing out the worst in humanity towards bats [3].

Figure 1: Bats
(Source: https://cdn.newsapi.com.au/image/v1/a24eb21ba67489939a1643fc306d88d4)

Bats come in large numbers. One in five mammals on the Earth are bats. In other words 20% of us are bats!! Since bats can fly, they spread in large numbers from one community to another

over large areas. This habit makes them a safe haven for different pathogens. Bats teem with as many as 200 types of coronaviruses because they live in huge colonies in caves - a niche for infection. As they fly around, dropping feces, they spread the virus to other species - then to us. Or, if we eat bats, our exposure is more direct.

A long-standing mystery is: how do the bats protect themselves from the pathogens for whom they act as the pre-emergence niches? Since bats are so good at suppressing viruses, there is a lot interest in studying their immune system, from a physiological and immunological perspective through to genomics.

"[Bats] have lots of viruses but there are very few viral diseases that actually make them sick," said Vikram Misra, a bat expert and microbiologist at the University of Saskatchewan [4]. "They also seem to have for some of these viruses a very balanced relationship...they don't get rid of the viruses, the viruses just sort of come along or multiply at a very very low rate."

The problem for bats is that when they are under stress, that delicate balance tips. In other words, when a bat is stressed, its immune system is challenged and finds it harder to cope with pathogens it otherwise took in its stride.

There are several factors that can lead to higher levels of stress in bats, including hunting, loss of habitat by deforestation, fungal disease, having to fly long distances for food and being confined in cages, a situation that may sometimes be seen in wet markets in China where bats are sold as food for human consumption.

When bats fly, they generate so much internal heat that, according to many scientists, their bodies are able to fight off the germs they carry. This is known as the "flight as fever hypothesis [5]."

"When they fly they have a peak body temperature that mimics a fever," said Andrew Cunningham, Professor of Wildlife Epidemiology at the Zoological Society of London. "It happens at least twice a day with bats - when they fly out to feed and then they return to roost. And so the pathogens that have evolved in bats have evolved to withstand these peaks of body temperature."

Cunningham goes on to say that this poses a potential problem when these diseases cross into another species. In humans, for example, a fever is a defence mechanism designed to raise the body temperature to kill a virus. A virus that has evolved in a bat will probably not be affected by a higher body temperature, he warned [6].

## 5.3 Why are Bats Valuable?

Bats are critically important participants in the ecosystem. Despite a long tradition of being misunderstood and feared, perhaps it is because of their nocturnal habits and erratic flight that bats have an outstanding record of living safely with humans. Millions living in backyard bat houses, city parks, and bridges have proven to be safe neighbours.

Bats play a key role in pest control. Bats eat insects which are considered pests to humans. Insects make up two-thirds of bats' diets and they are able to consume (at least) a quarter of their body mass in insects nightly. This ferocious appetite is important in protecting crops, making bats an essential part of the global food system. As the natural predator of insects, including mosquitoes, bats help to control the mosquito population, protecting our health in the process [2].

Bats gobble up so many insect pests in fields of cacao, cotton, corn and countless other cultivated species. Researchers in Indonesia conservatively estimate that bats save cacao growers more than $700 million annually in avoided insect damage. In Mexico, tequila and mescal production worth billions annually relies on bats that pollinate agaves. From South-east Asia to the Mediterranean, bats provide key pest control for rice growers. In South Africa, it is found that bats foraging around Macedonia farms eat stinkbugs - a major agricultural pest saving Macedonia growers millions of dollars on insecticides.

Another significant role played by the bats is in pollination. Many plants heavily rely on bats for pollinating their flowers and dispersing their seeds. It has been found that the fruits pollinated by bats, called chiropterophily are superior in taste and quality. It is estimated that the bats pollinate around $200 billion worth of crops, which represented around 10% of the world food crop production in 2005 [2]. Thus bats provide intangible economic benefits.

Bats are also 'indicator species,' because changes to the bat populations can indicate changes in biodiversity. Bats might suffer when there are problems with insect populations (because our bats feed on insects) or when habitats are destroyed or poorly managed (for example, some bats only live in large woodlands).

That bats play multifarious roles proves beyond doubt their indispensability in the ecosystem. Any sort of fiddling with bats would be at our own peril.

