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No Funds for BioScience in 20 lakh crore AtmaNirbhar Package

By Anonymous Writer

Despite having huge money flow in this biological pandemic Indian Bioscience sector is looking at the backfront in recent announcement of G.O.I of AtmaNirbhar Package

Rs 20 lakh crore package announced in five tranches by FM Sitharaman stood at Rs 20,97,053 crore, included the Rs 1.92 lakh crore stimulus from measures announced by PM Modi recently such as the Pradhan Matri Garib Kalyan Package worth Rs 1.7 lakh crore.

The first set of relief measures announced by Nirmala Sitharaman focused on enabling the Indian economy's backbone – MSMEs that employ around 11 crore people and have a GDP share of approximately 29 per cent.

Second tranche of measures catered to migrant workers and street vendors.

The third tranche of the measures worth Rs 1.5 lakh crore focused on the agriculture and allied sectors including dairy, animal husbandry and fisheries as the government announced steps to strengthen the overall farm sector.

The fourth instalment of the Rs 20 lakh crore package comprised of reforms for sectors including coal, minerals, defence production, air space management, airports, MRO, distribution companies in UTs, space sector, and atomic energy.

The minister also announced the commercial mining in the coal sector and privatizing discoms in metros to streamline their functions for better accountability.

The minister allocated an additional Rs 40,000 crore for the Mahatma Gandhi National Rural Employment Guarantee Act (MGNREGA) for job creation in India's hinterland.

In all above mentioned schemes biological science has not been discussed for even a single time when we have been victimized of biological pandemic. Is this a punishment to Indian scientists or the ignorance of govt is a matter of great speculation.

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From the very first issue, Biotech Express team has been delivering what's best for Biosciences community. The audience of this magazine includes students, researchers, faculties and executives of highly prestigious organizations of India. In year 2016, BEM has made new editorial Board combining experience of eminent Advisory Board Members who have been into Award winning Research and head prestigious Administrative positions.

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Editorial

Why Indian Bioscience Response is "Not Enough" to curb Global "COVID19" Biological Pandemic: What are We Missing?

By Kamal Pratap Singh and Seema Pavgi Upadhye

Introduction

India is a country of around 1.3 billion living in as congested places like Dharavi in Mumbai to spacious lush green Lutyen's zone of Delhi. Handling world's second most population is not an easy task but the situation till now is under the control. However, there are few who speculate that we have just postponed the pandemic which will come after lifting up the lockdown or may recur like other viral infections.

There has been around two months (in India) since the lockdown which has led life to travel on road. The strategy has been proved successful till now, but we were not able to find rocket science behind this act, when it was asked for 21 days only as time window for scientific and other preparations and then extended for around 60 days.

Despite having complete Genome sequence(s) and biochemical information which can further help to prepare recombinant vaccine, unavailability of COV-2 vaccine anywhere is the most embarrassing situation for scientific fraternity in world when the institutions and companies of world declare themselves as world's no.1 including in the field of biosciences. It is important to refer Remdesvir here because it has become first drug of emergency use in COVID19 by FDA (not by WHO) but has failed to gain trust of market, it is in the market since 2004. According to a recent update of WHO, no Indian Vaccine has entered human trial as on 15th May. (Reference 1)

On the many occasions Biotech Express magazine has reported accomplishments of India's scientific developments but we at this occasion have nothing great to show as there is still no 'Make in India' diagnostic method and/or treatment available from the country. In this COVID19 pandemic too, we are lagging behind many nations when we could control whole attention through a vaccine or a cure. In this article we are discussing about current status of India in Virus research, what has been done by Indian science leaders and scientists to combat this virus and its transmission and what more is expected to become global leader in Biological sciences.

NOTE: Chinese research and products are not mainly included in this article.

Major decisions taken by global bodies

- World Health Organization is facilitating collaboration, accelerated research, and international communications with a goal to raise US$8 billion
- Coalition for Epidemic Preparedness Innovations (CEPI) is working with global health authorities and vaccine developers to raise US$8 billion. The United Kingdom, Canada, Belgium, Norway, Switzerland, Germany and the Netherlands had already donated US$915 million by early May.
- The Gates Foundation, a private charitable organization dedicated to vaccine research and distribution, is donating US$250 million for research and public educational support.
- Global Alliance for Vaccines and Immunisation (GAVI) is financing and organizing clinical groups in under-developed countries with COVID-19 vaccination preparedness.
- Global Research Collaboration for Infectious Disease Preparedness (GLoPID-R) is coordinating among the international funding and research organizations to maintain updated information on vaccine progress and avoid duplicate funding.
- The International Severe Acute Respiratory and Emerging Infection Consortium organizes and disseminates clinical information on COVID-19 research to inform public health policy on eventual vaccine distribution.

COVID19- India's Approach(es)

To start with Indian healthcare and medical science, health of a common man of this country is supported by Ministry of health and family welfare (MHFW) headed by Dr. Harsh Vardhan. MHFW supports health infrastructure required for medical treatment and/or research activities in this field. The budgetary allocation for the MHFW in 2019-20 was Rs 60,908.22 crore, with Rs 6,400 crore earmarked AB-PMJAY. Ministry of Health and Family Welfare has three Departments- Department of Health & Family Welfare, Department of Health Research (ICMR as its flagship organization) and recently added Department of AYUSH. Directorate General of Health Services (DGHS) is attached office of the Department of Health & Family Welfare.

The next important organization of Govt. which supports science activities is Ministry of science and technology, it mainly look up research activities in the country. The Ministry of Science and Technology (S&T) has three wings under it — the Department of Science and Technology (DST), Department of Biotechnology (DBT) and Council for Scientific and Industrial Research (CSIR). In 2019-20, the DST has been allocated Rs 5,321 crore, the DBT has been allocated Rs 2,580 crore and the CSIR has been allocated Rs 4,895 crore. (Reference 2)

To know the efforts of Indian science to this biological pandemic it is important to see and understand the activities of these two ministries MHFW and MST in current times, which together are premiere authorities for health infrastructure and research and are responsible to provide urgent plan for combating and curing this health hazard now and in recurrent future.

A. Indian COVID19 Science Task forces and their assigned tasks

To address the COVID19 pandemic, various task forces/committees/groups were made in these two ministries, their departments, councils and organizations each one with their own leaders and peers. Analysis of various task forces revealed lack of harmony among these groups which we will discuss later. The various groups made are as under:

1. Central Govt. Task forces

COVID-19 task force was set up on March 29, 2020 which directly operates under the Prime Minister. This task force, with handpicked bureaucrats and key officials, operates around the powerful Prime Minister's Office. These include cabinet secretary Rajiv Gauba, health secretary Pritee Sudhan and home secretary Ajay Bhalla, three officers--principal sec-

retary to the PM, P.K. Mishra; principal advisor to the PM, P.K. Sinha; and newly-appointed secretary to PM, Amarjeet Sinha. Reporting to the PM's task force are V K Paul, NITI Aayog member for health, and Balram Bhargava, secretary, health research, and also director-general of the Indian Council of Medical Research (ICMR). Another key official in this grid is K. Vijay Raghavan, principal scientific advisor to the government. The government's public interface includes the daily press briefing at the National Media Centre. The briefings are given by Lav Agarwal, joint secretary in the health ministry, ICMR DG Bhargava, ICMR chief scientist R. Gangakhedkar, home ministry spokesperson P.S. Srivastava and K.S. Dhatwalia, director-general of the Press Information Bureau. (Reference 3, 4)

On April 19, the centre has formed again a **high-level task force** to track and monitor the work being carried out **to develop vaccine** against COVID-19. The panel has been led by Member (Health), NITI Aayog and PSA to the PM. AYUSH, ICMR, DST, DBT, CSIR, DRDO, DG Health Services and Drug Controller are members of the task force. In this task force the Department of Biotechnology has been asked to become a central coordination agency to identify pathways for vaccine development. (Reference 5)

2. DHR-ICMR

As per records, the first high-level technical committee of 21 scientists and Public Health Experts for COVID-19 was established on 18th March under the Chairmanship of Dr Vinod K Paul, Member, NITI Aayog, to guide the prevention and control activities in the country. (Reference 6)

On 6th April, National Task Force for COVID-I9 has constituted the following research groups to identify the research priorities and quickly initiate research studies. (Reference 7)

1. Clinical Research Group
2. Research on Diagnostics and bio-markers
3. Epidemiology and surveillance
4. Operations Research
5. Vaccines/Drug Research and Development

ICMR's Rapid Response Team for COVID-19 appeared on 26th April (Reference 8).

3. CSIR

CSIR has not constituted any formal task force but has been seen to coordinate with other science agencies on regular basis.

On April 29, CSIR and **Cadila** started clinical trial of Sepsivac' drug in PGIMER Chandigarh to evaluate efficacy of an existing gram-negative sepsis drug, called Sepisvac for COVID19 patients.

On 5th May, CSIR-IGIB and TATA Sons signed a MoU for licensing of KNOWHOW for FNCAS9 EDITOR LINKED UNIFORM DETECTION ASSAY (FELUDA) FOR RAPID DIAGNOSIS OF COVID-19. (Reference 9).

On 8th May, CSIR under its New Millennium Indian Technology Leadership Initiative (NMITLI) has sanctioned a project to develop human monoclonal antibodies as therapy for COVID-19 infections. National Centre for Cell Science (NCCS), IIT-Indore and a Gurgaon-based company, PredOmix Technologies will also collaborate with Bharat Biotech on the project. The cost of project has not been disclosed. (Reference 10)

More info about CSIR strategies and drugs being considered by CSIR for followup can be found here- https://urdip.res.in/covid19/vertical2.jsp (Reference 11)

4. Department of Science and Technology

On March 27, the Department of Science and Technology (DST) said it has set up a Covid-19 task force for mapping of technologies to fund nearly market-ready solutions in the area of diagnostics, testing, healthcare delivery solutions and equipment supplies. The capacity mapping group consists of representatives from DST, DBT, ICMR, Ministry of Electronics and Information Technology, and CSIR. It also has representative from the Atal Innovation Mission (AIM), Ministry of Micro, Small and Medium Enterprises (MSME), Startup India and All India Council

for Technical Education (AICTE). (Reference 12)

5. ISRC (Non-Govt.)

Indian Scientists' Response to CoViD-19 (ISRC) started as a group of Indian scientists who came together voluntarily in response to the COVID-19 pandemic. It has now grown to include **more than 500** scientists, engineers, technologists, doctors, public health researchers, science communicators, journalists and a number of students; they hail from a range of disciplines but principally the physical and life sciences; they are affiliated to eminent research institutes of science and technology, universities, colleges, hospitals and private laboratories. The group also includes Indian scientists from laboratories all over the world. The few initiators of the group include S Krishnaswamy, Sandhya Koushika (TIFR, Mumbai), L S Shashidhara (Ashoka University), Rahul Siddharthan (IMSc, Chennai), Reeteka Sud (NIMHANS, Bengaluru) and many more. (Reference 13)

6. Principal Scientific Advisor's Task forces

The first meeting of the **Empowered Committee for COVID-19** response in India was held on March 21, 2020. The meeting was co-chaired by Dr. Vinod Paul, Member NITI-Aayog and Professor K. Vijay Raghavan, Principal Scientific Advisor (PSA) to Prime Minister, Government of India. The Committee was constituted to co-ordinate, amongst science agencies, scientists and regulatory bodies, and take speedy decisions on R&D implementation related to the SARS-Cov-2 virus and the COVID-19 disease.

According to an official release from PSA office, Indian research institutions and organizations were directed for speedy implementation of solutions related to COVID-19. "National research labs (defined as labs of DBT/DST/CSIR/DRDO/DAE for this directive were permitted to carry out clinical testing for COVID19 based on self-assessment and willingness to follow established protocols and all applicable reporting regulations as defined by the DHR/ICMR,". Also "Labs with BSL-3 or BSL-3^{+} facilities, with DBT/DST/CSIR/DRDO/DAE, were permitted to culture the virus and serve as additional testing and validation sites for research, based on self-assessment of BSL-3 facilities and willingness to follow established protocols as defined by the DHF2/ICMR. (Reference 14)

The Principal Scientific Advisor to the GoI, Dr K VijayRaghavan, has constituted a S&T Core Group '**PSA Task Force on Repurposing of Drugs for COVID19'** on 16th March 2020 (in short "**TFORD-COVID19**"). The Task Force is being coordinated by: Dr V Premnath, Head, NCL Innovations at CSIR-NCL and Director, Venture Center and Dr Anurag Agarwal, Director, CSIR-IGIB. Key components planned for this task force are to Compile information on Drug Candidates, Reports by Nerve Center Team to PSA, Inter-disciplinary Advisory Group; Position/ Strategy Papers, Virtual Translation Network, Information on Path to Market/ Bedside, Requests to PSA etc. (Reference 15)

B. Vaccine Research and Manufacturing in India

The first two vaccines in India were developed by Dr Haffkine of British Government in 1893. The first recombinant vaccine made in India was Hepatitis-B made by Dr Ramareddy V Guntaka in 1996 for a company of first generation entrepreneur Varaprasad Reddy, Padma Bhushan who conceptualized the impossible task and fought against many odds. Since then Biotechnology has opened new avenues and interests for Indian Pharmaceutical sector. Now, India occupies a prominent position in Biologics drugs industry.

1. Early Background & Development

In India, till 1850, the vaccine was imported from Great Britain. Anna Dusthall, a three year old child from Bombay (now Mumbai) became the first person in India to receive smallpox vaccine on June 14, 1802. In 1893, Dr Haffkine conducted vaccine trials in Agra, Uttar Pradesh, and showed the efficacy of Cholera vaccine in the effective control of the disease. Later he developed plague vaccine in 1897 and it is arguably, the first vaccine developed in India. This

laboratory was called Plague Laboratory since 1899, renamed as Bombay Bacteriological Lab in 1905 and then finally named as Haffkine Institute in 1925, as it is known today.

In early twentieth century, four vaccines (smallpox, cholera, plague, and typhoid) were available in the country. Feeling growing demand, the Government of India decided to set up new vaccine institutes. The initial vaccine research unit was Haffkine Institute for plague vaccine. The smallpox vaccine lymph was being produced in Shillong since 1890. In 1904/1905, Central Research Institute was set up in Kasauli, Himachal Pradesh and then Pasteur Institute of Sothern India in Coonoor in 1907, in the same year the Pasteur Institute of India (PII) produced neural tissue Anti-rabies vaccine in 1907. The PII in due course of years, developed influenza vaccines, trivalent oral polio vaccines conducted landmark research and production of tissue culture and then Vero cell derived DNA purified rabies vaccine for human use.

Then many developments and reorganization of vaccine industry has taken place and can be found in the article published by IJMR in 2014. (Reference 16)

2. Current Landscape: Vaccine R&D and manufacturing infrastructure in India

What we have now and how to use it to fight this COVID19 enemy is a question of the hour. In virology research, India's position is not that much weak when compared to west, over the years the vaccine research and manufacturing infrastructure has developed into world class facility in the country.

