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BIOTECH EXPRESS

The monthly magazine of Biotechnology

Call for BRSI Annual Awards

Views

FDA and WHO Puppets of Lancet NEJM and such journals? The case of HCQ in COVID19

Image: A plague Doctor

Editorial: A correlation between environmental deterioration and Pandemic

Guest Article: Disinfection – A silent soldier

Guest Article: Coronavirus and the heat - A realistic perspective

Guest Article: COVID-19 and Primary Health Infrastructure: Is Rural India in Ruins?

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Editorial

Does information from pre-prints servers serves purpose in a pandemic like COVID19?

by Kamal Pratap Singh, Email-kamal9871@gmail.com

Summary

Preprints publish articles without peer review.

Important articles are retracting from these servers too.

Unlike normal journal which shows only published articles, preprints accumulates unpublished and unverified research on their servers which becomes available for public interpretation.

Introduction

Like we post updates on fb/Ln/Tw etc. and expect audience's response, preprints like bioRxiv/medRxiv platforms posts scientific research papers and leave it on readers to understand, accept or reject the research. Earlier it was task of peer reviewers who used to carefully analyze the study and then either approve study if it is not found satisfactory on certain grounds. Let us see if these preprints servers are doing any good in pandemic times by taking the example of BioRxiv and MedRxiv.

Preprint and its benefits

A preprint is a full draft of a research paper that is shared publicly before it has been peer reviewed. Some of the benefits of preprints are:

1. Publishing a preprint is almost instantaneous.

2. Publish research with open access for free .

3. Preprints achieve many of the goals of journal publishing, but within a much shorter time frame.

4. When you post a preprint with your research results, you can firmly stake a claim to the work you've done.

5. Mass feedback can be provided publicly through commenting, or privately through email.

6. Posting a preprint led to a significant increase in altmetric attention scores and citations for the final published paper.

It was by Maimuna Majumder and Kenneth Mandl first, in March (https://www.thelancet.com/journals/langlo/article/PIIS2214-109X(20)30113-3/fulltext), analyzing media and other interest in preprints versus journal articles about the reproduction number for the new coronavirus when they concluded that because of the speed of release of preprints, they were driving the discourse, not journal articles. Decision-making can be informed quickly, they point out, but it can go

badly wrong, too, as when a preprint had to be retracted after an outcry, because it erroneously claimed that COVID-19 virus contained HIV insertions.

Later the preprint of the **Santa Clara seroprevalence study** (https://www.medrxiv.org/content/10.1101/2020.04.14.20062463v2), a highly contested piece of research, one of the authors of which is John Ioannidis attracted criticism. James Heathers wrote an informative and entertaining **recap (**https://medium.com/@jamesheathers/preprints-arent-the-problem-we-are-the-problem-75d29a317625**)** of the preprint and reaction to it, as well as the arguments about preprints themselves it provoked. He wrote, "the idea of releasing work previous to 'formal' publication isn't the problem — it's us". He argues that a critical part of the preprint process is responding to criticisms. Heathers also criticized the authors' media campaign: "The preprint-followed-by-immediate-formal-demand-for-attention is a disgusting new normal".

An essential aspect of the scientific process is the thorough examination of manuscripts by other scientists. They read the article critically and then either suggest that its acceptance, rejection, or -most frequently- revision before it is published. In fact, most scientists will not consider a scientific pronouncement as valid unless it has been approved by this anonymous process, known as peer review. Without such an external seal of approval, they would consider any results presented as preliminary, potentially flawed and generally of the same self-serving status as a press release.

Preprint on the other hand publishes research (mainly online now) which may put a needle in haystack of scientific knowledge. There are not many publishing houses that remain untouched by Retraction Watch and Pubpeer but the phenomenon of retraction has seen in recent times of COVID19 on preprint servers also.

Taking example of medRxiv and bioRxiv which publishes articles related to biosciences and medical sciences only, have published around 5200 preprints (4201 medRxiv, 1002 bioRxiv) on COVID-19 SARS-CoV-2 (as on June 14 2020), the first paper being published on September 25, 2019.

According to Retraction Watch, the retracted or controversial papers of medRxiv and bioRxiv are:

1. "Uncanny similarity of unique inserts in the 2019-nCoV spike protein to HIV-1 gp120 and Gag," bioRxiv preprint published January 31, 2020 and withdrawn February 2, 2020.

2. "Epidemiological and clinical features of the 2019 novel coronavirus outbreak in China," medRxiv preprint published February 11, 2020 and withdrawn February 21, 2020.

3. "Hydroxychloroquine plus azithromycin: a potential interest in reducing in-hospital morbidity due to COVID-19 pneumonia (HI-ZY-COVID)?" preprint published on medRxiv, May 11, 2020, withdrawn on May 20, 2020.

4. "From SARS-CoV to Wuhan 2019-nCoV Outbreak: Similarity of Early Epidemic and Prediction of Future Trends," preprint posted on bioRxiv, January 25, 2020, withdrawn January 28, 2020.

5. "Analysis of Ten Microsecond simulation data of SARS-CoV-2 dimeric main protease," preprint posted on bioRxiv, April 12, 2020, withdrawn April 16, 2020.

6. "Computational analysis suggests putative intermediate animal hosts of the SARS-CoV-2," preprint posted on bioRxiv, April 5, 2020, withdrawn April 20, 2020.

7. "Mental health status and coping strategy of medical workers in China during The COVID-19 outbreak," preprint posted on medRxiv, February 25, 2020, withdrawn March 7, 2020.

The total controversial articles on COVID19 on Retraction Watch website are 19, thus out of these total, 7 are from either BioRxiv or MedRxiv which makes around 36 percent. https://retractionwatch.com/retracted-coronavirus-covid-19-papers/

On the BioRxiv or MedRxiv servers, through advanced search option we noticed that both servers have published around 93700+ papers from November 2013. A different picture was found when looked at the other dataset from http://api.biorxiv.org/reports/. It reveals that from November 2013 to May 2020 biorxiv has published around 116,420+ (cu-

mulative) articles (http://api.biorxiv.org/reports/content_summary), whereas it is 93000+ cumulatively on BioRxiv and MedRxiv database.

https://www.biorxiv.org/search/jcode%3Amedrxiv%7C%7Cbiorxiv%20numresults%3A10%20sort%3Arelevance-rank%20format_result%3Astandard).

Further out of 116,421 cumulative papers published/ submitted only around 32,000 could find place in journals i.e. only 27.46% whereas 72.53 percent study is still floating on the platform without any verification.

Conclusion

This paper conclude that Preprint servers though are good for free rapid publications there are many drawbacks which outweigh its benefits like the process can compromise with quality, absence of peer review leads to delayed or afterward assessment, unclean study becomes available in public domain, many studies goes in PseudoJournals etc. In light of the above analysis author strongly condemn use of preprint servers for pandemic situation like COVID19 as they do not publish verified research. The same can make catastrophic changes (either positive or negative) unless seen and understand by a field expert.

About bioRxiv

bioRxiv (pronounced "bio-archive") is a free online archive and distribution service for unpublished preprints in the life sciences. It is operated by Cold Spring Harbor Laboratory, a not-for-profit research and educational institution. By posting preprints on bioRxiv, authors are able to make their findings immediately available to the scientific community and receive feedback on draft manuscripts before they are submitted to journals.

medRxiv (pronounced "med-archive") is a free online archive and distribution server for complete but unpublished manuscripts (preprints) in the medical, clinical, and related health sciences. medRxiv was founded by Cold Spring Harbor Laboratory (CSHL), a not-for-profit research and educational institution, Yale University, and BMJ, a global healthcare knowledge provider. The server is owned and operated by CSHL.

Warning from BioRxiv

Caution: Preprints are preliminary reports of work that have not been certified by peer review. They should not be relied on to guide clinical practice or health-related behavior and should not be reported in news media as established information.

