

The Institution of Engineers (India) A Century of Service to the Nation

COMBATING VID-19

Role of Engineers and Doctors

Combating COVID-19: Role of Engineers and Doctors

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Book on 'Combating COVID-19: Role of Engineers and Doctors'

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Foreword

The recent pandemic due to COVID-19 is straining the existing medical systems and changing every aspect of the daily life of human beings. The Medical professionals are on the frontline to fight against COVID-19 to care for patients as the work to vaccinate the people proceed ahead. These unprecedented times have led for brainstorming by other professionals as to how they can contribute to help the society through this pandemic. To assess the roles and contributions of the engineering fraternity worldwide during this pandemic, The Institution of Engineers (India) has tried to bring to the fore the technical intervention in support of fighting against this pandemic.



It is heartening to inform all readers that some eminent personalities have shared their views on combating COVID-19. We are really proud to have the article on "Global Engineering Innovations in response to the Corona virus Pandemic" written by Dr Marlene Kanga, Former National President, Engineers Australia and Former President, World Federation of Engineering Organisations (WFEO). Apart from that, the eminent person like, Prof Harish Hirani, Director, CSIR-Central Mechanical Engineering Research Institute, Durgapur, West Bengal has shared his experiences on "Oxygen Enrichment Technology". The thought on "Solar-Powered Vaccine Carrier with a Tracking Device" has been expressed by Mr Mayur Shetty, Chief Executive Officer, Blackfrog Technologies. The experiences were also shared by Dr C R S Kumar, Department of Computer Science & Engineering, Defence Institute of Advanced Technology, Pune on "COVID-19 Social Vaccine Toolkit (C19-SVT)", "Stockdale Paradox: Ten Lessons to deal with COVID-19 Pandemic" and "Arogva Kshem App: COVID-19 Infection Self Assessment Test C19-SVT: COVID-19 Social Vaccine Toolkit". We are also proud to have the articles on "Ultraviolet (C-Type) Germicidal Irradiation Based Covid-19 Sterilization Chamber" by Cdr Vinod Kumar, HoF (Engineering), Naval Institute of Aero Nautical Technology, Cochin University of Science & Technology; "Role of Engineers in combating COVID-19" by Dr Manoj Kumar Patel, Principal Scientist, CSIR-Central Scientific Instruments Organisation, Chandigarh; "Engineering Intervention in COVID Management" by Mr Soumen Sen, Department of Electronics & Communication Engineering, Asansol Engineering College, West Bengal; "Engineers' Achievement and Role in COVID Management -Some Thoughts" by Mr AK Saxena, Chairman, Sustainable Development Forum, IEI, Ranchi and "A Scientist's Perspective on the Impacts of Face Covering in Combating COVID-19" by Dr Vineeta Tanwar from Ohio State University, USA.

I am thankful for the help in preparation of this Book on **"Combating COVID-19: Role of Engineers and Doctors"** to the Secretariat of the Institution. I am quite confident that this Book would be useful for the stakeholders and will be an inspiration for all leading practicing engineers.

Er Narendra Singh, FIE President The Institution of Engineers (India)

Preface



The heralding of a new decade in 2020 would be forever etched in our memory as it took a massive toll of human lives while testing to the core the resilience of our healthcare system as the COVID-19 pandemic took centre stage. The subsequent

developments saw the plummeting of global economy pushing millions into penury while, at the same time, the digital technology was pushed over its tipping point transforming business, services and most importantly our lives forever.

The global COVID-19 pandemic has impressed upon the need of synergy between medical practitioners and engineers making them work together in unison to come up with synergistic solutions for the entire healthcare sector.

In backdrop of the above developments, the leadership from The Institution of Engineers (India) felt appropriate to come-up with a compiled volume comprising of works bearing testimony to the deep insights of our enterprising healthcare and engineering professionals. I must thank our leadership especially our President, Er Narendra Singh, for his tacit patronage in bringing out this book.

This corona virus is here for the long haul and as we move along, the biggest challenge at hand will be getting back on track and accepts the new normal. The future will very much depend on how we interact socially and what kind of preventive measures we adopt. This book, which contains articles from eminent engineers and doctors, deserves admiration and will serve as a reference material for many with an inchoate understanding of the subject. I must mention that the content of the book has been thoroughly enriched with some of the authoritative articles coming from eminent personalities like Dr Marlene Kanga, National President (2013), Engineers Australia, President (2017-2019), World Federation of Engineering Organizations.

This book, "Combating Covid-19: Role of Engineers and Doctors" has a comprehensive coverage of the nuances of this Covid19 pandemic and also discusses well-crafted strategy to deal with such crisis. I would like to believe that documenting these in the form of a book will enable us to cope with the challenges posed by the current pandemic and what lies beyond.

Er Pradeep Chaturvedi, FIE Chairman Interdisciplinary Coordination Committee The Institution of Engineers (India)

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Global Engineering Innovations in response to the Coronavirus Pandemic

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ABSTRACT

Engineering innovations have developed quickly and been more important than ever before with the urgent demand for technical solutions to respond to the global pandemic in 2020 and 2021. This paper presents the extraordinary breadth of new technologies that were developed and implemented across the world, by leading engineers and engineering institutions in every continent, including India, and in the shortest possible time. These included the development of new vaccine technologies including breakthrough m-RNA technology, agile and advanced manufacturing processes such as 3D printing, the use of Artificial Intelligence and the development of new diagnostic tools to detect the coronavirus, the development of vaccine manufacturing and cold chain logistics for vaccine delivery and software technologies for geo-spatial mapping, communication and analysis of the virus spread and progress of vaccinations. The importance of these advances and their impact on populations around the word is enormously significant especially for the health and well-being of billions. The World Federation of Engineering Organisations is committed to building capacity for all engineers, to understand these technological advancements and their implementation, in all parts of the world, essential for sustainable development and to ensure that no one is left behind.

Keywords: COVID-19; Innovation; Pandemic; AI; 3D Printing; World Federation of Engineering Organisations

INTRODUCTION

The spread of the coronavirus and the global pandemic of 2020 that followed, galvanised scientists and engineers into developing and delivering innovative solutions to deal with the virus and its impacts in a wide range of ways. Engineers have always been recognised as being ingenious and the word 'engineer' itself comes from the Latin Ingenium which is also the root of ingenuity and which means innate quality and especially mental power. This mental acuity has been on display like never before with remarkable developments that are benefiting millions today and will continue to deliver benefits for decades to come. Leading

engineers and engineering institutions in every continent, including the Indian Institute of Technology (IIT) Bombay and Imperial College, University of London, both institutions where I studied chemical engineering, have been at the forefront of breakthrough research, developing innovations to detect, control, track and prevent the spread of the corona virus in the shortest possible time. Engineers have been recognised as the hidden heroes of the pandemic [1]. Many leading institutions, such as Imperial College London, have developed an integrated approach, across various disciplines, to fast track innovative ideas and bring them to fruition[2]. This paper explores some of the technologies that have underpinned the response to the pandemic and enabled the global response.

WORLD FEDERATION OF ENGINEERING ORGANISATIONS KNOWLEDGE SHARING AND CAPACITY BUILDING

As the peak body for professional engineering institutions internationally, the World Federation of Engineering Organisations (WFEO) has some 100 national, international and regional/ continental members representing more than 30 million engineers. Our members reported the work of engineers round the world in response to the pandemic. For example, the Maltese Chamber of Engineers, our National Member of Malta, reported the work of their members in developing respirators, face masks and other solutions, winning awards for these innovations [3]. The Institution of Civil Engineers (ICE), our UK National Member, in partnership with the Infrastructure Client Group, released a White Paper that examines the impact of the pandemic on the future shape of infrastructure systems in the UK [4]. Our National Member from Portugal, The Ordem dos Engenheiros de Portugal (OEP) developed a series of initiatives aimed at preventing the COVID-19 pandemic and mitigating its consequences [5]. Our National Member for France, produced information for 3D printing of face masks and our Associate Member, TH Georg Agricola University produced face protection, door openers and much more for the Metropole Ruhr, using 3D printing [6]. The National Member for India, The Institution of Engineers (India), is producing a special publication on the work of engineers in addressing COVID-19, where this article is being published.

WFEO has developed an information portal to disseminate knowledge on engineering responses to COVID-19 to its members in 100 nations representing 30 million+ engineers. The goal is to share knowledge between developed and developing countries, train users and develop institutional capacity, all essential for sustainable development through engineering, a key strategic objective of the Federation [7]. WFEO has also developed a knowledge hub with links to important engineering information from public health departments and engineering organisations around the world, to facilitate the sharing of engineering information and innovations internationally[8]. The portal showcases the importance of engineering as a key lever for sustainable development, which has also been recognised by the United Nations [9].

VACCINE DEVELOPMENTS AND BREAKTHROUGHS

The global pandemic itself spread rapidly as a result of international travel made possible by modern aircraft technology developed by engineers. The coronavirus spread from Wuhan, China, to more than 140 other countries in just three months as travellers crossed the globe in a few hours. By comparison, the bubonic plague spread the Black Death from China to Italy in the course of some sixteen years, between 1331 and 1347. However, engineers and scientists have also been the source of solutions. For example, scientists developed a treatment for malaria by extracting quinine, from the bark of the Andean cinchona tree. In the 1980s, a number of antiviral medicines were developed and turned the HIV infection that had affected millions, from a nearly certain death to a chronic and controlled infection. Engineers have been essential in the manufacture of these medicines and their distribution. This has resulted in the eradication or control of many diseases, including in India such as tuberculosis, tetanus, typhoid, malaria and poliomyelitis [10].

The development of vaccines to respond to the coronavirus has been no less remarkable. It usually takes about 10 years to develop and approve a new vaccine. The mumps vaccine took four years [11]. Yet not one but several coronavirus vaccines have been developed in less than one year.

Advances in genomic sequencing enabled researchers to discover the viral sequence of coronavirus in January 2020, just 10 days after the first reported cases in Wuhan, China. Worldwide cooperation and funding by governments contributed to the rapid development of vaccines. In the U.S., Operation Warp Speed (OWS) partnered with multiple institutions, including the National Institutes of Health (NIH) and the Centres for Disease Control and Prevention (CDC), to develop, manufacture, and distribute the vaccines. OWS invested in multiple companies and vaccine platforms at once, increasing the odds of success. The European Commission also funded several vaccine candidates and worked with others in pledging \$8 billion for COVID-19 research. The UK government Vaccine Taskforce contributed to vaccine research for the Oxford/ AstraZeneca vaccine [12]. The World Health Organisations reports 180 vaccines in development as on 13 July 2021 around the world [13].

India also is in the race to manufacture and distribute the coronavirus vaccine.COVAXIN®, is India's indigenous COVID-19 vaccine,developed by Bharat Biotech in collaboration with the Indian Council of Medical Research (ICMR) - National Institute of Virology (NIV) [14]. The Novavax vaccine is being produced by the Serum Institute of India (SII).The government has also ordered 300 million doses of another vaccine from Indian firm, Biological E. At June 2021, India had given more than 260 million doses of three approved vaccines - Covishield, Covaxin and Sputnik V and approved Indian pharmaceutical company Cipla, to import the Moderna vaccine [15].

The extraordinary drive to develop COVID-19 vaccines was like a moonshot —and producing a vaccine in just over six months after the first vaccines were authorized for use, delivering more than 3 billion doses around the globe, is a remarkable feat of engineering [16]. Engineers had a key role, developing Artificial Intelligence tools to identify key vaccine candidates in a very short time [17]. The methods are also important to develop vaccines to mutations of the virus, ensuring the best possible vaccines are quickly identified.

Engineers have also played a key role in developing m-RNA technology to fast track the development of a new category of vaccines. Moderna, co-founded by two chemical engineers, Noubar Afeyan and Robert Langer, developed m-RNA vaccines that can be manufactured and distributed more efficiently. While conventional vaccines require vast resources to make large amounts of proteins, Moderna's technology can produce mRNA much more quickly in smaller manufacturing plants, and the human body becomes the protein factory. Moderna m-RNA vaccines were ready for human trials in just 63 days, an extraordinary achievement (Figure 1) [18].



Fig 1: Moderna, a biotechnology company, has developed a vaccine based on m-RNA technology [18]

Importantly, the Moderna vaccines can be manufactured in miniature factories creating capacity in shorter time frames and lower cost. A conventional factory would cost hundreds of millions of dollars and 12-18 months to build. However, the innovative "factory in a box" developed by engineers at Kings College, University of London, can produce m-RNA vaccines at scale at lower cost and in a shorter time [19]. This will dramatically increase current global manufacturing capacity of 5 billion vaccines per annum and will also provide agility to manufacture new vaccines to respond to mutations of the coronavirus (Figure 2).



Fig 2: Factory in a Box to manufacture m-RNA vaccines, Kings College, University of London [19]

RAPID DIAGNOSTICS

Engineers have a key role in the development of rapid diagnostics using new approaches that are cheaper and faster than conventional ones. For example, engineers from Columbia Engineering have established Rover Diagnostics to commercialise their invention of a rapid diagnostic tool [20]. The affordable, portable, and ultrafast point-of-care Rover platform provides reverse transcription polymerase chain reaction (RT-PCR) results in eight minutes, faster than any other test of its kind, with targeted accuracy to match laboratory-based tests. The system uses a new approach to thermal cycling, bypassing the standard approach of Peltier device—a semiconductor that heats and cools the sample from outside the vial with radiant heat. Instead, Rover's system uses a photo thermal process that relies on nanoparticles to generate heat from inside. It can be used to test a wide range of infectious diseases.

Professor Chris Toumazou, Regius Professor of Engineering at Imperial College London, is an electronic engineer, who has developed Covid Nudge, an innovative, lab-free, cartridge-based COVID-19 PCR test that combines advances in microfluidics, biochemistry, and electronic engineering to deliver test results in just over an hour, dramatically accelerating testing workflows. The same cartridge can simultaneously test for other viruses such as various influenza strains [21].

DETECTING AND MITIGATING TRANSMISSION OF THE VIRUS

The droplet transmission of the corona virus was identified in March 2020 and medical teams were alerted worldwide [22]. An engineering analysis of the fluid dynamics in air-conditioned room resulted in guidelines to reduce transmission, including by aerosol transmission, which included, the need for good ventilation and/or short exposure times. Recommendations were made for air recirculation in HVAC systems and for high quality filters to be installed to avoid

transmission through the air. Additional personal protective equipment (PPE) was recommended for tasks which required close proximity [23]. The application of fluid dynamics analysis tools has thus been important to fight the COVID-19 pandemic and to enable health authorities to prescribe measures to reduce virus spread. With the evidence from engineers that corona virus could be spread by tiny particles suspended in the air, the World Health Organisation began to advise widespread use of face coverings in July 2020 [24].

ADVANCED MANUFACTURING TECHNOLOGIES FOR DETECTION, PREVENTION, TREATMENT AND VACCINE MANUFACTURING

Engineers have had a key role in the detection of the corona virus, the design of preventative measures and equipment, equipment to support clinical treatment and technologies for vaccine manufacturing.

Engineers in India also made significant contributions, designing, prototyping and testing new hospital equipment in a few weeks, meeting regulatory requirements, including PPE gels and UV sanitisers and inexpensive throwaway bag respirators, through to supportive breathing devices with additional features, to full-scale ICU invasive ventilators. For example, Dr Pawan Goenka, Mechanical Engineer and Managing Director of automotive firm Mahindra and Mahindra, fast-tracked a major project to manufacture affordable respirators. The Tata Group and engineers in Tata Motors worked to build robots to sanitise hospitals. Other innovations developed at the Indian Institute of Science (IISc) and India Institute of Technology (IIT) Bombay include low-cost ventilators as well as sanitising equipment and processes using gels and UV light, the design and manufacture of 'tunnels', through which materials can be sanitised, and smaller mobile sanitisation units and portable room sanitiser for hospitals (Figure 3) [25].

Other innovations developed by Indian engineers include a drive through booth for COVID-19 testing, low cost PPE and masks and no-touch advanced washbasins [26].



Fig 3: The Dwaar Pro, a sanitising facility to allow students to enter the Indian Institute of Science [25]

Engineers around the world have also used 3D printing, consisting of direct manufacture of physical objects from digital models, to fabricate medical devices using low-cost materials and from complex geometries. This has enabled the supply of low cost masks, face shields, medical ventilator valves, clinical test kits and other personal protective equipment (PPE). For example, the start-up founder of Issinova, Christian Fracassi, developed a digital model of the Venturi valve that was required urgently in hospitals in Brescia, Italy, to supply oxygen and used 3D printing to fabricate these in two days, Fracassi and his team designed, tested and manufactured 100 valves for the hospital and saved many people's lives. The 3D printed valves were donated to the hospital (Figure 4) [27].



Fig 4: Original Venturi valve (left) and 3D printed Venturi valves. Source: [27]

3D printing has also been used to manufacture nasal swabs for COVID-19 testing kits, essential for the collection of biological samples to detect the corona virus and to manufacture several components of biosensors, including electrodes, substrates, parts for liquid handling and of devices [28]. Some of these innovations have been recognised with awards from the Royal Academy of Engineering, including a high-performance ventilator, a personal respirator for healthcare workers and an environment friendly face shield [29].

ARTIFICIAL INTELLIGENCE (AI) TO DETECT AND MANAGE THE CORONA VIRUS

AI applications to deal with the coronavirus pandemic include the early detection and diagnosis of infection; monitoring of treatments performed; tracking personal contacts of infected individuals; projection of cases and mortality; development of medicines and vaccines; and prediction of survival in severe cases of the disease. For example, AI is being used to detect COVID-19 from chest X-rays (Figure 5) [30, 31].

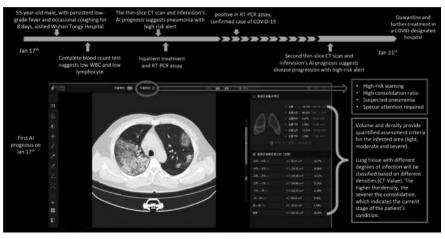


Fig 5: AI being used to detect Coronavirus from Chest X-rays. Photo: Ming-Ming Chen, China [31]

AI has also been used to identify molecular structures than can become effective vaccines [32], to optimise inpatient care [33] and for COVID-19 management including contact tracing [34].

My company iOmniscient, has developed iQ-FeverCheck, an AI-based multi-sensory capability instrument for crowded spaces such as airports, sports stadiums, railway stations and other public spaces as well as in hospitals, nursing and aged care homes and other health care facilities, where it is necessary to detect when individuals are suffering from a fever. The system can also be used to monitor and manage mask wearing, social distancing and limiting numbers of people in particular areas in an unobtrusive manner while maintaining privacy (**Figure 6**) [35].

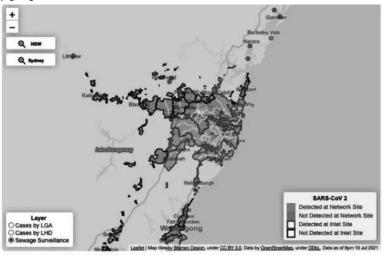


Fig 6: AI used for tracking and tracing people with fever in crowded public spaces [35]

An AI international vaccination certificate to authenticate if a person has been vaccinated has also been developed [36].

WASTEWATER SAMPLING TO MONITOR THE SPREAD OF CORONA VIRUS

Civil engineers at Stanford University have developed a process to test wastewater — a robust source of COVID-19 as those infected shed the virus in their stool-to track and supplement information on the spread of the virus. This is important for public health officials as they develop measures to combat the virus. The test works by identifying and measuring genetic material in the form of RNA from SARS-CoV-2, the virus that causes COVID-19. The trends in concentrations of SARS-CoV-2 RNA in wastewater aligns with trends of new COVID-19 infections in the community and is used by public health officials to manage outbreaks[37].For example, testing of wastewater to detect the virus is being used effectively in the state of New South Wales Australia and in public health messages and warnings. The map below is at 25 June 2021 (Figure 7) [38].