Since we are discussing CoV2 here which require a specialized BSL-4 facility for handling, it is little sad to know that we have only three facilities with BSL-4 rating, in a country of 1.3 billion where viral infections are common thing. The three facilities are Microbial Containment Complex(MCC), ICMR- National Institute of Virology, Pune; High Security Animal Disease Laboratory, ICAR- National Institute of High Security Animal Diseases (NIHSAD), Bhopal; and CSIR-Centre for Cellular and Molecular Biology(CCMB), Telangana. Recently, DBT-RGCB announced to establish BSL 4 facility.

List of CDSCO Licensed Human Vaccine indigenous Manufacturing Facilities in India (Reference 17)

Private

1. Biological E. Ltd.
2. Bharat biotech
3. Cadila healthcare
4. Cadila Healthcare Limited
5. Cadila Pharmaceuticals
6. Chiron Behering
7. Dano Vaccine & Biological Pvt. Ltd.
8. Green signal BioPharma Ltd.
9. Panacea
10. Ranbaxy Lab
11. Serum Institute of India
12. Shantha Biotechnics Ltd.
13. GSK Asia Pvt. Ltd.
14. Sanofi Pasteur India Pvt Ltd.

PSUs

1. BIBCOL
2. Haffkine Bio Pharma Corporation
3. Human biological institute
4. HLL Biotech Ltd.

Government

1. BCG vaccine, Guindy, Chennai.
2. CRI, Kasauli, District Solan, HP.
3. Pasteur institute

Other players

1. Avesthagen
2. Aventis Pharma Limited
3. CPL Biologicals Limited
4. Eli Lilly India

5. Indian Immunologicals Limited
6. Intervet India
7. Lupin
8. Merck
9. USV Biopharmaceuticals Limited
10. Venkateshwara Hatcheries Limited
11. Wyeth

Other Avenues of Indian science in Vaccinology

The Department of Health Research (DHR)/Indian Council of Medical Research (ICMR) took a far sighted decision of enhancing the country's capacity for early identification and diagnosis of all viral infections of public health importance. This initiative of DHR/ICMR has been rolled out on approval of the **VRDL Scheme** by the Union Cabinet wherein it was envisaged to set up 160 Virus Research & Diagnostic Laboratories (VRDLs) in most of the Government Medical Colleges of the country in 12th Plan Period (2012-2017). (Reference 18)

A Multi **Vaccine Development Program** (Not For Profit Research Society) is committed to undertake, outsource, assist, promote and encourage scientific studies, epidemiology studies, product development, clinical studies & establish field sites with the object of advancing the development of vaccines against *P. falciparum* and *P. vivax* malaria identified by Research Institutes. Dr. Salunke current Director of the International Centre for Genetic Engineering and Biotechnology and Dr. T.S. Rao presently working as Adviser in the Department of Biotechnology, Ministry of Science & Technology, Govt. of India are among the governing board member of this initiative. (Reference 19)

C. Translational Research after COVID19 pandemic

1. Diagnostic kits

Pune-based Mylab Discovery Solutions was the first Indian company to give Make in India diagnostic test. Mumbai-based Meril Diagnostics Pvt Ltd., Delhi based Medsource Ozone Biomedicals Pvt. Ltd., and others are among current manufacturers. (Reference 20)

On April 22, Indian scientists from the Institute of Genomics and Integrative Biology (IGIB) also declared to have successfully developed a low-cost, paper strip test which can detect the Coronavirus2 within an hour. It uses the cutting-edge, gene-editing tool - Crispr-Cas9 to target and identify the genomic sequences of the novel Coronavirus. The team led by Souvik Maiti and Debjyoti Chakraborty is currently testing the kit in a patient cohort for its accuracy and sensitivity and hope to seek validation from a regulatory body of the Indian Council of Medical Research (ICMR). (Reference 21)

However, with the accuracy in question there are questions on whether these kits can reliably help indicate the spread of the infection.

2. Vaccine or Treatment

There are no drugs or other therapeutics presently approved by the U.S. Food and Drug Administration (FDA) to prevent or treat COVID-19. Current clinical management includes infection prevention and control measures and supportive care, including supplementary oxygen and mechanical ventilatory support when indicated. (Reference 22)

Global Efforts

The National Institutes of Health, an agency within the Department of Health and Human Services, has been fast-tracking work with biotech company Moderna which is developing mRNA vaccine to prevent Covid-19. The company began the first phase 1 human trial on 45 volunteers testing a vaccine to prevent the disease in March and has been approved to soon start its phase 2, which would expand the testing to 600 people, by late May or June.

Inovio began its early stage clinical trials for a potential vaccine on April 6, making it the second poten-

tial Covid-19 vaccine to undergo human testing after Moderna.

Vaccine ChAdOx1 nCoV-19 (recombinant) developed by researchers at Oxford University began phase 1 human trials on April 23. British Health Minister Matt Hancock said that he would provide £20 million, ($24.5 million), to help fund the Oxford project.

Many others treatment options are in either preclinical, clinical stage or Midstage trial, some are BNT162, NVX-CoV2373, Remdesivir, Hydroxychloroquine, Favipiravir, Kevzara, Baricitinib etc. (Reference 23, accessed on 11 May 2020)

The FDA issued a warning against taking the drug outside a hospital or formal clinical trial setting after it became aware of reports of "serious heart rhythm problems" in patients. Similarly, even though remdesivir was granted FDA nod for emergency use, there are still several ongoing clinical trials testing whether it's effective in stopping the coronavirus from replicating and The Lancet reported that Treatment with remdesivir did not speed up recovery or reduce deaths from COVID-19. (Reference 24)

India

More than 30 vaccines are in various stages of development in India, scientists informed Prime Minister Narendra Modi on May 5.

\University of Oxford's vaccine is also being developed with multiple partners including India's Serum Institute of India. The WHO document says out of the 100 projects under pre-clinical stages,

Indian companies like Zydus Cadila, Codagenix-Serum Institute of India, Indian Immunologicals with Griffith University, Bharat Biotech in association with Thomas Jefferson University,

Biological E Ltd, and the UW Madison-FluGen-Bharat Biotech combine are all working on potential vaccine candidates to cure the coronavirus infection. (Reference 25)

Remarks:

So far we discussed the organizational setup of Indian healthcare system and their working in covid19 pandemic through science tasks forces for COVID19, current research and manufacturing infrastructure and the output till now. It is imperative that India does not have any promising innovative product nor her scientists could utilize the time they were seeking for preparation by putting lockdown in place; She is using diagnostic kits of other nations and in treatment too she is not in the hit lists of COVID19 Landscape drugs.

Where Indian Science is lagging? Why even after these many organizational set-ups and efforts Indian scientists could not make a single entity of great scientists who would find drug/vaccine for this disease.

We tried to find out more reasons why it is taking this much time to make a vaccine by Indian scientist when around 10,000 crore is going to DST, DBT and CSIR alone, where top most scientists are working. We could not figure out how much is going to DHR's medical research from 62,000 crore but believing it must be having significant contribution in figures.

How the chaos is creating problem can understand by taking excerpts from one article - "Everything is fine as long as you take action," Naveet Wig, head of the department of medicine at the All India Institute of Medical Sciences told other members of the government's task force of public health experts on Covid-19 on 29 March 2020. "This discussion has gone on for too long and no action has been taken. No. No. We will have to tell the truth." (Reference 26)

The records also show, while imposing the lockdown, the government had ignored recommendations from its top scientists. Instead of the current coercive lockdown, these scientists had advised "community and civil-society led self-quarantine and self-monitoring," through their research in February 2020. However later concerned Indian organization denied the claims.

This can be the problem over fight for leadership, the next problem that holds a place here is leaders' ignorance of national as well as internationally skilled sci-

entists who have played with the viruses. According to a survey by Biotech Express magazine many senior scientists of concern field were not contacted to see their views.

Lack of infrastructure is also a concern here because not all virologists can use same facility in single time, we have 24 hours only. In this situation, which warrant future preparation there is need of establishing most advanced multiple scientific infrastructure for translational research.

Lack of appropriate choice of expertise was revealed as an important factor which was seen while formations of task forces. It mainly revolve around current employees irrespective of their specialization whereas many famous Indian Microbiology and Biotechnology researchers like Jacob John, G Padmanabhan, Madhavi, Rajeev Bhargava, N K Ganguly, Satyajit Rath and many more have not been appearing in any of the task forces.

Concept of domination by misinformation in science came from an observation of a video of Prof K Vijayraghavan where he was seen ignoring his expertise when News anchor called him a Microbiologist. Our observation found that he is not a Microbiologist but a Drosophila Developmental Geneticist who have never experienced virus research, at least not in his published research studies. (Reference 27)

Lack of manpower and its positioning is another concern that needs to be addressed in times of such pandemics. Working Chair has his own duties but professionalism should come first in emergency situations like this. We saw that how many task forces were made for each and every task but these forces have different leaders and soldiers and one of the main leader has not come to front at a single location or time till now i.e. Dr V K Paul, the first Member of the various committees, which shows either of his incapability(which seems illogical here) or inconsistency of science fraternity toward combating this science problem.

Indian Govt has not tried the Brain Drain of the Indian scientists who otherwise are doing great in other nations. Indian Human Resources for Health supported Sustainable Development Goal (SDG) 3, which 'ensures healthy lives and promotes well-being for all at all ages', the US order prioritised SDG 8, which states: 'Promote sustained, inclusive and sustainable economic growth, full and productive employment and decent work for all'. Notably, the US order exempted foreign doctors, nurses, researchers and other healthcare workers and their dependents from the ban. (Reference 28)

We apologize that despite our duty we cannot spell more on Indian sciences as everyone is waiting for some working results but they are yet to come.

As Romila Thapar said somewhere, ''History is not written by committees but by individuals''. Whenever a major activity like combating this 'public Health crisis' is undertaken by very intelligent and competent human beings, you will not always hear beautiful symphony music. Some jarring notes are bound to appear. Team work is very difficult to execute without discipline, commitment and command structure.

Authors' Note: These are observations and views of authors' only, communicating their personal views.

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Letter to PM: from Virology Expert

Dear Honorable Prime Minister Modi ji:

As I am aware of the fact that you have to listen scientific people around you for scientific suggestions but let me bring some facts to you.

World Health Organization puts out statistics on various causes of deaths in each country every year. I checked for one recent year, in India, 1.23 million people died of diarrhoeal diseases compared to 18000 in China. Influenza, pneumonia and TB together killed about 1.1 million people compared to 0.75 million in China. Another 4 or 5 million people are dying in each year from heart problems, stroke, cancer, diabetes etc.

Today Coronavirus is making the whole world panicked with deaths. This shows how important to control infectious diseases. There are no proper diagnostic kits to detect this virus; they don't have antibody testing kits to check how many people got infected already (seroprevalence). Everybody is rushing to make poor quality kits, which don't have the required specificity and sensitivity. These ventures are now becoming big news items in various media.

They could have tested the genomes of the coronavirus that is prevalent in India. This would give some idea how it is evolving. Many research labs can do but we did not see many genome sequences of the virus from India whereas all the major countries in the world including China and Korea published a large number of these sequences, inspite of the fact that India has excellent genetic sequencing facilities all around the country through its lab's network of CSIR, DBT, DST, ICMR, Private companies etc.

How many diagnostic kits are they "making" in India? How many kits are imported into India? From which countries? Are they assessing the quality of the kits with respect to its specificity and sensitivity? Because Millions of coronavirus kits are necessary to detect and determine the seroprevalence in India, meaning what percentage of people were infected and recovered. These are done by testing for the coronavirus antigens and antibodies.

Are these kits (both Ag and Ab) available in India? To my knowledge, not even a single State in India has the capability to develop these kits and even if some small companies developed, they can't produce in quantities required. Everybody depends on countries like China and South Korea etc. As you all know the quality of Chinese kits and reagents are not good.

If we minimize political interference and influence in healthcare and other science and technology agencies and give highest priority to high quality research, India can be in the forefront of Research and Development and can compete with anybody in the world.

Ask your Health Department, the ICMR, the DST and DBT, who are spending several thousands of crores rupees on Research. Ask what the prestigious All India Institutes of Medical Sciences doing?
If we minimize political interference and influence in healthcare and other science and technology agencies and give highest priority to high quality research, India can be in the forefront of Research and Development and can compete with anybody in the world. Indians have enormous talent but most of it is wasted in India without doing much, whereas the same Indians are excelling in all fronts in USA and in other countries.

Locking down 130 crores of people in their homes and putting millions of policemen to achieve this, will not solve the problem. It is a big mistake. It might be prudent to do for 2 to 3 weeks initially but prolonged lock down will not do any good; it will only prolong the pandemic. Wiser decisions to protect the seniors and letting the younger (who are at minimal risk) work, would alleviate the problem.

In areas where there is one positive case, police are working at full force to block the people going out. They can spend that time to identify and isolate those positive cases and devote more time in taking care of and helping senior citizens.

Wise decisions by the Government with the advice of experts will slow down the current pandemic instead of locking down the whole country.

ONLY HEAVENS CAN HELP INDIA AND THE WORLD!

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Editorial in News

India's Pioneer Scientific Work Towards the COVID-19 Vaccine

by Kamal Pratap Singh, Managing Editor, Biotech Express
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In India, 'Lockdown' was imposed on March 21, 2020 but a team of scientists headed by Prof Shailendra Saxena from KGMU performed the best possible experiments in early January, as soon as World Health Organization published out first Disease Outbreak News on the new virus, with a cluster of cases of pneumonia in Wuhan, to know about the genetic and biochemical machinery and tried to get as much information as possible for the risk assessment and making a vaccine for prevention. In his pioneer original research paper from India, his team not only suggested to rename this virus as SARS-CoV-2 which later was done by WHO, but also reported its pandemic potential.

Prof Shailendra K Saxena, KGMU, and his team of researchers published an original research article which was sent to journal on 24 January 2020, it was further accepted on 21st February 2020 and published online eventually, much before Indian scientists started to see CoV pandemic around the world. This earliest study from India has been planned to determine the sequence variation, structural and antigenic divergence of S glycoprotein which aimed to provide help for the management of 2019-nCoV infection.

The various strains of viruses used for the experiment are Wuhan seafood market pneumonia virus isolate

Collectively, for the first time their results exhibited that the emergence of human 2019-nCoV is closely related to predecessor SARS-CoV and provide the evidence that 2019-nCoV uses various novel glycosylation sites as SARS-CoV does and may have a potential to become pandemic owing its antigenic discrepancy.

Wuhan-Hu-1 2019-nCoV (MN908947.3), Wuhan seafood market pneumonia virus isolate Wuhan-Hu-12019-nCoV (NC_045512.2), Bat SARS-like Coronavirus isolate bat-SL-CoVZXC21 (MG772934.1), Bat SARS-like coronavirus isolate Rs4084 (KY417144.1), SARS Coronavirus MA15 isolate d3om4 (JF292919.1), SARS Coronavirus civet007 (AY572034.1) and SARS Coronavirus GD03T0013 (AY525636.1), whereas Japanese encephalitis virus (AF075723.1) was considered as an outlier.

The steps they performed were as following:

- The team used sequences of spike glycoprotein of SARS-CoV-2 (2019-nCoV) and SARS Coronavirus (SARS-CoV) for the comparison using EMBOSS Nee-

dle pairwise sequence alignment tools.

