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Short Communication

Coronavirus Disease Prevention: Opportunities and Challenges

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SARS-CoV-2 the most potent killer virus, which originated from Wuhan province of China, has created an unprecedented health and economic crisis worldwide [1-3]. At the time of this writing, according to Johns Hopkins Coronavirus-tracker, (coronavirus.jhu.edu/map.html; April 8th, 2021) globally, 133 million (mil) individuals have tested positive to this virus, and over 2.9 (mil) have died. In the USA, which represents 4% of the world population, there are 31 (mil) infected individuals and over 562,360 Covid-related deaths. Little is known about the epidemiology of this disease in low- and middle-income countries. In a first of a kind review, Indo-US collaborators, conclude that, "Among 575,071 individuals exposed to 84,965 confirmed cases, infection probabilities ranged from 4.7 - 10.7% for low-risk and high-risk contact types. Case fatality ratios spanned 0.05% at ages 5 - 17 years to 16.6% at ages greater than 85 years [4,5]. According to a CNN news report, "A national (ICMR) survey of more than 29,000 people across villages and wards found, that about one in 15 people above age of 10, has antibodies against coronavirus. More than 63 million people in India, may have contracted Covid-19, according to the health authorities in India. Currently USA, India, Brazil, France, and Russia rank as the top five contenders for the highest number of COVID-positive individuals. As far as COVID-related deaths are concerned, USA, Brazil, Mexico, India, and the UK are the top five contenders. Since the time it was discovered in China to this day, the virus has mutated several times into highly transmissible and deadly strains. At the time of this writing the British, Brazilian, South African, and Indian double mutant strains are causing a havoc worldwide. Various research groups have carried out genomic sequencing of the COVID-19 virus and shared these sequences on public databases, including GISAID. Since majority of countries have done limited testing for SARS-CoV-2 virus, it is estimated that the incidence and prevalence of infection may be at least ten-fold higher than reported.

At the population level, the only preventive option that is available is, 'to play hide and seek', with this novel killer virus. If the virus cannot find you, it will not be able to infect you. Using this simple logic, public health best practices have been developed and implemented in all the major countries. Having said that, this approach has not been adhered strictly in all the countries, hence the observed disparity in the rate of infection and case fatality rate. China, Taiwan, and Vietnam stand out as the best examples of public health success, in preventing the spread of this virus into large sections of populations. In China, -COVID-19 pandemic's epicenter, Wuhan, and its province, Hubei, Chinese Center for Disease Control-network, formed 1300 epidemic investigation teams, in addition to the 40,000 doctors and nurses. They used very clever tracing tools with big data support. In the first week of January the novel coronavirus infection was detected, and on 23 January 2020, they locked down the city of 11 million people and soon the rest of the Hubei-a province of nearly 60 million. The WHO-China Joint Mission on Coronavirus Disease 2019 Task Force concluded, "In the face of unknown virus, China has rolled out perhaps the most ambitious, agile, and aggressive, disease containment effort in history". Take home lesson from these Asian countries is, that in the absence of a cure, the best option we have is, to avoid the infection by using face masks, observing social distancing, washing hands with soap as and when needed, implementing strict contact tracing and containment of infected individuals. Therefore, first and foremost requirement, is the availability of a safe and cost-effective test, that can be performed at the population level. Since testing for COVID positive individuals is of primary importance, there is great oppor-

tunity to develop simple easy to use, cost-effective, tests that can detect the virus with great specificity and accuracy.