A map shows areas highlighted in red where Covid-19 has been detected in NSW. Source: NSW Health

Fig 7: Map showing spread of coronavirus in wastewater in New South Wales Australia by Local Government Authority (LGA), June 2021 [38]

Engineers in IIT Bombay and the University of Strathclyde have developed a low-cost sensor to detect the SARS-CoV-2 virus in wastewater. This low-cost technology can help several middle-to-low-income countries, who are struggling to control the prevalence of COVID-19. The project commenced in May 2021, led by Prof. Siddharth Tallur and Prof. Kiran Kondabagil at IIT Bombay. The sensor was tested with wastewater collected from a sewage treatment plant in Mumbai and can detect the genetic material at concentrations as low as ten pictograms per microlitre [39].

SOFTWARE AND COMMUNICATIONS ENGINEERING TO DEAL WITH COVID-19

The role of communications and software engineers were at the forefront of the battle against the coronavirus as billions were forced to work and study from home. The internet and communications technologies became essential to everyday life and engineers rapidly created new approaches to the accelerated digitisation of work and study [40].

Software engineers are also developing systems to manage the logistics of distribution and delivery of vaccines and websites and apps to manage registration, eligibility, and scheduling and integrate these into reminder and multipronged communication programs. Public health messaging is increasingly being provided through new technologies using social media, videos, and podcasts about COVID-related issues, including testing, recovery, and vaccination. All these require technical expertise and engineering. Clinicians from different health organizations require real-time access to its patients' vaccine information — helping to ensure that people receive their second dose of the right vaccine at the right time, while maintaining privacy and confidentiality [41].

The Indian Institute of Science and IIT Bombay are among leading engineering institutions that are developing software applications including for collecting anonymised data related to pandemic spread and virus tracing [42].

Technologies such as geospatial mapping has also been used to effectively trace the spread of the virus (Figure 8) [43].



Fig 8: Johns Hopkins University, Center for Systems Science and Engineering, Coronavirus Global Map, 24 June 2021, [43]

SUPPLY CHAIN LOGISTICS, DISTRIBUTION AND VACCINE DELIVERY

Needless to say, engineers are essential not only for the design of manufacturing facilities for the vaccine, but also for the logistics systems and cold storage required for the distribution of vaccines around the world.

The supply chain challenges for the delivery of the vaccine are the largest the world has seen[44]. In short, it is the biggest logistical challenge the world has ever seen with up to 100 million deliveries or more per month. Key elements for this supply chain are increased cold chain capacity, storage requirements at low temperatures and 'Last-Mile Delivery' logistics.

Cold chain capacity is one of the most important factors in distribution of any vaccine, but in the case of the Pfizer vaccine, which needs to be stored at below -70°C, this capability is lacking in many countries. Typically, cold supply chain carriers used to transport medical supplies operate roughly between two and eight degrees Celsius. This is fine for most vaccines, which are stored at around 4°C. However, requirements for the Pfizer vaccine are significantly different. This has implications for distribution in parts of South America, Asia, and Africa. Not only is the climate hotter in these areas, but the infrastructure to support such low temperature storage is lacking. For example, if a power outage causes refrigeration to fail, the vaccines would likely be rendered useless. Storage capabilities will be hampered further by the volumes required, given that these areas are home to over six billion people combined. Engineers will be needed to ensure access to reliable power supplies and for the construction of large scale refrigerated storage warehouses. Engineers are innovating in this area, for example the development of the reusable Credo Cube, available for minus 80°C, storage [45].

Last-mile delivery is a challenge due to the need for trained truck drivers and staff to deliver from port to end destination and the need to maintain cold temperatures. This situation becomes more acute in rural and regional centres. Once the vaccine arrives, there is the added complexity of different interval periods for a second dose and the process of prioritizing and tracking those who will be offered the vaccine.

RESILIENCE AND RESPONSE BY ENGINEERS FOR THE FUTURE

This paper has shown the work of engineers around the world in responding to the coronavirus pandemic. It is also important to develop engineering capacity to respond to future challenges. For example, the Royal Academy of Engineering [46] has recommended measures for national infrastructure resilience, strengthening cyber security to mitigate risks arising from large-scale remote working, ensuring entrepreneurial ecosystems survive and thrive and supply chain agility, to minimise disruptions and reduce vulnerabilities.

Engineers have impacted not only the responses to the health aspects of the pandemic but have generated innovations, for example in India, for facilitating technologies for telehealth, making

medical care accessible in regional locations [47, 48] and accelerated the implementation of contactless mobile payment systems [49]. These innovations have social, economic as well as health benefits.

Reflections on the year that changed the world include considerations of inequalities in terms of access to education [50], healthcare and vaccines. India is well placed to develop low cost innovations in healthcare [51, 52]. Engineers are also needed for infrastructure especially electricity, clean water and sanitation. For the future, it is essential to build resilience, including through accelerated digitalisation, rapid innovation and scale-up and importantly to address the need for more engineering skills and a diverse engineering workforce to take advantage of the opportunities created by the engineering responses to the pandemic [53].

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Dr Marlene Kanga is the Immediate Past President of World Federation of Engineering Organisations (WFEO), the peak body for engineering institutions internationally representing some 100 engineering institutions and approximately 30 million engineers. A Chemical Engineer, she was the 2013 National President of Engineers Australia. She is a Fellow of the Academy of Technology Science and Engineering Australia and a Fellow of The Institution of Engineers (India). She is a Member of the Order of Australia, a national honour, in recognition of her leadership of the engineering profession. During her term as WFEO President, Dr Kanga led the initiative for the member states at UNESCO to declare 4th March, the founding Day of WFEO as World Engineering Day. The inaugural World Engineering Day was held on 4th March 2020. Dr Kanga has been listed among the 100 engineers making a contribution to Australia in the last 100 years as part of Engineers Australia. Dr Kanga is a Board Member and non-executive Director of some of the largest organizations in Australia in the utilities, transport and innovation sectors. She is an Honorary Fellow of the Institution of Engineers Australia, an Honorary Fellow of the Institution of Chemical Engineers (UK) and a Foreign Fellow of the ASEAN Academy of Engineering and Technology

Corona Virus (COVID- 19): A Literature Survey

Background

The current COVID-19 pandemic is caused by a corona virus named SARS-CoV-2. Corona viruses (CoVs) are a large family of viruses, several of which cause respiratory diseases in humans, from the common cold to more rare and serious diseases such as the Severe Acute Respiratory Syndrome (SARS) and the Middle East respiratory syndrome (MERS), both of which have high mortality rates and were detected for the first time in 2003 and 2012, respectively.

CoVs are divided into four genera: alpha-, beta-, gamma- and delta-CoV. All CoVs currently known to cause disease in humans belong to the alpha- or the beta-CoV. Many of these CoVs can infect several animal species as well. SARS-CoV infected civet cats and infected humans in 2002 and MERS-CoV is found in dromedary camels and infected humans in 2012. A virus that is regularly transmitted from an animal to a human is called a zoonotic virus. When a virus passes from animals to humans for the first time it is called a spillover event.

To identify the source or origin of a virus, it is helpful to look at the genetic makeup of the virus and see whether it resembles other known viruses. This may provide some clues as to its origin. Viruses that are genetically closely linked tend to come from a similar source or similar geographic area. SARS-CoV-2, the virus responsible for COVID-19, belongs to a group of genetically related viruses that includes SARS-CoV and a number of other CoVs isolated from bat populations. MERS-CoV also belongs to this group but is less closely related.

It is also necessary to investigate and interview in depth the first known human cases of the disease for indications as to where they may have become infected. This may help identify earlier possible cases and narrow the geographical areas and timeframes so that more specific investigations could be performed to identify the source.

Currently, the zoonotic source of SARS-CoV-2 is unknown. The first human cases of COVID-19, the coronavirus disease caused by SARS-CoV-2, were first reported from Wuhan City, China, in December 2019.

Structure and Genome of Corona Viruses

All SARS-CoV-2 isolated from humans to date are closely related genetically to corona viruses isolated from bat populations, specifically, bats from the genus Rhinolophus. SARS-CoV, the cause of the SARS outbreak in 2003, is also closely related to corona viruses isolated from bats.

These close genetic relations suggest that they all have their ecological origin in bat populations. Bats in the Rhinolophus genus are found across Asia, Africa, the Middle East, and Europe. SARS-CoV-2 is not genetically related to other known corona viruses found in farmed or domestic animals. The analysis of the virus genome sequences also indicates that SARS-CoV-2 is very well adapted to human cell receptors, which enables it to invade human cells and easily infect people [Fig 1].

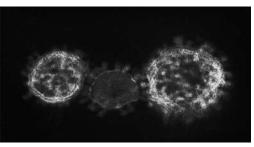


Fig. 1: Colorized transmission electron micrograph showing particles of the Middle East respiratory syndrome corona virus that emerged in 2012: Credit: NIAID

Corona viruses are spherical enveloped viruses containing a single strand of positive-sense RNA (similar to host mRNA) of approximately 26 to 32 kb.10 Their defining morphologic features are club-shaped projections from the viral envelope resembling a crown or a solar corona and made of a highly glycosylated protein named spike protein. Their other three structural proteins are the envelope, membrane, and nucleocapsid proteins as shown in Fig. 2.

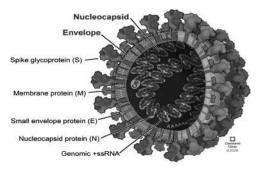


Fig 2: Structure of corona viruses [Courtesy: http://www.clevelandclinic.org]

The first two-thirds of the genome consists of two large overlapping open reading frames that encode 16 nonstructural proteins, including proteases, RNA-dependent RNA polymerase (prRdRp), RNA helicase, primase, and others, that form the viral replicase complex, a platform to propagate viral mRNAs.

All the published genetic sequences of SARS-CoV-2 isolated from human cases are very similar, suggesting that the start of the outbreak resulted from a single point introduction in the human population around the time that the virus was first reported in humans in Wuhan, China. The analyses of the published genetic sequences further suggest that the spillover from an animal source to humans happened during the last quarter of 2019.

First known Human COVID-19 Cases

As soon as the first cases of COVID-19 were reported in late December 2019, investigations were conducted to understand the epidemiology of COVID-19 and the original source of the outbreak. A large proportion of the initial cases in late December 2019 and early January 2020 had a direct link to the Huanan Wholesale Seafood Market in Wuhan City, where seafood, wild, and farmed animal species were sold. Many of the initial patients were either stall owners, market employees, or regular visitors to this market. Environmental samples taken from this market in December 2019 tested positive for SARS-CoV-2, further suggesting that the market in Wuhan City was the source of this outbreak or played a role in the initial amplification of the outbreak. The market was closed on January 01, 2020 and was cleaned and disinfected. The virus could have been introduced into the human population from an animal source in the market or an infected human could have introduced the virus to the market and the virus may have then been amplified in the market environment.

Subsequent investigations into the first human cases have determined that they had onset of symptoms around December 01, 2019. However, these cases had no direct link to the Huanan Wholesale Seafood Market and they may therefore have been infected in November through contact with earlier undetected cases (incubation time between date of exposure and date of symptom onset can be up to 14 days). Additional studies are ongoing to as whether unrecognized infections in humans may have happened as early as mid-November 2019.

SARS-CoV, the virus that caused the SARS outbreak in 2003 and probably also had its ecological reservoir in bats, jumped from an animal reservoir (civet cats, a farmed wild animal) to humans and then spread between humans. In a similar way, it is thought that SARS-CoV-2 jumped the species barrier and initially infected humans from another animal host. Since there is usually very limited close contact between humans and bats, it is more likely that transmission of SARS-CoV-2 to humans happened through an intermediate host, that is another animal species more likely to be handled by humans. This intermediate animal host could be a domestic animal, a wild animal, or a domesticated wild animal and, as of yet, has not been identified.

A number of investigations in the area believed to be the source of the outbreak in China are currently underway or planned. These include investigations of human cases with symptom onset in and around Wuhan in late 2019, environmental sampling from markets and farms in areas where the first human cases were identified, and detailed records on the source and type of wildlife species and farmed animals sold in these markets.

Symptoms

COVID-19 affects different people in different ways. Most infected people will develop mild to moderate illness and recover without hospitalization.

Most common symptoms:

- fever.
- dry cough.
- tiredness.

Less common symptoms:

- aches and pains.
- sore throat.
- diarrhoea.
- conjunctivitis.
- headache.
- loss of taste or smell.
- a rash on skin, or discolouration of fingers or toes.

Serious symptoms:

- difficulty breathing or shortness of breath.
- chest pain or pressure.
- loss of speech or movement.

On average it takes 5–6 days from when someone is infected with the virus for symptoms to show, however it can take up to 14 days.

Testing

Tests for COVID-19 can be divided into antigen or antibody tests, both of which use different kinds of samples to search for different hallmarks of the SARS-CoV-2 virus.

Over the course of the COVID-19 crisis, the importance of reliable, accessible testing to screen for the disease has become increasingly apparent. Tests for COVID-19 can be divided into antigen or antibody tests, both of which use different kinds of samples to search for different hallmarks of the SARS-CoV-2 virus. Medical Device Network takes a closer look at the different types of COVID-19 test.

Types of COVID-19 Test

- Polymerase chain reaction (PCR) tests are sent away to a lab to diagnose disease
- Lateral flow tests (LFTs) can diagnose COVID-19 on the spot, but aren't as accurate as PCR tests
- Antibody (or serology) tests can't diagnose active infection, but they can help to tell if a person has immunity to COVID-19

PCR Testing

PCR tests are used to directly screen for the presence of viral RNA, which will be detectable in the body before antibodies form or symptoms of the disease are present. This means the tests can tell whether or not someone has the virus very early on in their illness.

During COVID-19 PCR testing, substances known as reverse transcriptase or DNA polymerase are added to a nasopharyngeal sample in a lab. These substances work to make numerous copies of any viral RNA that may be present. This is so that enough copies of the RNA are present to signal a positive result, as specifically designed primers and probes attach themselves to sequences of the genetic code of the virus to signal that a pathogen has been found.

By scaling PCR testing to screen vast swathes of nasopharyngeal swab samples from within a population, public health officials can get a clearer picture of the spread of a disease COVID-19.

However, PCR still has its caveats. These types of COVID-19 test need to be sent away to a laboratory for analysis, meaning it can take days for people to find out their results.

False negatives can occur up to 30% of the time with different PCR tests, meaning they're more useful for confirming the presence of an infection than giving a patient the all-clear. They can also provide false positive results, as they're so sensitive they can potentially signal a positive result upon detecting dead, deactivated virus still present in the body of someone who has recovered from COVID-19.

During the course of the outbreak, the PCR testing has been refined from the initial testing procedures and with the addition of greater automation to reduce errors. The swabs are taken

from people, who have lots of other organisms floating around, it is essentially dealing with the question of how 'right' the result is.

Lateral Flow Test

LFTs are similar to PCR tests, in that they're both types of antigen test, designed to pick up active COVID-19 infection rather than antibodies to the disease. With a COVID-19 LFT, a nasopharyngeal sample is placed on a small absorbent pad, which is then drawn along the pad via a capillary line to a strip coated in antibodies, which bind to SARS-Cov-2 proteins. If these proteins are present, this will show as a coloured line on the test, indicating infection.

The major benefit of LFTs over PCRs is that they do not need to be sent away for confirmation, and instead provide results within 15 to 30 min. However, what they gain in speed they sacrifice in accuracy.

A review of studies from Europe and the US showed a wide variance in accuracy between different brands of LFT. The review also found that the tests were far better at identifying COVID-19 in people who had symptoms than those who did not. LFT sensitivity in symptomatic people ranged from 34% to 88%, with an average accuracy of 72%. In people without symptoms the LFTs correctly identified an average of 58% of those who were infected.

While the use of LFTs for mass asymptomatic screening has been encouraged in countries like the UK, experts have cast doubt on how useful these types of COVID-19 test really are in this context.

Antibody Testing

A study suggests that Immunity found in people who recover from even mild cases of COVID-19 produce antibodies for at least five to seven months, and could do so for much longer.

Studies have indicated that people who survived SARS outbreak in the early 2000s had antibodies in their blood for years after recovery. Both SARS and COVID-19 are caused by similar corona viruses, so it's not unreasonable to think that COVID-19 could have a similar effect.

If there's a high enough level of people in the population who have immunity, they will then stop this virus from circulating within the population, which is known as herd immunity.

Unlike PCR tests, which commonly use swabs to detect COVID-19, blood samples are usually used for antibody tests. This is because there will be a very small amount of COVID-19 circulating in the blood compared to the respiratory tract, but a significant and measurable antibody presence in the blood following infection. Antibody tests are being used to evaluate the immune responses in people who have been vaccinated against COVID-19.

CBNAAT Testing

Considered the gold standard for COVID tests, the RT-PCR can take a day to declare results and involves sample collections and testing. Although it runs the advantage of testing almost 92 samples at a time, CBNAAT is much quicker and produces results within 45 min.

This runs on the same technology of nasal and oral swabs except that the testing method is rapid and can take 45 minutes or even lesser if results are positive while the RT-PCR test takes more time due to its testing method. For an effective COVID filter the tests are needed that can enable regimens that will capture most infections while they are still infectious and with a shorter sample-result time.

The advantage of CBNAAT or TrueNAT(Indian variant) is that the machines are available across the country even in the remotest places. CBNAAT was also used in the National Tuberculosis Control program. Based on the cartridges system, the COVID cartridge was launched recently and is being used rampantly across the world.

PREVENTION

Ministry of Health and Family Welfare, Government of India issued symptoms and prevention in pictorial form to make population aware of prevention from Corona virus dieses. The same is shown in Fig 3.



Fig 3: Novel Corona Virus [Courtesy: Ministry of Health and Family Welfare, Govt of India] To prevent infection and to slow transmission of COVID-19, do the following:

• Wear proper mask

- Wash your hands regularly with soap and water, or clean them with alcohol-based hand rub.
- Maintain at least 1 metre distance between you and people coughing or sneezing.
- Avoid touching your face.
- Cover your mouth and nose when coughing or sneezing.
- Stay home if you feel unwell.
- Refrain from smoking and other activities that weaken the lungs.
- Practice physical distancing by avoiding unnecessary travel and staying away from large groups of people.

Therapeutic Management of Adults with COVID-19

Two main processes are thought to drive the pathogenesis of COVID-19. Early in the clinical course, the disease is primarily driven by replication of SARS-CoV-2. Later in the clinical course, the disease appears to be driven by a dysregulated immune/inflammatory response to SARS-CoV-2 that leads to tissue damage. Based on this understanding, it is anticipated that antiviral therapies would have the greatest effect early in the course of the disease, while immunosuppressive/anti-inflammatory therapies are likely to be more beneficial in the later stages of COVID-19.

No therapy has been proven to be beneficial in outpatients with mild to moderate COVID-19 who are not at high risk for disease progression. The COVID-19 Treatment Guidelines Panel (the Panel) recommends providing supportive care and symptomatic management to outpatients with COVID-19; steps should also be taken to reduce the risk of SARS-CoV-2 transmission to others. Patients should be advised about when to seek in-person evaluation.

In outpatients with mild to moderate COVID-19 who are at high risk for disease progression, anti-SARS-CoV-2 antibody-based therapies may have the greatest potential for clinical benefit during the earliest stages of infection. For these patients, the Panel recommends administering **bamlanivimab plus etesevimab (AIIa)** or **casirivimab plus imdevimab (AIIa)**, both of which are available through Emergency Use Authorizations (EUAs) from the Food and Drug Administration (FDA).