## 5.4 Are Humans Less Culpable?

Should bats be blamed for the pandemic? What is the role of humans in giving rise to COVID-19? Can we shake off our responsibility and absolve ourselves completely? These harrowing

questions must not be swept under the rug. It is as clear as crystal that hapless bats have been made the scapegoat in this unsavoury episode to exonerate humans of any wrongdoing.

In their native habitats, bats are very unlikely to shed these viruses into dense concentrations of domesticated animals [1]. With their homes in good shape, there is less need for bats to spend time in ours. Researchers believe that it is the humanity's destruction of the biodiversity that creates the conditions for new viruses and diseases such as Covid-19. The disruption of pristine forests driven by logging, mining, road building through remote places, rapid urbanisation and population growth is bringing people into closer contact with animal species they may never have been near before. Climate change is accelerating the loss of animal habitats. As climate change causes large disasters like floods and drought, human food sources are also lost, and growing food insecurity pushes people to further encroach on animal habitats, increasing animal contact. The direct damage from environmental destruction has been evident for years. We are only just now starting to get a sense of the collateral damage.

"We invade tropical forests and other wild landscapes, which harbour so many species of animals and plants – and within those creatures, so many unknown viruses," David Quammen, author of Spillover: Animal Infections and the Next Pandemic, recently wrote in the New York Times. "We cut the trees; we kill the animals or cage them and send them to markets. We disrupt ecosystems, and we shake viruses loose from their natural hosts. When that happens, they need a new host. Often, we are it."

"Human activities and encroaching upon wildlife habitats puts us at risk of encountering new viruses. We need to modify human practices to prevent the emergence of new pathogens.", says Arinjay Banerjee, a postdoctoral researcher at McMaster University, Canada in the release [7]. He studies bat viruses and was part of the team that isolated the COVID-19 virus.

The transmission of disease from wildlife to humans says Kate Jones, chair of ecology and biodiversity at University College, London, is now "a hidden cost of human economic development. There are just so many more of us, in every environment. We are going into largely undisturbed places and being exposed more and more. We are creating habitats where viruses are transmitted more easily, and then we are surprised that we have new ones."

"There are countless pathogens out there continuing to evolve which at some point could pose a threat to humans," says Eric Fevre, chair of veterinary infectious diseases at the University of Liverpool's Institute of Infection and Global Health. "The risk [of pathogens jumping from animals to humans] has always been there [8]."

The difference between now and a few decades ago, Fevre says, is that diseases are likely to spring up in both urban and natural environments. "We have created densely packed popu-

lations where alongside us are bats and rodents and birds, pets and other living things. That creates intense interaction and opportunities for things to move from species to species," he says.

Large-scale habitat restoration could decrease problematic contact between bats and people or our domesticated animals, a side perk of global reforestation efforts. We may even be able to take targeted steps like establishing artificial bat roosts and native fruit trees in appropriate settings, reducing dangerous contact while still retaining the valuable services bats provide us. Building support for all these efforts, however, is vastly more difficult if we continue demonizing bats [1]. More empathy for bats could bolster efforts to limit or even outright end the wildlife trade, since it is another common way in which bats are forced into direct or indirect contact with people.

We have to understand that we have only one Earth. Its capacity to support a thriving diversity of species, humans included, is large but fundamentally limited. When human demand on this capacity exceeds what is available - when we surpass ecological limits - we erode the health of the Earth's living systems. Ultimately the loss threatens human well-being.

Unless we drastically change the way we use planet's available resources, we may be hit by another pandemic that is going to be far more damaging. There is an urgent need for a complete rethink of how we treat the planet.

## 5.5 Conclusion

Wildlife harbours large number of pathogens, most of which are yet to be discovered. These pathogens in nature do pose threats, but the real damage is done by the human actions. Sars-Cov-2 makes it clear that anthropogenic environmental damage can kill humans fast. Rather than vilifying the bats, we humans should introspect and address our own culpability.

Blaming bats only increases already severe threats to their survival, despite scientific evidence about the enormous benefits they provide to both the environment and societies. Bats provide an increasingly compelling case for protecting animal habitats. Persecuting bats because of the diseases they harbor could easily backfire. Care about bats or not, we should see COVID-19 as a grim reminder that human well-being requires responsible stewardship of nature - not just dominance.