● Analysis for antigenicity was performed by NetCTL 1.2 and validated by IEDB Analysis Resource server. This server predicts the peptide MHC class I binding; proteasomal C terminal cleavage and transporter associated with antigen processing (TAP) protein transport efficiency.

● For structural divergence determination, the protein homology modeling was performed by using by using the spike glycoprotein sequences of SARS-CoV-2 (2019-nCoV) and SARS-CoV using HHPred server. The generated models for S glycoproteins of SARS-CoV-2 (2019-nCoV) (PDBA) and SARS-CoV (PDBB) were based on cryo-EM structure of the SARS coronavirus spike glycoprotein (PDB ID 6ACC). The generated models were superimposed to determine the structural divergence using SuperPose Version 1.0, which calculates the protein superposition using a modified quaternion approach.

● The variation in glycosylation sites was predicted by NetNGlyc 1.0 and validated by N-GlyDE server.

We found that this research from India suggested for the first time that SARS-CoV-2 (2019-nCoV) is closely related to SARS-CoV, which has only 12.8% of difference with SARS-CoV in S protein and has 83.9% similarity in minimal receptor-binding domain with SARS-CoV.

In glycosylation sites they found that the SARS-CoV-2 (2019-nCoV) spike glycoprotein exhibits common glycosylation sites that were also present in SARS-CoV such as NITN, NGTI, NITN, NFSQ, NESL, NCTF and NNTV. Their data suggests that the 2019-nCoV may interact with host receptor using novel glycosylation sites that may affect the internalization process and associated pathogenesis.

In addition, antigenic site analysis proposes that great antigenic differences exist between both the viral strains, but some of the epitopes were found to be similar between both the S proteins. They have found that most of the CTL epitopes are novel from the SARS-CoV. However, six epitopes RISNCVADY, CVADYSVLY, RSFIEDLLF, RVDFCGKGY, MTSCCSCLK and VLKGVKLHY were found to be identical in both the spike glycoproteins. In spite of the variation in S protein amino acid composition, they found no significant difference in their structures.

Collectively, for the first time their results exhibited that the emergence of human SARS-CoV-2 (2019-nCoV) is closely related to predecessor SARS-CoV and provide the evidence that SARS-CoV-2 (2019-nCoV) uses various novel glycosylation sites as SARS-CoV does and may have a potential to become pandemic owing its antigenic discrepancy.

Further, demonstration of novel Cytotoxic T lymphocyte epitopes may impart opportunities for the development of peptide based vaccine for the prevention of SARS-CoV-2 (2019-nCoV).

In his research paper written in January 2020 he concluded that human SARS-CoV-2 (2019-nCoV) is closely related to predecessor SARS-CoV, consequently, it should be renamed as SARS-CoV-2 and owing its pandemic potential it should be declared as a public health emergency of international concern at the earliest.

The research news was very well covered by Nature Asia and many other reputed Journals.

The Altmetric available on Springer article shows that the article has been accessed more than 14,000 times. Altmetric has tracked 14,991,487 research outputs across all sources so far and compared to these this one has done particularly well and is in the 94th percentile: it is in the top 10% of all research outputs ever tracked by Altmetric. Even a recent science show (Why Is SARS-CoV-2 So Contagious?) from USA, on SARS-CoV-2 (2019-nCoV) vs SARS-CoV, is based on this original research paper.

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Editorial

Detection of viruses in sludge, effluents and waters - The case of COVID-19

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Abstract

Viruses may occur, survive and/or decay much differently from bacteria in water. Pathogens, if not removed properly from wastewater may enter in water bodies and cause infections. Among the diseases caused by viruses some have been reported severe. COVID-19, SARS-CoV and MERS-CoV are recent examples of how coronaviruses infect humans. We have no tools to control the disease except social isolation. COVID-19 is enveloped, non-segmented, positive-sense RNA virus having high mutation rate and it may emerge in the future and pose challenges for the water and wastewater industries. COVID-19 is having very less literature available. It is very important that it should be treated by proper treatment at source i.e. Effluent Treatment Plants (ETP) and Sewage treatment plant (STP) operators/ Heath care facilities. Investigations regarding COVID-19 outbreak are on-going, and the information that we have right now may change as we learn more about this virus. Chlorination has been reported to be the proper treatment of it at source. If not treated properly this may enter in the water cycle. In this paper, exertions are mainly focused at methods of detection of various types of viruses. Future needs for the development of new technologies for virus elimination and source control have also been highlighted.

Key words: Coronaviruses, SARS, respiratory, Chlorination, Disposal

1. Introduction

Seasonal flu has been reported to be caused by viruses. During 1918-20 "Spanish" influenza virus, killed approximately 50 million people (Taubenberger and Morens, 2008). Severe respiratory illness by Severe acute respiratory syndrome coronavirus (SARS-CoV) has emerged in Hong Kong in 2003 has been noted (Leung et al, 2003; Cheng et al, 2004). The Middle eastern respiratory syndrome coronavirus (MERS-CoV) emerged in Saudi Arabia in 2012 is also an example of disease caused by coronavirus (Vana and Westover, 2008; Morens et al., 2012; Guery et al., 2013). H1N1 (from pigs) and Spanish flu (from birds) were deadly but it's RNA was slower to mutate. Recently, public fear is logical, because it has been reported that in Wuhan, China, at an animal market (December 2019), the coronavirus (COVID-19) mutated and made a jump from animal to humans, in just two week time, it mutated again and gained the ability to get transmitted from human to human. It has been reported to cause great damage to human lungs (OSHA, 2020; WHO, 2020a).Now it's a troublesome situation, because we have no natural or acquired immunity for this virus, hence it is difficult to fight with it. We have no vaccine to control the disease except social isolation.

COVID-19 is enveloped, non-segmented, positive-sense RNA virus having high mutation rate and it may emerge in the future and pose challenges for the water and wastewater handlers. As ETP plants are main entry and

expiry point of virus transmission, now a days there is a chance for presence of coronaviruses in drinking as well as domestic and industrial wastewater (Guery et al., 2013; Risku et al., 2010; WHO, 2020a).

Therefore in this paper, exertions are mainly focused at methods of detection of viruses from water/wastewater. The behaviour of viruses at each stage of treatment is reviewed. Particular attention is paid to the ETP unit operations, which play crucial roles in virus removals. Future needs for the development of new technologies for virus elimination and source control are also highlighted.

2. Occurrence of enveloped viruses in urban water cycle

In general, potential for presence of enveloped viruses in water/wastewater has been found very unstable but coronaviruses (e.g.SARS and MERS) are capable of holding infectivity for days to months in drinking and wastewater (Hewitt et al.,2013; Bibby et al., 2015). It may be excreted in human feces and can cause infection (Leung et al.,2003; dejong et al,2005). Coronaviruses, consists of lipids and proteins, are generally not associated with fecal routes of transmission but recently sewage samples have been reported to have some enveloped virus (Dumontet et al., 1999; Bibby et al., 2015). Human viruses do not replicate in the environment, therefore one way of transmission of a virus may the urban water cycle (Hewitt et al., 2013;Masclaux et al., 2013; Kitajima et al, 2014).

Transmission through domestic wastewater: The coronavirus most likely transmitted through aerosols during wastewater treatment and through human waste (Liu et al., 2003). The persistence of coronaviruses in hospital wastewater and domestic sewage is estimated to be 2-3 days (Wang et al., 2005). Further, if wastewater treatment is insufficient to remove or inactivate coronaviruses, or combined sewer overflows/bypasses are operational, the viruses may be released into the environment likely via aerosols (Casanova et al., 2009; WHO, 2020a).

3. Detection of Viruses

The methods available for detecting small numbers of viruses in large volumes of water are still inefficient for detection of coronaviruses. Membrane filter technique has been reported for virus detection in water as viruses can be adsorbed efficiently by cellulose nitrate membranes (Berg et al, 1972, Fong et al., 2005).

Cell culture with the aid of biotechnological tools such as molecular biological methods (Polymerase chain reaction (PCR)) has been recognized as the standard method for detection of infectious viruses Leung et al, 2003; Dejong et al, 2005; Fong et al., 2005; Vabret et al., 2006; Wong et al., 2012a; Xagoraraki et al., 2014; Guery et al.,2013). Thus, integrated technologies combining modern molecular biology and animal cell culture are the future development trends for virus detection. Role of metagenomic technologies is also gaining momentum for the rapid detection of viruses in sludge, water and wastewater.

4. Survival of viruses in urban water cycle

Studies suggest that survival of coronaviruses is reliant on various parameters (CDC, 2002; Rabenau et al., 2005). Coronaviruses rapidly lose their infectivity in aqueous environments (WHO, 2020b). Inactivation rates are highly dependent on the water temperature, salinity (Gundy et al., 2009; Casanova et al.,2009). Studies suggest that the survival of Human Coronavirus (HCoV) and SARS-CoV is reliant on temperature (CDC, 2002). Survival of coronaviruses in primary wastewater effluent at temperatures greater than 20°C has been reported as 4 days. However, the same study reported that the survival time increases at cold temperatures i.e. near 4°C as more than 4 weeks (Rabenau et al.,2005).

To the best of our knowledge the survival of coronaviruses in wastewater and sludge has not been reported but is expected to vary significantly depending on site-specific. Based on a study these viruses may be detected in urine and stools from infected individuals for more than 100 days after initial infection (Liu et al., 2003; Gundy et al., 2009).

5. Disease outbreaks due to waterborne viruses

Waterborne viruses can infect human beings with various diseases that may be fatal to sensitive populations such as infants, children and immune compromised individuals. Many recently reported disease outbreaks have been reported related to contaminated drinking and recreational waters (Wong et al., 2012a; Wong et al., 2012b; Wigginton et al., 2015; Zhang et al., 2016).

6. Elimination of viruses from urban water cycle

Wastewater treatment is typically conducted by

Table 1. Common viral diseases

Name of Virus	Major disease(s)	Virus elimination
Polioviruses	Poliomyelitis, paralysis, meningitis, fever	More effectively removed by secondary treatment compared to primary processes. Disinfection performance depends on various parameters such as pH, temperature, turbidity, residual chlorine, disinfectant dose. Hence all parameters should be continuously monitored. Lime treatment, activated carbon and UV technique, chlorination can be used to remove viruses from effluents
Echoviruses	Meningitis, respiratory disease, rash, fever, gastroenteritis	
Coxsackieviruses	Enteroviral vesicular pharyngitis, meningitis,respiratory disease, enteroviral vesicular stomatitis with exanthem (hand, foot andmouth disease)	
Hepatitis A virus	Hepatitis	
Adenoviruses	Conjunctivitis, respiratory disease, gastroenteritis	
Rotaviruses	Gastroenteritis, diarrhea	
Norovirus	Diarrhea, fever, vomiting, gastroenteritis	
Polyomavirus	Sarcoma, cancer	
Ebolavirus	Ebola	
SARS coronavirus	Severe Acute Respiratory Syndrome	
MERS coronavirus	Middle Eastern Respiratory Syndrome	
Avian influenza	Influenza	

conventional activated sludge process, including sedimentations, biological decomposition and disinfection. Filtration by sand filters or membranes may also be employed for tertiary treatment especially when water reuse is to be practiced. Generally, most of these unit operations, except for disinfection, are not designed for virus elimination but they mainly eliminate suspended solids (SS), organic substances and nutrients from wastewater (Dumontet et al., 1999).

6.1 Elimination of viruses by primary treatment: Enveloped viruses are poorly removed from primary wastewater treatment i.e. settling steps. The presence of suspended solids and organic material increases survivability of enteric viruses in aqueous environments. Hence there are chances for survival of coronaviruses in unfiltered primary effluent than in filtered water/wastewater. Viruses may easily be absorbed onto or may be trapped within suspended particles in wastewater (Irving and Smith, 1981; Cao et al., 2010; Wong et al. 2012b; Xagoraraki et al., 2014; Templeton et al., 2008).

Lime treatment, produces high alkalinity and high pH, which may remove all viruses from effluents or waters to achieve the disinfection. The coronaviruses are most stable between pH 7.4 - 8.2, with rapid inactivation below pH 6.5 and above pH 10. The coagulation-flocculation-settling process has not been reported very effective but ultrafiltration and chlorination has been reported effective in removal of influenza virus (Berg, 1973; Lucio-Forster et al., 2006).

The effectiveness of chlorination for inactivating viruses in wastewater is dependent upon numerous water quality factors like, presence of ammonia, which reacts with chlorine to form chloramines. Over-all, chloramines are much poorer virucides as compared to free available chlorine. Thus, it is important to consider the level of ammonia before the disinfection process to adequately determine its virucidal efficiency. Chemical disinfection of wastewater with free available chlorine is expected to be effective for coronaviruses when applied at adequate levels (Wang et al., 2005; Katayama et al., 2008).

6.2 Elimination of viruses by secondary treatment: Enveloped viruses can be more effectively removed in secondary treatment. Secondary clarifiers and disinfection step reduces viruses in effluent(s) (Irving and Smith, 1981; Katayama et al., 2008; Hewitt et al., 2013).

In general, secondary wastewater treatment may be highly variable for removal of viruses (USEPA 1986a; USEPA 1986b; Hewitt et al., 2013). Because of this variability, the processes like chemical disinfection (i.e. chlorination) and/or disinfection by ultraviolet (UV) light for inactivation of viruses in wastewater treatment is very

prominent (USEPA 2006a; Li et al., 2011). Extended aeration, ammonia removal and activated sludge system may have great virus removal capabilities in other biological systems context (USEPA 2006b; Chaudhry et al., 2015). Although sand does not adsorb viruses, organic and other substances trapped in sand often do it. Thus, as organic matter accumulates in sand, the latter may retain viruses. Salts and pH also play a role in the whole process. And coagulation itself effects virus removal (Li et al., 2011; Hewitt et al., 2013; USEPA 1986a).

6.3 Elimination of viruses by tertiary treatment: Carbon does retain viruses but it is important in the disinfection process because it removes organic compounds that interfere with disinfectants. Chlorine has been the reported as standard disinfectant, but turbidity has been reported to effect on that (Berg et al,1973). UV disinfection of viruses in wastewater is not possible to estimate for general systems as it is not designed specifically for virus inactivation; however it is expected that it may help for inactivation of low-levels of viruses. However, Ultraviolet (UV) disinfection is regarded as an effective and competitive solution for the disinfection of secondary effluent, due to its merits of no chemical agent(s) addition, non-corrosive, simple installation, easy operation, and no formation of disinfection by-products. But the disinfection effect may be significantly hindered by turbidity and coloured substances which are residual in the secondary effluent (USEPA 2006a,b).Disinfection performance is hooked on various parameters like turbidity, disinfectant dose, residual chlorine, pH, temperature and flow in treatment plant hence all must be continuously monitored and heightened, so that conventional filtration can achieve the goal to make the water safe to drink(Health Canada, 2019a,b).