At the end of August, the US Food and Drug Administration (FDA) granted emergency-use approval, to a new credit-card-sized testing device (BinaxNOW COVID19Ag Card) for the coronavirus, which gives the results in 15 minutes and doesn't require a laboratory or a machine for processing, using proven lateral flow technology, with demonstrated sensitivity of 97.1% and specificity of 98.5% in clinical studies. The United States is spending 760 million on 150 million of these tests from health-care company Abbott Laboratories. These tests detect specific proteins-known as antigens – on the surface of the virus and can identify who are at the peak of infection, when the levels in the body are likely to be high. Abbott is offering a no-charge complementary NAVICA app, which allows people to display their 'BinaxNOW' test results, when asked by organizations where people gather, such as workplaces and schools. A set of agreements to make available, for low and middle-income countries, affordable, high-quality COVID-19 antigen rapid tests were today (September 28, 2020) announced by the Access to COVID-19 Tools (ACT) Accelerator. Organizations involved in the milestone agreement include the Africa Centers for Disease Control and Prevention (Africa CDC), the Bill and Melinda Gates Foundation, the Clinton Health Access Initiative (CHAI), the Foundation for Innovative New Diagnostics (FIND), the Global Fund, Unitaid, and the World Health Organization (WHO). As far as developing a reliable cost-effective testing is concerned there is still a great opportunity for innovation and product development.

Since the time the killer virus, SARS-CoV-2 made its appearance on world scene, it has become a public health workers nightmare [6]. This virus is uniquely equipped for forcing entry into cells. The receptor binding site of this virus is a better fit for the ACE2 than the SARS-CoV, its predecessor. In addition, this virus seems to make use of the enzyme 'furin' from the host, to cleave viral spike protein. Both ACE2 and furin are abundant in the respiratory tract, as well as throughout the body. Coronavirus disease is a multisystem disease and as such, affects all the tissues, systems, and organs of the human body. These observations provide great opportunities for drug discovery and development. Since the mode of entry as well as specificity of its binding sites are well defined, the pharma companies can design and develop specific interventions for this mode of transmission. For instance, Chinese researchers have demonstrated that Hydroxychloroquine and Remedesivir are effective in inhibiting SARS-CoV-2 infection *in vitro* [7,8]. Despite these earlier findings, several clinical studies have failed to show any preventive effect of Hydroxychloroquine on COVID-19 infection in human trials [7-10]. Therefore, these observations pose a great challenge for the pharma company in terms of the development of drugs that can effectively interfere with transmission both *in vitro* as well as *in vivo.* FDA has created a special emergency program for possible coronavirus therapies, the Coronavirus Treatment Acceleration Program (CTAP). Currently there are 590 development programs in planning stages, 390 trials in review and five authorized for emergency use, -none approved for use in COVID-19 management. There is another challenge, -as mentioned earlier this virus attacks all the tissue, systems and organs, therefore its infection is accompanied by multiple clinical symptoms. In view of these observations, there is a great opportunity for developing a series of interventions to manage all the associated clinical symptoms.

There is an urgent need for the development of preventive strategies for COVID-19. While industry giants are transfixed by the high-stake race to develop a COVID-19 vaccine, an equal crucial competition is heating up, to produce targeted, neutralizing antibodies that could provide, an instant immunity boost against this virus [11]. Immunologist Dennis Burton, whose group at Scripps Research has isolated highly potent monoclonal antibodies against SARS-CoV-2, -hopes to move this novel therapy into human studies. He is optimistic, that monoclonals will protect people from infection for months with a single shot. Pandemic Prevention Platform (P3), at the Defense Advanced Research Project agency has a novel approach, in which they aim to develop monoclonal antibodies, that can be made by the body itself, instead of in large fermentation tanks. The idea, which has not been tested in humans for COVID-19, is to inject people with DNA or messenger RNA that encodes a desired antibody, allowing their own cells to make it. A cocktail antibody therapy on the other hand, uses two or more lab-engineered antibodies. Regeneron's cocktail includes a monoclonal antibody that targets the spike protein, the virus uses to drill into the healthy cells, and another antibody that targets a different part of the novel coronavirus. With two, the hope is to trap and shut down virus replication. According to Dr Leonard Schleifer, co-founder of Regeneron, phase 3 trial starts soon for COVID antibody drugs, that might treat and prevent infection. There are at least 70 different antibody treatments under investigation according to Bio, an association that represents major biotechnology companies. Research-

ers at the National Institutes of Health (NIH, USA) have isolated tiny antibodies or "nanobodies" against SARS-CoV-2. They seem to work equally well in either liquid or aerosol form suggesting that it could remain effective after inhalation.