Remdesivir, an antiviral agent, is currently the only drug that is approved by the FDA for the treatment of COVID-19. It is recommended for use in hospitalized patients who require supplemental oxygen. However, it is not routinely recommended for patients who require mechanical ventilation due to the lack of data showing benefit at this advanced stage of the disease [Fig 4].

Dexamethasone, a corticosteroid, has been found to improve survival in hospitalized patients who require supplemental oxygen, with the greatest benefit observed in patients who require mechanical ventilation. Therefore, the use of dexamethasone is strongly recommended in this setting.

Adding tocilizumab, a recombinant humanized anti-interleukin-6 receptor monoclonal antibody, to dexamethasone therapy was found to improve survival among patients who were exhibiting rapid respiratory decompensation due to COVID-19. The following Figure shows pharmacologic management of patients with COVID 19 based on disease severity.

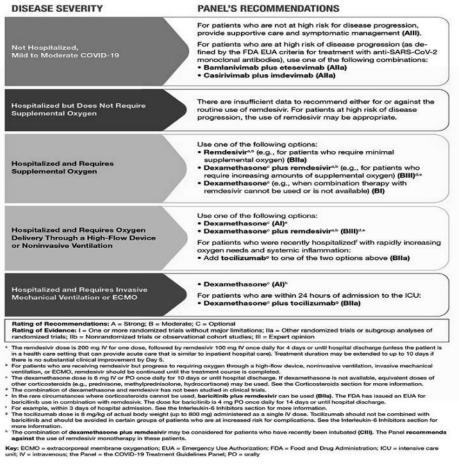


Fig 4: Pharmacologic Management of Patients with COVID-19 based on Disease Severity Doses and durations are listed in the footnotes.

Patients with Mild to Moderate COVID-19 who are not Hospitalized

The experts have following recommendations

For patients who are not at high risk of disease progression:

• The Panel recommends providing supportive care and symptomatic management (AIII).

For patients who are at high risk of disease progression, as defined by the EUA criteria for treatment with anti-SARS-CoV-2 monoclonal antibodies:

- The Panel recommends using one of the following combination anti-SARS-CoV-2 monoclonal antibodies (treatments are listed in alphabetical order):
- o Bamlanivimab 700 mg plus etesevimab 1,400 mg (AIIa)
- o Casirivimab 1,200 mg plus imdevimab 1,200 mg (AIIa).
- Treatment should be started as soon as possible after the patient receives a positive result on a SARS-CoV-2 antigen test or a nucleic acid amplification test and within 10 days of symptom onset.

Patients who are Hospitalized with Moderate COVID-19 but who do not Require Supplemental Oxygen

- The recommendations against the use of **dexamethasone** or other **corticosteroids (AIIa)**. Patients who are receiving dexamethasone or another corticosteroid for other indications should continue therapy for their underlying conditions as directed by their health care provider.
- There are insufficient data to recommend either for or against the routine use of remdesivir in these patients. The use of remdesivir may be appropriate in patients who have a high risk of disease progression.

In the Randomised Evaluation of COVID-19 Therapy (RECOVERY) trial, a multicenter, openlabel trial in the United Kingdom, hospitalized patients with COVID-19 were randomized to receive either dexamethasone plus standard of care or standard of care alone (control arm). In the subgroup of participants who did not require supplemental oxygen at enrollment, no survival benefit was observed for dexamethasone. 17.8% of participants in the dexamethasone arm and 14% in the control arm died within 28 days of enrollment (rate ratio 1.19; 95% CI, 0.91–1.55). Based on the data, the Panel recommends against the use of dexamethasone (AIIa) or other corticosteroids (AIII) for the treatment of COVID-19 in this subgroup, unless the patient has another indication for corticosteroid therapy. Experts Opinion on Rationale use of Remdesivir

The Adaptive COVID-19 Treatment Trial (ACTT-1) was a multinational randomized controlled trial that compared remdesivir to placebo in hospitalized patients with COVID-19. Remdesivir showed no significant benefit in patients with mild to moderate disease, which was defined as oxygen saturation >94% on room air or a respiratory rate <24 breaths/min without supplemental oxygen (rate ratio for recovery 1.29; 95% CI, 0.91–1.83); however, there were only 138 patients in this group.

For Hospitalized Patients with COVID-19 who Require Supplemental Oxygen but who do not Require Oxygen Delivery through a High-Flow Device, Noninvasive Ventilation, Invasive Mechanical Ventilation, or Extracorporeal Membrane Oxygenation

The recommendations are one of the following options for these patients:

- Remdesivir (e.g., for patients who require minimal supplemental oxygen) (BIIa);
- Dexamethasone plus remdesivir (e.g., for patients who require increasing amounts of oxygen) (BIII); or
- **Dexamethasone** (e.g., when combination therapy with remdesivir cannot be used or is not available) **(BI)**.

Additional Considerations

- If dexamethasone is not available, an alternative corticosteroid such as **prednisone**, **methylprednisolone**, or **hydrocortisone** can be used **(BIII)**. See Corticosteroids for dosing recommendations.
- In the rare circumstances when corticosteroids cannot be used, **baricitinib plus remdesivir** can be used (**BIIa**). Baricitinib **should not be used** without remdesivir.
- There is insufficient evidence to determine which patients in this group would benefit from adding tocilizumab to dexamethasone treatment. Some Panel members would add tocilizumab to a patient's dexamethasone treatment in cases where the patient has rapidly increasing oxygen needs and C-reactive protein (CRP) levels ≥75 mg/L but does not yet require oxygen through high-flow nasal canula (HFNC) or noninvasive ventilation.

For Hospitalized Patients with COVID-19 who Require Delivery of Oxygen through a High-Flow Device or Noninvasive Ventilation but not Invasive Mechanical Ventilation or Extracorporeal Membrane Oxygenation

- The recommendations are one of the following options for these patients:
 - o Dexamethasone alone (AI); or
 - o A combination of dexamethasone plus remdesivir (BIII).
- For patients who were recently hospitalized and who have rapidly increasing oxygen needs and systemic inflammation, add **tocilizumab** to one of the two options above **(BIIa)**.

Additional Considerations

- The combination of dexamethasone and remdesivir has not been rigorously studied in clinical trials. Because there are theoretical reasons for combining these drugs, the Panel considers both dexamethasone alone and the combination of remdesivir and dexamethasone to be acceptable options for treating COVID-19 in this group of patients.
- The recommendations **against** the use of **remdesivir alone** because it is not clear whether remdesivir confers a clinical benefit in this group of patients (AIIa).
- For patients who initially received remdesivir monotherapy and progressed to requiring high-flow oxygen or noninvasive ventilation, dexamethasone should be initiated and remdesivir should be continued until the treatment course is completed.
- If dexamethasone is not available, equivalent doses of other corticosteroids such as **prednisone, methylprednisolone**, or **hydrocortisone** may be used **(BIII)**.
- In the rare circumstances where corticosteroids cannot be used, **baricitinib plus remdesivir** can be used (**BIIa**). Baricitinib **should not be used** without remdesivir.
- Tocilizumab should be given only in combination with dexamethasone (or another corticosteroid at an equivalent dose).
- Some clinicians may choose to assess a patient's clinical response to dexamethasone before deciding whether tocilizumab is needed.
- Although some patients in the Randomised, Embedded, Multifactorial Adaptive Platform Trial for Community-Acquired Pneumonia (REMAP-CAP) and RECOVERY trials received a second dose of tocilizumab at the discretion of their treating physicians, there

are insufficient data to determine which patients, if any, would benefit from an additional dose of the drug.

• The combination of dexamethasone and tocilizumab may increase the risk of opportunistic infections or reactivation. Prophylactic treatment with ivermectin should be considered for patients who are from areas where strongyloidiasis is endemic.

Vaccination

Vaccines are supported by decades of medical research. They work by preparing the body's own immune system to recognise and defend against a specific disease. The volume of information available about vaccination can be overwhelming, so it's important to talk through the topic.

Typically, many vaccine candidates will be evaluated before any are found to be both safe and effective. For example, of all the vaccines that are studied in the lab and laboratory animals, roughly 7 out of every 100 will be considered good enough to move into clinical trials in humans. Of the vaccines that do make it to clinical trials, just one in five is successful. Having lots of different vaccines in development increases the chances that there will be one or more successful vaccines that will be shown to be safe and efficacious for the intended prioritized populations.

The Different Types of Vaccines

There are three main approaches to designing a vaccine. Their differences lie in whether they use a **whole** virus or bacterium; just the **parts** of the germ that triggers the immune system; or just the **genetic material** that provides the instructions for making specific proteins and not the whole virus [Fig 5].

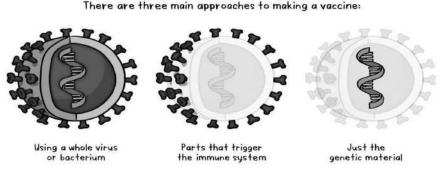


Fig 5: Approaches to designing a vaccine

The Whole-microbe Approach

Inactivated Vaccine

The first way to make a vaccine is to take the disease-carrying virus or bacterium, or one very similar to it, and inactivate or kill it using chemicals, heat or radiation. This approach uses technology that's been proven to work in people – this is the way the flu and polio vaccines are made – and vaccines can be manufactured on a reasonable scale.

However, it requires special laboratory facilities to grow the virus or bacterium safely, can have a relatively long production time, and will likely require two or three doses to be administered.

Live-attenuated Vaccine

A live-attenuated vaccine uses a living but weakened version of the virus or one that's very similar. The measles, mumps and rubella (MMR) vaccine and the chickenpox and shingles vaccine are examples of this type of vaccine. This approach uses similar technology to the inactivated vaccine and can be manufactured at scale. However, vaccines like this may not be suitable for people with compromised immune systems.

Viral Vector Vaccine

This type of vaccine uses a safe virus to deliver specific sub-parts – called proteins – of the germ of interest so that it can trigger an immune response without causing disease. To do this, the instructions for making particular parts of the pathogen of interest are inserted into a safe virus. The safe virus then serves as a platform or vector to deliver the protein into the body. The protein triggers the immune response. The Ebola vaccine is a viral vector vaccine and this type can be developed rapidly [Fig 6].

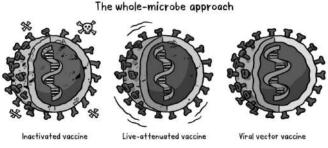
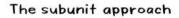


Fig 6: Three types of whole microbe approach

Subunit Approach

A subunit vaccine is one that only uses the very specific parts (the subunits) of a virus or bacterium that the immune system needs to recognize. It doesn't contain the whole microbe or use a safe virus as a vector. The subunits may be proteins or sugars. Most of the vaccines on the childhood schedule are subunit vaccines, protecting people from diseases such as whooping cough, tetanus, diphtheria and meningococcal meningitis [Fig 7].





Only uses the very specific parts (the subunits) of a virus or bacterium that the immune system needs to recognize.

Fig 7: Subunit Approach

The Genetic Approach (Nucleic Acid Vaccine)

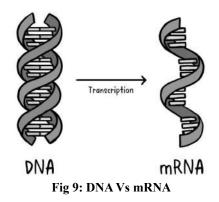
Unlike vaccine approaches that use either a weakened or dead whole microbe or parts of one, a nucleic acid vaccine just uses a section of genetic material that provides the instructions for specific proteins, not the whole microbe. DNA and RNA are the instructions our cells use to make proteins. In human body cells, DNA is first turned into messenger RNA, which is then used as the blueprint to make specific proteins.

The genetic approach (nucleic acid vaccine)



Uses the genetic material for specific proteins - the DNA or RNA.

Fig 8: Genetic Approach for vaccine



A nucleic acid vaccine delivers a specific set of instructions to our cells, either as DNA or mRNA, for them to make the specific protein that we want our immune system to recognize and respond to [Fig 8].

The nucleic acid approach is a new way of developing vaccines. Before the COVID-19 pandemic, none had yet been through the full approvals process for use in humans, though some DNA vaccines, including for particular cancers, were undergoing human trials. Because of the pandemic, research in this area has progressed very fast and some mRNA vaccines for COVID-19 are getting emergency use authorization, which means they can now be given to people beyond using them only in clinical trials.

Company	Doses	1	Storage	
RNA				
Pfizer (BioNTech)	11	۵	-80 to -60°C (6 months) and 2 to 8°C (for up to 5 days)	
Moderna	11	ā	-25 to -15°C (6 months) and 2 to 8°C (for 30 days)	
Viral vector				
Oxford-AstraZeneca	11	6	2 to 8°C (6 months)	
Sputnik V (Gamaleya)	11	6	-18.5°C (liquid form) 2 to 8°C (dry form)	
Johnson & Johnson (Janssen)	1	6	2 to 8°C (3 months)	
Inactivated virus				
CoronaVac (Sinovac)	11	۵	2 to 8°C	
Sinopharm	11	ā	2 to 8°C	
Covaxin (Bharat Biotech)	11	ā	2 to 8°C	
Protein-based	\$	1		
	11	6	2 to 8°C	
ource: Wellcome Trust, BBC	research	1	88	

Fig 10: Clinical Trial in Various Countries

Side Effects of COVID-19 Vaccines

Vaccines are designed to give you immunity without the dangers of getting the disease. It's common to experience some mild-to-moderate side effects when receiving vaccinations. This is because your immune system is instructing your body to react in certain ways: it increases blood flow so more immune cells can circulate, and it raises your body temperature in order to kill the virus.

Mild-to-moderate side effects, like a low-grade fever or muscle aches, are normal and not a cause for alarm: they are signs that the body's immune system is responding to the vaccine, specifically the antigen (a substance that triggers an immune response), and is gearing up to fight the virus. These side effects usually go away on their own after a few days.

Common and mild or moderate side effects are a good thing: they show us that the vaccine is working. Experiencing no side effects doesn't mean the vaccine is ineffective. It means everybody responds differently. Study has been conducted in India which recommended any marginal side effects in India the observation

Common Side Effects of COVID-19 Vaccines

Like any vaccine, COVID-19 vaccines can cause side effects, most of which are mild or moderate and go away within a few days on their own. As shown in the results of clinical trials, more serious or long-lasting side effects are possible. Vaccines are continually monitored to detect adverse events.

Reported side effects of COVID-19 vaccines have mostly been mild to moderate and have lasted no longer than a few days. Typical side effects include pain at the injection site, fever, fatigue, headache, muscle pain, chills and diarrhoea. The chances of any of these side effects occurring after vaccination differ according to the specific vaccine.

COVID-19 vaccines protect against the SARS-CoV-2 virus only, so it's still important to keep yourself healthy and well.

Experts are collecting Data on performance and efficacy of vaccines for protection against virus for long period of time. Artificial Intelligence is being used for Data analytic and its impact.

Less Common Side Effects

Upon receiving the vaccine, a person should be requested to stay for 15–30 minutes at the vaccination site so health workers are available in case of any immediate reactions. Individuals should alert their local health providers following vaccination if they experience any unexpected side effects or other health events – such as side effects lasting more than three days. Less common side effects reported for some COVID-19 vaccines have included severe allergic reactions such as anaphylaxis; however, this reaction is extremely rare.

National authorities and international bodies, including WHO, are closely monitoring for any unexpected side effects following COVID-19 vaccine use.

Long-term Side Effects

Side effects usually occur within the first few days of getting a vaccine. Since the first mass vaccination programme started in early December 2020, hundreds of millions of vaccine doses have been administered.

There have been concerns about COVID-19 vaccines making people sick with COVID-19. But none of the approved vaccines contain the live virus that causes COVID-19, which means that COVID-19 vaccines cannot make you sick with COVID-19.

After vaccination, it usually takes a few weeks for the body to build immunity against SARS-CoV-2, the virus that causes COVID-19. So it's possible a person could be infected with SARS-CoV-2 just before or after vaccination and still get sick with COVID-19. This is because the vaccine has not yet had enough time to provide protection.

Experiencing side effects after getting vaccinated means the vaccine is working and your immune system is responding as it should. Vaccines are safe, and getting vaccinated will help protect you against COVID-19.

Impact to the New Variants of COVID-19 Virus have on Vaccines

The COVID-19 vaccines that are currently in development or have been approved are expected to provide at least some protection against new virus variants because these vaccines elicit a broad immune response involving a range of antibodies and cells. Therefore, changes or mutations in the virus should not make vaccines completely ineffective. In the event that any of these vaccines prove to be less effective against one or more variants, it will be possible to change the composition of the vaccines to protect against these variants.

Data continues to be collected and analysed on new variants of the COVID-19 virus. WHO is working with researchers, health officials and scientists to understand how these variants affect the virus's behaviour, including their impact on the effectiveness of vaccines, if any. WHO's Disease Outbreak News to get up-to-date information on the impact of COVID-19 virus variants on the effectiveness of the different vaccines. This is an area where the evidence remains preliminary and is developing quickly.

At the learning stage, it is need to do everything possible to stop the spread of the virus in order to prevent mutations that may reduce the efficacy of existing vaccines. In addition, manufacturers and the programmes using the vaccines may have to adjust to the evolution of the COVID-19 virus: for example, vaccines may need to incorporate more than one strain when in development, booster shots may be required, and other vaccine changes may be needed. Trials must also be designed and maintained to allow any changes in efficacy to be assessed, and must be of sufficient scale and diversity to enable clear interpretation of results. Studies of the impact of vaccines as they are deployed are also essential in order to understand their impact.

Impact of Virus Variants on the Efficacy of COVID-19 Vaccines

Research groups have carried out genomic sequencing of the COVID-19 virus and shared these sequences on public databases, including GISAID. This global collaboration allows scientists to better track how the virus is changing. WHO recommends that all countries increase the sequencing of the COVID-19 virus where possible and share data to help one another monitor and respond to the evolving pandemic.

WHO has also established a SARS-CoV-2 Risk Monitoring and Evaluation Framework to identify, monitor and assess variants of concern. It will involve components like surveillance, research on variants of concern, and evaluation of the impact on diagnostics, therapeutics and vaccines. The framework will serve as a guide for manufacturers and countries on changes that may be needed for COVID-19 vaccines.

Prevention of Future New Variants of the COVID-19 Virus

Stopping the spread at the source remains key. Current measures to reduce transmission – including frequent hand washing, wearing a mask, physical distancing, good ventilation and avoiding crowded places or closed settings – continue to work against new variants by reducing the amount of viral transmission and therefore also reducing opportunities for the virus to mutate.

Scaling up vaccine manufacturing and rolling out vaccines as quickly and widely as possible will also be critical ways of protecting people before they are exposed to the virus and the risk of new variants. Priority should be given to vaccinating high-risk groups everywhere to maximize global protection against new variants and minimize the risk of transmission. Moreover, ensuring equitable access to COVID-19 vaccines is more critical than ever to address the evolving pandemic. As more people get vaccinated, we expect virus circulation to decrease, which will then lead to fewer mutations.

Vaccines are a critical tool in the battle against COVID-19, and there are clear public health and lifesaving benefits to using the tools we already have. It should not put off getting vaccinated

because of our concerns about new variants, and proceed with vaccination even if the vaccines may be somewhat less effective against some of the COVID-19 virus variants. It is needed to use the tools in hand even while continuation to improve those tools. All are safe only if everyone is safe. Worldwide experts are involved in data analytics for different variants however no conclusive evidence for new variants till date.

Specific Case Study of Singapore's New Plan to 'Live with COVID'

The country has been one of the world's most successful at combating COVID-19 has announced it will soon fundamentally change how it manages the pandemic. The city state of Singapore has stated COVID will be treated like other endemic diseases such as flu. **There will be no goals of zero transmission.** Quarantine will be dumped for travellers and close contact of cases will not have to isolate. It also plans to no longer announce daily case numbers. But you may need to take tests to head to the shops or go to work.

It means that the virus will continue to mutate, and thereby survive in our community.