COVID-19 is just the tip of the iceberg. The threat of the next pandemic is looming large. If we don't mend our ways, virus with a strange concoction of COVID-19's communicability and Ebola's mortality is lurking round the corner to unleash carnage. It's an opportune moment for humans to give up hubris and bow down to the nature's supremacy.

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# 6. Approaches to the Elusive Vaccine for COVID-19

*-Dr. Pruthul Desai*

**The COVID-19 pandemic has ravaged the world in a short span of four months causing nearly four hundred thousand deaths. The galloping number of deaths is a real matter of concern and anxiety. Vaccines are widely regarded as the best hope of stopping or at least slowing the pandemic. To combat the virus, scientists are putting in valiant efforts to discover a vaccine. Different groups are using novel approaches in a bid to cross the finish line at the earliest. In this article, a brief summary of different approaches adopted by the scientists to discover the vaccine is presented. The path followed by the virus to enter human cells and the response of the body's immune system provides a deep insight which helps us devise a strategy to develop vaccine. The method used by the virus to infect human cells and immunity's response to it is also discussed.**

## 6.1 Introduction

COVID-19 has unfurled its tentacles engulfing the entire globe at a breathtaking speed. The most advanced species on the Earth has been brought to its knees by a very humble assailant which barely measures a billionth of a meter in diameter. Even in the 21st century, the response of humans to the pandemic has been to say the least, medieval. Quarantine was the way people fought plagues in the distant past, and with COVID-19 our response has been not too different.

To combat the virus, almost all the countries used the bluntest tool of all in the outbreak management toolbox - lockdown, India being no exception. Extensive Lockdowns over two months have had devastating impact on the economy and emotional well-being of the populace at large. Countries all over the world are grappling with the problem of soaring unemployment. Governments are promoting non-pharmaceutical interventions, such as social distancing in order to circumscribe spread of the virus. We are absolutely clueless about how long these restricted movements would remain in place.

On its part, the virus has been found to work with ruthless efficiency and remarkable persistence. Countries like South Korea, who have apparently battled hard to tame the first wave of infections and achieved "flattening of the curve," are nervously eyeing "the second wave." No one knows when the spread will settle into an endemic equilibrium or how many times such waves of infections are going to reoccur and with what ferocity. Scientist believe that only when nearly 80% of the population of the world gets infected and develops immunity, the spread of the virus will be petered out. It is estimated that for the vast majority of people to get

infected, the time duration will stretch well over a year clearly indicating that the virus is going to stay, to say the least, for a year.

The picture appears grim and and the threat menacing. Under the circumstances, entire humanity is yearning for a quick fix solution to the problem which arose in the first place because of immoderate human actions spanning decades. In other words, humans are pretending to be naively innocent to expect a quick fix for a problem compounded over the years because of the prodigal usage of natural resources. The current pandemic is nature's own way of settling the scores and we are paying a heavy price for our wrongdoings in the past.

Looking at the ruthless efficiency of the virus, the development of a vaccine - a purported panacea- has to be done expeditiously. Around the world, more than 135 vaccines against the coronavirus are in the pipeline and extensive extensive efforts are made to hasten the process. Vaccines typically require years of research and testing before reaching the clinic, but scientists are racing to produce a safe and effective vaccine by next year. It would be instructive to look at how the virus attacks our body. This insight about the machinations of the virus will give us vital clues for the development of the much anticipated vaccine.

## 6.2 The Enemy Within

Viruses as we all know don't have their own biochemistry because they borrow ours. Viruses are weird microscopic particles consisting of a tiny piece of genetic information (about 10,000 times less than that contained in the human genome) and a protein or lipid (fatty molecule) shell.

Coronaviruses are enveloped, single-stranded RNA viruses, which means that their genome consists of a strand of RNA (rather than DNA) and that each viral particle is wrapped in a protein "envelope." Researchers have found that the SARS-CoV-2 virus which is responsible for the current COVID-19 pandemic has a spike (S) protein that protrudes out from the viral membrane which drastically increases its ability to hitch itself to the human cells as a route to enter it. These protrusions are observed to bind, in particular, with the protein named angiotensin-converting enzyme 2 (ACE2) - a viral receptor, on the surface of human cells.