7. Virus elimination from water

7.1 Sludge and domestic wastewater: Oxidation pond or lagoon can be considered as practical and simple sludge and domestic wastewater treatment method as it is well suited for destroying pathogens, because this treatment has relatively long retention times. It is combined with sunlight, elevated pH levels, biological activity and other factors which serve to accelerate pathogen destruction (Dumontet et al., 1999; WHO and UNICEF2020). It has been reported that greater numbers of viruses disappeared from sewage when settling was allowed to continue for 12-24 hrs retention time and this also depends on temperature, sunlight and perhaps the condition & microbial flora ofsoil present in the pond (Dumontet et al., 1999).

7.2 Drinking water: Contamination from upstream in raw water supply can leads to the occurrence of viruses in surface water treatment plants. Conventional treatment with chlorination cause inactivation of viruses in the water (Health Canada, 2019a). However, continuous analysis of turbidity, residual chlorine, pH, temperature is mandatory (Health Canada, 2019a, b). It has been reported that UV effluence can achieve inactivation of poliovirus, rotaviruses, adenoviruses in the drinking water (Health Canada, 2019b; USEPA 2006 a,b).

8. Potential response actions

Respiratory illnesses usually spreads at community level by contact with aerosols and by hand-to-mouth transmission in operators of wastewater treatment. Therefore, it is recommended that wastewater treatment operators and sludge handlers use personal protective equipment(s) such as face masks, goggles and gloves to prevent exposure to aerosols (OSHA, 2020; WHO, 2020b). Further, strict sanitation practices should be implemented and frequent handwashing with soap should be performed. Separation of eating areas from work areas and minimization of contact between hands & face should be practiced.

9. Protective measures for wastewater treatment facility operators/Heath care facility operators: Special focus to COVID 19

Wastewater treatment facility operators/Wastewater analyst/Heath care facility operators should take extra precautions to protect themselves from the COVID-19 virus infections. Particular safeguards are recommended for staff involved in wastewater analysis/COVID 19 treatment and diagnosis operators. Employee should wear appropriate personal protective equipment(s). While planning for long-term management, above immediate solutions are often needed to minimize the spread of disease during emergencies, and should include community education basic hygiene practices for the above facility handler(s). Below are the compiled general sanitation practices that prevent the spread of respiratory viruses (CDC, 2002; OSHA, 2020; WHO 2020b).

- People who work with wastewater treatment/ collection/analysis/COVID 19 diagnosis or treatment facility operation should avoid direct contact with wastewater, and should avoid ingesting, swallowing, breathing in wastewater spray or mist.

- Frequently wash hands with soap and water for at least 20 seconds. When soap and running water are unavailable, use an alcohol-based hand rub with at least 60% alcohol. Always wash hands that are visibly soiled.
- Wash hands before eating and after each toilet visit.
- Clean and disinfect surfaces.
- Wear appropriate Personal protective equipment such as protective outerwear/clothing, gloves, boots, and goggles (Covering the eyes completely) or face shield masks (N95 or FFP3 respirator mask).
- Maintain good hand hygiene
- Avoid touching your eyes, nose, or mouth with unwashed hands
- Avoid close contact with people who are sick.
- Avoid spray aerosols because aerosols containing virus can enter the body through eyes, nose or mouth.
- Avoid contact with others if they have cold and flu like symptoms.
- Use the inside of elbow to cover sneezes or coughs.
- Once work is complete take complete shower with shampoo and soap because aerosols settles on clothes/body/hair.

Note: Proper disinfection/treatment of the generated waste at the source is highly recommended.

10. Conclusions and perspectives

Enveloped viruses are more effectively removed in secondary treatment compared to primary treatment. History has shown that fast and immediate steps taken in proper direction, which have helped to limit the spread of the disease. Long retention time during settling may help in removal of viruses. Coronaviruses showed lower survival rates in wastewater than other enteric viruses. They do rapidly lose their infectivity in aqueous environments. As ETP plants are main entry and expiry point of virus transmission, based on behaviour of viruses at each stage of treatment, particular attention needs to be paid by ETP unit operations, which play crucial roles in virus removal from wastewater. Operators of sewage treatment plants/ effluent treatment plants/solid waste management facilities related with treatment of solid/liquid waste generated by healthcare facilities/COVID-19 diagnosis laboratories should follow standard operating procedures with basic hygiene practices including use of proper PPEs. Lime treatment process can be one of the options to remove viruses from effluents. Disinfection performance is affected by various parameters hence all relevant parameters should be continuously monitored during the treatment processes. Chlorination has been reported to be the proper treatment of it at source. If not treated properly this may enter in the water cycle.

It is to remember that much literature on effectiveness of water and wastewater treatment processes for COVID 19 is not available. The treatment is as always site-specific due to which variation in water-quality would be observed. Very limited data has been published on the fate of COVID 19 in natural waters and in water treatment processes. More experimental work is required on enveloped viruses in water treatment processes before major conclusions can be drawn on their fate in wastewater and drinking water treatment. As reported by WHO (2020a), investigations into the COVID-19 outbreak are on-going, and the information that we have right now may change as we learn more about this virus. The brief notes made in this document are based on best practices and procedures from reputed organizations. Analyst health and safety risks are likely to vary among specific locations. Trained health and safety professional should be consulted to create site specific health and safety plans.

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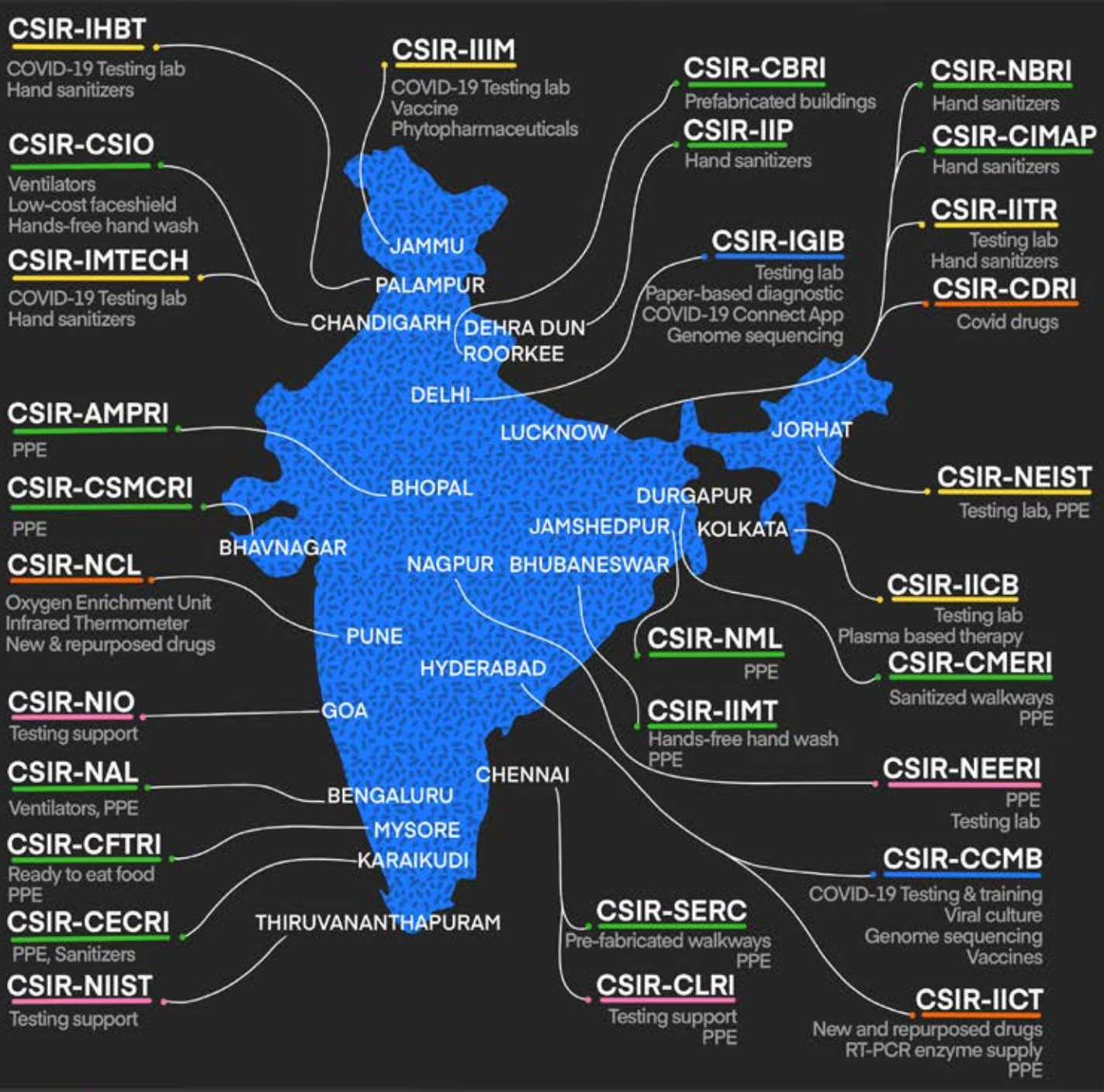
CSIR-Corona Combat Mission

Even as COVID-19 entered India, CSIR and its 38 constituent laboratories consisting of about 3,500 scientists and thousands of students geared-up to mitigate the pandemic. From developing diagnostics using cutting-edge technologies to repurposing drugs, from genome sequencing to viral cultures, from making and distributing masks & sanitizers to developing personal protection equipment, Team-CSIR has been at the frontline.



CSIR's five-pronged approach to mitigate COVID-19 in India.

1. Surveillance and Digital Monitoring
2. Diagnostics and Testing
3. Development and Repurposing of Drugs
4. Personal Protection Equipment & kits
5. Supply Chain for Products

- COVID-19 Sequencing labs
- Testing labs
- Testing support labs
- New & Repurposed drugs
- Personal Protection Equipment

Expert Views: Stem Cells

Stem Cells as Clinical and Research Tools For COVID-19

S Dravida, PhD

Founder, CEO, Transcell Biologics

World Health Organization (WHO) has named SARS-CoV2 (a new format of corona virus) as COVID-19 while declaring it as causative agent of the pandemic outbreak in 2020 with roots from China. According to a recent publication of the International Society for Stem Cell Research (ISSCR), currently, there are no approved stem cell-based approaches neither for prevention nor treatment of COVID-19 infection. Mesenchymal stem cells (MSCs) are being researched and trialed as one of the therapeutic tools in the treatment of COVID19. The hypothesis on which MSCs are being trialed is that this particular stem cell type opposes viral infection due to the secretion of specific cytokines by them. These ancillary secretory components are present in MSCs in their intrinsic forte and so they survive even if they are transplanted into a patient with a confirmed COVID-19 infection.

COVID-19 is shown to trigger a destroying immune overreaction in the body while the immune system produces large amounts of inflammatory factors, causing a cytokine storm that includes an overproduction of immune cells and cytokines. MSCs are postulated to prevent the storm release of cytokines by the immune system and stimulate endogenous repair by reparative properties owing to their stemness. Typically, after intravenous injection, portion of the injected MSCs entangle in the lung, which in otherwise systemic infusion is perceived as a limitation, while it is a blessing in disguise for COVID-19 patients that could positively influence the recovery in the pulmonary microenvironment by way of protecting alveolar epithelial cells, intercepting pulmonary fibrosis, and ultimately curing lung dysfunction and pneumonia caused by the virus.

MSCs type has attracted attention to be considered as therapeutic tool for COVID-19 infection due to source availability, their high proliferation rate supporting in culturing in the labs, low invasive procedure when being injected, and with no ethical issues. As MSCs can be stored for repetitive therapeutic usage, **biobanks** could play a quintessential role in the supply with safety and efficacy of MSCs documented in several clinical trials.

Pathological microenvironment induced by viral infections in cell cultures contribute tremendously to a researcher's work on host-virus interactions. If the cell cultures are harvested from human system, they become an amazing alternative *invitro* systems that accurately re-create in vivo human physiology that can support the study of viral pathogenesis.

Adult stem cells especially MSCs can be handy to mimic the human host environment when modeling viral pathogenesis *invitro*. Noroviruses, rotaviruses, enteroviruses, adenoviruses, zika virus and many other viruses were studied by infecting stem cell cultures *invitro* while genome-wide analysis of host-virus

crosstalk, identification of host factors critical for viral pathogenesis, and the study of viral pathogens are some of the lab based research findings supporting the discovery and development of solutions to diagnose and cure viral diseases. Human biological discards sourced MSCs could be an ideal stem cell type for *invitro* infection studies with COVID-19 strain while addressing the otherwise known challenges dealing with biopsies, availability, ethics etc.

About Transtoxbio

Transtoxbio (www.transtoxbio.com) is a portfolio with all new league of human biological discards sourced (ethically immuned) primary progenitor cell based platforms for specialty next generation *invitro* applications in preclinical basic and translational research. Primary stem cells are amenable to any research specific modelling and are cost-effective in the scheme of operations with relevant human specific read outs obtained as experimental end points.

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About Author

S Dravida leads the team and collaborations responsible for discovering druggable formulations across therapeutic areas and platforms. Her role requires converging and executing both laboratory, clinical research programs across touch points.

Her Past Affiliations include University of North Carolina, Ottawa Health Research Institute and Center for Cellular and Molecular Biology, Hyderabad Eye Research Foundation.

Expertise: Adult stem cell technologies, Predictive platform development and screening, Primary cells, Tumorospheres, Low throughput and High throughput platform technologies, Cancer progenitor cells, Repository of patient sourced screening platforms, Cell based readouts, Drug discovery, pre-discovery process

Featured News

Overall strategy of DBT-BIRAC COVID-19 Research Consortium for funding in Vaccines, Diagnostics, Therapeutics and other Technologies

MAY 10, 2020

To urgently develop safe and effective Biomedical solutions against SARS CoV-2, Department of Biotechnology and Biotechnology Industry Research Assistance Council (BIRAC) had invited applications for COVID-19 Research Consortium. In addition, BIRAC has also created a provision to fund COVID-19 solutions that are ready for immediate deployment under a '*Fast Track Review Process'*.

Under the research consortium, DBT and BIRAC have continuously been evaluating applications with an intent to support Industry/ Academia and Jointly Academia & Industry for developing Diagnostics, Vaccines, Novel Therapeutics, Repurposing of Drugs or any other intervention for control of COVID-19. Through a rolling multitiered review mechanism, 70 proposals of devices, diagnostics, vaccine candidates, therapeutics and other interventions have been recommended for receiving financial support. **The shortlisted proposals includes10 Vaccines candidates, 34 Diagnostics products or scale-up facilities, 10 Therapeutics options, 02 proposals on Drug Repurposing and 14 projects which are categorised as preventive interventions**

To be able to provide an accelerator approach for vaccine development, DBT has identified institutes which will provide animal models for testing pre-clinical efficacy and also make available neutralization assays. IIT Indore will produce Pseudovirus SARS CoV-2 which can be used for development of in-vitro assays. Enzene biosciences limited will make available Spike protein and Receptor Binding Domain protein in large quantities to vaccine and diagnostic companies as a reagent. The portfolio of vaccine candidates has further been enhanced by providing support for development of Next-generation mRNA vaccine candidate by Gennova and also separately to CMC, Vellore for a lipid encapsulated mRNA based vaccine.