Like most countries, Singapore had an initial peak of cases last year, topping out at 600 cases a day in mid-April. Following a smaller wave in August, COVID-19 hasn't flared up since. However, the nation of 5.7 million, slightly larger than Sydney, has had a steady undercurrent of around 20-30 cases every day. The nation has recorded 35 deaths in total. Singapore has strict border controls in place with most countries including tests on arrival, hotel quarantine and stay at home orders. It's not dissimilar to Australia, but Singapore varies the demands on travellers depending on the risk in the location where they last visited. Every year, many people catch the flu. The overwhelming majority recover without needing to be hospitalised, and with little or no medication. But a minority, especially the elderly and those with comorbidities, can get very ill, and some succumb. Vaccination was key. The road map out of the current measures couldn't begin until more people had been jabbed. Testing would also have to be easier and quicker. Selfadministered tests, such as breathalysers, should replace the uncomfortable ear bud down the back of the throat method.

Coronavirus Modeling, Impact on India's Pandemic Response

Four months since the first case of COVID-19 in Wuhan, China, the SARS-CoV-2 virus has engulfed the world and COVID-19 has been declared a global pandemic. The number of confirmed cases worldwide stands at a staggering 303,594 (as of 6:00 PM EST March 21, 2020, Microsoft bing coronavirus tracker). Of these, only 315 confirmed cases are from India (Figure 11), the world's largest democracy with a population of 1.34 billion (compare China at 1.39 billion and USA at 325.7 million).

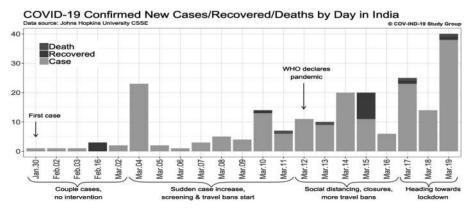


Fig 11. Description of the cases, recovered and fatalities in India with landmark policy/recommendations

Fig. 11 is shown the case study for combating COVID 19 by India in year 2020. However after second wave India response has improved and India has vaccinated more than 75 crore people till 15 September 2021.

India is being vigilant and wise in instituting the right public health interventions at the right time including sealing the borders with travel ban/canceling almost all visas, closing schools and colleges in certain states and diligently following up with community inspection of suspected/ exposed cases with respect to adherence of quarantine recommendations. While India seems to have done well in controlling the number of confirmed cases compared to other countries in the early phase of the pandemic.

The COVID-19 pandemic in India is a part of the worldwide pandemic of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The first case of COVID-19 in India, which originated from China, was reported on 30 January 2020. Currently, India has the largest number of confirmed cases in Asia. As of 12 June 2021, India has the second-highest number of confirmed cases in the world (after the United States) with 29.3 million reported cases of COVID-19 infection and the third-highest number of COVID-19 deaths (after the United States and Brazil) at 367,081 deaths.

The first cases of COVID-19 in India were reported in the towns of Thrissur, Alappuzha and Kasargod, all in the state of Kerala, among three Indian medical students who had returned from Wuhan. Lockdowns were announced in Kerala on 23 March, and in the rest of the country on 25 March. By mid-May 2020, five cities accounted for around half of all reported cases in the country: Mumbai, Delhi, Ahmedabad, Chennai and Thane [Fig 12]. On 10 June, India's recoveries exceeded active cases for the first time. Infection rates started to drop in September,

along with the number of new and active cases [Fig. 13 & Fig. 14]. Daily cases peaked mid-September with over 90,000 cases reported per-day, dropping to below 15,000 in January 2021. (First wave)

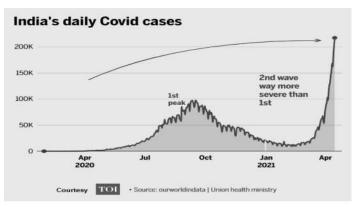


Fig 12: Comparision of Peak of COVID cases in 1st Wave and 2nd Wave in India

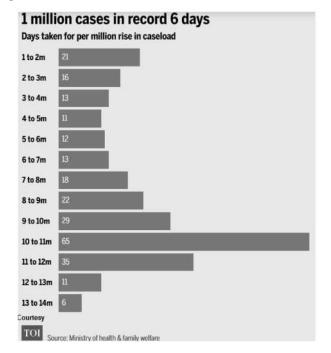


Fig 13: India Caseload per million

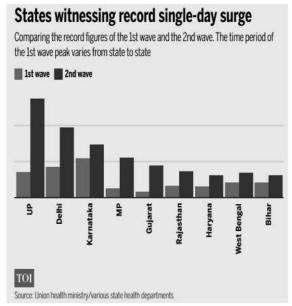


Fig 14: State wise comparison of first wave Vs Second wave

A second wave beginning in March 2021 was much larger than the first, with shortages of vaccines, hospital beds, oxygen cylinders and other medicines in parts of the country. By late April, India led the world in new and active cases. On 30 April 2021, it became the first country to report over 400,000 new cases in a 24-hour period. Health experts believe that India's figures have been underreported due to several factors.

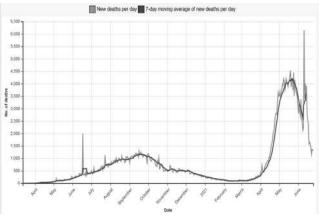
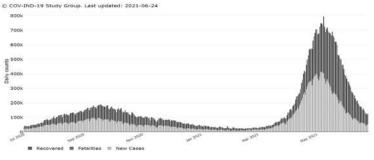


Fig 15: Trends of Virus in India

The COV-IND-19 shiny app aim to provide a resource to describe the COVID-19 outbreak in India to date as well as prediction models under various hypothetical scenarios. The figure and forecasting models update as new data becomes available (i.e., at least daily).

Daily number of new COVID-19 cases, fatalities and recovered in India based on COV-IND-19 shiny app data analytic are pictorically represented in figure below:



Cases© COV-IND-19 Study Group. Last updated: 2021-06-24

Fig 16: Analytical data band on COVID-19 app.

Cases© COV-IND-19 Study Group. Last updated: 2021-06-24

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COVID-19 Social Vaccine Toolkit (C19-SVT)

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ABSTRACT

COVID-19 Social Vaccine Toolkit (C19-SVT) addresses social and behavioral modalities which to combat the corona virus. The users become aware of number of measures which include social distancing, use of masks, sanitisation etc. The C19-SVT further introduce the awareness of various prophylactic tasks to combat the COVID-19. Unlike a biological vaccine, the C19- SVT prevents the spread of COVID-19 infection through knowledge dissemination and training skill sets, that are mandatory. A person who has better understanding of how the corona virus spreads, symptoms of the disease, social distancing measures, washing hands, biological vaccination and other dos and don'ts will be better prepared to prevent this highly infectious disease. Good understanding of fundamentals of COVID-19 preventive measures is the necessity at this critical moment. The C19-SVT is informative, timely, interactive, state of the art tool for the masses.

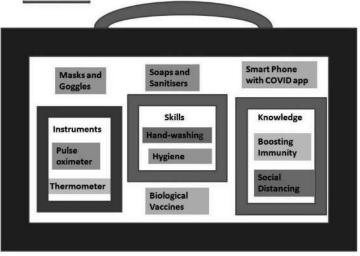
Keywords: Social Vaccine Toolkit; Biological Vaccination; Pandemic

INTRODUCTION

COVID-19 stands for Corona Virus Disease of 2019[1]. The COVID pandemic was started in December 2019 in Wuhan, China. It has been spreaded world-wide and resulted Global infection of more than 13 million people and death of more than half a million[2] based on WHO Dashboard as on 17th July 2020. The highly infectious COVID-19 has resulted in worldwide lock down and serious distress. Number of biological vaccines have developed safer and there are many biological vaccines under development[3]. However, till the biological vaccines are fully in use, in order to control and contain the spread of COVID-19 infections, the only solution is Social Vaccine. The social vaccine is for the new normal with social and behavioural modalities. Some of the measures of social vaccines are social distancing, wearing masks, sanitisation etc.

The Social Vaccine Toolkit for COVID-19 (C19-SVT) is a specific toolkit addressing the COVID 19 pandemic. It is the collection of best practices and lessons from COVID pandemic. The steps and tasks identified are addressing the measures to contain and control the spread of the COVID 19 infection. The various sources from which the prophylactic tasks are collected are highly reliable scientific bodies. The C19-SVT is a compilation of the effective measures for monitoring, modifying and activating social and behavioural modalities. The C91-SVT is continuously evolving with new learning methods on the emerging COVID-19 pandemic.

C19-SVT is deployed on Microsoft Sway and Microsoft Forms platform for general public access. C19-SVT took kit is easy to access, browse and understand. The content is presented in a layman language for easy understanding. The scientific explanations for different steps are provided in order to be convincing.



C19-SVT : ARCHITECTURE AND COMPONENTS

Figure 1: C19-SVT; COVID-19 social vaccine toolkit

The C19-SVT is proposing multi-pronged strategy which incorporates principles of redundancy and diversity. The C19-SVT is based on scientific approach with solid concepts from reliable sources as the basic components. The C19-SVT robust, fault tolerant architecture is shown in the figure and consists of the following components, also as shown in Figure 1.

- Face Masks: Face masks protect the nose and mouth from getting infected from Corona virus. The Corona virus propagates through cough and sneeze droplets from infected patients to others. A person can protect themselves and others by wearing face masks. Corona virus can infect human through nose, mouth and eyes. Hence it is important to cover mouth and nose with masks and eyes by goggles/spectacles.
- **Soaps and Sanitisation:** Frequent hand washing using liquid soap and water or sanitizer is advised. This is to prevent the virus sticking to hands. The corona virus is killed with soap water or sanitizer and thus when a person touches any surface or object carrying the virus, hand washing will remove the traces of virus. Also, avoid touching nose, mouth and eyes with hands.

- **Nasal and Oral Hygiene:** Anterior Nasal Washing using Jal-Nethi: This is a technique found to be effective to keep inside the nose clean through the process of washing using distilled water. The technique is effective when practiced daily. Oral and Throat cleansing using mouth wash and salt water gargling are equally important to keep the virus away.
- Smart Phone with COVID Apps: There are apps released by Governments across the globe to facilitate safety of the users through warnings and exposure notifications. (i.e. Aarogya Setu, Arogya Kshema App etc.). A person who is regularly using such mobile applications better equipped with the preventive measures. These apps use bluetooth and Cellular networks to keep track with the users and their contacts. Whenever a person is diagnosed with COVID-19, all their contacts are notified about the exposure.

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Stockdale Paradox: Ten Lessons to Deal with COVID-19 Pandemic

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ABSTRACT

The COVID-19 pandemic has unleashed global havoc and resulted in millions of deaths. To deal with difficult scenario created by the pandemic, the paper is prepared inspired by "Stockdale Paradox" when the lessors have derived. These lessons are precious in the current scenario and discuss in detail various issues and challenges with solutions. The lessons are useful for anyone in successfully dealing with brutal facts of pandemic and overcome the odds.

Keywords: Pandemic; Stockdale Paradox; Isolation; Lockdown

INTRODUCTION

The COVID-19 pandemic has been highly unpredictable. The unexpected second wave arrived in the middle of April 2021 resulted in death count reaching more than 3 million worldwide as per WHO[1]. The highly infectious disease has been spreaded rapidly in spite of many harsh lockdowns and countermeasures. Some may survive and some may not in the pandemic. Also, the pandemic seems to be endless with many mutant viruses spreading rapidly out of control. The way to deal with harsh reality of COVID-19 pandemic finds parallels with Stockdale Paradox.

The Stockdale Paradox is named after Admiral Stockdale who was imprisoned during Vietnam War[2]. The Stockdale Paradox has been made popular by Jim Collins book on Good to Great[3]. The Stockdale Paradox states that "you must maintain unwavering faith that you can and will prevail in the end, regardless of the difficulties, and at the same time, have the discipline to confront the most brutal facts of your current reality, whatever they might be".

The paper explores how Stockdale Paradox can find application in dealing with COVID-19 Pandemic. One can observe the current reality with rapidly spreading disease with thousands dying everyday. Also, there is no endpoint visible with second wave of COVID-19 pandemic coming in. The COVID-19 pandemic is also posing difficulties in finding right medicines and vaccinations. The situation is unparalleled as the virus, the disease causes, symptoms and treatments that are all completely new.

The first statement of the Stockdale Paradox, it must be maintained the unwavering faith that can prevail at the end, regardless of the difficulties can be implemented as follows,

There are many infections and also the possibilities that one may get infected at any point of time in future. However, one should have unwavering faith that we will survive no matter whatever difficulties may arise. There may be lockdowns, restriction in movements and difficulties in finding right medicine, healthcare facilities etc. While one needs to be prepared to deal with the brutal facts of current reality, as per the second part of the paradox, one needs to maintain discipline. The discipline may involve strict adherence to COVID-19 protocols such as wearing masks, maintaining social distancing, washing hands, vaccination etc. There may be situations of quarantines where one is faced with isolation and hardship. This also requires psychological preparation to deal with hardships. Mental toughness and unwavering faith to prevail at the end are tools for survival. One may even get infected and end up in ICU, but never give up hopes. The best way to deal with current scenario of COVID-19 Pandemic is to apply the Stockdale Paradox and survive. There are growing literature in finding application of Stockdale Paradox for COVID pandemic and lockdown[4-5].

TEN LESSONS:

The following lessons derived from "Stockdale Paradox" can be life savers for many.

Lesson 1: There are many predictions regarding when the COVID-19 pandemic will end [6-7]. There are mathematical models, computer simulations and AI based predictions[8]. However the second wave with mutant variants of COVID-19 virus have taken everyone by surprise. This surprising twist in the COVID-19 pandemic can be handled without heartbreaks if one were to fully understand the concept of Stockdale Paradox.

Lesson 2: Medicines and vaccinations have been developed for COVID-19. However, there is no silver bullet till now to solve the COVID-19 conundrum. Further, the virus is mutating day by day and new variants may or may not be controlled with the medicines or vaccines developed for original virus strains. Researchers and scientists are on their toes to come up with better medicines and vaccines.

Lesson 3: During pandemic, misinformation and conspiracy theories are flooding the internet. These are misguiding the people about the pandemic. The current situation requires that we get news and updated information from trusted sources. As the number of infections are exponentially increasing, there are many messages and information flooding the social media.

Lesson 4: The exponential growth of the infections during pandemic resulted big rush of patients in the hospitals. There is a sudden shortage of medicines, ICU beds, Oxygen concentrators, Ventilators, Doctors and nurses. This can be an anxious moment for many who are in isolation and stranded due to lockdown and curfews. The need of the hour is to plan well in advance for many possible outcomes and be prepared to face the situation as it arises. In planning, one needs to take the Murphy's law into account: "Anything that can go wrong will go wrong"[9].

Lesson 5: Emergence of alternative medicines and immunity booster medications. There are many alternatives as the vaccinations are slowly becoming available. Homeopathic, Ayurvedic

and other alternative medicines and immunity boosters are becoming available. There are also many mobile apps which facilitate one to stay safe during the pandemic[10].

Lesson 6: Emergence of new normal of lockdowns, wearing masks, Social distancing etc. The pandemic has unleashed certain brutal facts and needs to be quickly adjusting to new normal. One needs to be updated about the various measures and protocols and dos and don'ts and strictly follow them. Social Vaccine plays an important role in the control of spreading of COVID[11].

Lesson 7: Psychological effects and mental toughness. Stockdale while being captured by his enemies was constantly tortured. For enduring such scenerios, one needs to be tough. The current pandemic can trigger psychological problems due to isolation and sad situation. One needs to face the brutal facts with awareness about how to deal with them through counselling and relationships. The social networks, video conferencing etc can connect people and they can seek help through these mediums. One should visualize the most happiest moments once the Pandemic has ended and keep the hopes alive all the time. Also, the psychological technique things getting better each day will have healing effect and enhance ones confidence in coming out of the pandemic safely.

Lesson 8: Discipline is the central point in the concept of Stockdale Paradox. The current scenario requires one to follow strict protocols of wearing masks, maintaining social distance, washing hands etc. One needs to be disciplined and adhere to the protocols of COVID pandemic.

Lesson 9: While the gyms, sports facilities and swimming pools remain closed, one can easily follow the fitness routines such as walking, jogging, running, yoga, exercising etc to keep oneself fit. The fitness and health consciousness can contribute to overall wellbeing and may also aid in beating the infection.

Lesson 10: Faith and the pandemic should not be mixed up. While one prays for the safety and wellbeing, one needs to maintain unflinching faith in passing through the pandemic. From Stockdale's experience, one sees that many of the optimists suffered heart breaks when they were not freed as per their expectations [12]. There is a similarity in the current pandemic where one can see new wave of infection while there was a short period of relief. The Pandemic has had first wave and second wave. While it may end anytime, one needs to be prepared to deal with if it does continue for more time.

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Ultraviolet (C – Type) Germicidal Irradiation based COVID -19 Sterilization Chamber

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INTRODUCTION

Ultraviolet Germicidal Irradiation¹ (UVGI) is an established means of disinfection and can be used to prevent the spread of certain infectious diseases. Low-pressure mercury (Hg) discharge lamps are commonly used in UVGI applications and emit shortwave ultraviolet-C (UV-C, 100–280 nanometre [nm]) radiation, primarily at 254 nm. UV-C radiation kills or inactivates microbes by damaging their Deoxyribonucleic Acid (DNA). The principal mode of inactivation occurs when the absorption of a photon forms pyrimidine dimers between adjacent thymine bases and renders the microbe incapable of replicating. UVGI can be used to disinfect air, water, and surfaces, although surface disinfection is limited by micro shadows and absorptive protective layers. Air disinfection is accomplished via several methods like irradiating the upper-room air, irradiating the full room (when the room is not occupied or protective clothing is worn), and irradiating air as it passes through enclosed air circulation and heating, ventilation, and airconditioning (HVAC) systems. In this project, UVGI is used in specially designed chambers to disinfect the personal protective equipment (PPEs).

AIM

The aim of the project is to design and develop a low cost Ultraviolet Germicidal Irradiation Chamber to sterilize the Personal Protective Equipment (PPEs) like face masks, gloves, google, head gears and other items which are prone to COVID - 19 attack. Using this chamber PPEs can be sanitized and reused to overcome the production shortages and supply issues during this pandemic.

SCOPE

Understanding Ultraviolet irradiation spectrum, selection of suitable wavelength and required dosage for the purpose of sterilizing COVID - 19.

^{1.} The History of Ultraviolet Germicidal Irradiation for Air Disinfection. Public Health Reports / January -February 2010.

Designing a disinfection chamber based on the calculated UVC exposure dosage, availability of UVC lights in domestic market and quantity of PPEs to be sterilized in a single cycle of operation.

Training the personnel to handle and operate UVC chamber effectively with proper protective gears and to safeguard from direct exposure to UVC irradiation from the chamber.

ULTRAVIOLET IRRADIATION

Sunlight emits Ultraviolet rays. In early 19th century it was discovered that sunlight has ability to neutralize bacteria. It was dependent on intensity, duration, and wavelength of sun's light. Shorter wavelengths of the solar spectrum were observed to be effective in disinfection of microbes. Early investigations in this domain coined the term "Ultraviolet Germicidal Irradiation (UVGI)" for shorter wavelength light emitted by sun for disinfection of microbes. Further investigations, also pointed towards some key factors that influenced Ultraviolet Germicidal Irradiation (UVGI) performance. Inactivation (also called as sterilization) of a given fraction of microorganisms is dependent on the dose of radiation received. Dose ($J \times m^{-2}$) is the product of intensity ($W \times m^{-2}$) and exposure duration (s). Inactivation is also dependent on the wavelength of received radiation.