Articles are not peer-reviewed, edited, or typeset before being posted online. However, all articles undergo a basic screening process for offensive and/ or non-scientific content and for material that might pose a health or biosecurity risk and are checked for plagiarism. No endorsement of an article's methods, assumptions, conclusions, or scientific quality by Cold Spring Harbor Laboratory is implied by its appearance in bioRxiv/ medRxiv. An article may be posted prior to, or concurrently with, submission to a journal but should not be posted if it has already been accepted for publication by a journal.

References:

Gannon, F. (2001), The essential role of peer review. EMBO reports, 2: 743-743. doi:10.1093/embo-reports/kve188

Scientific work in the time of Corona by By Carina Fron

A CRITICAL LOOK AT A PREPRINT INFERRING THE COVID-19 INFECTION FATALITY RATE http://hildabastian.net/index.php/91

Note: The article is highly pliagiarized with given due references; the views expressed here are personal of author's.

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PUBLIC NOTICE

Dated: 15.06.2020

Subject: Extension / Revision of Last Dates for submission of Online Application Forms for various Examinations conducted by the National Testing Agency (NTA).

In view of many requests and representations received from students and the hardships faced by them due to COVID-19 epidemic, the National Testing Agency (NTA) has further extended the last dates of submission of Online Application Forms for various Examinations to be conducted by the Agency.

Accordingly, the Extended last dates for submission of Online Application Forms shall now be as follows-

S. No	Examination	Current Last Date	Revised/Extended Last Date*	Email for any Clarification
01	Indira Gandhi National Open University (IGNOU) Ph.D. and OPENMAT (MBA) Entrance Examination-2020	15.06.2020	**30.06.2020**	ignou@nta.ac.in
02	Indian Council of Agricultural Research (ICAR) AIEEA 2020	15.06.2020	**30.06.2020**	icar@nta.ac.in
03	Jawaharlal Nehru University Entrance Examination (JNUEE)-2020	15.06.2020	**30.06.2020**	jnu@nta.ac.in
04	UGC-National Eligibility Test(UGC-NET)-June 2020	15.06.2020	**30.06.2020**	ugcnet@nta.ac.in
05	Joint CSIR-UGC NET Examination (CSIR-UGC NET)-June 2020	15.06.2020	**30.06.2020**	csirnet@nta.ac.in
06	All India AYUSH Post Graduate Entrance Test (AIAPGET)-2020	15.06.2020	**30.06.2020**	aiapget@nta.ac.in

'*' Submission of Online Application Forms shall be accepted up to 05.00 PM and Submission of fee up to 11.50 PM.
The requisite fee can be paid through Credit/Debit Card/ Net Banking/UPI and PAYTM.

The detailed schedule mentioning revised dates of downloading of Admit Cards and of Examination will be displayed separately on respective examination website(s) and **www.nta.ac.in** later on. NTA would keep students updated about the latest developments and would inform about changes with ample time.

The candidates and their parents are advised to keep visiting the respective examination website(s) and **www.nta.ac.in** for latest updates.

The candidates can also contact at 8287471852, 8178359845, 9650173668, 9599676953, 8882356803 for any further clarification.

Editorial

A correlation between environmental deterioration and Pandemic

By Seema Pavgi Upadhye

Dr Peter Daszak, who is preparing the next Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services' (IPBES) assessment, writes that rampant deforestation, uncontrolled expansion of agriculture, intensive farming, mining and infrastructure development as well as the exploitation of wild species, all have created a "perfect storm" for the spillover of diseases. These activities can cause pandemics by bringing more people into contact and conflicts with animals, from which 70% of emerging human diseases originate.

The COVID-19 pandemic has compelled us to think again that whether this all is due to heavy destruction of the natural world or due to some other reason(s).

If we see nature then all living organisms are attached either within a food chain or food web. Whether we stand anywhere in chain? Which make us think whether we are required in nature or not? If we are not required then at least we should make ourselves useful to the nature, but ultimately we are playing a role of a villain not a hero.

Urbanisation and explosive growth of global air travel has enabled a harmless virus in Asian bats to bring lot of human suffering and put a halt for economies and societies around the world. If we call SARS-CoV2 a human made pandemic then we can say the COVID -19 is only beginning.

The list of diseases that have jumped from animals to humans ("zoonotic diseases") includes HIV, Ebola, Zika, Hendra, SARS, MERS and bird flu. Like its precursor SARS, SARS- CoV2 is thought to have originated in bats and subsequently transmitted to humans via another animal host, possibly at a wet market which involve in trading of live animals in Wuhan, China.

Ebola virus emerged in Central Africa when land use changed and altered climatic conditions forced bats and chimpanzees to come together around concentrated areas of food resources. Hendra virus is associated with urbanisation of fruit bats following habitat loss. Such changes are occurring worldwide.

Climate change makes us more vulnerable to such pandemics. Climate change is undermining human health globally in other profound ways. It is a risk multiplier, exacerbating our vulnerability to a range of health threats.

Earlier this year, all eyes were on the life-threatening bushfires and the resulting blanket of smoke pollution. This exposed more than half of the Australian population to health harm for many weeks, and led to the deaths of more than 400 people. For infectious communicable diseases such as COVID-19, air pollution creates another risk. This new virus causes a respiratory illness and, as with SARS, exposure to air pollution worsens our vulnerability. Particles of air pollution also act as transporter of pathogens, contributing to the spread of viruses and infectious disease across large distances.

Future pandemics are likely to happen more frequently, spread more rapidly, have greater economic impact and kill more people if we will not become extremely careful about the possible impacts of the choices we make today.

It is indeed essential that trillions of dollars must be invested to save environment, which will ultimately save human health.

Professor Thomas Lovejoy, at the United Nations foundation and George Mason University in the US, who coined the term " Biological diversity " in 1980, said that the pandemic is not nature's revenge; we did it to ourselves. It is due to our persistent and excessive intrusion in nature and the vast illegal wildlife trade, and the wet markets.

The growing global demand for food, fibre, fuels, shelter and freshwater is driving the loss and degradation of natural forests, wetlands, coastal areas and other ecosystems. It has had devastating consequences for biodiversity and the life-sustaining services that ecosystems provide, such as clean air, safe drinking water and a stable climate. Biodiversity (all biological diversity from genes, to species, to ecosystems) is declining faster than at any time in human history.

The explosive growth of towns and cities and land use changes — forestry, agriculture, mining — destroyed an astonishing 3.3 million square kilometres of terrestrial wilderness (an area larger than India) between 1993 and 2009.

The high seas haven't escaped the breadth and reach of human activity either. Today, industrial fisheries, pollution and marine traffic are threatening more than 87 per cent of the world's oceans.

Studies like these have helped draw attention to the astonishing pace and scale of global habitat loss at a time when policy-makers are expected to increase the coverage of protected areas.

We are fast approaching the 2020 deadline for achieving the United Nations' Strategic Plan for Biodiversity and its 20 Aichi Biodiversity Targets, including Target 11. That initiative obligates countries to protect 17 per cent of terrestrial areas and inland water, and 10 per cent of marine and coastal areas.

A mid-term analysis of progress on the Aichi Targets, published in 2014, showed that most countries would likely fail to meet their own goals. But there is a promising way forward where countries can protect biodiversity and recognize Indigenous peoples as conservation partners.

The Aichi Biodiversity Targets

Strategic Goal A- Address the underlying causes of Biodiversity loss by mainstreaming biodiversity across government and society.

Strategic Goal B- Reduce the direct pressures on biodiversity and promote sustainable use.

Strategic Goal C- Improve the status of biodiversity by safeguarding ecosystems, species and genetic diversity

Strategic Goal D- Enhance the benefits to all from biodiversity and ecosystem services.

Strategic Goal E- Enhance implementation through participatory planning, knowledge management and capacity building.

At the global scale, the number of terrestrial and marine protected areas have expanded since 2011. As of July 2018, there were 238,563 designated protected areas recorded in the World Database on Protected Areas. These areas collectively protect more than 20 million square kilometres of land (14.9 per cent of the Earth's land surface) and six million square kilometres of oceans (7.3 per cent).

While the global community is on track to achieve its spatial goals by the 2020 deadline, there are concerns that the focus on quantity of protection instead of the quality of protection is undermining biodiversity conservation.