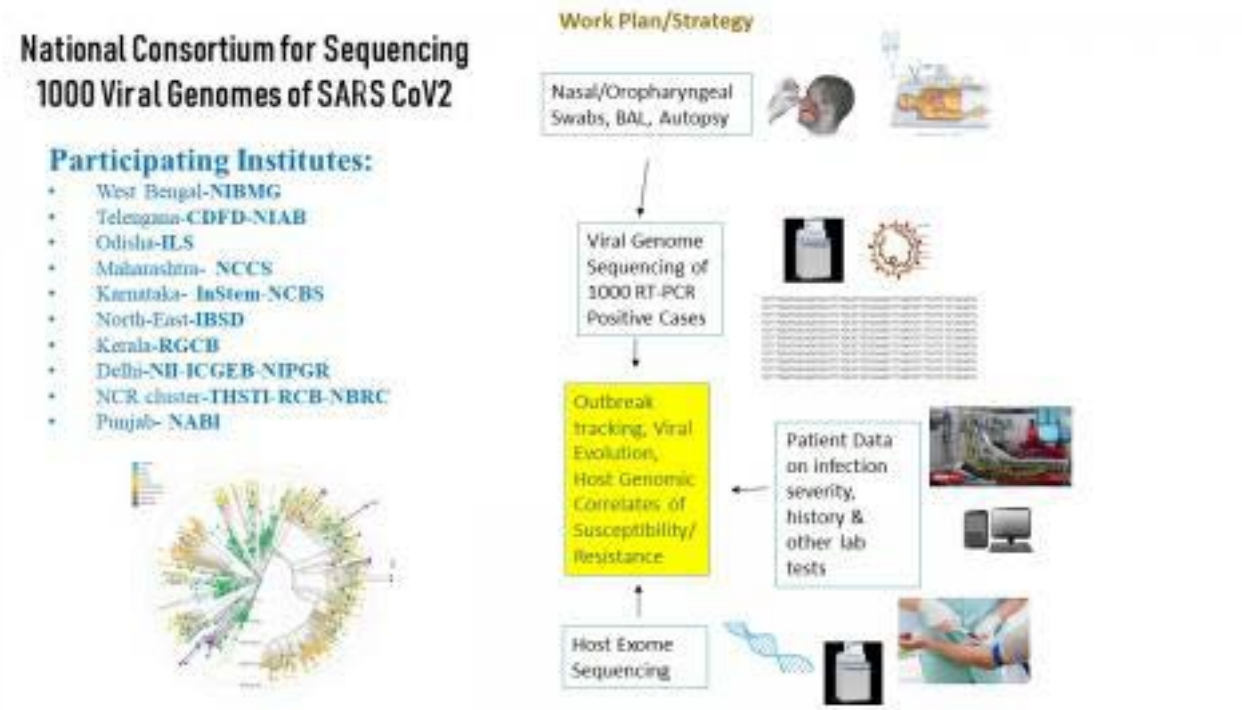
Early development work for developing an Intranasal vaccine candidate for COVID-19 has also been awarded to Indian Institute of Chemical Technology.

University Delhi South Campus has initiated work towards discovering neutralizing antibodies from an existing phage display based library and are being supported under National Biopharma Mission of DBT.

To ensure complete indigenization of COVID diagnostics, support has already been provided to AMTZ and other companies to scale-up production of RT PCR kits. In addition anticipating long term need for diagnostics, DBT/ BIRAC have also committed support for different types of diagnostics platforms like: Fluorescence and Electrochemistry Mediated Rapid Detection of SARS-Cov-2 Nucleic Acid from Bennett University, Greater Noida; portable microfluidics embedded on chip rRT-PCR and microelectrode array coupled point-of care optoelectronic device for large scale screening: JNU, Delhi; Development and evaluation of aptamer based lateral flow assay kit for detection of SARS-CoV2 detection to IIT Delhi and CRISPER based diagnosis of Covid-19 using paper microfluidics form IIT Guwahati. Other companies to get funding support are Denovo, Biolabs, ShineBiotech, Prantae, Proma Therapeutics, Achira. In total, 34 companies and academic institutes will receive financial support for ensuring there is no shortage of indigenous diagnostic kits in the near future.

Department of Biotechnology has also launched a **National Biomedical Resource Indigenization Consortium** (NBRIC) in a Public Private Partnership model to foster indigenous innovation focused on developing reagents and resources for diagnostics, vaccines and therapeutics for COVID19 which is in partnership with ABLE and CII and is being hosted by C-CAMP.

Under its 'Fast Track Review Process' Process BIRAC has created a provision to fund COVID solutions that are ready for immediate deployment. Through this initiative Startups with PPE solutions have been approved for supporting manufacturing of "Full body coverage suits" to Aarna Biomedical Products and for "Face Shields" to Alpha Corpusles Pvt Ltd. Automoted Sanitizer to MicroGO, Remote patient monitoring Stasis Health Pvt Ltd. Turtle Shell for DOZEE a sleep monitoring device, Monitra for remote monitoring of patients, Perisodhana for N-95 Mask's and Remidio for Ambu bags.



Complications in Plasma therapy for COVID19

APRIL 28, 2020 | Plasma therapy was approved for trial and clinical research proposals were also floated to see whether plasma therapy can be a cure for Coronavirus2 which has made more than 2 lakh fatalities around the world. But the therapy has been declared unproven and unsafe by ICMR, India as on 28th April 2020.

Plasma therapy involves isolation of plasma (blood component) which carries important molecules like antibodies, other proteins, metals etc. This plasma of infected might have two important characteristics, one is presence of specific antibodies (Abs) (for viral proteins or RNA) and second is to have these in sufficient quantities (to elicit antibody generation and virus neutralization).

Earlier it was suggested that the generation of specific Ab takes around 21 days. So finding plasma which might have components required becomes too difficult because patient does not survive beyond 14-17 days in severe CoV2 infection.

Vaccine on other hand contains specific molecules unlike plasma. It either have specific Ab or material that can start production of Abs against the virus.

Finding patients having right plasma is still a subject of investigation and Convalescent plasma therapy can create life-threatening complications in a Covid-19 patient and is still experimental, the ministry of health and family welfare warned. Thus ICMR has put a ban on use of plasma therapy.

Why India is throwing out Rapid testing kits for COVID19 worth Rs. 30 Crore?

APRIL 23, 2020 | The ICMR has issued notice on 27th April to halt surveillance testing of COVID-19 through Rapid testing kits in India as the test kits procured from China were reported to be faulty.

Two Chinese companies — Livzon Diagnostic Inc and Wondfo — which supplied 6.0 lakh kits to India on April 16, say that they were validated by NIV, Pune and then cleared by ICMR for supply.

According to details provided in the Delhi High Court, the kits procured from China, whose delivered cost was ₹245 a test, were sold to ICMR for ₹600 a test — a mark up of 145%. The matter came to light when Rare Metabolics Life Sciences Pvt Ltd and Aark Pharmaceuticals, distributors of Chinese Wondfo Biotech's kits imported by Matrix Labs, approached the High Court recently to get delivery/payment disputes cleared.

This is not the first time Chinese companies were blamed for fake products, Spain on 28th March reportedly found out that rapid coronavirus test kits purchased from a Chinese firm could only identify 30% of the virus, according to a report in Spanish newspaper El País.

According to China's official reaction in the El País report, one of its biotechnology companies which supplied test kits to Madrid did not figure in the list of firms approved by the Chinese government for trading in corona related medical items. The Chinese government said it did not give licence to the company to sell its products.

Paper strip based COVID-19 test kit developed in India?

APRIL 23, 2020 | Scientists from the Council of Scientific and Industrial Research (CSIR),, India have found great success in developing a new kit for rapid testing of Covid-19.

This kit can detect viral RNA of the novel corona virus (SARS-COV-2) in less than an hour. Scientists say this paper-strip kit is much cheaper than commonly used testing methods and may help meet the challenge of large-scale corona testing once it is developed.

IGIB scientist Dr. Debjyoti Chakraborty told India Science Wire that "this paper-kit used state-of-the-art technique of gene-editing crisper-cas-9 to identify the genomic sequence of the corona virus in susceptible individuals of infection."

Dr. Debjyoti Chakraborty said, "The validity of this test kit is currently being tested, after its completion it will be used for testing new corona virus.

CSIR Director General Dr. Shekhar C. Mande has said – "The primary results associated with the development of this kit are encouraging. However, the primary results are still seen on limited samples and are being tested extensively. It will also be tested on samples sourced from other countries. Regulatory bodies may get permission for its use soon, after which this kit can be used for testing. "

Academic curriculum guidelines for new session after COVID19

APRIL 29, 2020 | The new academic session for freshers may begin in universities from September and for already enrolled students in August in the wake of the coronavirus COVID-19 outbreak in the country, the University Grants Commission (UGC) told universities on Wednesday.

"Universities may follow a six-day week pattern and devise proforma to record travel or stay a history of staff and students for the lockdown period. Extension of six months will be granted to MPhil, PhD students and viva-voice be conducted through video conference," it added. The commission clarified that the guidelines are advisory in nature and varsities may chalk out their own plan taking into consideration issues pertaining to the COVID-19 pandemic.

It added that a COVID-19 cell will be constituted in every university which will be empowered to solve the issues of students related to academic calendar and examinations. A COVID-19 cell in the UGC will be created for faster decision making.

These UGC guidelines were issued in presence of Union HRD Minister Ramesh Pokhriyal 'Nishank' in New Delhi. Secretary, Higher Education, MHRD Amit Khare and senior officials of the Ministry and UGC were present on the occasion.

Universities may adopt efficient and innovative modes of examinations by reducing the time from 3 hours to 2 hours. Universities may conduct Terminal / Intermediate Semester / Year examinations in offline/online mode, as per their Ordinances/Rules and Regulations, Scheme of Examinations, observing the guidelines of social distancing and keeping in view the support system available with them and ensuring a fair opportunity to all students, it added.

In case the situation does not appear to be normal in view of COVID-19, in order to maintain "social distancing", safety and health of the students, grading of the students could be composite of 50% marks on the basis of the pattern of internal evaluation adopted by the universities and the remaining 50% marks can be awarded on the basis of performance in previous semester only (if available). The internal evaluation can be continuous evaluation, prelims, mid-semester, internal evaluation or whatever name is given for student progression, it added.

After Remdesivir 2 out of 4 COVID19 Solidarity trial drug candidates failed to achieve results

Remdesivir after Hydroxychloroquine have been abandoned as promising cure of COVID19.

MAY 1, 2020 | Remdesivir is an investigational nucleotide analog with broad-spectrum antiviral activity both in vitro and in vivo in animal models against multiple emerging viral pathogens, including Ebola, Marburg, MERS and SARS. Remdesivir is not yet licensed or approved anywhere globally and has not yet been demonstrated to be safe or effective for the treatment of COVID-19.

The Union Health Ministry on 1st May said that none of the international studies on Covid-19 have produced any conclusive results yet. On being asked about US study on remdesivir, Health Ministry's Joint Secretary Lav Aggarwal said that the researches conducting the study have said that the trial is still on with some positive outcome, "but again, this is still inconclusive."

Lav Aggarwal cautioned against hoping too much too soon from studies underway as he said that studies take time and have to go through various stages.

Earlier, the Centre had cautioned the public against seeking the convalescent plasma therapy as the cure Covid-19. While the therapy is being administered at various Covid-19 hospitals across India on a trial basis, Lav Aggarwal had said that it is still an experimental drug.

What's new about Italy and Israel's first COVID-19 vaccine

Israel's Defence Minister Naftali Bennett said scientists at the Israel Institute of Biological Research (IIBR) had developed an antibody to COVID-19. The IIBR is a secretive organisation that works directly under the Israel Prime Minister's Office. The Times of Israel reported that the antibody's development had been completed and that researchers will approach international companies to produce the antibody on a commercial scale. However, the report also said that the antibodies were yet to be tested on humans.

Takis in collaboration with Applied DNA Sciences Inc. is working on a vaccine. The researchers claimed that they have successfully developed a vaccine that can help contain the novel coronavirus that causes COVID-19. The DNA-based vaccine was able to produce an antibody response against the spike protein of the virus in mice. As per tests conducted in Rome's infectious-disease Spallanzani Hospital on mice, the vaccine has antibodies that work on human cells, blocking the virus from infecting people. The team of researchers further observed that the five vaccine candidates generated a large number of antibodies, and selected two with the best results. Luigi Aurisicchio, CEO of Takis, the firm developing the medication, said that a coronavirus candidate vaccine has neutralised the virus in human cells for the first time, the Arab News reported. According to reports, the company is likely to commence human trials soon.

Chinese scientists said they have successfully tested the country's first vaccine against COVID-19 in monkeys

May 8, 2020 | In yet another significant development in the race to find a cure for the deadly novel coronavirus, Chinese scientists said they have successfully tested the country's first vaccine against COVID-19 in monkeys. According to reports, PiCoVacc, an inactivated COVID-19 vaccine candidate made by Beijing-based Sinovac Biotech, has shown promising results as the experimental vaccine could help protect the rhesus macaques, a type of monkey originating in India, from the virus.

The researchers isolated the virus from 11 patients. Among those, five were from China, three were from Italy, one was from Switzerland, one was from the UK and one was from Spain.

For the trial, the researchers injected the vaccine into the monkeys who were then exposed to the SARS-CoV-2 that causes COVID-19 three weeks later. The report in Science Magazine stated that the vaccine triggered an immune response to produce antibodies against the virus. These antibodies can also attack normal viruses. The researchers observed that the monkeys administered the largest dose of PiCoVacc did not have the virus in their lungs after a week, whereas those monkeys that didn't receive the vaccine contracted the virus and developed severe pneumonia.

Reports suggest that China has been testing the vaccine in humans since mid-April. Also, another vaccine made by a Chinese military institution is currently being tested on humans. Meanwhile, both Italy and Israel this week claimed success in developing COVID-19 vaccines.

News of Focus

Flawed Covid-19 Database Source to Ease Lockdown

15 May, 2020

According to an article by MRIDULA CHARI & NITIN SETHI on 15th May, 2020, The Centre's 'single source of truth' in easing lockdowns is a database of Covid-19 cases ridden with unverified data, duplicate names and other flaws.

On 29 April, the ICMR database used by the Centre recorded 5,024 different active Covid-19 cases than the National Centre for Disease Control (NCDC) database used by the states, with the two databases showing the same figures in only five states and three union territories, with no more than 16 cases between them. The rest showed either fewer or more cases from state to state.

On complaints from states, India's premier medical-research body has frequently revised protocols and processes of collecting these data, in one instance changing a data-collection form 10 times over 60 days. But the Centre, which makes all decisions related to lockdowns, has said only the ICMR data will prevail.

The ICMR database was unreliable even on 1 May, when the Union government extended the lockdown for the second time, up to 17 May, according to the presentation sent to the states.

"The ICMR database has duplicate names, wrong and vague phone numbers and address details," a senior officer of an eastern state told Article 14 on 3 May. The officer requested anonymity because of the sensitivity of the issue and requested that the state not be identified.