Myriad research work following these initial investigations were carried out in finding the suitable wavelength for germicidal action of light. As a result, the following wavelength of Ultraviolet light was proved to be effective against bacteria, fungi, viruses and various pathogens. **UV-C** radiation (100 nm to 280 nm). This radiation is called "far UV" and "germicidal UV".

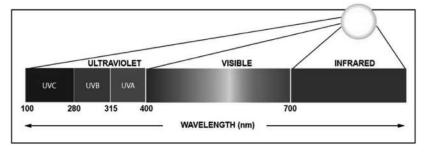


Fig 1: Spectrum of Sunlight

Ultraviolet – C radiation (UVC) exposure inactivates microbial organisms such as bacteria and viruses by altering the structure and the molecular bonds of their DNA^2 (Deoxyribonucleic acid). DNA is a "blue print" these organisms use to develop, function and reproduce. By

^{2.} Introduction to UV Disinfection. (https://www.trojanuv.com/uv-basics)

destroying the organism's ability to reproduce, it becomes harmless since it cannot colonize. After UVC exposure, the organism becomes dead leaving no offspring and the population of the microorganism diminishes rapidly.

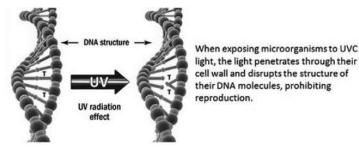


Fig 2: Action of UVC on DNA

It is now evident that UVC irradiation is an effective means of disinfecting PPEs. However, the it is essential to understand whether this UVC radiation is effective against COVID - 19.

UVC DISINFECTION FOR COVID - 19

The International Ultraviolet Association (IUVA) believes that UVC can be used to disinfect COVID-19 virus based on current disinfection data and empirical evidence. UVC is a known disinfectant for air, water and surfaces that can help to mitigate the risk of acquiring an infection in contact with the COVID-19 virus when applied correctly.

UVC has been effective to achieve a high level of inactivation of a near-relative of COVID-19's virus (i.e. SARS-CoV-1, tested with adequate dose of 254nm UV while suspended in liquid). Therefore, a similar results can be expected when treating COVID-19's virus, SARS-CoV-2. However, the key is applying UVC in such a way that it can effectively reach any remaining viruses on those surfaces. The effectiveness of UV light in practice depends on factors such as dosage, exposure time and the ability to reach the viruses on surfaces and in crevices of any materials.

Based on the paper³ published by the International Journal of Transfusion Medicine, it is observed that, treatment of surface with half to three-fourths of the full UVC dose (0.2 J*cm⁻²) reduced the infectivity of SARS-CoV (\geq 3.4 log) to the limit of detection (LOD) in platelet concentrates. Therefore, a UVC disinfectant chamber has to be designed to radiate UVC dosage of 0.1 J*cm⁻² to effectively sterilize the COVID – 19 virus.

3. Inactivation of three emerging viruses – severe acute respiratory syndrome coronavirus, Crimean–Congo haemorrhagic fever virus and Nipah virus – in platelet concentrates by ultraviolet C light. 2020.

DESIGNING UVC STERILISATION CHAMBER

In order to produce UVC dosage of 0.1 J*cm⁻², Phillips UVC lamp (model : TUV T8, 30 Watt) was selected based on availability in local market. Therefore the source of UVC has been identified from a Chennai firm named M/s Electro Science and procured.

The design, size and shape of sterilization chamber has been evaluated based on the following factors:-

- (a) Chamber should be portable.
- (b) Accommodation of 24 face masks per operating cycle. (one operating cycle is 120 seconds)
- (c) Timer with "Auto cut-off" function to prevent over exposure of UVC.
- (d) Temperature sensor to monitor temperature raise inside chamber.
- (e) Chamber should work with 230 V, 50 Hertz domestic power supply.

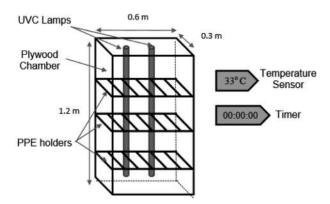


Fig 3: UVC Sterilization chamber design

The material used for construction of outer body is 12 mm thick plywood, which is a good absorbent of UV lights emitted from the source. Inner surface of the chamber is coated with thin aluminium foil for enhancing the exposure to UVC. Three wire mesh grills or holders made up of aluminium are used to hold the PPEs during sterilization. Two UVC lamp holders (frames) are placed inside the chamber to accommodate two UVC lamps and driver units are placed outside the chamber. Temperature sensor is place inside the chamber with a display outside the chamber. The power supply is connected to a timer circuit for automatic cut-off post pre-set exposure time.

CALCULATION OF EXPOSURE TIME

The following calculations were carried out to determine the exposure time to sterilize the PPEs:-

(a)	Surface area of the Chamber in m ²	2.52 m ²	
(b)	Energy produced by two 30 Watt Philips TUV T8 Lamps (J/s)	30 J/s	
(c)	UVC dosage required to inactivate COVID 19 per $(m^2)^4$	1000 J/m ²	
(d)	UVC dosage required to terminate COVID 19 for 2.52 m^2	2520 Joules	
(e)	Time required to produce 2520 Joules of UVC dosage	84 Seconds	

From the above calculation it is observed that, for a chamber having surface area of 2.52 m², 2520 Joules of dosage is required to inactivate COVID – 19 viruses present on the surface of PPEs. Therefore, PPEs can be sterilized when they are exposed to UVC for 84 seconds inside the chamber. For effective sterilization, it is recommended that exposure time of PPEs inside chamber may be increased to 120 seconds per operational cycle. The temperature rise inside the chamber for the said exposure time is approximately 10C, as measured by the temperature sensor.

SAFETY GUIDELINES FOR OPERATION OF STERILIZATION CHAMBER

UV lamps must be used in designated areas with limited access. Operation from within a closed, well-ventilated room or a draped area reduces the risks of exposure.

The UV lamp should never be viewed directly. Operators must wear UV-filtering face shields, long-sleeved shirts, gloves, and long pants. Most UV-filtering face shields and spectacles are made of polycarbonate plastic, which is capable of absorbing 99% of UV radiation up to 400 nm (violet light).



Fig 4: Personal Protective Equipment

^{4.} Inactivation of three emerging viruses – severe acute respiratory syndrome coronavirus, Crimean–Congo haemorrhagic fever virus and Nipah virus – in platelet concentrates by ultraviolet C light and in plasma by methylene blue plus visible light. International Journal of Transfusion Medicine.

Safety warning signs like shown below are to be pasted on the sterilization chamber to caution the personnel nearby.



Fig 5: Safety Warnings

FINANCIAL IMPLICATION

Based on the above calculations and references from international journal, the sterilization chamber was fabricated inhouse with help of skilled personnel and the pictures of the same is shown in **Fig 6**.

Timer with temp sensor



Fig 6: Fabricated UVC sterilization chamber (front view, rear view, UVC and rack arrangement) List of components and sensors are as follows:

Sl	Item	Quantity	Price (Rs)
(a)	Marine 'A' grade plywood 18 mm thickness	2.52 sq m	1500
(b)	Aluminium foil 18 micron	24 sqft	300
(c)	Analog timer- 22.5 MM DIN RAIL (SELCE, Pt No.800SQ-A, 230V AC)	01 in nos	1000
(d)	Temperature sensor with digital display (MULTISPAN, P.No.CC-5020-B1-00-R, 230V AC)	01 in nos	1000
(e)	UV-C lamp TUV 30W (Philips)	02 in nos	4500
(f)	Wire mesh holders with fixtures	03 in nos	550
(g)	Lamp fixtures	04 in nos	100

(h)	Door Handle	01 Nos	50
(j)	Aluminium rack	03 Nos	500
(k)	Door seal and paint	-	500
	Total	10,000/-	

CONCLUSION

The said project is a cost-effective technique to neutralise the corona virus and can be used for sterilisation of PPE (masks, helmets etc), personnel electronic devices viz phones, laptops, chargers, badges, stationery items etc. Customized chambers can also be fabricated utilising the above said calculations which are scientifically proven. The cost of the project has been conceived at 1/10th of the cost of commercially prepared off the shelf sterilisation chambers for the said volume. Prior usage of the chamber, every personnel has to be trained to operate the timer, sensitivity of instrumentation and safety precautions.

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Oxygen Enrichment Technology

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ABSTRACT

The huge requirement for oxygen has surged during COVID-19, as most of patients hospitalized with acute respiratory problem and required oxygen support. Due to the huge demand, the liquid oxygen supplied to the hospitals get affected which forced the patients & hospitals to opt for alternate oxygen generator devices such as O_2 concentrators. However, there are shortfall of commonly available O_2 concentrators. There is a need to innovative oxygen enrichment device, which can act like O_2 concentrators to overcome most of the drawbacks of the concentrators. The device must generate medical oxygen (appropriate mixture of air and oxygen under controlled condition of pressure and moisture contents) to treat the patient. In addition, the device shall have the capacity to provide necessary oxygen supplements to small hospitals, primary healthcare unit and established hospitals. The present manuscript detailed scientific solutions for decentralized generation of Oxygen at affordable price to reduce the dissipation of Coronavirus and ensure more democratic and widespread network of Oxygen Generation hubs across the Nation.

Keywords: COVID-19; SARS CoV-2; Oxygen Enrichment Unit; Oxygen Concentrator; Oxygen therapy; Oxygen saturation.

INTRODUCTION

Oxygen supplies have been disrupted since the advent of the COVID-19. A huge requirement for oxygen has surged during COVID-19, as most of the patient hospitalized with acute respiratory problem and required oxygen support. Question arises: Is there genuine shortage/scarcity of Oxygen? Answer is NO. One of the major projected obstacles for the seamless flow of Oxygen across the healthcare facilities is unavailability of appropriate vehicles for transportation of liquid oxygen (requiring specialised capital intensive Cryogenic Tanks) and frequent refilling of medical gaseous O_2 Cylinders. In fact, installing a plant to utilize liquid oxygen can only be justified at larger hospitals requiring huge volume of oxygen.

The second constrain is the wastage of remaining 5-10% of Oxygen which cannot be used due to absence of sufficient pressure in cylinders. Third reason is a myth about oxygen saturation (SpO_2) level, that when it is below 92, the concerned patient requires more than 90% of Oxygen; which is NOT always correct. Often patient with low SpO2 does not require oxygen purity of

more than 60% and there is a need to utilize Oxygen effectively. As an alternative to Oxygencylinders, Oxygen PSA plants & Concentrators appear to be better options in many ways. Reason being, cylinders require frequent refilling, involving transportation difficulties and leakage risks leading to fire-hazards. Whereas PSA plants and Concentrators are free from such drawbacks. A PSA plant (to deliver more 500 LPM oxygen) may not be an appropriate proposal for source of oxygen at the rural (primary) healthcare facility due to its high capital cost, whereas it might be an economical solution for a large hospital. The present manuscript is restricted to oxygen enrichment technology required for primary health care and home units, which can also be used for critical patients for life support before the patient is hospitalised.

The technology of O_2 concentrator is already established. The oxygen concentrators work like air purifiers. It sucks around 5 units of the ambient air, removes majority of nitrogen and provides one unit of concentrated oxygen. As shown in Fig 1, O_2 concentrators work on 'pressure swing adsorption' principle where the nitrogen and CO_2 are adsorbed from the air using zeolite minerals and leaving oxygen as the primary gas. Two zeolite sieve columns are used to switch between Nitrogen adsorption and Nitrogen purge cycles. It requires oil free compressor, filters (dust, antibacterial, etc.), Zeolite (i.e. Lithium exchanged), pneumatic fitting, alarm system, flow meter, regulators, power switch, accumulator, etc.

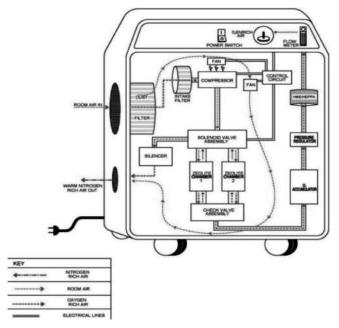


Fig 1: Schematic diagram of Oxygen Concentrator

As per WHO report "Oxygen concentrator: An electrically powered medical device designed to concentrate oxygen from ambient air. It is used to deliver oxygen at the bed side, typically through an attached nasal cannula (or prongs), to a patient requiring oxygen therapy. The intended use or clinical purpose is the delivery of low-flow, continuous, clean and concentrated oxygen (> 82%) from room air (21%)". This has raised a big question of usage of O₂ concentrator for disease like COVID-19.

As per the available literature, concentrator using nasal cannula to deliver oxygen to patient may spread COVID virus [1-3]. Mardimae et al [1] recommended modified N95 mask along with nasal cannula to prevent the spread of COVID virus. Cournoyer et al. [2] reviewed the Oxygen delivery systems and concluded that the existing oxygen therapies generate air dispersion and increase the risk of infection. Montiel et al. [3] studied usage of surgical mask on the top of nasal cannula and concluded the essential need of appropriate mask for usage of nasal cannula. Possibility of spread of virus through nose is illustrated in Fig 2.

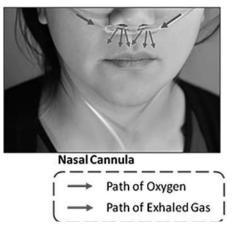


Fig 2: Spread of Virus during Exhaling

While using cannula, one inhales Oxygen enriched air from concentrator (maximum 5 LPM) along with remaining air flow from outside environment. But while exhaling, exhaled flow (containing Coronavirus) goes to the environment and increased the possibility of spreading the disease. It has been mentioned a number of times that a person suffering from COVID-19 releases coronavirus during coughing and/or exhaling. People may get COVID-19 by breathing air or exhaled by the patient. Often, the infection is mild and most of people recovered in few days time. In other words, viral transmission from respiratory particles from COVID patients (during first 7-10 days when viral load is high) who are undergoing oxygen therapy without shielding their nose & mouth is high. Therefore using mask over nasal cannula interface is essential in

reducing spreading of aerosol particles. Therefore the usage of nasal cannula without covering nose as well as mouth of COVID patient, must be treated as "COVID Inappropriate behaviour" (as shown in Fig 3). However, some experience more serious illness and may require hospital care. Risk of serious illness rises with age, people with weakened immune systems and people having comorbidities (diabetes, heart and lung diseases). From his/her single cough, more than 105 droplets containing viruses may get generated and remain airborne [4]. To minimize the virus spread from COVID-patient, the nasal cannula must be used with appropriate mask such as N95, as shown in Fig 4.



Fig 3: COVID Inappropriate usage



Fig 4: Nasal Cannula with N95 mask

As per Dr. Russel Blaylock [5] there is danger of wearing N95 mask by person infected with COVID virus, as he/she will be constantly rebreathing the virus, raising the concentration of the virus in the lungs and the nasal passages. In addition, in the present N95 masks, there is a

possibility of inhaling back the previously exhaled air which unnecessarily increases the chances of dead space, which in turn creates the possibility of bacterial/viral transmission as the patient is exposed to the danger of inhaling contaminated gas.

To fulfil the need of rising demand of Oxygen due to unprecedented consumption of Medical Grade Oxygen, it is necessary to develop alternative technology to supply the required Oxygen to COVID patients with emphasis on reducing virus diffusion to minimize the risk of infection transmitted to doctors, nursing staff and family caring members. In this manuscript 'Oxygen Enrichment Technology' has been presented which overcomes the drawbacks of Oxygen Concentrators. The proposed technology will also be useful for the hospitals having compressor pipeline for supply of medical air, as generated oxygen will provide support to the existing oxygen delivery system established in various hospital.

NEED OF OXYGEN ENRICHED AIR

In normal cases, the lungs enable the human body to absorb oxygen from the air (containing 20-21 percentage of oxygen by volume) and expel carbon dioxide enriched air. If the coronavirus has caused pneumonia, patient may feel breathless as infected lungs struggle to get enough oxygen, which is essential nutrient for every organ of the body.

The SARS-CoV-2 coronavirus can infect respiratory epithelial cells and disturbs the gas exchange process. Therefore most patients with COVID-19 have infected respiratory tract causing shortness of breath. The body's immune system fights such infection that triggers inflammation. When this inflammatory immune response continues, it hinders the transfer of oxygen in the lungs. In addition, there is a build-up of fluids in the lungs too, consequently it becomes difficult to breathe and require supplementary oxygen from other sources. As per report, 54.5% of hospital admissions during the second wave required supplementary oxygen during treatment [6]. As per established standards, oxygen therapy at 0.5-5 litres/min is recommended. However, if SpO₂ of the patient does not recover, then high-flow nasal cannula oxygen therapy or non-invasive ventilation can be considered.

To approximate the required air intake, following equation can be considered:

Air requirement to move throughlungs (LPM) $= Tidal \ volume\left(\frac{mL}{kg}\right)$ $* Ideal \ weight(kg)$ $* Respiratory \ rate\left(\frac{1}{minute}\right)$ It is worth to be mentioned that the Ideal weight is not the same as the actual body weight, but it is related to height. There are a number of approximations, one of them is:

Ideal weight (kg) = Height in cm-100

Tidal volume ranges between 6 to 8 mL/kg. The respiratory rate may vary from 12 to 25 per minute depending upon the breathing rate during sleeping, walking, exercise etc. Using these parameters and equations, 8 to 10 LPM is the requirement of fresh air moving through lungs. As it is known that ventilation is the movement of a volume of gas into and exhaled-out of the lungs. On assumption of I:E (Inspiratory : Expiratory) ratio equal to 1:1, the requirement of blended air enriched with oxygen delivered by device will be double (as oxygen enriched air supply devices are continuous and supply air even when patient is exhaling), which means device must provide 15-20 LPM of oxygen enriched air. Based on this discussion, it can be concluded that in normal case (FiO₂ = 0.21), the requirement of oxygen will be lesser than 4 LPM. That's why usage of Oxygen Concentrators @ 5 LPM is sufficient. As per one report 10 LPM of Oxygen is being supplied to the COVID patients in normal wards of hospitals and 24 LPM Oxygen is given in ICUs.

It is necessary to understand that the concentration of oxygen in the gas mixture can be evaluated using the Fraction of inspired Oxygen (FiO_2),

$$FiO_2 = \frac{LPM \ ofO_2 * Purity \ ofO_2 + LPM \ of \ air}{Total \ inhaled \ air}$$

Using above equation, it is clear that in normal air environment $FiO_2 = 0.21$. For COVID patients, who requires total 20 LPM and inhales 5 LPM of 0.93 purity from Oxygen concentrator (using nasal cannula), FiO_2 will be

$$FiO_2 = \frac{5*0.93 + 15*0.21}{20} = 0.39$$

Using this example of inhaling 5 LPM from nasal cannula of O_2 concentrator and remaining 15 LPM from open environment indicates contradiction and proves that Oxygen concentrator should not be used for COVID like transmissible disease. As per the available Medical Journals, the usage of Nasal Cannula without masks leads to significant transmission of Viral Load to nearby attendants. The COVID appropriate behaviour demands that nasal cannula be used with N95 type masks, so that virus exhaled during breathing-out get trapped into N95 mask. But person infected with COVID needs to inhale remaining 15 LPM from environment through N95 mask, which forces that patient to constantly rebreathing the virus, raising the concentration of

the virus in the lungs and the nasal passages. In addition N95 masks might hinder the breathing process of patients, having breathing problem. Therefore, the contradiction is that COVID patient needs to wear mask to protect others, but needs to remove mask to recover fast. This contradiction can be overcome if patient is supplied desirable oxygen enriched air directly from the device and such a device developed by CSIR-CMERI is described in the next subheading.