There is also the danger that in the rush to meet the 2020 deadline, many new protected areas will simply be "paper parks" that remain open to the consumption of biodiversity within them, such as industrial fishing, or suffer from inadequate resources and enforcement.

The global biodiversity crisis necessitates conservation action that is both effective and equitable. Recent progress to expand the global coverage of traditional parks and protected areas is encouraging, but we must not loose sight of the critical need for new and innovative forms of conservation governance.

Habitat destruction like deforestation and agricultural

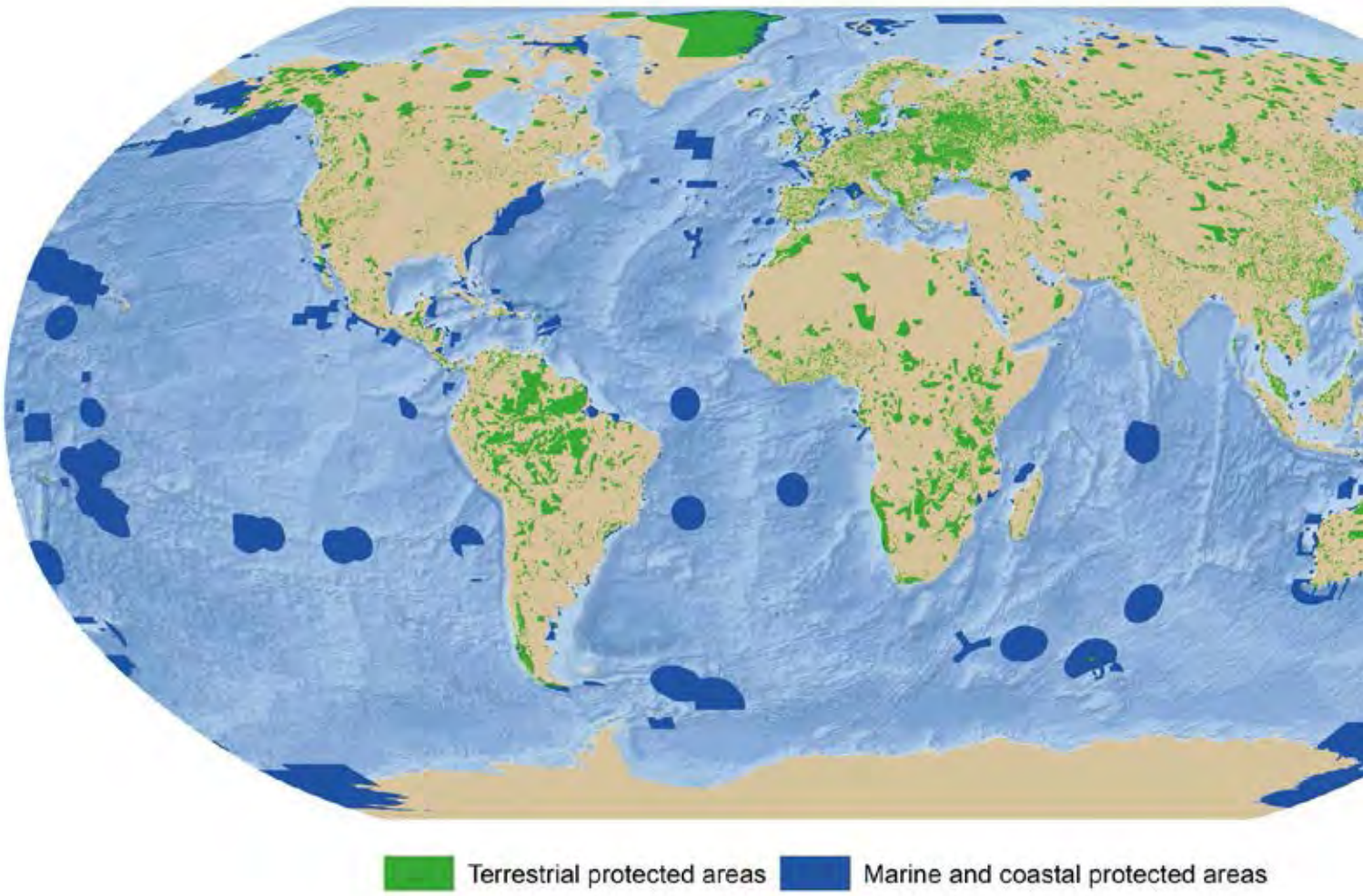

Fig. Map of the world, showing the locations of protected areas on land and in the ocean, based on spatial data derived from the WDPA43. Source: UNEP-WCMC and IUCN (2019). Protected Planet: The World Database on Protected Areas (WDPA, January 2019, Cambridge, UK: UNEP-WCMC. Available at www.protectedplanet.net (accessed January 2019).

development on wild lands are increasingly forcing disease-carrying wild animals to come closer to humans, allowing new strains of infectious diseases to thrive.

"When you cut down trees and remove the forest, you eliminate the natural environment of some species. But those species don't just disappear," said Roger Frutos, an infectious diseases researcher at the University of Montpellier in France. "We instead create a patchwork, a mosaic of their environment that is closer to ours, with houses that attract insects or sheds where bats can rest and find shelter," he said.

Scientists say the coronavirus pandemic is the most recent instance of how human degradation of wildlife habitats is linked to the spread of infectious diseases.

Bats are less likely to transmit viruses to humans when they are in wild habitats, but land conversion has increased their exposure to humans and upped the chances of virus transmission. There is now a higher density of bat-borne viruses and pathogens near human dwellings worldwide.

Some researchers estimate that more than 3,000 strains of coronavirus could already exist in bats and could be transmitted to humans.

"When you're building human homes right up on forest edges, you're destroying wildlife habitats and squeezing animals' habitats into smaller areas," leading to a more likely transmission of disease to humans, according to Tierra Smiley Evans, an epidemiologist at the One Health Institute at the University of California.

Only about 15% of the world's forests, which are key to maintaining biodiversity, remain intact after degradation from logging, fires and agricultural expansion, according to the World Resources Institute. Millions of animal and plant species currently face extinction because of habitat destruction.

South America is a prime area of concern over infectious disease spread due to rapid deforestation of the Amazon rainforest from logging and mining, which researchers say will aggravate wildfires and Covid-19 spread in the region.

"Preserving habitats for wildlife and preserving our world is a human health issue, not just a wildlife or environmental issue," said Smiley, who studies deforestation and virus spread in Myanmar.

Scott Weaver, director of the Institute for Human Infections and Immunity at the University of Texas Medical Branch in Galveston, said deforestation will increase the risk of many mosquito-borne viruses in areas like the tropics, Latin America and Southeast Asia.

Poorer countries will suffer the most from diseases made worse by climate change, since warmer temperatures will increase the spread of viruses like dengue fever in places where people can't afford air conditioning and general protections against disease exposure, Weaver said.

For instance, the West Nile virus, a mosquito-borne disease, replicates a lot faster in hotter climates. Researchers believe that global warming is allowing the virus to spread more efficiently in wild birds, which then infect people.

"We're in this predicament with the coronavirus because we've under invested in public health across the world and we haven't taken scientific information into account in political decisions," Weaver added.

In this pandemic situation every country is looking to end lockdown, if it is safe. It has hurt largely economic and also political shocks. But at the same time we should not forget biosphere and its future. Off course brake on the economic activities has led to cut in carbon emissions, less air pollution, clean waters, less noise better to wildlife; Deterioration of environment have paused. Carbon emissions are cut by 15-20% in various countries but it is also associated with fall in economy.

If we gain back our economy then all this environmental gains will be temporary or reversed. Off course some benefit will stay back like wildlife protected from accidents, more grasslands and less poaching, but how longer, is the question. The other side of coin is that less money cannot conserve endangered species and habitats, this can increase illegal activities like poaching, mining and logging. Therefore loss in economy is not a benefit to nature.

So the need of the day is to grow and flourish by green jobs, clean energy and many natural things without spoiling our environment.