Indian Pharma companies are not known for drug discovery and innovation. Having said that, we need to assure the readers, that Indian Pharma is well placed and competent in drug development, scale up of generics, biologicals, and vaccines. Abhirup Roy and Euan Rocha report in Healthcare Pharma (May 22, 2020), - "How one Indian company, could be the world's door to a COVID-19 vaccine. If the World is to gain access to a vaccine for COVID-19, there's a good chance it will pass through the doors of the Serum Institute India (SII)." The fight against COVID-19 has seen unprecedented vaccine development worldwide at a record speed, with more than 170 different vaccines in trials. All of them are trying to achieve the same goal, - achieving development of immunity to the virus as well as for reducing further transmission. They achieve this goal by stimulating an immune response to an antigen molecule that is typically found on the virus. Majority of the vaccines are concentrating on the spike proteins which are responsible for transmission of the virus. There are four categories of vaccines in clinical trials: whole inactivated virus, protein subunits, viral vectors, and nucleic acid (RNA and DNA) Nucleic acid vaccine use either RNA or DNA to provide cells with the instructions to make the antigen. Viral vector vaccine also provides genetic instruction to produce antigens. In the US Pfizer-BioNTech COVID-19 vaccine, Moderna COVID-19 vaccine, and Janssen COVID-19 vaccine are authorized for emergency use.

Pfizer, BioNTech COVID-19 (mRNA-based) vaccine is a multinational product authorized for emergency use in majority of the countries. Moderna, BARDA (NIAID) also an mRNA based vaccine is also widely authorized for emergency use. AstraZeneca (AZD1222), a UK product also produced in India by the Serum Institute, Pune, (Covishield) is widely distributed and authorized in many countries for emergency use. Sputnik V, a recombinant adenovirus vaccine (rAd26and rAd5) developed by Gamaleya Research Institute, Russia is authorized in several countries and may be produced under a licensing agreement in India. Janssen (JNJ Ad26.COV2.S) is a non-replicating viral vector and is produced by Janssen Vaccines (Johnson and Johnson), developed by the bilateral collaboration between the US and the Netherlands. It is a single shot vaccine and may become popular because of it cost, safety and efficacy. China has developed three vaccines, CoronaVac (Sinovac) (inactivated virus), BBIBP-CorV (Sinopharm) and Convidicea (Ad5-nCoV) by CanSino Biologics. India has developed Covaxin (inactivated virus) at Hyderabad by Bharat Biotech, whereas Serum Institute Pune has several vaccines under development. What role will India play in the global COVID-19 vaccine supply chain? The country plans to vaccinate over a billion of its own population and the government has donated millions of doses across 10 countries.

Indian companies will soon start selling COVID vaccines globally. COVID-19 is not going to be a once in century pandemic. It may turn itself into an endemic. In view of this possibility there is a great opportunity as well as a challenge for the Indian entrepreneurs to develop innovative ideas and come up with various interventional strategies in addition to COVID-vaccines, for combating this menace at all levels of its manifestation.

According to the National Institutes of Health (NIH) USA, and the US Food and Drug Administration (FDA), there are no approved therapies for COVID-19 management. FDA has created a special emergency program for possible coronavirus therapies, the Coronavirus Treatment Acceleration Program(CTAP). Currently, there are 590 drug development programs in planning stage, 390 trials are in review, and five authorized for emergency use, -none approved for use in COVID-19 management. Again, in palliative and preventive therapies, there are great opportunities for drug discovery and development. This is a challenging time, we have the science to help us get through this pandemic and future ones, - we need to use it, together says, Gangadeep Kang, Professor, Christian Medical College, Vellore. In a short overview like this, it is not possible to cover all aspects of this unprecedented pandemic. Readers are urged to refer to original articles, reviews and monographs on this topic for additional information [12-18].

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