CSIR-CMERI'S OXYGEN ENRICHMENT TECHNOLOGY

The CSIR-CMERI Oxygen Enrichment Unit is an in-situ Oxygen Technology, which concentrates Oxygen from the ambient air using the Pressure Swing Adsorption Methodology (Fig 1). The Oxygen Enrichment Unit (OEU), helps to increase oxygen concentration by filtering away the nitrogen, using two modules i.e. Compressor Unit and Oxygen Concentration Unit, as shown in Fig 5. The modular design has the added advantage of flexibility of placement of the product. The CSIR-CMERI Technology has multiple competitive advantages in terms of Performance, Efficiency and Endurance. The OEU can also be termed as a 'Mini-PSA Plant' as it can provide enough Oxygen in a day equivalent to the volume of a Jumbo Cylinder.

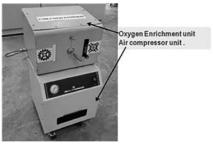


Fig 5: Standalone Oxygen Enrichment Unit (OEU)

Compared to the standard available concentrator, the OEU has a large sized compressor to provide flow rate in the range of 0.5 to 30 LPM considering the specific and optimum requirement of the patients. The operating temperature range of OEU has been extended to 40°C while the available concentrators can operate in the range of 12°C to 32°C. An optional passive moisture control unit has been provided. Molecular sieve Li -exchanged zeolite material having spherical particle size varying in the range of 200 to 400 micron has been used to develop adsorbent columns having aspect ratio of length to diameter of less than 5. The pressure drop across the adsorbent columns remains lesser than 25 kPa. The device is developed to utilize nasal cannula with necessary N95 masks to avoid spread of harmful virus. The developed Oxygen Enrichment Unit is unique in these aspects, which are lacking in other Oxygen Concentrators. The variation in oxygen percentage with flow rate and time has been demonstrated in Fig 6. The list of technical specification parameters with comparison between OEU and standard concentrator is provided in Table 1. The performance shown in the Fig 6 and Table 1 provide confidence in the CSIR-CMERI developed Oxygen Enrichment Unit. With an optional plug-in module, this unit can work up to an altitude of 14000 ft with a penalty on flow rate thereby making it very handy for high altitude terrain battlefield in contingencies. The commercially available concentrators generally work up to 8000 ft from sea level.

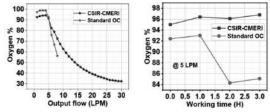


Fig 6: Comparison of CSIR-CMERI developed Oxygen Enrichment Unit and available Oxygen Concentrator

Table 1 : Performance Parameters of Standard Concentrator and OEU				
Parameters	Standard Oxygen Concentrator (OC), 5 LPM	CSIR-CMERI OEU, 5 LPM	Remarks	
Average Power Consumption	350 W	550 W	Slightly higher power to provide flow up to 30 LPM	
Oxygen concentration	93 +/- 3 %	93 +/- 3 %	At 5 LPM	
Weight	14 kg	18-20 kg	Slightly bulky as the compressor rating is higher	
Standard Flow	0.5-5 l/min	0.5-5 l/min		
Higher Flow	Not possible	up to 30 LPM @33%	This facility is completely absent in the competitor	
Outlet Pressure	5.5 PSI	5.5 PSI		
Sound level	45 (typical) dB	60 (typical) dB	Due to higher rated compressor	
Operating Temperature	12°C to 32°C	up to 40°C	Very much suitable for Indian conditions	
Operating Humidity	up to 95 %	up to 95 %		
Operating Altitude (standard)	0 to 7500 ft	0 to 7500 ft		
High Altitude	Not Possible	0 to 14000 ft (with an additional module)	This facility is completely absent in the competitor	

ADVANCED OXYGEN ENRICHMENT UNIT

There are two important parameters: Flow rate and FiO_2 to be considered while delivering supplemental oxygen to the COVID patient. It is necessary to understand that the breathing pattern, tidal volume, I:E ratio, dead space, etc. for every patients is different and the device to deliver Oxygen must have uncoupled flow rate and FiO_2 parameters to titrate to provide appropriate oxygen therapy. Advanced OEU provides independent control on the Oxygen enrichment (FiO₂) as well as on Flow Rate. This has been illustrated in Fig 7.

With independent control on flow rate and FiO_2 , 50 LPM and 100 LPM models of Advanced OEU can be utilized in 5-10 bedded smaller dispensaries, local/Mohalla clinics and primary healthcare centres of the rural areas. Fig 8 illustrates Oxygen Enrichment Unit of 100 LPM capacity to supply Oxygen for 10-bedded facilities (Upto 10 LPM for each bed). This is possible owing to the fact that the Compressor Unit and the Concentration Units are separate. Thus, this enables the entire system to function with a Single Compressor that makes overall Oxygen supply cost effective. Further, setting up separate oxygen enrichment unit at every bed is advantageous as malfunctioning of any one unit does not affect the entire loop. The Oxygen Enrichment Unit would be located on the bedside with control on flow rate and FiO_2 . Advanced OEU can be Integrated/Hybridized with existing oxygen lines of the hospitals.

Further, Hybrid Version of the Advanced Oxygen Enrichment Technology, having the added advantage of being able to function along with Hospital Oxygen/Oxygen Cylinders (illustrated in Fig 9) for Intelligent Switching and Interventions in a variable manner can be developed. This technology will help in complementing Oxygen shortfalls, if the situation arises.

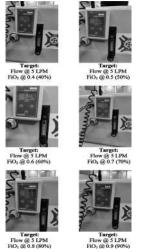


Fig 7: Variations of a FiO₂ with 5 LPM through Manual Control

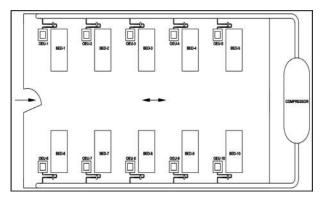


Fig 8: Arrangement of Advanced OEU for Local Clinics, Small Dispensaries and Primary Healthcare Units

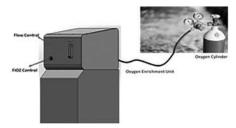


Fig 9: Hybrid System Configuration

FUTURE STRATEGY

The Advanced Oxygen Enrichment Unit is being developed having Independent Controls for Oxygen Enrichment (FiO₂) and Flow Rate. It can be equipped with SpO₂ sensor and C-PAP with an estimated capacity of 15 LPM of enriched Oxygenated Air (93+3%). The Prototype experiments have been showing encouraging results and might soon see the light of the day.

CONCLUSIONS

Most of the Oxygen Concentrators come with nasal cannula having potential risk of spreading the virus exhaled from COVID patient. The present paper is related to Oxygen Enrichment Technology (OEU and advanced OEU) to provide supplemental oxygen to COVID-19 patients minimizing the chances of spreading virus among health care medical and non-medical workers. The advanced OEU provides independent control on FiO_2 and oxygen enriched air flow. With the above mentioned facts of CSIR-CMERI developed technology, it can be stated that device will be useful at homes even after this deadly pandemic and can be a life-saver therapy in other diseases too.

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- 7. To learn further about the Technology Click the Link below and Contact: https://www.cmeri.res.in/ technology/oxygen-enrichment-unit

About the author

Prof Harish Hirani is presently the Director of CSIR- Central Mechanical Engineering Research Institute (CMERI), Durgapur, India. He assumed the leadership from 16th March 2016 after taking lien from IIT Delhi, New Delhi. Before joining as Director, CSIR-CMERI, he was an academic leader for 17 years at IIT Bombay and IIT Delhi. For his research achievements, Prof Hirani had been accorded the prestigious 'BOYSCAST fellowship' and worked at Massachusetts Institute of Technology, Cambridge, USA. He has 160 research publications and 114 IPR (granted/ applied) in his credit. His book on 'Fundamentals of Engineering Tribology with Applications', published by Cambridge University Press has proven to be a success. He has organized and conducted more than 25 training courses for 1000+ engineering faculty and 300+ industry executives. With a robust research experience of more than 25 years, 20+ years teaching experience in IITs and more than 7 years of academic & scientific administrative experience, Prof Hirani always strived to inculcate the value of developing innovative thinking among Scientists/ Researchers and learners for realising substantial socio-economic impact. He being at the helm of affairs at CSIR-CMERI envisions an emboldened and socio-economically empowered India through Technology Innovations and Impact Investment. He is a firm believer of inclusive growth and paves the ways of technology transfer to micro and small enterprises so that common people are benefited. There has been an almost 500% rise in Technology Transfers since 2015-16, when compared to the preceding period.

Role of Engineers in Combating COVID-19

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ELECTROSTATIC DISINFECTION DEVICE

Electrostatic spraying is one of the most efficient and effective methods to apply the liquid based solutions such as surfactants, disinfectants and sanitizers. Basically, by providing the charge to fine droplets, the aerodynamics conditions are controlled in the desired manner. Charged droplets cover the directly exposed and obscured surfaces uniformly with increased efficiency and efficacy.

The sudden outbreak of novel coronavirus SARS-CoV-2E also termed as COVID-19 has become a global thread for human being and it has put the world in tremendous crisis. Disinfection and sanitization has become one of the most essential tasks to stop the spread of novel Corona virus. Disinfection is the process to destroy or inhibit the growth of disease causing the microorganisms thriving on the living and non-living surfaces. CSIR-CSIO has designed and developed an electrostatic disinfection machine to sterilize the indoor and outdoor surfaces to stop the spread of Corona virus effectively and efficiently.

The technology know-how of electrostatic disinfection machine has been transferred to three industries for commercial production and the products are available in the market with the brand name of "ENCESPRAY", "Micro-Sprayer" and SMQRT-ES by Rite Water Solutions (I) Pvt. Ltd., Nagpur, India, Bharat Heavy Electricals Limited (BHEL) Haridwar, India and Jhosna Corporation, Raichur, India, respectively. The device is mobile, handy environment friendly and easy to use.



Fig 1: Electrostatic disinfection machine

TECHNOLOGY KNOW-HOW TRANSFER

- The know-how of technology, "Electrostatic Disinfection Machine" has been transferred to Jhosna Corporation, for commercial production on December 18, 2019.
- The know-how of technology, "Electrostatic Disinfection Machine" has been transferred to Rite Water Solutions (I) Pvt. Ltd., as well (https://www.ritewater.in/) for commercial production on April 22, 2020.
- The know-how of technology, "Covid-Spray" was also transferred to BHEL, (https://www. bhel.com) for commercial production on March 27, 2020. The technology transfer took place in presence of the Director General, CSIR & Secretary, Department of Scientific & Industrial Research (DSIR) and other Directors of CSIR.

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About the author

Dr Manoj K Patel has received his BTech degree from NIT Jamshedpur and completed his PhD from Academy of Scientific & Innovative Research (AcSIR). He is currently working as Principal Scientist in CSIR-Central Scientific Instruments Organisation, Chandigarh. Dr Patel has started his research career in charged particulate technology, electro-hydrodynamics of liquid sprays and aerodynamics of charged particulate matter. His current research interests are electrostatic liquid atomization, electrostatic spraying technology, airborne charged particulate technology for and air-pollution abatement, electrostatic spraying for surface decontamination and effective disinfection and sanitization, food safety and nutrition, nanogenrators, precision agriculture, autonomous robotic systems for agricultural tasks, UAVs and aerial electrostatic spraying. He has received three patents, published several research articles in refereed journals. He has completed seven projects successfully funded by private as well as public funding agencies. Dr Patel has transferred seven technology know-how to various industries for commercial production and created three startups. Currently, he is a Project Leader of various national and international projects funded by USISTEF, DST, CSIR, Govt. of India and private industries. Dr. Patel has received several Awards, such as, CSIR Young Scientist Award 2020, IETE- Hari Ramji Toshniwal Award 2020, Shushila Sharma New Idea Award 2020, IEI Young Engineers Award 2019, NRDC National Societal Innovation Award 2017, Gandhian Young Technological Innovation Award 2016, SKOCH Smart Technology Award 2015 and Order-of-Merit Award 2015. He is a recipient of TATA Cummins Meritorious Scholarship from TATA CUMMINS (2009-2010). Dr Patel is a Fellow of IETE, Member of IEI, Indian Society of Agricultural Engineers (ISAE) etc. He is serving as an External Member, Board of Studies, NIT Jamshedpur.

ArogyaKshem App: COVID-19 Infection Self Assessment Test C19-SVT: COVID-19 Social Vaccine Toolkit

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Arogya-Kshema

COVID 19 Infection Self Assessment Test has been developed at the Department of Computer Science & Engineering, DIAT. The Android App is made available using Google Play store to the general public. The App is useful in self assessment and freely made available for general public. The app checks the symptoms of the users through series of multiple choice quiz and provides an appropriate feedback. The App is updated with the latest symptoms of the COVID-19 Infection.

C19-SVT

COVID-19 Social Vaccine Toolkit has been developed at the Department of Computer Science & Engineering, DIAT. The C19-SVT is useful for general public in gaining knowledge about various preventive measures for COVID-19 Infection. It is deployed on Microsoft Sway platform and provides set of recommendations based on scientific literature. The C19-SVT was found 100s of users, which has been downloaded 250 times.

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Solar-Powered Vaccine Carrier with a Tracking Device

Mayur Shetty

Blackfrog Technologies

About 120 km away from Imphal, Manipur, India, M Zinghorla's day, for the past few months, has been starting at dawn. A nurse at the Kamjong Community Health Center (CHC), heads out to the centre to collect Covid-19 vaccines which she places carefully in a carrier. Then she sometimes a vehicle, but on most days by walking, going door-to-door, immunising families in remote areas.

While the first wave of the Covid-19 pandemic was limited largely to urban India, the second wave has severely hit rural India and the lack of health infrastructure has only become more evident. A recent report by SBI Research pointed out that between March and May 2021, the percentage of rural districts with Covid-19 cases across India surged from 36.8 to 48.5 and like Zinghorla, there are a number of healthcare workers across the country, who have been struggling to treat patients due to the lack of infrastructure, availability of medication and now, lack of tests and vaccines in rural India.

Now, a handful of startups—for-profit and non-profit—are using various innovations or pivoting their models to help rural India fight Covid-19.



Fig 1: Solar powered vaccine carrier

"Some of the areas we travel to are extremely remote, and often there aren't decent roads, and electricity is always an issue. Earlier, this was a major issue for delivering vaccines because we had to carry large bulky ice-boxes," recalls Zinghorla.

Over the past few months, Zinghorla and her team have switched to Manipal-based Blackfrog Technologies' Emvólio, a solar-powered vaccine carrier with an IoT device (to track the vaccine) that can be worn like a backpack. "With this new technology we can travel to remote areas and immunise entire communities easily," she said.

According to Ministry of Health and Welfare estimates, 25% of all vaccines (not just Covid-19) end up getting wasted due to temperature fluctuations. This is even more relevant in the current scenario since both Covaxin and Covishield vaccines need to be stored at a temperature between 2°C and 8°C, and are freeze-sensitive—meaning storing them in ice-boxes is unsafe because the temperature often drops below 0°. Ice boxes usually end up freezing the vaccine, and one risks accidentally administering vaccines that have lost potency. Emvólio helps in reducing the economic burden of these vaccines and nullifies the chances of inefficacious vaccines being administered.

Emvólio's patented technology ensures that the contents in the cold chamber are blanketed in strictly temperature-controlled air. Blackfrog has a production capacity of 1,500 units per month and Emvólio is now being deployed in large volumes across North-East India under the National Health Mission.

While during the first wave, Blackfrog's technology was useful—especially in urban India in handling Covid-19 test samples, which due to a change in temperature might lead to false negatives, by November 2020, they launched a newer version focusing on vaccine delivery.

The company, which started in 2015 as an engineering design and consultancy firm, in 2017 transitioned into a product development company. In an attempt to solve the issues with immunisation—vaccines being wasted due to lack of temperature control—Shetty and his team developed the patented technology called Emvólio. The researchers stated that, this product is a portable medical-grade refrigeration system for last-mile delivery of vaccines, blood cultures and all other biologicals. The startup began with vaccines for polio, BCG and MMR, which also require 2°C-8°C refrigeration, and is funded by BIRAC and leading impact investors, including Venture Centre (CSIR-National Chemical Laboratory, Pune), CCAMP, Bengaluru, and Social Alpha.

Engineering Intervention in COVID Management

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INTRODUCTION

Since December 2019, the entire nation alongwith the world is panicked and attacked by COVID-19 issues. As a part of the engineering and teaching fraternity, five corona related projects have been developed by us for serving the society in this precarious scenario. The students of Asansol Engineering College have contributed their best under my mentorship and college management extended their whole hearted support by way of funding etc to bring real life solutions to the problems encountered in covid period.

"Non Contact Switching System" project, using ATmega ϕ 328 Microcontroller and Ultrasonic Sensor was developed to operate switches and public electrical points avoiding physical touch in COVID crisis in June 2020. This project was published in various press and media. The project achieved **JIS SAMMAN 2020** in Best Project Category by JIS group held on 01 February, 2021. This project work is very necessary to avoid the contact on a surface by multiple users at common places like switch boards. So, it is going to help us fight against COVID-19.

A compact non-contact switching electrical system used in an electrical box mounted on a wall, has one ultrasonic sensor for detecting a hand placed at different distances in front of the sensor that reads the distance and a CPU for receiving the values for determining which function is to be performed, such as turning on or off a switch according to the distance recorded by the ultrasonic sensor. The CPU can be used to generate one or more control signals for controlling the multiple switches.

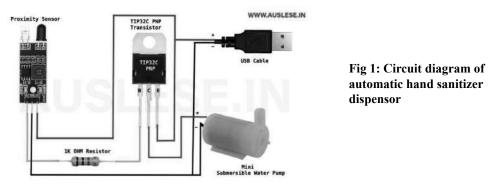
Advantages of "Non-Contact Switching System" technology are as follows:

- It is very easy to operate.
- It stores the data inside EEPROM, so that a power restart will not result in losing the last (on/off) state of switch.
- It is very simple to install inside any switchboard that is commonly used.
- It is very cost effective solution to the problem.

Some of the applications of "Non-Contact Switching System" technology are as follows:

- This is very helpful for the cardiac patient with artificial cardiac pacemaker because a very minute accidental leakage of current from the switchboard may damage the pacemaker installed in their heart. So it gives a non contact operation of switches.
- This is very helpful in prevention of contagious diseases dur to non contact operation.
- It can also be operated with wet hands without having risk of electric shocks.

"Automatic Hand Sanitizer Dispenser" project developed by Subha Sundar Chakraborty, student of ECE dept, Asansol Engineering College using transistor and proximity sensor was developed to operate sanitizer dispenser automatically without touching and intimate if sanitizer is empty by sensor in June, 2020. This project was awarded Best Jury Award in "CII Innovation 2020: Innovation in New Era" on 04 December, 2020 by Confederation of Indian Industry(CII). In the COVID 19 situation we are following some rules. We are using hand sanitizer every time and every place. It is harmful to touch same sanitizer container by many people like in school, college, house, office, etc. where there is a common sanitizer and is used by many people and this make situation very dangerous. We all know that in the Covid19 situation same sanitizer used by so many people it is harmful. This is basically a touchless hand sanitizer container. This automatic sanitizer container is very low-cost solution because here only infra-red sensor and transistor are used. Anyone can buy it because it is a very low cost device and is easy to use. When anyone give their hands in front of the sensor then automatically sanitizer liquid cames out. This project also detects sanitizer level easily. Fig 1 shows the circuit diagram of the project.



"Smart Lock and Switches" project was developed By Kamran Hassan, Student of CSE dept, Asansol Engineering College using Internet of Things (IoT). This project won Best Top 5 project award in **"CII Innovation 2020: Innovation in New Era"** on 04 December, 2020 by Confederation of Indian Industry (CII). It is used to operate door locks, switches without physical contact. This is an IoT based project. In this project, our home electrical switches and door locks are controlled with our mobile phone remotely from wherever we want over the globe, the only

condition is having an internet connection. This device has a control unit that is having some relay that can be controlled by the instructions received from the user via internet and as per the instruction the relay operates, and devices connected to those relays can be controlled remotely. The block diagram of the device is given in Fig 2.