After binding, proteases, which are human enzymes that clip other proteins into pieces, cut, or "prime," the spike protein to remove its outer segment, named S1, and reveal the inner segment, named S2. The spike protein S2 segment then causes fusion of the viral membrane with the human cell membranes, letting the the viral genetic material enter the cell and start replicating. Therefore, ACE2 and its interaction with SARS-CoV-2, as well as other proteins involved in this process, are conceivably valid targets for anti-COVID-19 agents. Let us have an in-depth

look at the mechanism of the interaction of the spike protein and the ACE2 cells.

### 6.2.1 The Spike Protein of SARS-CoV-2

The spike protein of corona virus causing COVID-19, forms club-shaped protrusions that stick out all over the ball and a longer, thinner stalk, as shown in the fig.(1), resembling a crown or the sun's corona - hence the name. Different parts and organs of human body such as the respiratory system, gastrointestinal track, blood vessels etc. have ACE2 receptors on their surfaces. Three spike proteins bind to each other to form a trimer, which is shaped, predictably,

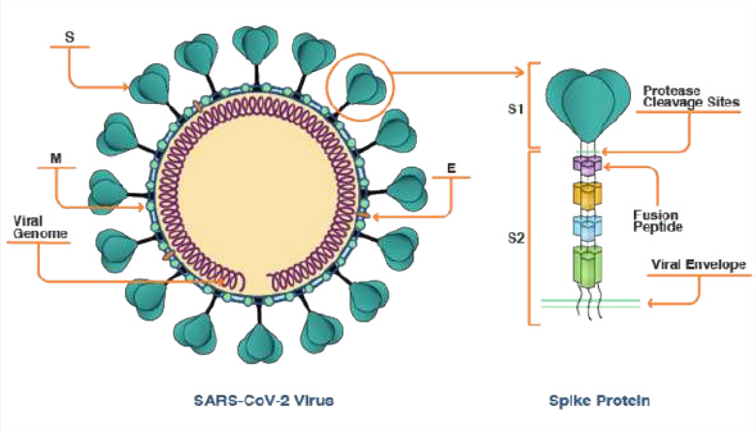


Figure 1: Viral spike protein structure
(Source: https://www.cas.org/blog/covid-19-spike-protein)

like a bigger screw. The stalk is inserted into the viral membrane and holds the head outwards away from the virus. The larger head region and part of the stalk are called the S1 region of the spike protein. The remaining part of the stalk that's closer to the viral membrane is called the S2 region [1].

Once the virus enters human body, the spike protein's S1 region binds to ACE2 on the cell surface and tethers the virus to the outside of the human cell. This is the first step in the viral replication process.

### 6.2.2 How Virus Enters into the Human Cells

Once the virus piggybacks on to the human cells it has two different potential pathways to enter the cell as shown in the fig.(2). Which pathway is used depends on whether or not human proteases are present to "prime" the spike protein. The presence of proteases depends on the type of human cell that the virus is entering and on the particular conditions at that cell. Several

human proteases can cleave the spike protein, including transmembrane serine proteinase 2 (TMPRSS2), furin, elastase and trypsin. TMPRSS2 is expressed by human lung cells. Thus, it is thought that it plays an important part in virus entry into respiratory system cells [1].

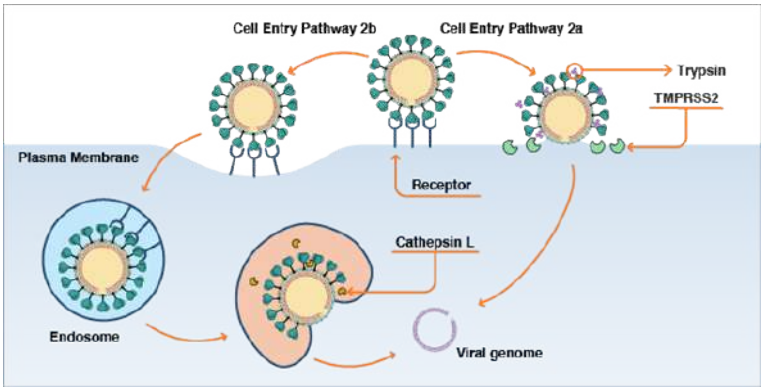


Figure 2: Two possible pathways for SARS CoV-2 to enter the human cell
(Source: https://www.cas.org/blog/covid-19-spike-protein)

If these proteases happen to be present near the spike-ACE2 binding interface, they will cleave the spike protein to expose the S2 region, and specifically the fusion peptide region, of the spike protein. This fusion peptide region of spike is made of more hydrophobic, or lipid-like, amino acids, and it inserts into the lipid-containing cell membrane to induce viral membrane - cell membrane fusion and subsequent entry of the viral genome into the cell (Figure 2a). This cleavage must occur after spike-ACE2 binding. If it occurs before, the virus becomes less potent and loses its ability to infect the cell.