Guest Article

COVID-19 and Primary Health Infrastructure: Is Rural India in Ruins?

Sukanya Chakraborty[1] , Aparajita Chattopadhyay[2]

Indian Institute of Science Education and Research, Berhampur
International Institute of Population Sciences, Mumbai

The Novel Coronavirus 2019 has taken the world by a storm and brought life to a standstill. Caused by the SARS-CoV-2 virus, the disease presents as mildly symptomatic in most afflicted individuals, with possibilities of complications in those with co-morbidities. The devastation does not end there. The socio-economic landscape of the world has suffered irrevocable damages, particularly, in developing nations such as ours. A dearth of essential resources and an ineffective workforce, make it unlikely for India to be rescued from the impending doom in time.

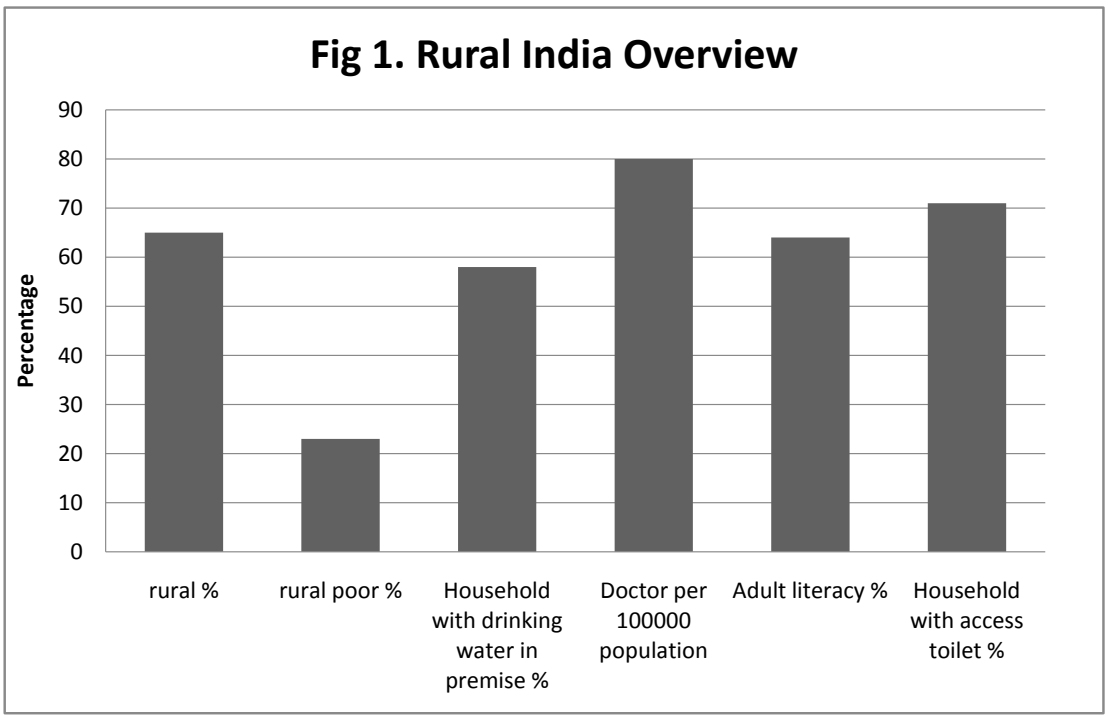

Fig 1: Different sources from Government of India records and World Bank, 2018

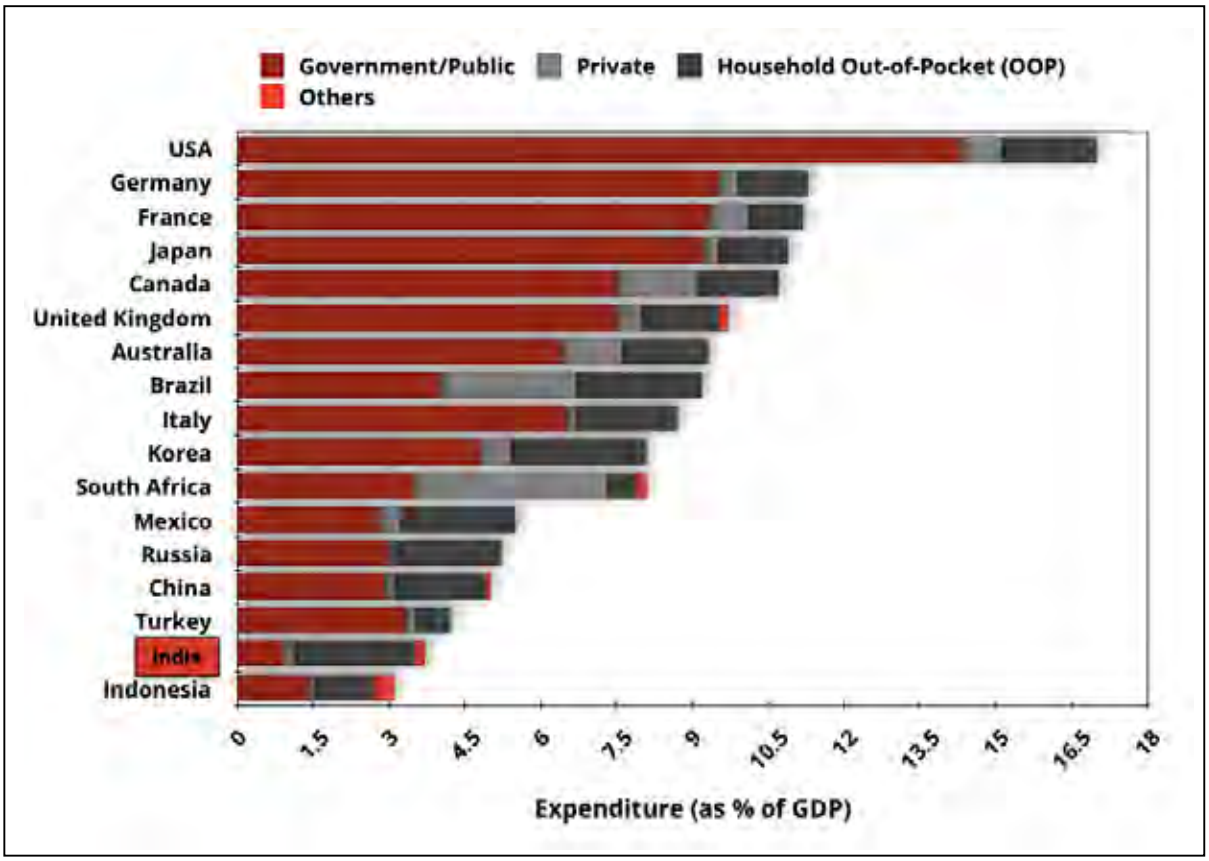

Fig 2: Amount spent by various sectors on Healthcare in different countries Health at a Glance, OECD, 2018

Rural India, as stated by Dr. Soumya Swaminathan, WHO's Chief Scientist, may become the next coronavirus epicentre. Lack of social distancing, temporary unemployment, poor health infrastructure, restricted activities of rural health workers, misinformation and confusion, deficient water and sanitation facilities altogether may turn rural regions into COVID19 hotspots. This opportunity should be utilised to strengthen the country's primary health care system. Although an impossible feat under current time constraints, the right steps in this direction will definitely help in the future.

We need to understand the overall health scenario of our country. Deaths in India due to Communicable Diseases are higher than the Global Average (IHME, Global Burden of Disease 2017). Expenditure on Healthcare by different sectors is alarmingly low. Maximum share of health expenditure in India, including rural areas is 'Out of Pocket' expenses, one of the highest compared to other countries (**Fig 2**). Contagious Respiratory Diseases in India **(Fig 3)** account for more than 50% of total deaths. Rural regions that support 70% of the Indian population, lacks enough health facilities or manpower in many aspirational districts demarcated by the Government.