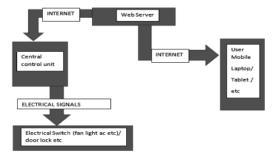


Fig 2: Block diagram of smart lock switchs

"Automatic Door Bell" project developed by Suryadeep Sen, Student of CSE Dept, Asansol Engineering College in June,2020. This project is Arduino Uno microcontroller based project which was developed in COVID period. Door bells are prevented from outside contacts automatically. In this project, there is no contact with automatic doorbell. This prevents or decreases the chances of disease causing pathogens passing from one person to the other. Figure 3 shows the circuit diagram of the project.

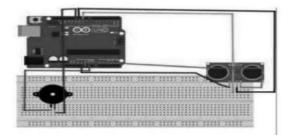


Fig 3: Circuit diagram of automated door bell

"Voice activated home and office appliances" project developed by Ayan Roy, Student of CSE dept, Asansol Engineering College. This project is Arduino Uno microcontroller based project developed in COVID period in the year 2020. All appliances are being controlled by voice without physical contact. The concept of home automation is gaining popularity as it helps in reducing human effort and errors and thus increases the efficiency. With the help of home automation system, we can control different appliances like lights, fans, TV, AC etc.

Additionally, a home automation system can also provide other features like security, alarms, emergency systems etc. that can be integrated. The voice activated home automation project is implemented using Arduino Uno, bluetooth and a smart phone. There are many types of home automation systems like bluetooth controlled, internet controlled, RF controlled, remote controlled (IR remote) etc. Each type has its own advantages and disadvantages. In this project, we have designed a voice activated home automation system, where different appliances are controlled by sending a voice command.

In this project, a simple voice activated home automation system is designed. Voice commands are used to control different appliances. We will now see the working of the project. All the connections are made as per the circuit diagram shown in Fig 4. After making the necessary connections, we have to switch on the power supply to the circuit. Now, we need to pair the Phone's Bluetooth to the HC – 05 Bluetooth Module. Before that, we have to install the App mentioned above in the phone. The home screen of the app looks something like this. Next step is to connect the phone with the Bluetooth module. For this, choose the option "Connect Robot" and select the appropriate Bluetooth Device. If the devices aren't paired earlier, we need to pair them now using the Pin of the HC – 05 Bluetooth Module. After successful connection, the devices are ready to transmit data. For that, press the microphone icon on the app and start giving voice commands. The Voice Activated Home Automation system will help us control different loads (electrical appliances) with simple voice commands. This kind of system is very useful for people with disabilities. Further, the project can be expanded by adding different sensors (light, smoke, etc.).

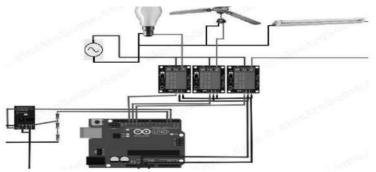


Fig 4: Circuit diagram of voice activated house automation systems

ACKNOWLEDGEMENT

The authors are thankful to the entire management of Asansol Engineering College for giving the valuable support by way of funds, motivation and for giving me this responsibility of executing the corona related projects along with my students.

Engineers' Achievement and Role in COVID Management – Some Thoughts

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INTRODUCTION

Disease and illnesses have plagued humanity since the earliest days. However, it was not until the marked shift to agrarian communities, urbanization, opening of trade routes, and increased contact with different populations of people, animals, and ecosystems increased the probability of occurrence of pandemics. Some of the major pandemics that have occurred over time are given in **Table 1**.

Name	Time period	Type / Pre-human host	Death toll
Antonine Plague	165-180	Believed to be either smallpox or measles	5M
Japanese smallpox epidemic	735-737	Variola major virus	1M
Plague of Justinian	541-542	Yersinia pestis bacteria / Rats, fleas	30-50M
Black Death	1347-1351	Yersinia pestis bacteria / Rats, fleas	200M
New World Smallpox Outbreak	1520 – onwards	Variola major virus	56M
Great Plague of London	1665	Yersinia pestis bacteria / Rats, fleas	100,000
Italian plague	1629-1631	Yersinia pestis bacteria / Rats, fleas	1M
Cholera Pandemics 1-6	1817-1923	V. cholerae bacteria	1M+
Third Plague	1885	Yersinia pestis bacteria / Rats, fleas	12M (China and India)
Yellow Fever	Late 1800s	Virus / Mosquitoes	100,000- 150,000 (U.S.)

Table 1: List	of pandemics	over time
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Russian Flu	1889-1890	Believed to be H2N2	1M
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		(avian origin)	
Spanish Flu	1918-1919	H1N1 virus / Pigs	40-50M
Asian Flu	1957-1958	H2N2 virus	1.1M
Hong Kong Flu	1968-1970	H3N2 virus	1M
HIV/AIDS	1981-present	Virus / Chimpanzees	25-35M
Swine Flu	2009-2010	H1N1 virus / Pigs	200,000
SARS	2002-2003	/ Bats, Civets	770
Ebola	2014-2016	Ebolavirus / Wild animals	11,000
MERS	2015-Present	Coronavirus / Bats,	850
		camels	
COVID-19	2019-Present	Coronavirus – Unknown	218,700 (Johns
		(possibly pangolins)	Hopkins
			University
			estimate as of
			8.58am PT,
			April 29, 2020)

COVID-19 is the most tumultuous, catastrophic and defining epoch of our lifetime. This crisis has no precedent. The high and the mighty have all met their match in this lowly virus. The tiniest primitive invisible life form is now controlling the behavior of entire mankind. It has made us feel humble and made us to think about what and how we need to act and behave.

The lockdown last year was required to get systems in place, to prepare ourselves, whether with testing kits, or personal protective equipment, or ventilators or hospital infrastructure. Since the last quarter of 2020 the country eased out from previous restrictions, with all sectors encouraging borders to reopen. As a result, we were caught off guard when the cases went up in such a huge surge from mid-March 2021. In the absence of a nationwide lockdown and with COVID-19 cases on a steady rise, a number of states in India have imposed complete lockdowns to reduce the spread of the coronavirus virus amid a deadly second wave. At present based on several indicators, it does appear that the second wave is subsiding and the COVID-19 case counts dropping.

Medical professionals are on the frontlines in the fight against COVID-19 as they care for patients and work to create a vaccine. These unprecedented times have left other professionals wondering what they can do and how can they contribute to help society through this pandemic. Doctors, nurses and medical researchers are on the frontline, but engineers are also playing a crucial supporting role amongst the crisis.

The COVID-19 outbreak has brought with it several logistical challenges. The contributions from engineering are apparent and numerous. Few are listed below.

- Engineers have helped in enabling flow of essential services in cities during lockdown.
- Providing clean water, sanitation, waste disposal, etc
- Providing uninterrupted power to our homes and for essential services
- Providing internet connection, Wifi, platforms like Zoom, computers, and microelectronics, which allow people to telework and communicate, digitization and end-to-end data analytics support to police to maintain law and order.

Note: Many of the death toll numbers listed above are best estimates based on available research. Some, such as the Plague of Justinian and Swine Flu, are subject to debate based on new evidence.

• Production of medical devices, diagnostics, and safety clothing, face-shield manufacture; Personal Protective Equipments (PPEs), to mechanical and test engineers working to double our supply of intensive care respirators / ventilators to oxygen concentrators and monitors, scale up the production and distribution of vaccines, therapeutics and telemedicine.

When the virus reached India on January 30, 2020, local manufacturers did not have the capability to produce PPE kits like body coveralls, which are required during pandemic situations and classified as Class-3 protection level under ISO 16603 standards. India was entirely dependent on imports. In March 2020, Niti Aayog estimated that we would need 20 million PPE kits and 40 million N-95 masks, which translated to 20,000 PPE kits and 400,000 h-95/FFP-2 class masks per day by July 2020. Engineers along with entrepreneurs rose to the occasion to meet the demand.

India has traditionally imported ventilators primarily from Europe and China to meet its requirements. Before the pandemic, the sector had eight manufacturers with an annual capacity to supply 3,360 ventilators. The COVID crisis saw nine more players enter the field, raising the manufacturing capacity to 396,260 a year, according to industry data. Maintaining supply chain of materials and chemical precursors like sanitizers, phenyl etc; food items, oxygen.

The railways helped Food Corporation of India (FCI) to transport a record 1.7 lakh tonnes of food grains every day, more than double the normal average movement of 80,000 tonnes a day.

Total available production capacity of oxygen has been increased to 9,200 tonnes by converting high purity industrial oxygen to medical oxygen. Indian Railways, started running 'Oxygen Express' to supply medical oxygen to various states amidst increased demand due to COVID-19. Also Indian Air Force and Navy were pressed into service to supply oxygen to needy places.

• Taking initiatives focused on improving infrastructure like organizing hospital space and beds and trying to deal with the shortage of personal protection equipment (PPE) for hospital staff.

It was estimated that India has approximately 1.9 million hospital beds, 95 thousand ICU beds, and 48 thousand ventilators. To meet the emergency requirements efforts to increase the hospital beds by converting facilities like temples, mosques, utilities, etc. into hospitals. The Indian Railway's workshops, quickly converted some 5,000 air conditioned sleeper coaches into care units and stabled them at various locations for hospital overflows.

In the first week of February 2020, only 14 laboratories were testing for COVID-19. At present there are there are 2661 laboratories (Government laboratories: 1271 Private laboratories: 1390).

Further, engineers have been working hard behind the scenes to help flatten the curve and building life-saving equipment. Keeping people healthy is complicated, and no single engineering discipline can do it alone. Different types of engineers have different skill sets and will do that in different ways.

Aerospace engineers COVID-19 had dealt the aerospace industry a severe blow. However, transportation of essentials like oxygen, etc. is being carried out.

Agriculture engineers the impact of COVID-19 on agriculture sector has been varied starting from supply of agricultural inputs to marketing of produce. The long lockdown not only affected the agricultural activities but it has also badly affected the livelihood of farmers and laborers. Farm mechanization, automated irrigation, precision farming, soil and water conservation matters, post-harvest management are some of the areas where agriculture engineers are involved.

Architectural, Civil and Environment engineers are looking into environmental health, civil infrastructure security, and sustainable resource engineering, design buildings that increase health infrastructure. They also make sure that drinking water is clean, and waste is disposed of safely. This makes it urgent for environmental engineers and civil engineers to collaborate on pinpointing viral and environmental characteristics that affect transmission of virus via surfaces, the air and fecal matter. While lockdown has reduced pollution and positive impacts have been observed it puts pressure on all to adhere to pollution control and management post lockdown.

Chemical engineers are involved in development of drug / vaccines, researching on fluid dynamics aspects since they are directly linked to the spread of disease from the transmission routes by air and droplet dynamics, innovative strategies such as the use of reverse engineering and additive manufacturing, exploring some state-of-art technologies in the disease diagnostics and the pandemic monitoring.

Computer / IT engineers - develop and maintain programs and algorithms for modern medical

equipment and modeling tools analyze health data and create health apps (aarogyasetu) and secure tele-health protocols. Several companies that have embraced the remote-working model are likely to continue to do so even after the pandemic end.

Electrical engineers - COVID-19 has not only affected the people's well-being and our economy but also has affected the electricity sector. During lockdown almost all the offices and educational institutions are closed. Thousands of professionals are working from home and students are attending classes online. This has led to a substantial reduction in power consumption of industrial / commercial sectors due to lower demand. Railway's power demand has also reduced substantially. Along with this, the health care systems are operating at their full capacity, making the role of electrical infrastructure more critical. The electric grid is experiencing variations in the load patterns. This has underlined the prominence of delivering reliable and resilient services to various sectors of society

Electronics and Telecommunication engineers role is significant in providing automated resolutions like infection supervision, aarogyasetu app, sensor-related sanitizer dispenser, thermal scanner etc. so, utilisation of electronics components, incorporation with sensors, Wi-Fi connectivity, and remote workability etc. are the basic requirements for this epidemic. Drones are now dominant equipment to visualize and communicate in complicated and infected areas, sanitize infected regions most effectively.

Marine engineers - like aerospace maritime industry has suffered heavily due to COVID. However, they have also contributed in transportation of Oxygen from other countries, supplying to islands and along coastal regions.

Metallurgical & Materials engineers Modern drug delivery systems are comprised of a variety of materials—glass, polymers, ceramics, and metals. For many of us, our interaction with vaccines is at the point of a needle. Austenitic stainless steels find widespread use in medical devices as a result of a good combination of biocompatibility, corrosion resistance, strength, manufacturability, and cost. These attributes are necessary to produce hollow hypodermic needles to incredibly fine sizes through a repeated process of tube drawing and annealing. The finest needles have an outside diameter of about two tenths of a millimetre—approximately twice the diameter of a human hair—with inner diameters about half as much. Developing technologies for anti-viral coating on masks and PPE with metals like copper.

Mechanical and Production engineers work to design health products and plan the large-scale production of masks, face shields, complex medical devices from ventilators to heart monitors, oxygen concentrators, etc. The range of equipment is wide, from PPE, gels and UV sanitizers and inexpensive throwaway bag respirators, through to supportive breathing devices with additional features, to full-scale ICU invasive ventilators. IISc has established a manufacturer for 'tunnels',

through which materials can be sanitised, and smaller mobile sanitization units as well. IITB similarly has developed a large-scale and portable room sanitizer for hospitals

Mining engineers - there has been an impact on the mining sector. However, this is likely to vary from one commodity to another. Thermal coal, building materials will remain buoyant but minerals like iron ore which are exposed to consumer demand, will come under pressure. Engineers have to maintain mining and supplies.

Textile Engineering-Universal masking as a public health intervention is currently mandatory. To avoid PPE shortage crisis for medical staff and other frontline workers, health authorities are recommending the use cloth masks. Although in theory, cloth masks can be helpful to limit the spread of the COVID-19, serious consideration should be given to the choice of textile, the number of layers of cloth used, pre-treatment of the material with water repellent material and other compounds that can enhance the filtration efficiency of the masks without compromising their breathability. Development washable masks and PPE kits, textile based bags for disposing bodies so as to replace plastics is essential.

Interdisciplinary engineers / **Biomedical engineers** combine in-depth knowledge of mechanical and electronic engineering, human physiology and medical applications to design devices like ventilators, diagnostic devices and prosthetic limbs. Biomedical Engineers from a range of industry backgrounds have been putting their normal tasks to one side to build ventilators and PPE to help care for the increasing numbers of patients. Many are using reverse engineering techniques to help them better understand the make-up of the equipment and the optimum methods needed to recreate them, modeling the transport of aerosol droplets as it relates to transmission of the coronavirus between two individuals and among groups, so that effective countermeasures such as enhanced ventilation can be taken. Development of nanobased materials, such as disinfectants, personal protective equipment, diagnostic systems and nano carrier systems, for treatments and vaccine development, as well as the challenges and drawbacks are some of the areas where they are providing inputs.

Every time there is a crisis or a major problem, there are opportunities that lead to improvements. Post COVID, a new global order will emerge. The way are done business will change. Companies will change their governance and business management models with greater focus on corporate social responsibility and the well-being of people. With the changing landscape of business operations, innovation in business will be essential for businesses to survive.

The current practice of work from home could permanently shift working patterns. New norms will be established for these working conditions, redefining work life and personal life boundaries. The workplace will no longer be simply an office where people come to each day, increasingly, workplaces will become collaboration hubs to achieve common objectives, compared to just providing a place for people to work. Companies may have to take steps to adopt technology advancements, and modernize culture, organizational structures, measurement systems and operating architectures. Up skilling and reskilling of the work force would be essential. Companies may go for on-demand workforce models. This would require workforce planning, financial management and access to diverse skills.

COVID-19 has exposed lack of basic healthcare and major gaps in it. The pandemic has created a burning platform for healthcare reform in the country. The healthcare industry will create new opportunities for many. The need for emotional connectivity will increase as remote working, social isolation and social distancing practices become more common. Companies will increase focus on employee's mental health and well-being.

Another area where engineers are playing a role is in telemedicine, the scale-up of therapeutics manufacturing and up scaling manufacture of vaccines. This is a huge engineering challenge. Also scale of diagnostic tests for COVID-19 has improved greatly, and engineers have brought artificial intelligence, automation, and process control to industry's development. As 5G internet becomes more widely available, it will increase the use of online internet systems leading to less dependence or elimination of centralization.

This pandemic has shaken up and laid bare a lot of our country's deep seated problems. With the rapidness of change we are undergoing as a society, if people and companies do not change they will be left behind / perish. Technology will continue to drive innovation across business models in various industries, re-engineering and allowing new businesses to enter the market In the post COVID-19 era, there will be a greater need to increase innovation and move away from the comfort of operating 'business as usual' as old ways of doing things may not work.

About the author

Nearly five decades of experience in Public and Private Sectors in Design and Engineering, Project Monitoring and Management, Turnkey Projects, Corporate Business Management, academics and applied research, etc. Mr Saxena was the General Manager with MECON, Executive Director, BPSL, Independent Director (India) RUSSULA, Spain, Chairman SEAC, Jharkhand constituted by MOEF&CC, Government of India. Currently, he is the EIA Assessor with NABET, QCI; Consultant and Advisor to organizations; Secretary, GB, Yogoda Satsanga Mahavidyalaya. He was Adjunct Faculty with NIFFT, MHRD, Government of India and is associated with other Academic Institutions (Central University, Jharkhand, JRU, Ranchi, IEI, etc.), Spiritual and Philanthropic organizations. Disciplines served Water Supply, Water and Effluent Treatment, Environment, Tailing Dams, Energy, Slurry transportation. Has published / presented over 100 papers / talks. He was awarded Dr. Visveswaraya / SAIL Medal on seven occasions and has also received other awards and is well known figure in Industry. He has travelled widely in Middle East, Europe, USA, Africa and South East Asia. Mr Saxena is Associated with IEI from Student days (Student Chapter) and with Jharkhand State Center for over three decades and at National Level (for 15 years) in various capacities. Currently he is the Chairman, IEI- Sustainable Development Forum at Ranchi.

A Rapid Nucleic Acid Based Point-of-Care Test for Detecting Pathogenic Infection in Resource-Poor Settings

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ABSTRACT

We innovated a new generic piece-wise isothermal nucleic acid test (PINAT) device as a platform technology for diagnosing pathogen-associated infections, including but not limited to COVID-19. The specific innovations in the diagnostic procedure include: single-dispensingstep with single-microchamber integration of all possible process elements for nucleic acid based testing including sample extraction/ lysis, reverse transcription, amplification, specific hybridization probing (with provision for multiple nucleic acid probing) in a thermo-kinetically controlled, automated, time-synchronized manner without any external field-mediated operative intervention. This innovation leads to seamless sample-to-result integration in an inexpensive, scalable, pre-programmable and customizable portable device, with mobile app-integrated interpretation and analytics involving minimal manually operative procedures that can be undertaken by unskilled personnel outside controlled lab environment in a resource-constrained setting. The resulting ultra-low-cost yet highly accurate testing device has been proven highly successful in COVID-19 screening at underserved locations interfaced by minimally trained frontline rural health workers.

Keywords: Nucleic acid testing; Point of care; Rapid diagnostics, COVID-19.