"The ICMR database has duplicate names, wrong and vague phone numbers and address details," a senior officer of an eastern state told Article 14 on 3 May. The officer requested anonymity because of the sensitivity of the issue and requested that the state not be identified

Another officer in-charge of Covid-19 data management for a western state said, "Sometimes the person had [been] tested in one district, but came from another and originally belonged to a third place. Verification of these discrepancies can only be done by state agencies. But, till recently ICMR did not have a process to allow state and district authorities to verify and fix it." This officer also did not want to be quoted fearing retaliation from the central government.

Article 14 sent emails seeking comment to India's Health Minister Harsh Vardhan, Health Secretary Preeti Sudan, ICMR Director General Balram Bhargava and ICMR chief of Epidemiology and Communicable Diseases Raman Gangakhedkar about the discrepancies in the two databases.

The secretary, who heads the ministry of health and family welfare (MOHFW) forwarded our email to others in the ministry and ICMR and copied us. Bhargava replied to the email thread saying, "The matter… is related to MOHFW and not to ICMR." Bhargava did not reply to a separate email with questions connected to the ICMR.

CSIR, India to let firms defer fee on use of its technology

APRIL 27, 2020

Technology will include diagnostic kits, personal protective equipment, drugs and health equipment. Currently the 38 labs of the organisation have 41 dedicated technologies to deal with the pandemic.

They include a paper strip-based test to detect the virus, various kinds of hand sanitizers, a pre-fabricated makeshift hospital and a 3-D printed ventilator.

Under normal circumstances, being a publicly funded organisation, technologies developed by the CSIR are generally available to the industry on a non-exclusive licensing basis, that is any company can earn the right to manufacture and sell a product provided they pay a technology fee.

CSIR Director-General Shekhar Mande told that the deferment would not apply if a firm planned on exporting such equipment.

US study on remdesivir inconclusive: Indian Health Ministry

April 30, 2020

Lav Aggarwal cautioned against hoping too much too soon from studies underway as, he said, that studies take time and have to go through various stages.

On being asked about US study on remdesivir, Health Ministry's Joint Secretary Lav Aggarwal said that the researches conducting the study have said that the trial is still on with some positive outcome, "but again, this is still inconclusive."

Earlier as well, the Centre had cautioned the public against deeming the convalescent plasma therapy as the cure Covid-19. While the therapy is being administered at various Covid-19 hospitals across India on a trial basis, Lav Aggarwal had said that it is still an experimental drug.

DBT Launched 1000 Genome sequencing project of SARS-Cov-2

May 1, 2020

During a review of COVID 19 activities by Hon'ble Minister, the DBT announced Launch of 1000 Genome sequencing of SARS-Cov 2 Virus by DBT Autonomous Institutions consortia to understand viral and host genomics of COVID-19 outbreak.

This study will sequence 1000 SARS Cov-2 genomes from the clinical samples to understand the evolving molecular phylogeny of the virus and the emerging mutations in the viral RNA as well as identify the host genetic variations which correlate with transmission, susceptibility and disease severity.

This study is being coordinated by NIBMG, Kalyani with active participation from CDFD, Hyderabad; ILS, Bhubaneswar; NCCS, Pune; InStem, Bengaluru along with other DBT Autonomous Institutions. The findings of this study will also assist development of efficient diagnostic assays, vaccine and drug candidates and help formulate policies for containment of the outbreak.

"For any virus to make it a epidemic or pandemic, would usually take about a decade. These viruses, like other RNA viruses, have unusually high rate of mutation, which make them constantly change".

Prof Ramareddy V Guntaka, Professor, Department of Microbiology, Immunology & Biochemistry, University of Tennessee, USA. Published in April 2020 issue of Biotech Express Magazine

Coronavirus antibody tests have 'really terrible' accuracy, says US researchers

May 1, 2020

Of the 12 antibody tests that were studied by the COVID-19 Testing Project, one of the tests gave false positives more than 15% of the time, or in about one out of seven samples. Three other tests gave false positives more than 10% of the time.

"That's terrible. That's really terrible," said Dr. Caryn Bern, one of the authors of the study that looked at the 12 tests.

She said while it's unrealistic to think all tests will be 100% accurate all the time, their false positive rates should be 5% or lower, or ideally 2% or lower.

The COVID-19 Testing Project is a consortium of researchers and physicians at the University of California San Francisco, the University of California Berkeley, the Chan Zuckerberg Biohub, and the Innovative Genomics Institute.

IICT to make affordable RT-PCR kits

May 2, 2020

To make RT-PCR Kits, the IICT is partnering with Hyderabad-based Genomix Biotech, which is already into manufacturing rapid diagnostic kits and PCR based molecular diagnostic assays. Senior scientists at IICT said the collaboration would bring down the cost of the PCR Kits and at the same time also make it readily available because at the moment, all the testing kits for diagnosing SARS-CoV-2 are being imported.

"We are in the process of approaching the Indian Council of Medical Research (ICMR) for the required approvals and validation. There is no doubt that indigenously manufactured test kits will be affordable and readily available," said senior principal scientist, IICT. Dr Anthony Addlagatta.

"We are ready to produce the kits at the earliest in Hyderabad. We need just regulatory permissions to start making them," he said. Director, IICT, Dr. S Chandrasekhar said that the collaboration will enable to produce affordable quality RT-PCR kit and help meet the huge demand of the country during this COVID-19 pandemic.

IITR is now working on three verticals, out of five taken up by CSIR against the Coronavirus

May 02, 2020

CSIR has devised a five-pronged strategy in the fight against Covid-19. The five verticals to fight Covid-19 are Surveillance, Rapid and Cheap Diagnosis, Development of New Therapies (including Repurposing of Drugs and New Drugs), Hospital Assistive Devices and Supply Chain and Logistics. Among these verticals, CSIR-IITR is participating in the three verticals, namely prevention, diagnostics and therapeutics.

CSIR-IITR has set up a state-of-the-art facility for Covid-19 testing as per national norms. A team of about 24 personnel will be participating in this exercise and have been imparted training by the Department of Microbiology, King George's Medical University (KGMU) on issues related to biosafety and handling of samples.

In a meeting held with Suresh Khanna, Minister of Medical Education, and Chief Secretary, Government of Uttar Pradesh, Professor Alok Dhawan, Director, CSIR-IITR, apprised them of the Institute's full pre-

paredness for testing and assured support to the state to enhance the testing capacity for Covid-19.

Director-General of CSIR and Secretary, Department of Scientific and Industrial Research (DSIR), as well as the Indian Council of Medical Research (ICMR), Ministry of Health and Family Welfare, have given their approval for testing of Covid-19 at CSIR-IITR.

CSIR pins hope on repurposed Sepsivac

May 3, 2020

CSIR is currently testing Cadila Pharmaceuticals' "Sepsivac" against COVID-19.

This treatment was developed as a result of a partnership between CSIR and Cadila Pharmaceuticals many years ago. This immunotherapy treatment, which boosts "innate immunity", was initially approved by the Drug Controller General of India (DCGI) for gram negative sepsis which is a disease caused by bacteria.

CSIR got the approval to test "Sepsivac" against Covid-19 in a Phase 2 clinical trial about 10 days ago. The trial is being conducted on 50 patients at the All India Institute of Medical Sciences (AIIMS), New Delhi, AIIMS Bhopal, and Post Graduate Institute of Medical Education & Research (PGIMER), Chandigarh.

"We expect the results from this Phase 2 trial within 30-45 days from now. And if the results are encouraging, we will seek approval from the drug controller because of emergency and keep on continuing the Phase 3 trial. That's how it happens," Ram Vishwakarma, Director, Integrative Medicine (Council of Scientific & Industrial Research), Jammu, told IANS.

Meanwhile, Vishwakarma informed that CSIR has also got approval for conducting Phase 3 clinical trial of "Sepsivac" against Covid-19.

"The Phase 3 trials will be done on 1,100 people -- 600 will be those who have tested positive but non-symptomatic, and 500 will be those who are out of hospital," Vishwakarma said. "Sepsivac will be an immunomodulator, which will have protective effect and therapeutic effect both," he said.

Sepsivac contains mycobacterium, an immunomodulator which is a non-pathogenic mycobacterium. As a result of the immunomodulator effect, Sepsivac effectively saves more lives in sepsis. Randomized trials in sepsis patients showed 11% absolute reduction and 55.5% relative reduction in mortality.

COVID-19 has unmasked significant health disparities in the U.S.

May 4, 2020

The COVID-19 pandemic has unmasked long-standing racial and ethnic health-related disparities, according to a new article published today in the American Heart Association's flagship journal *Circulation*. The perspective essay notes higher rates of COVID-19 hospitalizations, deaths or positive cases among blacks, Hispanic/LatinX and Native Americans are being reported at local and national levels. Among the potential solutions, the writers note:

- Health care entities must collect and present COVID-19 data according to socio-demographic characteristics.
- COVID-19 testing must be easily available in all communities, and contact tracing must be relentless.
- Housing availability should be expanded. Facilities such as hotels and dorms should be used to quarantine symptomatic individuals to avoid spread to family members and neigh-

bours. Suspension of foreclosures and evictions should occur.

- Incentives to provide free or discounted food delivery to low-income neighbourhoods and the elderly are necessary. Food banks will benefit from additional funding to reduce food insecurity.
- Due to the increased reliance on telemedicine and distance learning, policymakers should support broad access to computers and free internet for vulnerable communities.
- Employers should provide paid sick and quarantine leave to help reduce the risk of unwitting spread.

Blueprint to protect the mental health of front-line medical workers

May 6, 2020

University of Queensland researchers have developed a set of recommendations to manage the mental health of frontline medical workers during viral outbreaks, such as COVID-19. Researchers developed the recommendations after analysing 59 international studies on the psychological effects of treating viral outbreaks.

"These include clear communication, providing training and education, enforcing infection control procedures, ensuring adequate supplies of protective equipment and providing access to psychological interventions,". "Implementing screening stations to direct patients to relevant infection treatment clinics, redesigning high-risk procedures and reducing the number of patients in hospital wards will all help to protect the mental health of frontline workers." They found clinicians who were younger, in a junior role, parents of dependent children or had an infected family member were at greater risk of psychological distress.

Longer periods of quarantine, lack of practical support and stigma were also negative contributors.

The study's lead author Professor Steve Kisely said supervisors should consider staff needs when assigning duties -- especially if staff had been redeployed to meet rising clinical demands -- and where possible, make redeployment voluntary.

"Staff need regular breaks and appropriate rosters, so they can access food and other daily living supplies, and make video contact with their families to alleviate concerns," Professor Kisely said.

"They may also need alternative accommodation to reduce the risks of infecting their families." The studies considered staff impacts during SARS, MERS, H1N1, H7N9, Ebola and COVID19 in countries that included; China, Taiwan, Canada, Hong Kong, Singapore, South Korea, Saudi Arabia, Greece, Mexico, Japan, The Netherlands, Germany and Liberia.

An exponential blast of Covid-19 scientific research

May 6, 2020

More than 7,000 papers on the pandemic—covering everything from virology to epidemiology—have appeared in the past three months (see chart). A fifth of them have come out in the past week alone.

This is astonishingly fast. Researchers usually take years to design experiments, collect data and check results. Scientific journals, the self-appointed keepers of the gate between those researchers and the rest of the world, can easily take six months, often a year, to grind through the various steps of their procedure, including editing and the process of checking by anonymous outside experts, known as peer review.

The current public-health emergency has, however, turbocharged all this. With physicians, policymakers and prime ministers all needing the latest science in order to make immediate life-and-death decisions, speed has become paramount. Journals have responded to sharp rises in submissions by working overtime. In so doing they have squeezed their normal processes down to days or weeks.

Dr Lipsitch recommended that preprints form a bigger part of a faster information "ecosystem" during future emergencies. And his wish, it appears, has been granted. The two biggest relevant preprint servers for covid-19 are bioRxiv, set up in 2013, and medRxiv, launched in 2019, both of which are run by Cold Spring Harbor Laboratory in New York state. (The "x" in the names represents the Greek letter "chi", making them pronounceable as "bioarchive" and "medarchive".

Anyone can submit a manuscript to one of these servers and see it made available to the world within hours. Submissions are given a cursory check, to weed out opinion pieces and to ensure that they have the parts expected of a scientific paper—an abstract and sections describing methods and results. If the topic is controversial, the checkers may flag up outlandish claims. But beyond this they do not attempt to review the scientific contents of the paper. Once a preprint is online, anyone with access to the internet can read it and, if they so wish, leave detailed comments.

This process—essentially a free-for-all version of peer review—can be brutal. But it often works. Conspiracy theories about SARS-CoV-2 being an artificial, laboratory creation were fuelled by a preprint posted to bioRXiv in January, by Indian scientists. This claimed "uncanny" similarities between the genetic sequences of SARS-CoV-2 and HIV, the cause of AIDS. The study was torn apart as soon as it appeared, though, by other researchers who weighed in and pointed out serious methodological flaws. As a consequence, the manuscript has now been withdrawn.

This incident does, however, highlight a repeated criticism of preprint posting, which is that dodgy material may be misused, either accidentally or deliberately, by overzealous patients, politicians, journalists or just plain troublemakers. It is certainly a risk. But in the opinion of many, that risk does not outweigh the advantage of the free and fast flow of information between researchers that preprints provide.

Another Hype of world's first Covid-19 vaccine: Italy's claims

May 06, 2020

Italy has announced that it has successfully developed a vaccine to contain coronavirus. Italy has claimed that the vaccine works on humans, Arab News reported.

As per the tests carried out at Rome's infectious-disease Spallanzani Hospital, the coronavirus vaccine has antibodies generated in mice that work on human cells, CNBC TV 18 reported.

"This is the most advanced stage of testing of a candidate vaccine created in Italy," Luigi Aurisicchio, CEO of Takis, the firm developing the medication told Italian news agency ANSA in a report.

"Human tests are expected after this summer," Aurisicchio was quoted as saying. So it is not yet certain whether this vaccine is going to work or not.

COVID-19: Indian Govt. to conduct randomised controlled clinical trial of Ashwagandha

May 7, 2020

This will be a joint initiative of the ministries of AYUSH, health, and science and technology through the Council of Scientific and Industrial Research (CSIR) with technical support from the Indian Council of Medical Research (ICMR), Union Health Minister Harsh Vardhan said.

Simultaneously, the efficacy of ayurvedic drugs yashtimadhu, combination of Guduchi and Pippali and a poly-herbal formulation (AYUSH-64) along with ashwagandha will also be evaluated as a prophylaxis and add on to standard care in mild to moderate COVID-19 patients, Secretary in the Ministry of AYUSH Vaidya Rajesh Kotecha said.

"These randomised controlled clinical trials will help us assess the benefit of these ayurvedic drugs as a preventive intervention and as an add on therapy in arresting the progression of the respiratory ailment," Kotecha said.

An interdisciplinary AYUSH Research and Development Task Force with a group of experts under the chairmanship of Dr Bhushan Patvardhan, Vice Chairmen of University Grant Commission, has formulated clinical research protocols for prophylactic studies and add-on interventions in COVID-19 positive cases thorough review and consultative process for studying these four different interventions -- ashwagandha, yashtimadhu, guduchi and pippali, and AYUSH-64.

The study will be carried out through four research councils under the Ministry of AYUSH and national institutes in 25 states and several state governments covering around five lakh people, he said.