In a country whose foundations rely upon a major fraction of workers earning wages on a daily basis without insurance and adequate savings, the economic scenario is unstable. Migrants exasperated with their emotional turmoil have taken to the roads. This may exacerbate the situation

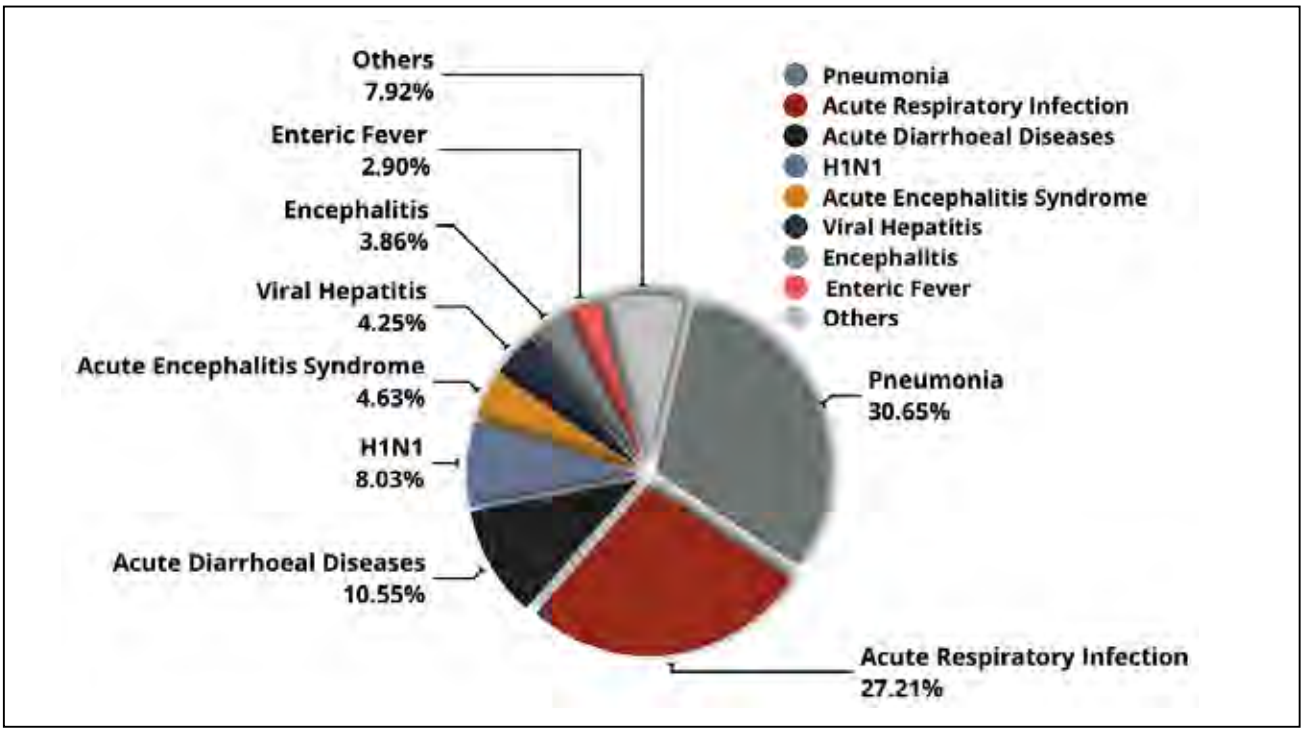

Fig 3. Proportion of Deaths due to Infectious Diseases, National Health Profile, 2019, Central Bureau of Health Intelligence

by increasing chances of widespread transmission. Information about their exposure and status of infection is extremely limited. Guidelines have been stated in many tertiary medical colleges,

regarding the screening and quarantine of incoming labourers. However, these rely on them approaching the hospital authorities and revealing their travel history. This isvery unlikely to happen considering their mindset and the stigma surrounding the disease. As a result, thousands of cases will go unnoticed, and community transmission through the asymptomatic carriers among the migrants may increase rampantly. With the lack of proper scientific temper in our country, these serve as added burdens to an already frail health system.

Healthcare facilities are underfunded to support current demands, hampering most provisions. The primary health care centres and lower tiers in rural regions are involved in spreading awareness regarding infectious diseases such as dengue, malaria, tuberculosis among others, through home visits by health workers. Maternal and child-care duties, such as antenatal and postnatal care are also disseminated through the same medium.

"Recently, due to the outbreak, all such activities have come to a complete halt. Despite orders to normalize the situation from authorities, most rural areas are still deprived of these programs, highlighting one of the many failures of our health system.", says Dr. Somajita Chakraborty, HOD, Obstetrics and Gynaecology, Diamond Harbour Medical College and Hospital, West Bengal. Rural morbidity and

mortality are mainly associated with respiratory and water borne diseases that are preventable. However, the COVID-19 emergency has diminished all regular actions of identification and prevention.

Until recently, India had only 126 government based COVID-19 testing centres to handle a population of over 1.35 billion people (ICMR, April 2020). The surveillance in our country is hindered by a severe lack of awareness. Reports of patients trying to flee from isolation wards and conceal their travel records have been rampant. Lack of proper intervention on the part of hospitals have been noticeable. In fact, there is sceptic evidence on incorrect results being released and numbers being withheld.

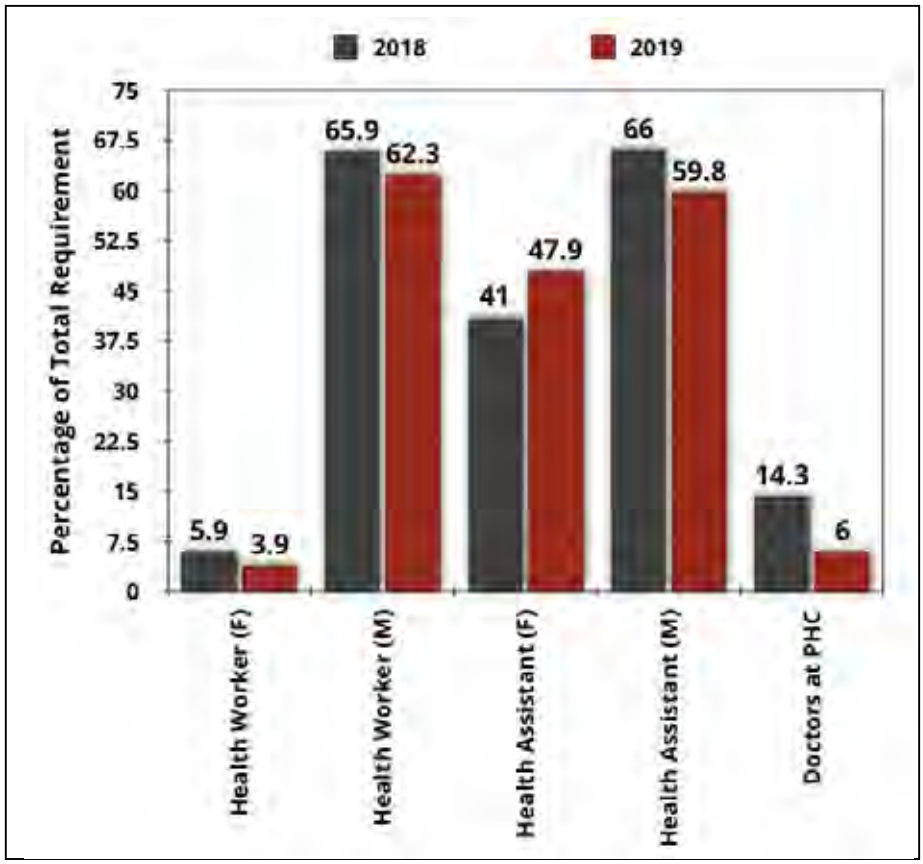

Fig 4. Shortage of Manpower in Sub-centers and Primary Health Centers
Ministry of Health and Family Welfare Statistics Division, RHS 2018 – 2019
[M = Male, F = Female]

Rural population is at the verge of poverty, uncertainty and ill health. Without rigorous monitoring of asymptotic COVID cases by grass root workers and a strong referral system, it would be impossible to check spread of the virus. Incidence of catastrophic expenditure due to health care costs will offset the gains of income, further questioning the Government schemes aiming to reduce poverty.