If proteases don't happen to be present near the spike-ACE2 binding interface, the virus will enter the cell by a different pathway called endocytosis (Figure 2b). In this process, the coronaviruses bound to ACE2 proteins outside the cell are engulfed by an indentation in a small region of the cell's membrane, which then pinches off to form an endocytic vesicle that brings the outside material into the cell. After this happens, the endocytic vesicle fuses with an intracellular membrane-walled vesicle called an endosome. In the endosome, there are proteases present, including one called cathepsin L, that can cleave the spike protein and expose its fusion peptide region. The fusion peptide then mediates fusion of the viral membrane with the endosome's membrane and thereby induces subsequent entry of the viral genome into the cell [1].

Although SARS-CoV-2 is very similar to SARS-CoV, the virus that caused SARS (Severe Acute Respiratory Syndrome), a few mutations in the receptor binding domain of the S protein have significantly increased the SARS-CoV-2 virus' binding affinity to ACE2. These differ-

ences may underpin the higher transmissibility of COVID-19. There is evidence that ACE2 is expressed in our lungs, digestive systems, hearts, arteries and kidneys. ACE2 expression also increases with age and is higher in patients suffering from cardiovascular diseases, potentially explaining the increased severity of COVID-19 in these subgroups [2].

Researchers have grasped the basic mechanism adopted by the virus to infect the human cell. It becomes imperative for us to find out ways of impede this process and that is precisely where all the attention is currently focussed at. We hope to find a potent vaccine which will trigger the human body to develop appropriate counter measures to fend off the infection. But to achieve this aim a through understanding of how the body's immune system works is the key. So let us have a look at this important mechanism which would catapult us to develop the elusive vaccine.

## 6.3 Orchestrated Response by the Immune System

In discussions of immunity, antibodies often end up hogging the spotlight - but they're not the only weapons the body wields against invaders. The sheer multitude of molecules at work helps explain why "immunity" is such a slippery concept [3]. When the pathogens infiltrate, our body adopts a two pronged defence strategy. The first line of defence comes from the innate immune response - a blunt, broad-acting ensemble, also called macrophages, that attacks any invader that doesn't resemble a normal-looking human cell. The second line of defence is brought into action when the invading pathogen slips through the first line. The second lined up defence mechanism is slow but specific and is called the adaptive immune response. The body custom-builds these second wave of assailants to recognize the unique features of the intruding pathogen.

This second wave includes antibodies, which are manufactured by immune cells called the B cells. One particular category of antibodies called neutralizing antibodies are potent weapons necessary to combat most of the pathogens that plague humans. A hallmark of a good vaccine is its ability to induce immune response via large scale production of these neutralizing antibodies. The most amazing thing about the immune system is that it retains some of the B cells which produced antibodies, though the antibodies disappear from the blood in few weeks or months. If the same pathogen attacks, then these cellular factories profusely produce the antibodies to defend against the intruder thus generating long term immunity against a particular pathogen. But antibodies alone aren't enough to quash an infection, says Diane Griffin, an immunologist at Johns Hopkins University's Bloomberg School of Public Health. "You need an orchestra of responses [for protection] to really be effective."

Another important player are the T-cells. There are two main types of T-cells: helper T-cells

and killer T-cells. Helper T-cells stimulate B-cells to make antibodies and help killer cells develop. Killer T-cells directly kill cells that have already been infected by a foreign invader. T-cells also use cytokines as messenger molecules to send chemical instructions to the rest of the immune system to ramp up its response.

"You can't have a great antibody response without T cells," says Akiko Iwasaki, a virologist and immunologist at Yale University. Among a slew of helpful functions, T cells help young B cells mature into antibody-making machines. "These things really go hand in hand." T cells are also formidable fighters in their own right. In a bid to stop the spread of a pathogen throughout the body, some T cells will trigger infected cells to self-destruct. Others linger after an illness has resolved, patrolling tissues so germs can't re-establish a foothold [3].