Nearly Everyone Who Recovers From COVID-19 Makes CoV Antibodies: Dr. Francis Collins on NIH Blog

May 7, 2020

There's been a lot of excitement about the potential of antibody-based blood tests, also known as serology tests, to help contain the coronavirus disease 2019 (COVID-19) pandemic. There's also an awareness that more research is needed to determine when—or even if—people infected with SARS-CoV-2, the novel coronavirus that causes COVID-19, produce antibodies that may protect them from re-infection.

A recent study in *Nature Medicine* brings much-needed clarity, along with renewed enthusiasm, to efforts to develop and implement widescale antibody testing for SARS-CoV-2. Antibodies are blood proteins produced by the immune system to fight foreign invaders like viruses, and may help to ward off future attacks by those same invaders.

In their study of blood drawn from 285 people hospitalized with severe COVID-19, researchers in China, led by Ai-Long Huang, Chongqing Medical University, found that all had developed SARS-CoV-2 specific antibodies within two to three weeks of their first symptoms. Although more follow-up work is needed to determine just how protective these antibodies are and for how long, these findings suggest that the immune systems of people who survive COVID-19 have been be primed to recognize SARS-CoV-2 and possibly thwart a second infection.

Specifically, the researchers determined that nearly all of the 285 patients studied produced a type of antibody called IgM, which is the first antibody that the body makes when fighting an infection. Though only about 40 percent produced IgM in the first week after onset of COVID-19, that number increased steadily

to almost 95 percent two weeks later. All of these patients also produced a type of antibody called IgG. While IgG often appears a little later after acute infection, it has the potential to confer sustained immunity.

To confirm their results, the researchers turned to another group of 69 people diagnosed with COVID-19. The researchers collected blood samples from each person upon admission to the hospital and every three days thereafter until discharge. The team found that, with the exception of one woman and her daughter, the patients produced specific antibodies against SARS-CoV-2 within 20 days of their first symptoms of COVID-19.

Meanwhile, innovative efforts are being made on the federal level to advance COVID-19 testing. The NIH just launched the Rapid Acceleration of Diagnostics (RADx) Initiative to support a variety of research activities aimed at improving detection of the virus. As I recently highlighted on this blog, one key component of RADx is a "shark tank"-like competition to encourage science and engineering's most inventive minds to develop rapid, easy-to-use technologies to test for the presence of SARS-CoV-2.

On the serology testing side, the NIH's National Cancer Institute has been checking out kits that are designed to detect antibodies to SARS-CoV-2 and have found mixed results. In response, the Food and Drug Administration just issued its updated policy on antibody tests for COVID-19. This guidance sets forth precise standards for laboratories and commercial manufacturers that will help to speed the availability of high-quality antibody tests, which in turn will expand the capacity for rapid and widespread testing in the United States.

Finally, it's important to keep in mind that there are two different types of SARS-CoV-2 tests. Those that test for the presence of viral nucleic acid or protein are used to identify people who are acutely infected and should be immediately quarantined. Tests for IgM and/or IgG antibodies to the virus, if well-validated, indicate a person has previously been infected with COVID-19 and is now potentially immune. Two very different types of tests—two very different meanings. There's still a way to go with both virus and antibody testing for COVID-19. But as this study and others begin to piece together the complex puzzle of antibody-mediated immunity, it will be possible to learn more about the human body's response to SARS-CoV-2 and home in on our goal of achieving safe, effective, and sustained protection against this devastating disease.

CSIR NMITLI program approves a multi institutional project to develop human monoclonal antibodies (hmAbs) to neutralize SARS-CoV-2

08 MAY 2020

CSIR is also supporting new ideas and projects from other academic and industries through its flagship New Millennium Indian Technology Leadership Initiative (NMITLI) program.

Given the importance of deploying multiple strategies against Covid-19, CSIR through NMITLI program has approved a project towards development of human monoclonal antibodies (hmAbs) that can neutralize SARS-CoV-2 in patients. This project on generation of neutralizing human monoclonal antibodies as a therapeutic strategy will be implemented by a multi-institutional and multi-disciplinary team. The team comprises of academic institutes and industry with participants from NCCS, IIT-Indore, PredOmix Technologies Pvt. Ltd. and Bharat Biotech International Ltd (BBIL)

The project aims to generate hmAbs to SARS-CoV-2 from convalescent phase of COVID-19 patients and select high affinity and neutralizing antibodies. The project also aims to anticipate future adaptation of the virus and generate hmAbs clones that can neutralize

the mutated virus so that could be readily used for combating future SARS-CoV infections.BBIL will be the commercial partner and responsible for subsequent development and commercialization of the hmAbs generated.

Indian Researchers Submit 53 Genome Sequences of Coronavirus

May 07, 2020

CSIR, has submitted as many as 53 genome sequences of the virus to a global genome database, a move that may help in better understanding of the virus and developing a vaccine.
The Council for Scientific and Industrial Research (CSIR) is also planning to submit additional 450 genome sequence data of coronavirus by May 15, its Director General Shekhar Mande told news agency Press Trust of India.

CSIR's Institute of Genomics and Integrative Biology (IGIB), Delhi, Centre for Cellular and Molecular Biology (CCMB), Hyderabad and Institute of Microbial Technology, Chandigarh are currently sequencing the genomes of the novel coronavirus, he said. Other CSIR institutes are also expected to join the process.

Launched in 2008, the GISAID, a public–private partnership between the German government and the nonprofit organization, promotes the rapid sharing of data from all influenza viruses and the coronavirus causing COVID-19.

This includes genetic sequence and related clinical and epidemiological data associated with human viruses, and geographical as well as species-specific data linked to avian and other animal viruses.

This enables researchers to understand how viruses evolve and spread during epidemics and pandemics.

According to GISAD, more than 16,000 genome sequences of the coronavirus have been shared with it by different institutes in the world.

Glenmark initiates Phase 3 clinical trials on antiviral Favipiravir for COVID19 patients, first in India

May 13, 2020

- COVID-19 patients from over 10 leading government and private hospitals in India are being enrolled for the study
- Trial completion and study results expected by July/ August 2020
- Glenmark was the first pharmaceutical company in India to be given an approval by the regulator to conduct Phase 3 clinical trials in India on Favipiravir Antiviral tablets for COVID -19 patients.

Glenmark has successfully developed the API and the formulations for the product through its inhouse R&D team. Favipiravir has demonstrated activity against influenza viruses and has been approved in Japan for the treatment of novel influenza virus infections. The molecule if commercialized, will be marketed under the brand name 'FabiFlu®' in India.

Commenting on this development, Dr. Monika Ta don, Vice President & Head, Clinical Development, Global Specialty/Branded Portfolio, Glenmark Pharmaceuticals Ltd., said, "Several health and medical experts, both in and outside of Glenmark are eager to see the effect that Favipiravir has on COVID-19 cases. We believe the study results will be significant as there is currently no effective treatment for the virus." She added, "The data we get from these trials will point us in a clearer direction with regard to COVID-19 treatment and management."

COVID19 Research

Hydroxychloroquine linked to increased risk of cardiac arrhythmias

May 1, 2020

In a brief report published today in JAMA Cardiology, a team of pharmacists and clinicians at Beth Israel Deaconess Medical Center (BIDMC), part of Beth Israel Lahey Health, found evidence suggesting that patients who received hydroxychloroquine for COVID-19 were at increased risk of electrical changes to the heart and cardiac arrhythmias. The combination of hydroxychloroquine with azithromycin was linked to even greater changes compared to hydroxychloroquine alone.

"While hydroxychloroquine and azithromycin are generally well-tolerated medications, increased usage in the context of COVID-19 will likely increase the frequency of adverse drug events (ADEs)," said co-first author Nicholas J. Mercuro, PharmD, a pharmacy specialist in infectious diseases at BIDMC.

In this single-center, retrospective, observational study, Mercuro and colleagues evaluated 90 adults with COVID-19 who were hospitalized at BIDMC between March 1 and April 7, 2020, and received at least one day of hydroxychloroquine. More than half of these patients also had high blood pressure, and more than 30 percent had diabetes.

Seven patients (19 percent) who received hydroxychloroquine alone developed prolonged QTc of 500 milliseconds or more, and three patients had a change in QTc of 60 milliseconds or more. Of the 53 patients who also received azithromycin, 21 percent had prolonged QTc of 500 milliseconds or more, and 13 percent experienced a change in QTc of 60 milliseconds or more.

"In this study, patients who were hospitalized and receiving hydroxychloroquine for COVID-19 frequently experienced QTc prolongation and adverse drug events," said co-first author Christina F. Yen, MD, of BIDMC's Department of Medicine. "One participant taking the drug combination experienced a potentially lethal tachycardia called torsades de pointes, which to our knowledge has yet to be reported elsewhere in the peer-reviewed COVID-19 literature."

Journal Reference:
Nicholas J. Mercuro, Christina F. Yen, David J. Shim, Timothy R. Maher, Christopher M. McCoy, Peter J. Zimetbaum, Howard S. Gold. Risk of QT Interval Prolongation Associated With Use of Hydroxychloroquine With or Without Concomitant Azithromycin Among Hospitalized Patients Testing Positive for Coronavirus Disease 2019 (COVID-19). JAMA Cardiology, 2020; DOI: 10.1001/jamacardio.2020.1834

Two repuprposed drugs from Korea showed promise against COVID-19

May 4, 2020

Korean researchers have screened 48 FDA-approved drugs against SARS-CoV-2, and found that two, that are already FDA-approved for other illnesses, seem promising. The investigators tested the drugs in Vero cells, a cell line developed from kidney cells of the African Green Monkey, which are commonly used to grow viruses for vaccine production.
An anti-helminthic drug called niclosamide demonstrated "very potent" antiviral activity against SARS-CoV-2, according to coauthors Sangeun Jeon, Meehyun Ko, and their collaborators, of the Zoonotic Virus Laboratory, Institut Pasteur Korea, Seongnam, Korea. "Not surprisingly, its broad-spectrum antiviral effect has been well documented in the literature, including antiviral properties against SARS- and MERS-CoV," they write.

A downside of niclosamide is low absorption, which undercuts the drug's power by reducing the dose that reaches the target tissue.

Despite substantially lower antiviral potency, ciclesonide, an inhaled corticosteroid used to treat asthma and allergic rhinitis, also showed promise against SARS-CoV-2. Intriguingly, the investigators note that a study published earlier this year (by Matsuyama et al.) a treatment report of 3 patients infected by SARS-CoV-2, demonstrated antiviral activity and revealed the drug's molecular target to be a viral protein called Nsp15.

Journal Reference:
Sangeun Jeon, Meehyun Ko, Jihye Lee, Inhee Choi, Soo Young Byun, Soonju Park, David Shum, Seungtaek Kim. Identification of antiviral drug candidates against SARS-CoV-2 from FDA-approved drugs. Antimicrobial Agents and Chemotherapy, May 4, 2020; DOI: 10.1128/AAC.00819-20

Blood thinners may improve survival among hospitalized COVID-19 patients

May 7, 2020

The study found that hospitalized COVID-19 patients treated with anticoagulants had improved outcomes both in and out of the intensive care unit setting. The research also showed that the difference in bleeding events among patients treated with and without anticoagulants was not significant. The Mount Sinai researchers say their work outlines an important therapeutic pathway for COVID-19 patients.

"This research demonstrates anticoagulants taken orally, subcutaneously, or intravenously may play a major role in caring for COVID-19 patients, and these may prevent possible deadly events associated with coronavirus, including heart attack, stroke, and pulmonary embolism," says senior corresponding author Valentin Fuster, MD, PhD, Director of Mount Sinai Heart (the nation's number six ranked hospital in Cardiology/Heart Surgery) and Physician-in-Chief of The Mount Sinai Hospital. "Using anticoagulants should be considered when patients get admitted to the ER and have tested positive for COVID-19 to possibly improve outcomes. However, each case should be evaluated an individualized basis to account for potential bleeding risk."

The publication of this study follows recent research out of the Icahn School of Medicine at Mount Sinai that shows a large number of patients hospitalized with COVID-19 have developed high levels of life-threatening blood clots, leading to potentially deadly thromboembolic events.

The observational study also explored the association

of systemic anticoagulant treatment with bleeding events. Major bleeding was defined as 1) hemoglobin <7 g/dL and any red blood cell transfusion; 2) at least 2 units of red blood cell transfusion within 48 hours; or 3) a diagnosis code for major bleeding including intracranial hemorrhage; hematemesis; melena; peptic ulcer with hemorrhage; colon, rectal, or anal hemorrhage; hematuria; ocular hemorrhage; and acute hemorrhagic gastritis. Among those who did not receive anticoagulants, 38 (1.9 percent) patients had bleeding events, compared to 24 (3 percent) among those who received anticoagulants, p=0.2).

Journal Reference:
Ishan Paranjpe, Valentin Fuster, Anuradha Lala, Adam Russak, Benjamin S. Glicksberg, Matthew A. Levin, Alexander W. Charney, Jagat Narula, Zahi A. Fayad, Emilia Bagiella, Shan Zhao, Girish N. Nadkarni. Association of Treatment Dose Anticoagulation with In-Hospital Survival Among Hospitalized Patients with COVID-19. Journal of the American College of Cardiology, 2020; DOI: 10.1016/j.jacc.2020.05.001

Scientists discovered Antibody blocks infection by the SARS-CoV-2 in cells

May 4, 2020

"This research builds on the work our groups have done in the past on antibodies targeting the SARS-CoV that emerged in 2002/2003," said Berend-Jan Bosch, Associate Professor, Research leader at Utrecht University, and co-lead author of the Nature Communications study. "Using this collection of SARS-CoV antibodies, we identified an antibody that also neutralizes infection of SARS-CoV-2 in cultured cells. Such a neutralizing antibody has potential to alter the course of infection in the infected host, support virus clearance or protect an uninfected individual that is exposed to the virus."

Dr. Bosch noted that the antibody binds to a domain that is conserved in both SARS-CoV and SARS-CoV-2, explaining its ability to neutralize both viruses.

Journal Reference:
Chunyan Wang, Wentao Li, Dubravka Drabek, Nisreen M. A. Okba, Rien van Haperen, Albert D. M. E. Osterhaus, Frank J. M. van Kuppeveld, Bart L. Haagmans, Frank Grosveld, Berend-Jan Bosch. A human monoclonal antibody blocking SARS-CoV-2 infection. Nature Communications, 2020; 11 (1) DOI: 10.1038/s41467-020-16256-y

High blood pressure medications safe for patients with COVID-19 disease, study finds

May 1, 2020

Published online May 1 in the New England Journal of Medicine, the study was launched in response to a March 17 joint statement issued by the American Heart Association, the American College of Cardiology, and the Heart Failure Society of America.

Led by researchers from NYU Grossman School of Medicine, the study found no links between treatment with four drug classes -- angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs), beta blockers, or calcium channel blockers -- and increased likelihood of a positive test for COVID-19.

Further, the study found no substantial increase in risk for more severe illness (intensive care, use of a ventilator, or death) with any of the treatments in patients with the pandemic virus.