Most hospital facilities in districts lack state-of-the-art infrastructure to address emergencies such as this. Although by now, much of the mayhem and tumult has considerably subsided, we do need to remember that the Indian health system deserves immediate attention.A severe shortage of adequately trained staff **(Fig 4)** has rendered us helpless to contain the infection, particularly in densely populated states and low-resource regions, which India is replete in. We are highly deficient in health care services as per the recommended levels advisable by the World Health Organization.

Challenges are discernible at every turn and the dream of a fruitful health order today, seems no less than a mirage. The coming weeks and months are challenging for India and we need to take strong measures to meet this emergency and its inevitable aftermath.

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Guest Article

CORONAVIRUS AND THE HEAT - REALISTIC PERSPECTIVE

by Rama S Verma and Steffi SV

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INTRODUCTION:

The **2019–20 coronavirus pandemic** is an ongoing pandemic of coronavirus disease 2019 (COVID19) caused by severe acute respiratory syndrome coronavirus 2 (SARSCoV2). Severe acute respiratory syndrome coronavirus (SARS-CoV)-2, a novel coronavirus from the same family as SARS-CoV and Middle East respiratory syndrome coronavirus, has spread worldwide leading the World Health Organization to declare a pandemic. The disease caused by SARS-CoV-2, coronavirus disease 2019 (COVID-19), presents flu-likeand respiratory symptoms The outbreak was identified in Wuhan, China, in December 2019.The World Health Organization declared the outbreak a Public Health Emergency of International Concern on 30 January, and a pandemic on 11 March. As of June 12, 2020, more than 7.273 million cases of COVID-19 have been reported in 187 countries and territories, resulting in more than 413,372 deaths. More than 3.09 million people have recoveredand categorised in a high-risk disease.

Human-to-human aerosol transmission is undoubtedly the main source of contagion, which happens mainly through contaminated droplets, hands or surfaces. Virus particles, which are present in secretions from an infected person's respiratory system, infect others through direct contact with mucous membraneswith a median incubation period of between 2 and 12 days (median 5.1 days) (1).

1. ORIGIN OF CORONAVIRUS:

The most recent common ancestor of all coronaviruses is estimated to have existed as recently as 8000 BCE, although some models place the common ancestor as far back as 55 million years or more, implying long term co-evolution with bat and avian species. The most recent common ancestor of the α-coronavirus line has been placed at about 2400 BCE, of the β-coronavirus line at 3300 BCE, of the -coronavirus line at 2800 BCE, and of the -coronavirus line at about 3000 BCE. Bats and birds, as warm-blooded flying vertebrates, are an ideal natural reservoir for the coronavirus (2).

MERS-CoV emerged in humans from bats through the intermediate host of camels. MERS-CoV, although related to several bat coronavirus species, appears to have diverged from these several centuries ago. The most closely related bat coronavirus and SARS-CoV diverged in 1986. The ancestors of SARS-CoV first infected leaf-nose bats of the genus *Hipposideridae*; subsequently, they spread to horseshoe bats in the species *Rhinolophidae*, then to civets, and finally to humans(2).

The emerging coronavirus disease (COVID-19) has swept across the world, and this outbreak was reported in Wuhan, China affecting more than 200 countries and territories. On 31st December 2019, the outbreak was traced to a novel strain of coronavirus, which was given the name 2019-nCoV by the World Health Organization (WHO), later renamed as SARS-CoV-2 by the International Committee on Taxonomy of Viruses. Genomic analysis suggests that the COVID-19 virus originated in bats and transmitted to humans through unknown intermediate hosts in the Wuhan seafood market, China, in December of 2019.

TYPES OF CORONAVIRUS:

The term 'coronavirus' refers to a large group of viruses known to affect the birds and mammals, including humans. COVID-19, which first appeared in China in December 2019, is a type of coronavirus. There are hundreds of coronavirus, but only seven types are known to affect the people. Four human coronavirus only cause mild cold or flu-like symptoms. Three other coronaviruses can cause more serious risks. The seven coronaviruses that affect the humans can be categorized into two groups:

i) Common human coronavirus

There are four common human coronaviruses namely 229E, NL63, OC43, HKU1. Common human coronaviruses usually cause mild to moderate symptoms. Most people around the world will develop at least one of these viral infections over their lifetime. Those who develop these kind of infections recover on their own most of the time.

ii) Other human coronavirus

There are three other human coronavirus-

1. **SARS-CoV-** SARS-CoV causes Severe Acute Respiratory Syndrome (SARS). This virus is said to have originated in bats and are transmitted to other animals before infecting humans.

2. **MERS-CoV-** MERS-CoV causes Middle East Respiratory Syndrome (MERS). This virus is spread through the contact with the camels that have carried the infection.

3. **SARS-CoV-2-** SARS-CoV-2 causes the illness known as COVID-19. This new coronavirus appeared in Wuhan, China, in late December 2019. Though the virus likely evolved from an animal source, its exact source is unknown. This virus is dangerous because it is transmitted easily from person-to-person, whether or not the person is exhibiting symptoms (3).

2. INFECTIVE STATUS OF DIFFERENT STRAINS:

Six species of human coronaviruses are known, with one species subdivided into two different strains, making seven strains of human coronaviruses altogether. Four of these coronaviruses continually circulate in the human population and produce the generally mild symptoms of the common cold in adults and children worldwide: -OC43, -HKU1, HCoV-229E, -NL63.

These coronaviruses cause about 15% of common colds, while 40 to 50% of colds are caused by rhinoviruses. The four mild coronaviruses have a seasonal incidence occurring in the winter months in temperate climates. There is no preference towards a particular season in tropical climates.

Four human coronaviruses produce symptoms that are generally mild: 1. Human coronavirus OC43 (HCoV-OC43), β-CoV. 2. Human coronavirus HKU1 (HCoV-HKU1), β-Co. 3. Human coronavirus 229E (HCoV-229E), α-CoV. 4. Human coronavirus

NL63 (HCoV-NL63), α-CoV

Three human coronaviruses produce symptoms that are potentially severe: 1. Middle East respiratory syndrome-related coronavirus (MERS-CoV), β-CoV. 2. Severe acute respiratory syndrome coronavirus (SARS-CoV), β-CoV.3. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), β-CoV (2).

The SARS-CoV-2 is a coronavirus, which is enveloped, non-segmented positive-sense RNA virus. Coronaviruses are divided into four genera, including α, β,-CoV. α and β-CoV infect the mammals, while -CoV tend to infect the birds. Six CoV's have been identified as human-susceptible virus, among which α-CoVs (HCoV-229E and HCoV-NL63) and β-CoVs (HCoV-HKU1 and HCoV-OC43) with low pathogenicity, cause mild respiratory symptoms similar to a cold. The SARS-CoV and MERS-CoV lead to severe and potentially fatal respiratory tract infections. It was found that the genome sequence of SARS-CoV-2 is 96.2% identical to a bat CoV RaTG13, whereas it shares 79.5% identity to SARS-CoV (1).

A recent study that was reportedly done at the National Institute of Biomedical Genomics, West Bengal suggested that there are at least 11 different strains of SARS-CoV-2 in the world. A strain is a subtype of a virus that is created due to a mutation in the genome (genes) of the said virus. For the study, scientists at the National Institute of Biomedical Genomics studied more than 3,600 samples of the SARS-CoV-2 genome collected from various countries (around 55) of the world. These samples were then studied to look for similarities and differences. As per the study, the original strain of the COVID-19 causing virus was named O type or ancestral type. But from this strain at least 10 different strains had originated. Out of these 10 new strains, a strain called A2a is currently the most prevalent in the world as well as in India. The study claims that if a vaccine is to be made, it should be made against A2a strain.The A2a strain reportedly has an advantage over its peers in that it can better bind with the ACE-2 receptors in the lungs which is what the SARS-CoV-2 virus uses to enter into healthy cells. This happens due to a change in a single amino acid from aspartic acid to glycine in the spike protein of the virus. The stronger this virus binds to its receptors the more chances of it entering a healthy cell and replicating.