## 6.4 What is a vaccine?

Vaccines work by tricking your immune system into thinking that it's being attacked by a virus. Your immune system then churns out antibodies that are custom made for that particular virus. That way, if you're exposed to that virus in the future, your body can quickly squash it out before it makes you sick [4].

Triggering that immune response takes two main components: a bit of the virus so the body knows what it's looking for and some kind of irritant to stir the immune system into action against that viral bit [4].

"If I just put purified protein under your skin, nothing would happen. You have to get the immune system kicked up," Rosemary Rochford, University of Colorado immunologist, says.

Unless we take cognizance of these two important components, the efficacy of the vaccine will be impaired and the vaccine will be rendered useless.

## 6.5 Basic Approaches for Developing a Vaccine

### 6.5.1 Gene Based Vaccines

Gene-based vaccines are the much-hyped underdog in the race to create a coronavirus vaccine. Most of the vaccine candidates that grabbed headlines or sent the stock market soaring are gene-based. Moderna, US based biotechnology company, which was the fastest to start testing its vaccine in volunteers in the US, has a gene-based vaccine. So does Pfizer, which is also in clinical trials [4]. Cautioning that a vaccine is still months, maybe even a year away, experts said the US-based biotechnology firm's results have propelled it to a pole position in the race to deliver the vaccine.

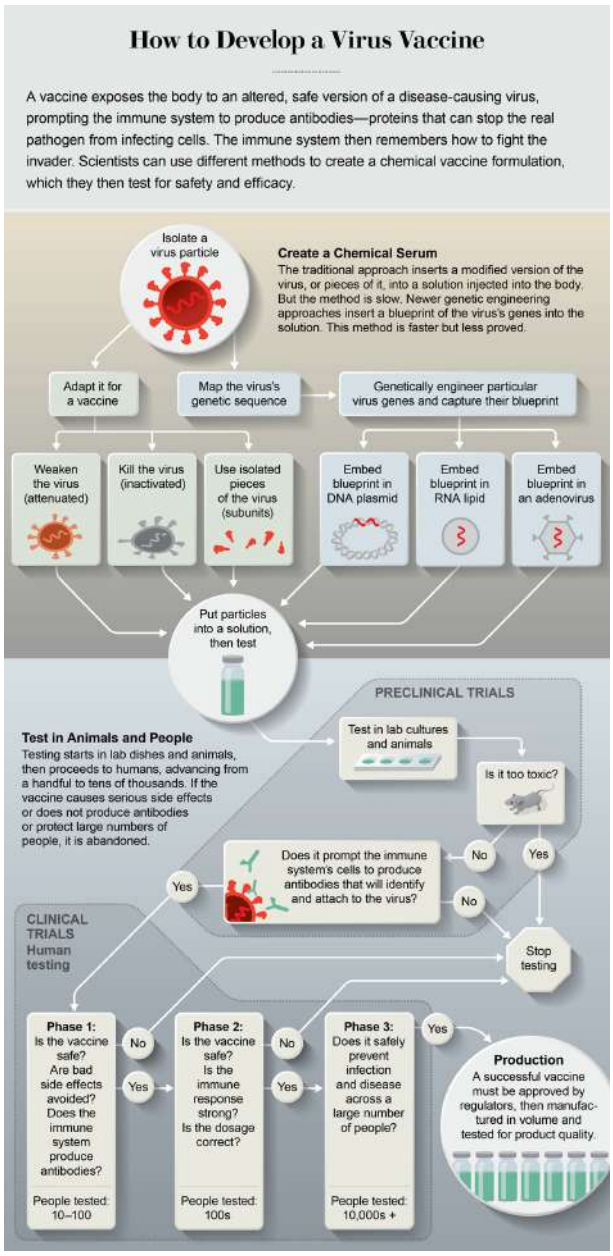


Figure 3: How to develop a virus vaccine
(Credit: Jen Christiansen)

Instead of directly delivering bits of virus to the immune system for target practice, gene-based vaccines give the body tools to make them on its own. The vaccines are made up of pieces of genetic material, either mRNA or DNA, that encode the instructions for making the protein. The mRNA or DNA then enters cells, which read the instructions and churn out copies of the protein for the immune system to rally against [4].

"Rather than producing the vaccine outside the patient, you make the patient make their own vaccine," Ross Kedl, University of Colorado immunologist, says.