The study revolves around drugs that act on the renin-angiotensin-aldosterone hormonal system, which

influences blood pressure. Central to this system is the signaling protein angiotensin II, levels of which are controlled by angiotensin-converting enzyme (ACE), say the authors. Angiotensin II narrows blood vessels to increase blood pressure, and the study drugs counter that, either by blocking ACE-induced increases in angiotensin II, or the ability of ACE to interact with its receptor signaling partners on cells.

According to the researchers, one version of ACE, angiotensin converting enzyme 2 (ACE2), is present in the outer membrane of lung cells. SARS-CoV-2, the current pandemic virus, has been shown to connect to ACE2 on lung cells, a first step toward viral infection.

This led to concern in the field that ACE inhibitors and ARBs might increase or worsen COVID-19 infection. Past studies in animal models had suggested that ACE inhibitors and ARBs increase ACE2 production in other organs, but how they related to ACE2 levels in the lungs was not known.

On the other hand, ACE inhibitors and ARBs had been shown elsewhere to reduce lung injury in certain viral pneumonias, creating speculation that they might be helpful. The new study was designed to address these contradictions.

Journal Reference:
Harmony R. Reynolds, Samrachana Adhikari, Claudia Pulgarin, Andrea B. Troxel, Eduardo Iturrate, Stephen B. Johnson, Anaïs Hausvater, Jonathan D. Newman, Jeffrey S. Berger, Sripal Bangalore, Stuart D. Katz, Glenn I. Fishman, Dennis Kunichoff, Yu Chen, Gbenga Ogedegbe, Judith S. Hochman. Renin–Angiotensin–Aldosterone System Inhibitors and Risk of Covid-19. New England Journal of Medicine, 2020; DOI: 10.1056/NEJMoa2008975

Most critically ill patients with COVID-19 survive with standard treatment, study reveals

May 6, 2020

During the COVID-19 pandemic, hospitals around the world have shared anecdotal experiences to help inform the care of affected patients, but such anecdotes do not always reveal the best treatment strategies, and they can even lead to harm. To provide more reliable information, a team led by C. Corey Hardin, MD, PhD, an Assistant Professor of Medicine at MGH and Harvard Medical School, carefully examined the records of 66 critically ill patients with COVID-19 who experienced respiratory failure and were put on ventilators, making note of their responses to the care they received.

The investigators found that the most severe cases of COVID-19 result in a syndrome called Acute Respiratory Distress Syndrome (ARDS), a life-threatening lung condition that can be caused by a wide range of pathogens. "The good news is we have been studying ARDS for over 50 years and we have a number of effective evidenced-based therapies with which to treat it," said Dr. Hardin. "We applied these treatments -- such as prone ventilation where patients are turned onto their stomachs -- to patients in our study and they responded to them as we would expect patients with ARDS to respond."

Importantly, the death rate among critically ill patients with COVID-19 treated this way -- 16.7% -- was not nearly as high as has been reported by other hospitals.

Journal Reference:
David R. Ziehr, Jehan Alladina, Camille R Petri, Jason H. Maley, Ari Moskowitz, Benjamin D Medoff, Kathryn A Hibbert, B. Taylor Thompson, C. Corey Hardin. Respiratory Pathophysiology of Mechanically Ventilated Patients with COVID-19: A Cohort Study. American Journal of Respiratory and Critical Care Medicine, 2020; DOI: 10.1164/rccm.202004-1163LE

Mutations in SARS-CoV-2 offer insights into virus evolution

May 5, 2020

Researchers found that a large proportion of the global genetic diversity of SARS-CoV-2 is found in all hardest-hit countries, suggesting extensive global transmission from early on in the epidemic and the absence of single 'Patient Zeroes' in most countries.

The findings, published today in Infection, Genetics and Evolution, also further establish the virus only emerged recently in late 2019, before quickly spreading across the globe.

Scientists analysed the emergence of genomic diversity in SARS-CoV-2, the new coronavirus causing Covid-19, by screening the genomes of over 7,500 viruses from infected patients around the globe.

They identified 198 mutations that appear to have independently occurred more than once, which may hold clues to how the virus is adapting.

The results add to a growing body of evidence that SARS-CoV-2 viruses share a common ancestor from late 2019, suggesting that this was when the virus jumped from a previous animal host, into people. This means it is most unlikely the virus causing Covid-19 was in human circulation for long before it was first detected.

The research team have developed a new interactive, open-source online application so that researchers across the globe can also review the virus genomes and apply similar approaches to better understand its evolution.

Journal Reference:
Lucy van Dorp, Mislav Acman, Damien Richard, Liam P. Shaw, Charlotte E. Ford, Louise Ormond, Christopher J. Owen, Juanita Pang, Cedric C.S. Tan, Florencia A.T. Boshier, Arturo Torres Ortiz, François Balloux. Emergence of genomic diversity and recurrent mutations in SARS-CoV-2. Infection, Genetics and Evolution, 2020; 104351 DOI: 10.1016/j.meegid.2020.104351

Repurposing existing drugs for COVID-19 offers a more rapid alternative to a vaccine

May 7, 2020

A team of researchers representing the International Union of Basic and Clinical Pharmacology today say there will be no 'magic bullet' to treat the disease and argue that a multi-pronged approach is needed to find new drugs. They caution that an effective and scalable vaccine is likely to take over a year before it can used to tackle the global pandemic.

"Any drug to treat COVID-19 will need to focus on the three key stages of infection: preventing the virus entering our cells in the first place, stopping it replicating if it gets inside the cells, and reducing the damage that occurs to our tissues, in this case, the lungs and heart," said Professor Anthony Davenport from the University of Cambridge, one of the authors of the review.

The review looks at potential therapeutic drug targets - the chinks in the virus's own armour or weak spots in the body's defences. Two key targets appear to be proteins on the surface of our cells, to which SARS-CoV-2 binds allowing it entry - ACE2 and TMPRSS2. TMPRSS2 appears to be very common on cells, whereas ACE2 is usually present at low levels that increase depending on sex, age, and smoking history.

The team say that we need to move quickly to identify existing drugs that are effective in clinical trials so that we can begin treating patients as rapidly as possi-

ble, but also because cases are likely to fall during the summer meaning there will be fewer people who can be recruited to clinical trials ahead of an anticipated second wave of the disease in autumn. They estimate there are currently more than 300 clinical trials taking place worldwide, though many of these investigational drugs are unlikely to be effective for widespread use because either it is not clear which part of the disease pathway they are targeting or they cause unpleasant side-effects.

Journal Reference:
S.P.H. Alexander, J. Armstrong, A.P. Davenport, J. Davies, E. Faccenda, S.D. Harding, F. Levi-Schaffer, J.J. Maguire, A.J. Pawson, C. Southan, M.J. Spedding. A rational roadmap for SARS-CoV-2/COVID-19 pharmacotherapeutic research and development. British Journal of Pharmacology, 2020; DOI: 10.1111/bph.15094

Vitamin D linked to low virus COVID19 death rate, study finds

May 7, 2020

Previous observational studies have reported an association between low levels of vitamin D and susceptibility to acute respiratory tract infections. Vitamin D modulates the response of white blood cells, preventing them from releasing too many inflammatory cytokines. The COVID-19 virus is known to cause an excess of pro-inflammatory cytokines.

Italy and Spain have both experienced high COVID-19 mortality rates, and the new study shows that both countries have lower average vitamin D levels than most northern European countries. This is partly because people in southern Europe, particularly the elderly, avoid strong sun, while skin pigmentation also reduces natural vitamin D synthesis.

The highest average levels of vitamin D are found in northern Europe, due to the consumption of cod liver oil and vitamin D supplements, and possibly less sun avoidance. Scandinavian nations are among the countries with the lowest number of COVID-19 cases and mortality rates per head of population in Europe.

Dr Lee Smith, Reader in Physical Activity and Public Health at Anglia Ruskin University, said: "We found a significant crude relationship between average vitamin D levels and the number COVID-19 cases, and particularly COVID-19 mortality rates, per head of population across the 20 European countries.

Journal Reference:
Petre Cristian Ilie, Simina Stefanescu, Lee Smith. The role of vitamin D in the prevention of coronavirus disease 2019 infection and mortality. Aging Clinical and Experimental Research, 2020; DOI: 10.1007/s40520-020-01570-8

Outpatient COVID-19 clinic clues to medical treatment

May 1, 2020

Now, a new analysis by researchers at Harvard Medical School and Harvard-affiliated Cambridge Health Alliance offers insights into this in-between category based on data collected from people presenting at an outpatient COVID-19 clinic in Greater Boston.

The team's observations, published April 20 in the journal Mayo Clinic Proceedings, are based on data from more than 1,000 patients who visited the clinic for respiratory illness since COVID-19 was declared a pandemic in March. The findings offer a compilation of clues that can help clinicians distinguish between patients with COVID-19 infections and those with other conditions that may mimic COVID-19 symptoms.

According to the report, COVID-19 typically pres-

ents with symptoms suggestive of viral infection, often with low-grade fever, cough and fatigue, and, less commonly, with gastrointestinal trouble. Shortness of breath usually emerges a few days after initial symptoms, becomes most pronounced upon exertion and may involve sharp drops in blood oxygen levels.

Chief among the team's findings are:
- Fever is not a reliable indicator. If present, it could manifest only with mild elevations in temperature.
- COVID-19 may begin with various permutations of cough without fever, sore throat, diarrhea, abdominal pain, headache, body aches, back pain and fatigue
- It can also present with severe body aches and exhaustion.
- A reliable early hint is loss of the sense of smell in the first days of disease onset.
- In serious COVID-19, shortness of breath is a critical differentiator from other common illnesses.
- Almost no one, however, develops shortness of breath, a cardinal sign of the illness, in the first day or two of disease onset.
- Shortness of breath can appear four or more days after onset of other symptoms.
- The first days after shortness of breath begins are a critical period that requires close and frequent monitoring of patients by telemedicine visits or in-person exams.
- The most critical variable to monitor is how the shortness of breath changes over time. Oxygen saturation levels can also be a valuable clue. Blood oxygen levels can drop precipitously with exertion, even in previously healthy people.
- A small number of people may never develop shortness of breath, but may have other symptoms that could signal low oxygen levels, including dizziness or falling.
- Anxiety -- common among worried patients with viral symptoms suggestive of COVID-19 -- can also induce shortness of breath.

Journal Reference:
Pieter A. Cohen, Lara Hall, Janice N. Johns, Alison B. Rapoport. The Early Natural History of SARS-CoV-2 Infection: Clinical Observations From an Urban, Ambulatory COVID-19 Clinic. Mayo Clinic Proceedings, 2020; DOI: 10.1016/j.mayocp.2020.04.010

Summer is not going to make this go away," Canadian study finds temperature, latitude not associated with COVID-19 spread

May 8, 2020

The Canadian study looked at 144 geopolitical areas -- states and provinces in Australia, the United States and Canada as well as various countries around the world -- and a total of more than 375 600 confirmed COVID-19 cases to estimate epidemic growth, researchers compared the number of cases on March 27 with cases on March 20, 2020, and determined the influence of latitude, temperature, humidity, school closures, restrictions of mass gatherings and social distancing measured during the exposure period of March 7 to 13.

They found little or no association between latitude or temperature with epidemic growth of COVID-19 and a weak association between humidity and reduced transmission.

The results -- that hotter weather had no effect on the pandemic's progression -- surprised the authors. The researchers did find that public health measures, including school closures, social distancing and restrictions of large gatherings, have been effective.

Journal Reference:
Peter Jüni, Martina Rothenbühler, Pavlos Bobos, Kevin E. Thorpe, Bruno R. da Costa, David N. Fisman, Arthur S. Slutsky, Dionne Gesink. Impact of climate and public health interventions on the COVID-19 pandemic: A prospective cohort study. CMAJ, May 8, 2020; DOI: 10.1503/cmaj.200920

Further evidence does not support hydroxychloroquine for patients with COVID-19

May 15, 2020

The anti-inflammatory drug hydroxychloroquine does not significantly reduce admission to intensive care or death in patients hospitalised with pneumonia due to covid-19, finds a study from France published by The BMJ today.

A randomised clinical trial from China also published today shows that hospitalised patients with mild to moderate persistent covid-19 who received hydroxychloroquine did not clear the virus more quickly than those receiving standard care. Adverse events were higher in those who received hydroxychloroquine.

Taken together, the results do not support routine use of hydroxychloroquine for patients with covid-19. Of 181 patients, 84 received hydroxychloroquine within 48 hours of admission and 97 did not (control group). They found no meaningful differences between the groups for transfer to intensive care, death within 7 days, or developing acute respiratory distress syndrome within 10 days.

By day 28, tests revealed similar rates of covid-19 in the two groups but adverse events were more common in those who received hydroxychloroquine. Symptom alleviation and time to relief of symptoms also did not differ meaningfully between the two groups.

Journal References:
Matthieu Mahévas, Viet-Thi Tran, Mathilde Roumier, Amélie Chabrol, Romain Paule, Constance Guillaud, Elena Fois, Raphael Lepeule, Tali-Anne Szwebel, François-Xavier Lescure, Frédéric Schlemmer, Marie Matignon, Mehdi Khellaf, Etienne Crickx, Benjamin Terrier, Caroline Morbieu, Paul Legendre, Julien Dang, Yoland Schoindre, Jean-Michel Pawlotsky, Marc Michel, Elodie Perrodeau, Nicolas Carlier, Nicolas Roche, Victoire de Lastours, Clément Ourghanlian, Solen Kerneis, Philippe Ménager, Luc Mouthon, Etienne Audureau, Philippe Ravaud, Bertrand Godeau, Sébastien Gallien, Nathalie Costedoat-Chalumeau. Clinical efficacy of hydroxychloroquine in patients with covid-19 pneumonia who require oxygen: observational comparative study using routine care data. BMJ, 2020; m1844 DOI: 10.1136/bmj.m1844

Detailed analysis of immune response to SARS-CoV-2 bodes well for COVID-19 vaccine

Published in today's online edition of Cell, the study documents a robust antiviral immune response to SARS-CoV-2 in a group of 20 adults who had recovered from COVID-19. The findings show that the body's immune system is able to recognize SARS-CoV-2 in many ways, dispelling fears that the virus may elude ongoing efforts to create an effective vaccine. The researchers found that all COVID-19 patients had a solid CD4, or "helper," T cell response, which helps antibody production. Almost all patients had produced virus-specific CD8, or "killer," T cells, which eliminate virus-infected cells. "Our data show that the virus induces what you would expect from a typical, successful antiviral response," says Crotty.

Journal Reference:
Alba Grifoni, Daniela Weiskopf, Sydney I. Ramirez, Jose Mateus, Jennifer M. Dan, Carolyn Rydyznski Moderbacher, Stephen A. Rawlings, Aaron Sutherland, Lakshmanane Premkumar, Ramesh S. Jadi, Daniel Marrama, Aravinda M. de Silva, April Frazier, Aaron Carlin, Jason A. Greenbaum, Bjoern Peters, Florian Krammer, Davey M. Smith, Shane Crotty, Alessandro Sette. Targets of T cell responses to SARS-CoV-2 coronavirus in humans with COVID-19 disease and unexposed individuals. Cell, May 14, 2020; DOI: 10.1016/j.cell.2020.05.015

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