3. VIRULENCE OF CORONAVIRUS:

The common human CoVs are generally associated with relatively mild clinical symptoms and cause a self-limiting upper respiratory tract disease. Several independent research groups have identified that SARS-CoV-2 belongs to β-coronavirus, with highly identical genome to bat coronavirus, pointing to bat as the natural host. The novel coronavirus uses the same receptor, angiotensin-converting enzyme 2 (ACE2) as that for SARS-CoV, and mainly spreads through the respiratory tract. The clinical symptoms of COVID-19 patients include fever, cough, fatigue and a small population of patients appeared gastrointestinal infection symptoms. The elderly and people with underlying diseases are susceptible to infection and prone to serious outcomes, which may be associated with acute respiratory distress syndrome (ARDS) and cytokine storm.

The virulence nature of this coronavirus vary significantly in risk factor and are as follows:

1. Symptoms of COVID-19 (SARS-CoV-2 syndrome) may occur within 2–14 days after exposure and can lead to difficulties in cilium beating of airway cells and to alveolar damage. 2. Infected patients experience mild to severe manifestations, such as fever, dry cough, dyspnoea, abdominal pain, and diarrhoea. 3. Can cause pneumonia and bronchitis. 4. Affects both upper and lower respiratory tracts. 5. Attacks artery walls and can cause organ failure. 6. Strokes and heart damage.7. Severe urinary complications and acute kidney injury.8. Skin lesions, neurological problems, sharp chest pains, loss of taste and smell.

4. GENETICS OF CORONAVIRUS:

Coronaviruses are large, enveloped RNA viruses of both medical and veterinary importance. At the mo-

lecular level, coronaviruses employ a variety of unusual strategies to accomplish a complex program of gene expression. Coronavirus replication entails ribosome frame shifting during genome translation, the synthesis of both genomic and multiple subgenomic RNA species, and the assembly of progeny virions by a pathway that is unique among enveloped RNA viruses. Progress in the investigation of these processes has been enhanced by the development of reverse genetic systems, an advance that was obstructed by the enormous size of the coronavirus genome.

A new genetic analysis of 10 genome sequences of 2019-nCoV in Wuhan found that the virus was most closely related to two bat-derived SARS-like coronaviruses. Comparing the 2019-nCoV genetic sequence with a library of viruses, a team of researchers from the China found that the most closely related viruses were two SARS-like coronaviruses of bat origin bat-SL-CoVZC45 and bat-SL-CoVZXC21 which shared 88% of the genetic sequence. The scientists found 2019-nCoV was genetically little distant to the human SARS virus (which shared about 79% of the genetic sequence) and the Middle East respiratory syndrome (MERS) virus (which shared about 50% of the genetic sequence).

SYMPTOMS OF COVID-19:

The primary symptoms of COVID-19 include: 1. Cough 2. Fever3. Shortness of breath 4. Fatigue

Less common symptoms of COVID-19 include:1. Sore throat 2. Nasal congestion 3. Muscle aches and pains 4. Diarrhoea 5. Loss of taste or smell 6. Headache 7. Chills, which may occur sometimes with repeated shaking (3).

PRECAUTIONS FOR COVID-19:

The following basic protective measures can help you protect yourself from COVID-19:

1. Stay home. The best way to protect yourself from the virus is to avoid being exposed to it. That means staying home to avoid coming into contact with people who might have the virus.

2. Wash your hands often and thoroughly. Wash your hands with soap and water for at least 20 seconds especially if you have been in a public area.

3. Use an alcohol-based hand sanitizer. When it's not possible to wash your hands, use a hand sanitizer with at least 60 percent alcohol content.

4. Avoid touching your face. The virus can survive on surfaces that you touch with your hands. If your hands come into contact with your mouth, nose, and eyes, the virus might enter your body.

5. Practice social distancing. If you need to leave your house, maintain your distance from anyone who might have the virus, especially if the virus is being transmitted in your community.

6. Seek regular updates. The situation is evolving rapidly. It's important to follow instructions from public health officials (3).

The virus is primarily spread between people during close contact, often via small droplets produced by coughing, sneezing, or talking. The droplets usually fall to the ground or onto surfaces rather than remaining in the air over long distances. People may also become infected by touching a contaminated surface and then touching their face.On surfaces, the amount of virus declines over time until it is insufficient to remain infectious, but it may be detected for hours or days.It is most contagious during the first three days after the onset of symptoms, although spread may be possible before symptoms appear and in later stages of theCommon symptoms include fever, cough, fatigue, shortness of breath, and loss of smell. Complications may include pneumonia and acute respiratory distress syndrome. The time from exposure to onset of symptoms is typically around five days, but may range from two to fourteen days.There is no known vaccine or specific antiviral treatment for this pandemic as of now. Primary treatment is symptomatic and supportive therapy.

Recommended preventive measures include hand washing, covering one's mouth when coughing, maintaining distance from other people, wearing a face mask in public settings, and monitoring and self-isolation for people who suspect they are infected. Authorities worldwide have responded by implementing travel restrictions, quarantines, curfews and stay-at-home orders, workplace hazard controls, and facility closures. Many places have also worked to increase testing capacity and trace contacts of infected persons.

HIGH TEMPERATURES INEFFECTIVE AGAINST CORONAVIRUS

The novel coronavirus can survive in high temperatures, researchers said, casting doubt on suggestions that the threat will subside in the summer. Researchers from the University of Aix-Marseille in France, led by Remi Charrel and Boris Pastorino, found that the virus survived in **140-degree Fahrenheit temperatures** typically used to disinfect research labs, The Jerusalem Post reported.

It took **15 minutes** of exposure to **197.6-degree temperatures** to kill the virus, the newspaper noted, adding that the study had yet to be peer-reviewed. Researchers did say the lower temperature should be sufficient to deactivate the virus in samples with smaller loads but added that the higher temperature was necessary for larger loads and concluded that disinfecting chemicals were a better option.Earlier research has reached similar conclusions.

A National Academies of Sciences (NAS) panel has told the White House in early April that previous research suggesting a connection between temperature and the virus's transmissibility was flawed. "There is some evidence to suggest that [the coronavirus] may transmit less efficiently in environments with higher ambient temperature and humidity; however, given the lack of host immunity globally, this reduction in transmission efficiency may not lead to a significant reduction in disease spread" without efforts such as social distancing, the NAS report stated, noting that SARS and MERS are not seasonal (4).

THE VIRUS DOES SEEM TO DIE FASTER IN SUNNIER, HOTTER, AND MORE HUMID LAB CONDITIONS

A handful of lab experiments in China and the United States suggest the coronavirus decays more quickly in summer versus winter conditions.Researchers in Hong Kong found that when a sample of the coronavirus in a cell culture was left at **39 degrees Fahrenheit**, it was still detectable after 14 days; at **71 degrees**, the virus degraded significantly over 7 days and was not detectable after 14 days. And when exposed to **98 degrees**, no virus was detectable by the second day, according to results published April 2 in the Lancet.

The preliminary DHS study announced similar findings though the agency did not release its methodology or raw data. The experiment exposed virus in droplets of simulated saliva on a stainless steel surface to different levels of solar radiation to simulate sunlight, as well as a range of temperatures and humidities. Under the **70 to 75 degree Fahrenheit** temperature range, with 20% humidity, the virus decayed by half over 18 hours; when humidity was increased to 80%, the virus decayed by half in only 6 hours. When the temperature was increased to **95 degrees**-Fahrenheit combined with the higher humidity, the virus half-life again dropped to 1 hour. And the virus rapidly decayed in 2 minutes when exposed to **75 degrees Fahrenheit**, 80% humidity, and intense solar radiation used to simulate sunlight.