Most of the coronavirus vaccines that use this method are introducing the gene that encodes a bit of protein on the outside of the virus called the spike protein. The virus depends on the spike protein to break into cells and replicate. If the immune system is trained to recognize and block that protein, the virus can't attack cells and continue to spread [4].

**Pros:** These types of vaccines are relatively easy for companies to make once they know the genetic sequence they're targeting. That's why Moderna was able to get a vaccine ready and start testing it in people so quickly. They're also easy to manufacture: if they work, companies could quickly generate millions of doses. "From a manufacturing standpoint, if you could shift everything to a nucleotide system, that would be brilliant," Kedl says.

**Cons:** But despite their simplicity and decades of work, gene-based viruses are still largely experimental, at least for people. There's never been a gene-based vaccine approved by the Food and Drug Administration. If a gene-based coronavirus vaccine makes it over the finish line, it would be the first of its kind.

mRNA and DNA vaccines sometimes work well in animals like mice, but they have previously sputtered out when they're introduced to humans, Kedl says. He says it may be because these vaccines aren't good enough at spurring the immune system to create antibodies.

### 6.5.2 Inactivated Virus Based Vaccines

In this technique scientists can take a virus and kill it with heat or radiation - rendering it harmless, but still retaining important traits which can be identified by the immune system. A handful of Chinese companies are developing coronavirus vaccines using this method. One company, Sinovac, showed that its vaccine could protect monkeys from COVID-19. Human trials are ongoing.

**Pros:** These types of vaccines have been around for decades, and scientists understand them well. Because these vaccines contain the whole (but non-replicating) virus, they're good irritants for the immune system. "It's got bacterial cell walls and all sorts of viral capsules and proteins and things that stimulate immunity very robustly," Kedl says.

**Cons:** Unlike gene-based vaccines, though, inactivated virus vaccines are tough nut to crack. Over the years we have gained expertise to manufacture inactivated viruses. But to scale them up to massive amounts is an excruciatingly slow process. "It's really hard to scale up and create enough of that," Rochford says. With the passage of time the immunity generated by these types of vaccines wanes and fizzles out. So people may need booster shots.

### 6.5.3 Adenovirus Vector Vaccines

They are attractive vaccine vectors as they induce both innate and adaptive immune response in mamlanian hosts. Adenovirus vectors are made from live — but heavily weakened — versions of the viruses. The viruses are so weak that they don't make you sick, but they still make your body think it's infected and set off the immune system [4].

To make the virus innocuous so that it is safe enough to be used as vaccine, is a long and tedious process. To speed things up, vaccine developers aren't even attempting to do that with the entire coronavirus. Instead, some teams are inserting sections of the coronavirus gene into weakened, live versions of other viruses. British pharmaceutical giant AstraZeneca, who has joined hands with the University of Oxford is trying to produce a vaccine based on a chimpanzee adenovirus called ChAdOx1. A vaccine prototype has reached the clinical trial stage. After early hiccups and observations, the researchers have now said that they are all set to "roll out" their vaccine candidate for the masses in the months of September or October, with production for two million doses underway.

**Pros:** Because this vaccine is based on a weakened, but living virus, the immune system mounts a strong response against it. "When a live, attenuated, vaccine works, they tend to give you longer immunity and a more robust and more durable immunity," Kedl says. With these vaccines, one shot may be enough — you wouldn't need a booster.

**Cons:** Even though we regularly use live virus vaccines, the adenovirus platforms are still experimental. They've never been used for infectious diseases. There's also a concern, Rochford says, that some people may be immune to the adenovirus that's shepherding the coronavirus gene into the body. "Adenoviruses circulate through the human population," she says. Even though research groups are using adenoviruses that are relatively uncommon, some people may have seen them before — so the vaccine wouldn't work for them [4].

### 6.5.4 Protein Subunit Vaccines

A protein subunit vaccine presents an antigen to the immune system without introducing viral particles, whole or otherwise.

One method of production involves isolation of a specific protein from a virus and administering this by itself. For the coronavirus, in most cases, that's the spike protein. These vaccines contain copies of the spike protein and a bit of something to stimulate the immune system.

**Pros:** Scientists are familiar with this approach, and it's worked well for other types of diseases. "We very much know exactly what we have to be going after," Kedl says. Because the vaccine only contains a piece of the virus, it's also less likely to trigger side effects.