INTRODUCTION

The COVID-19 pandemic has been rudely exposing the glaring limitations in public health due to non-availability of diagnostic technologies that are accurate yet low cost, accessible, userfriendly and amenable to massive manufacturing scale-up and parallelization. With the goldstandard diagnostic tests (such as RT-PCR) turning out to be prohibitively resource-intensive and the common rapid-tests (such as Rapid Antigen tests) proving to be alarmingly inaccurate, there is an unmet demand for low-cost novel diagnostic technologies for resource-limited settings with high specificity and sensitivity. However, the available rapid tests either are limited by compromised accuracy or are poorly performing outside a highly controlled laboratory

ambiance. Disrupting the perception that high-quality molecular diagnostics necessarily demands sophisticated technological and human resources, here we report a novel diagnostic procedure is the first of its kind, highly accurate ultra-low-cost point-of-care nucleic acid-based test having the simplicity and user-friendliness of a common rapid test. The extremely low cost per test (~50 Rs. Per test gene), as well as the capability of operation outside laboratory settings, hallmarks its value the proposition as an affordable alternative to RT-PCR for monitoring the spread of infection at the community level, and an excellent option for routine screening at community locations including schools, shopping complexes, offices, etc. during the regularization phase of the common daily activities post-pandemic. While relying on the same basic backbone of isothermal nucleic acid amplification as several other recently-introduced tests that have otherwise failed to perform satisfactorily on-field, the exclusive test exemplified here could by far successfully deploy the detection method stably outside controlled lab settings in more than 2000 cases of patient trials in rural and unsophisticated urban settings, without incurring carryover contamination despite strict laboratory controls not being adhered to. Summarily, some exclusive value propositions of this diagnostic procedure include: (i) one-step sample-toresult integrated low-cost universal platform device technology for nucleic acid based testing applicable to a wide variety of diseases, (ii) CRISPR-independent but complementary DNAprobe hybridization-based exclusive generic detection procedure favouring high specificity and sensitivity, (iii) simple, user-friendly, extremely low-cost (~INR 8000 per instrument as opposed to highly expensive Real time PCR machine) yet generic, robust, highly-scalable portable device, (iv) certified for satisfactory performance in resource-limited settings by regulatory authority, (v) unique amalgamation of advanced nucleic acid based diagnostics in the format of an affordable rapid test, (vi) deployment at point of care by frontline health workers outside controlled laboratory settings.

METHODOLOGY

In this work, we have resolved one outstanding technological challenge that had largely prohibited the LAMP-based tests to be deployed for community-level testing, which is the lack of a simple, user-friendly low-cost instrument that can seamlessly couple any arbitrary number of isothermal reaction steps as a generic requisite for all LAMP-based test protocols. We have developed a simple device (see **Fig. 1** below) to this end which may be assembled by minimally trained workers. The device comprises a pre-programmable thermal control cum reaction unit that is capable of performing all the heating-cum-reaction steps necessary for the entire test protocol in a time-stamped harmonized and automated sequence without manual intervention. The compact single-chamber arrangement is organized in our device via thermochemically synchronizing all the relevant procedures without any external field-mediated control. In terms of manufacturing, this proposition is realized by simple assembly of device

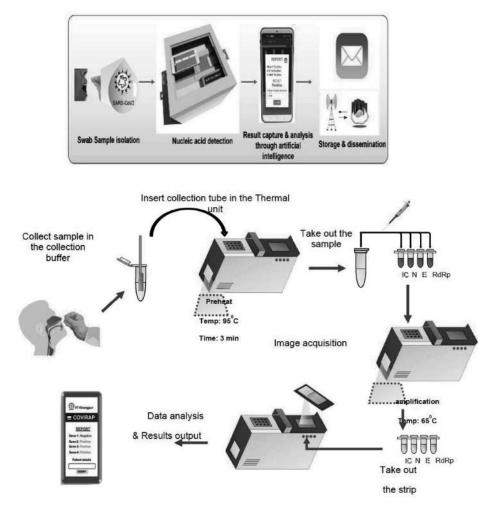


Fig 1: The test method workflow (adapted from ACS Sensors, 2021 Oct 22;6(10):3753-3764, DOI: 10.1021/acssensors.1c01573)

components that have obvious manufacturing scalability and does not require any specialized manufacturing control, rendering the technology dissemination at disruptively low cost as a platform device with minimal disposables. The manufacturing procedure of the device thus gets simplified to mere assembly of the heating block with a heater, temperature sensor, heat-sink fan assembly, microcontroller, opto-coupler-relay unit, and a power unit, with no need of any

sophisticated or complex micro-fabricated component as opposed to similar prior arts. Further, simple assembly of device components renders obvious manufacturing scalability without any specialized manufacturing control leading to the technology dissemination at disruptively low cost as a platform device with minimal disposables. The complete implementation workflow from sample collection to result dissemination using the portable device unit innovated by us is represented in Fig. 1 that includes some key schemes. The process flow from sample collection to test result disseminated via the integrated low-cost device, is as: (1) the swab/ saliva sample collected from the patient is subjected to a brief thermal step performed in heating slots present in the device; (2) the heat lysed sample is subsequently mixed with the test reagents containing primers, probes and enzymes and dispensed altogether in dedicated reaction-chambers (micro-chambers); (3) the piecewise isothermal time-stamped reactions are held in the portable device without intermediate manual intervention (4) colorimetric readouts of the products are captured using a smartphone camera, for subsequent image analytics and machine learning empowered algorithmic implementation and rapid dissemination of the test outcome (within ~45 minutes of sample collection).

The exclusive PINAT method developed here consists of three distinct and extremely generic steps. First, RT-LAMP reaction is executed in presence of biotinylated forward inner primer (FIP-5'Bt) and five unlabelled primers (F3, LF, BIP, B3, BF), resulting in the generation of 5' biotinylated RT-LAMP products. Second, a 6-fluorescein amidite (6-FAM) labelled DNA oligonucleotide (probe), complementary to the loop regions of the RT-LAMP products, gets hybridized through consecutive heat denaturation and annealing process, thereby generating dual labelled (Biotin + 6-FAM) products. Third, as an optional embodiment, the dual labelled products and the single labelled free probes get separated on a lateral flow assay strip and captured by the streptavidin and secondary anti-FAM antibody immobilized on the test line and control lines, respectively. RT-LAMP primer sets are exclusively designed against four highly conserved target regions in the SARS-CoV-2 genomic RNA that reside within the RNA dependent RNA polymerase (RdRp) gene, the nucleocapsid (N) gene, the envelope (E) gene, and the S gene (spike surface glycoprotein). It is important to mention here that a single-step single-microchamber execution of the entire test, central to our innovation, includes additional safeguards as this could potentially lead to adverse cross-interference of the nucleic acid amplification and probe hybridization reactions. To avoid such adverse artefacts, we have included a double modified DNA probe harbouring 6-FAM and a di-deoxy nucleotide at its 5'- and 3'-termini respectively, of our designed primers. It is also important to emphasize here that utilization of a non-amplifying probe hybridization method culminates to a novel two-tier labelling technology, thereby introducing a double layered specificity in the detection process.

VALIDATION

The technology developed by us was validated and benchmarked through patient trials at various levels, including trials supervised by authorized labs of ICMR. ICMR-NICED, one regional COVID-testing lab facilitated one round of clinical testing where the patient swab samples were tested by two independent methods: (i) real time PCR using standard approved kits (ICMR-National Institute of Virology (ICMR-NIV) and (ii) our method. Considering real time PCR as Gold Standard, RNA panel of 115 positive samples [balanced proportion of high viral load (Ct < 20), moderate (Ct 20-28) and high viral load (Ct 28-35)]; 75 SARS-CoV-2 negative samples (Ct undetermined) and 10 SARS-CoV-2 negative but Influenza A positive (Ct value 20-25) was prepared and coded by the ICMR experts. The coded panel was transferred to the designated kit validation unit in double-blinded form. The field study cohort could mimic the diagnostic procedure at a remote location in resource limited setting. We pre-aliquoted ready-to-use reaction-mixes in the forms of packed test kits that were transported in ice packs from our kit manufacturing unit to the patient sample testing centre over a road-travel duration of several hours before performing the test procedure. Purposefully, no specific attention was laid to perform the test in controlled ambience. After the test was run, the panel was de-coded and results of Real Time PCR (Ct values) were compared with the results from our assay. Successful validation was certified by the Head of the authorized ICMR unit. A second round of field trial of the single-step swab-toresult approach without any need of RNA extraction was conducted at the B.C. Roy Technology hospital, Indian Institute of Technology Kharagpur, which is a standard rural primary healthcare centre with limited resources. Samples were taken from patients and volunteers with their informed consent as per approval of the Institutional Ethical Committee. Swab samples were collected in phosphate buffer saline solution, preheated briefly and were directly used as inputs for the test without any need of additional pre-processing or purification steps. The entire testing was executed in a common room by unskilled operators with no special environmental control. The test kits were found to be highly stable in the common room with no specialized cold chain used for the reagent storage there. In parallel, rapid antigen test and/or gRT-PCR was performed with the same samples. qRT-PCR was performed with ICMR approved Quantiplus Multiplex Covid-19 detection kit V2.0. Data collected from more than 800 patient samples was used to estimate the sensitivity and specificity, which outweighed the typical performance parameters of POC-formatted low-cost rapid tests approved by regulatory authorities in India and globally for the detection of COVID-19 infection by manifold. This appears to be an extremely significant milestone towards bringing high-end molecular diagnostics from sophisticated labs to underresourced community settings without incurring any cost-penalty and unacceptable compromise in the predictive accuracy.

CONCLUSIONS

Currently, in India, there is no alternative RNA-extraction free low-cost point of care nucleic acid based test available in the market. The tests available in the Indian market are either resource intensive (like RT-PCR) or of limited accuracy (such as rapid antigen test) or cannot be made functional without including specialized procedures such as RNA extraction or using high end sophisticated instrumentation (like the available LAMP-based tests or their variants commercialized in India). In that perspective, the availability of such low-cost, easy-to-use, highly specific, and reasonably sensitive detection method as a generic platform technology has already been demonstrated to be highly successful in capturing commonly missed instances of early infection and asymptomatic disease presentation and reduce the opportunity for community-level transmission of COVID-19 infection, via organized field trials. Such a proven testing tool amenable for dissemination on a massive community scale in a decentralized manner (eradicating over-dependence on centralized RT-PCR labs) may be a decisive game-changer in re-establishing new-normalcy at workplaces and places of common gathering (including school, collage, community centres) post pandemic. This could result in dramatic improvements in disease management and epidemic/ pandemic control not just with specific relevance to COVID-19 but also in several unforeseen events in the future. The envisaged technological trade-off between the scientific standards of advanced molecular diagnostics and the elegance of common rapid tests for underserved community healthcare, eradicating any differential consideration between the rich and the poor, appears to be the future of molecular diagnostics in resource-limited constraints, bringing high-end lab tests to the ambit of the bottom of the community pyramid in the green field. This innovation is also likely to open up new sources of self-employment of MSMEs through opportunities of large-scale device manufacturing and employing frontline health workers (especially rural girls and youth) for disseminating the test. A Go-to-Market Strategy has also been implemented via licensing of the technology to selected Companies and further, in parallel, developing a rural-entrepreneurship-cum-dissemination ecosystem via the entrepreneurship incubation ecosystem at the Indian Institute of Technology Kharagpur, to ensure continuous endeavours and advancements in terms of reachability to the last mile of population.

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PATENTS

- 1. A Point of Care (POC) Device for Facilitating Nucleic Acid Based Testing and Method Thereof" (PCT/ IN2021/050218; US Patent Application Number 17201968)
- 2. A Method for POC-Based Detection of Pathogenic Infection via Nucleic Acid Based Testing (US Patent Application Number 17202903)
- 3. Detection of Viral RNA: A Portable Device and Method Thereof (202031031597)

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A Scientist's Perspective on the Impacts of Face Covering in Combating COVID-19

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In this article, the mechanism how SARS-CoV-2 virus infects human cells, what happens when virus enters human body, and what are the different phases of Covid-19 infection highlighting the causes of 'Cytokine Storm' has been discussed. For some COVID-19 patients, the body's immune response may be as destructive as the virus that causes the disease. The persistent high fevers, severe respiratory distress, and lung damage seen in some critically ill patients are all signs of an immune system in overdrive causing a cytokine storm. A strong immune system functions better when protected from environmental assaults and bolstered by healthy-living strategies such as: quit smoking, healthy eating, exercise regularly, maintaining blood pressure and healthy weight, and getting enough sleep. COVID-19 is primarily transmitted through viral particles that float in the air or through droplets containing viruses. Even people who are infected but do not have symptoms, or have not yet developed symptoms, can infect others. Masks help minimize spread, which is why the Centre for Disease Control and Prevention (CDC) has long advised mask wearing, in addition to physical distancing.

Soon after the WHO declared COVID-19 as a pandemic, various mitigation measures have been implemented by many countries to constrain the pandemic, including widely adopted social distancing, home isolation, hand sanitization, and mandated face coverings. The scientific data detailing their effectiveness individually or combined is still limited. Notably, face masks have been a matter of intense debate during the COVID-19 pandemic. Early on, several government officials and health authorities were discouraging healthy people from wearing masks because of the fact that there was little evidence showing its ability to prevent spread among people. Regardless of the debates in the medical community, more and more countries are moving forward with recommendations or mandates to wear masks in public.

Curbing the COVID-19 fatality relies on the scientific understanding of the virus transmission routes, which determines the effectiveness of the mitigation measures. Face covering can prevent viral transmission and reduce the risk of infection by the following three ways: it can (1) block the rapid turbulent jets generated while coughing/sneezing, (2) filter virus particles such as aerosols or droplets, and (3) prevent inhalation of virus-bearing aerosols.

EVIDENCE SUPPORTING THE EFFECTIVENESS OF MASKS

A growing body of research supports the use of different types of masks, though the quality of evidence varies. In a recent study [1], Zhang and co-workers analyzed the trend and mitigation measures in China, Italy, and New York City, from January 23 to May 9, 2020. The authors demonstrated that with social distancing, quarantine, and isolation in place worldwide and in the United States since the beginning of April 2020, airborne transmission represents the only viable route for spreading the disease, when mandated face coverings are not implemented.

In an experiment [2] using high-speed video, it was shown that while speaking simple phrases hundreds of droplets ranging from 20 to 500 micrometers were generated. But when the mouth was covered by a damp washcloth nearly all these droplets were blocked.

Another study published in The Lancet [3] systemically assessed 172 observational studies, looking at the effect of different mitigation measures such as physical distancing, face masks, and eye protection on the transmission of COVID-19. The N95 masks were found to offer 96% protection from infection whereas surgical masks (or comparable reusable masks) were 67 percent protective.

In another compelling case report [4], face mask has been shown to prevent COVID-19 transmission on an international flight. A COVID-19 positive passenger flew from China to Toronto. He wore a mask on the flight, and all other 25 passengers close to him on the flight tested negative for COVID-19.

LIMITATIONS OF FACE MASK

There are few rising concerns with the use of face masks as many think that covering the face fails to recognize several important facts such as:

The filter performance of a cloth material varies and does not necessarily represent its performance, transmission of a disease is much more intricate than merely a short interaction between people. Transmission of a disease relates to particulate matter concentration in the air and the duration of time exposed to that concentration, very small size particles of aerodynamic diameter $\leq 1 \mu m$ escape easily from cloth mask and face mask does not eliminate the risk of catching infection through the membranes in your eyes

Owing to such concerns, it can be speculated (not concluded) that face covering offer many benefits but also has certain limitations. Therefore, face masks offer have limited impact on lowering COVID-19 transmission, and caution should be given while considering them as a replacement for physical distancing or self isolation.

Wearing masks, if we are practicing social distancing

The other advocated mitigation measures such as physical distancing are equally important and are beneficial in preventing direct contact transmission but owing to rapid air mixing, it itself is insufficient without face masks to protect inhalation of virus-bearing aerosols/small droplets at intermediate proximity [5].

Mask is as important for vaccinated people as it is for unvaccinated ones

Vaccines appear to keep the vaccinated person from getting ill by stimulating the immune system to produce antibodies against the disease. But it is difficult to estimate the antibody pool in the vaccinated individual leaving an important question- whether vaccinated people wear mask or not? Here are few reasons for vaccinated people to continue wearing mask:

In order to reach same level of herd immunity, 50-80% of the population will need to be vaccinated. This is a time-consuming task as it requires humongous amount of antibody production and expediting its distribution.

After getting both the doses of vaccine, it takes some time to reach the optimum antibody pool in the body. Even after that, vaccines do not provide 100% protection; they only offer 94% to 95% protection. So there is always some risk among vaccinated individuals of getting infected. However, the severity of symptoms would be less compared to unvaccinated ones.

Moreover, vaccines prevent illness, but it is still not clear whether vaccines also prevent transmission of the disease. There is a concern among vaccinated people who can still become infected and spread it to others causing the virus to keep circulating. As the silent spreaders of the disease, vaccinated people should therefore continue to wear mask until more people are fully vaccinated.

CONCLUSIONS

Consider this example: We do physical exercise not because it is going to prevent us from getting a heart attack, but by doing so we are reducing our risk of getting it.

Similarly, face masks in compliance with hand hygiene, physical distancing and other infection prevention and control measures are critical to prevent transmission of COVID-19.

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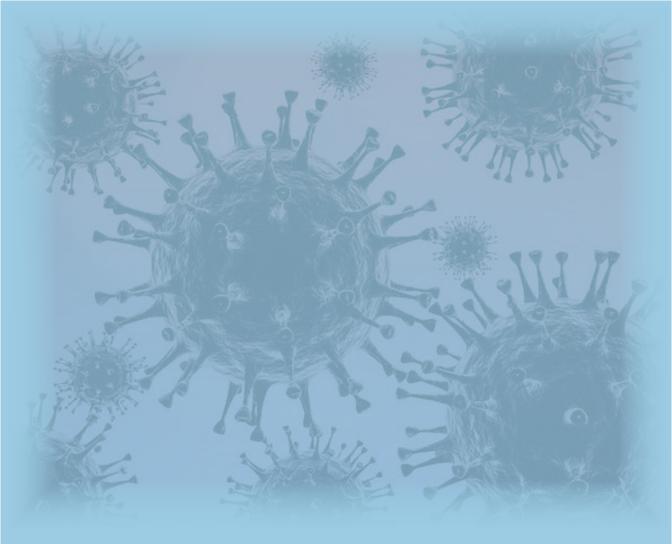
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ACRONYMS

ACTT	:	Adaptive COVID-19 Treatment Trial
BHEL	:	Bharat Heavy Electricals Limited
C19-SVT	:	COVID-19 Social Vaccine Toolkit
CDC	:	Centres for Disease Control and Prevention
CHC	:	Community Health Center
CII	:	Confederation of Indian Industry
CRP	:	C-Reactive Protein
DNA	:	Deoxyribonucleic Acid
EUA	:	Emergency Use Authorizations
FCI	:	Food Corporation of India
FDA	:	Food and Drug Administration
FIP	:	Forward Inner Primer
HFNC	:	High-flow Nasal Canula
HVAC	:	Heating, Ventilation and Air-conditioning
ICE	:	Institution of Civil Engineers, UK
ICMR	:	Indian Council of Medical Research
IIS	:	Indian Institute of Science
IIT	:	Indian Institute of Technology
IUVA	:	International Ultraviolet Association
LFT	:	Lateral Flow Tests
MERS	:	Middle East Respiratory Syndrome
MMR	:	Measles, Mumps and Rubella
NIH	:	National Institutes of Health
NIV	:	National Institute of Virology
OC	:	Oxygen Concentrator
OEP	:	Ordem dos Engenheiros de Portugal
OEU	:	Oxygen Enrichment Unit
OWS	:	Operation Warp Speed
PINAT	:	Piece-wise Isothermal Nucleic Acid Test
PPE	:	Personal Protective Equipment
REMAP-CAP	:	Randomised, Embedded, Multifactorial Adaptive Platform Trial for
		Community-Acquired Pneumonia
SARS	:	Severe Acute Respiratory Syndrome
RT-PCR	:	Rover Platform provides Reverse Transcription Polymerase Chain Reaction
SII	:	Serum Institute of India
UVGI	:	Ultraviolet Germicidal Irradiation
WFEO	:	World Federation of Engineering Organisations





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