**Cons:** Because these vaccines only use a piece of a virus, they sometimes aren't able to push the body to generate a strong enough immune response, even with a good irritant built in. People often need multiple shots to build up enough immunity to the disease. That's why, for example, most people get multiple doses of the HPV vaccine. During a pandemic, creating enough vaccines to give each person one shot is already a challenge.

Building the protein is also a challenge, Rochford says. Developers have to make sure that the version of the spike protein they build has the same properties as the one that's naturally on the virus. "Batching them up to scale is very challenging. It's not impossible, but it's a challenge," she says.

It often requires the incorporation of adjuvants (taken from the Latin, "adjuvare," meaning "to help" are designed to improve poorly immunogenic vaccines) to elicit a strong protective immune response because the antigens alone are not sufficient to induce adequate long-term immunity.

## 6.6 Conclusion

Getting a vaccine for the Sars-CoV-2 is a daunting task. Out of the different approaches discussed above, which one will eventually succeed in getting us the right vaccine is difficult to tell. But the frenetic pace at which scientists across the globe are working in unison with a sole aim of getting vaccine portends good omen.

We have learnt valuable lessons from different epidemics and pandemics that inflicted humanity in the past. Although what happened in the past isn't a template for what will happen with COVID-19 in the coming months, our experience of previous pandemics will come in handy for sure. It has given us a head start in the race to develop a vaccine and we hope to find a vaccine in a record breaking time.

There global race for vaccines by myriad companies has, apparently, entered into its stretch. When will the vaccine be eventually found? Whether it will have long lasting effect or periodic booster doses will be required? How long will it take to vaccinate the entire human population? These are some of the pressing questions and we don't have the a definitive answer to these

puzzles. Till then, an anxious wait is all that we are left to grapple with!

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# Covid-19 Awareness Campaign by Our Students During Lockdown







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SLOW THE SPREAD ...AS... MATTERS
STAY SAFE SAVE LIVES....
JAY HIND
STAY
HOME
STAY
SAFE
ptscs surat


National Service Scheme
Sir P.T.Sarvajanik collage of science
Surat, Gujarat
#MUSKURAYEGA_INDIA
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National Service Scheme
Sir P.T. Sarvajanik college of science
Surat, Gujarat
#TOGETHER_INDIA
#STAY_HOME
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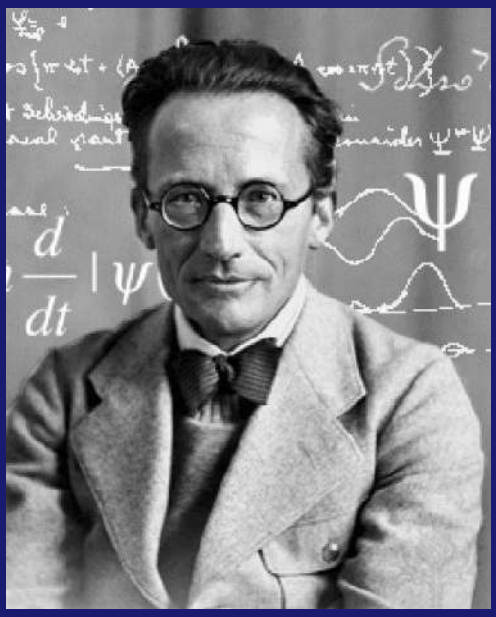
# Erwin Schrodinger




**August 12, 1887 - January 4, 1961**

***"Hence this life of yours which you are living is not merely a piece of the entire existence, but is in a certain sense the whole; only this whole is not so constituted that it can be surveyed in one single glance. This, as we know, is what the Brahmins express in that sacred, mystic formula which is yet really so simple and so clear: "Tat tvam asi", this is you. Or, again, in such words as 'I am in the east and in the west, I am below and above, I am this whole world.'***

***Thus, you can throw yourself flat on the ground, stretched out upon Mother Earth, with the certain conviction that you are one with her and she with you. You are as firmly established, as invulnerable as she, indeed a thousand times firmer and more invulnerable. As surely, she will engulf you tomorrow, so surely will she bring you forth anew to new striving and suffering. And not merely 'some-day': now, today, every day she is bringing you forth, not once but thousands upon thousands of times, just as every day she engulfs you a thousand times over. For eternally and always there is only now, one and the same now; the present is the only thing that has no end."***