SUNLIGHT, HUMIDITY DAMAGES NOVEL CORONAVIRUS, SAYS THE WHITE HOUSE

The coronavirus outbreak in the US has killed many Americans and has infected more than the death rate. The most striking observation to date is the powerful effect that solar light appears to have on killing the virus, both on surfaces and in the air. The similar effect is seen with both temperature and humidity as well. Increasing the temperature and humidity, or both, is generally less favourable to the virus. In a room at **70-75ºF (21-23ºC) temperature** with 20 percent humidity, the half-life of the virus is about an hour according to the study.But you get outside and

Increased temperature, humidity, and sunlight are detrimental to SARS-CoV-2 in saliva droplets on surfaces and in the air.				
CONDITION	**Temperature**	**Humidity**	**Solar**	**Half Life**
Surface	70-75˚F	20%	None	18 hours
Surface	70-75˚F	80%	None	6 hours
Surface	95˚F	80%	None	1 hour
Surface	70-75˚F	80%	Summer	2 minutes
Aerosol	70-75˚F	20%	None	˜60 minutes
Aerosol	70-75˚F	20%	Summer	˜1.5 minutes

it cuts down to a minute and a half, very significant difference when it when it gets hit with UV rays.

According to the same research, the virushalf-life on surfaces reduces dramatically with a combination increase of temperature and humidity. When the temperate is kept constant at **70-75ºF (21-23ºC)** and only the humidity is cranked up from 20 percent to 80 percent, the virus half-life is shown to crash from 18 hours to 6 hours. If the temperature is increased to **95ºF (35ºC),** the half-life sinks to barely 60 minutes (5).

EXPOSING YOURSELF TO THE SUN WON'T ELIMINATE CORONAVIRUS

Hot temperatures even those above **75 degrees**don't have an effect on the virus, and no area of the country has less of a risk than others right now because of its climate.

"You can catch COVID-19, no matter how sunny or hot the weather is. Countries with hot weather have reported cases of COVID-19," according to the World Health Organization.

"To protect yourself, make sure you clean your hands frequently and thoroughly and avoid touching your eyes, mouth and nose." (6).

COVID-19 CAN ALSO SPREAD IN HOT AND HUMID CLIMATES

There's still a question of seasonality with COVID-19. Early on in the outbreak, experts suspected the virus could be like other coronaviruses and have a shorter lifespan at higher temperatures and in higher humidity.

Most illnesses have an easier time surviving and reproducing in the colder months. But we won't know for sure this will happen with COVID-19 until the seasons change and more research comes."We don't have direct data for this virus, nor do we have direct data for a temperature-based cut off for inactivation at this point," according to the Centres for Disease Control and Prevention. "The necessary temperature would also be based on the materials of the surface, the environment, etc."(6).

COLD WEATHER ALSO CANNOT KILL CORONAVIRUS

There also isn't evidence that an extreme cold outside temperature will have an effect on the virus. WHO that there is "no reason to believe that cold weather can kill the new coronavirus or other diseases." Our normal body temperature typically remains around 98 degrees, give or take, regardless of the external temperature or weather (6).

DIRECT EXPOSURE TO INTENSE TEMPERATURES THROUGH OTHER METHODS WILL ALSO NOT ELIMINATE COVID-19

Hand dryers, hot baths, ice baths, UV lights and other related methods will likely not prevent a COVID-19 infection on their own.

WHO warns that attempting these methods may end up being harmful. For example, extremely hot showers can burn you, and UV radiation can cause skin irritation (6).

CONCLUSION:

From these information's we come to know that the novel coronavirus can survive in both the high and low temperatures. More researches need to be carried out upon this for a clear view of this virus being spread in hot, humid or cold conditions with respect to different environmental conditions. So, from this we come to know that neither the hot temperature nor the cold temperature can kill the virus.

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Call for BRSI Annual Awards Nominations for 2019 and Fellows for 2020

The Biotech Research Society, India (BRSI)

Nominations are invited for the following BRSI Annual Awards and election of Fellows:

1. Life-Time Achievement Award: Members of BRSI above the age of 55 years as on 31st December 2019 involved in Biotech R&D for life time contribution to the field of Biotechnology would be eligible. Award carries certificate, citation and Rs 50,000 cash.

2. Young Scientist Award: Members of BRSIof 35 years or below as on 31st December 2019 involved in Biotech R&D for outstanding contributions would be eligible. Award carries certificate, citation and Rs 25,000 cash.

3. Woman Scientist Award: Women members of BRSI below the age of 45 years as on 31st December 2019 involved in Biotech R&D for outstanding contributions would be eligible. Award carries certificate, citation and Rs 25,000 cash.

4. Industrial Medal Award: Members of BRSI involved in Biotech R&D for outstanding contribution, which has resulted in commercialization of a product/process. Award carries certificate, citation and Rs 25,000 cash.

5. Fellow of BRSI: Eminent members of BRSI above the age of 45 years as on 31st December 2019 having long-standing and significant contribution to the field working in various areas of biotechnology shall be considered to be elected as Fellow of BRSI (*FBRS*).

6. Honorary Fellow of BRSI: Eminent persons above the age of 45 years as on 31st December 2019 who have rendered distinguished service to the nation in Biotechnology shall be considered to be conferred as Honorary Fellow of BRSI. Award carries a citation and a memento. Nomination can be made by the members of the Board of BRSI. For this, the nominee may or may not be member of BRSI.

7. AU-CBT Excellence Awards for Research Scholars (Two awards): Members of BRSI registered for PhD studies in any Indian university/institute below the age of 30 years as on 31st December 2019 involved in Biotech R&D for outstanding performance. Award carries a citation and Rs. 5000 cash for each.

8. Malaviya Memorial Awards for Teaching Faculties (Two awards – one for Young Faculty below the age of 40 years and one for the Senior Faculty above the age of 40 years as on 31st December 2019): Members of BRSI working as teachers involved in Biotech R&D for outstanding contribution. Award carries certificate, citation and Rs 10,000 and Rs 15,000 cash, respectively.

9. SBC-MKU Genomics Award: Members of BRSI below the age of 40 years as on 31st December 2019 involved in R&D in the area of Molecular Biology/Genomics/Metabolic Engineering/ Genetics/Genetic Engineering for outstanding contribution. Award carries certificate, citation and Rs 10,000 cash.

10. Prof SB Chincholkar Memorial Award: Members of BRSI above the age of 40 years as on 31st December 2019 involved in R&D in the area of Food/Agriculture Biotechnology/ Bioenergy for outstanding contribution. Award carries certificate, citation and Rs 25,000 cash.

11. BHU Centennial Award (Two awards): Members of BRSI above the age of 50 years as on 31st December 2019 involved in Biotech R&D for outstanding contributions. Award carries certificate, citation and Rs 25,000 cash.

General terms and conditions:

1. Nominee should be a BRSI member on at least one year standing on the closing date of award call (i.e., should have joined on or before 1st August 2019).

2. A person getting an award in any under any categories will not be eligible to apply for next THREE years for any other category of award (i.e., those getting any award for the year 2016, 2017 or 2018, and Fellows in 2017, 2018 or 2019 will not be eligible to apply for any award against this call).

3. Age certificate (copy of passport, X class school certificate or birth certificate) is required as the proof of age.

4. The work for which nomination is made must have been carried out in India (except for Overseas Fellow award).

5. Each nomination must be proposed and seconded by two persons, out of whom one should be Fellow or Life member of BRSI.

6. For AU-CBT Excellence Awards for Research Scholars, the nominee should be a full-time registered scholar working in India (part-time researchers and persons working under FIP/QIP are not eligible). Those who have submitted the thesis would also not be eligible. Status certificate from the Head of Institute/ HOD of University department of current date required.

7. Malaviya Memorial Awards are meant only for the teaching faculties for their R&D contributions. Members from the R&D institute involved in research on full-time basis are not eligible for this. However, those getting this award would not be eligible to apply for BHU Centennial award.

8. Those getting BHU Centennial award would subsequently be eligible to apply only for Industrial Medal, Fellow and Time-Time Achievement award.

9. Those elected as Fellow subsequently would be eligible to apply only for Industrial Medal, BHU Centennial and Life-Time Achievement award.

10. The criteria for the awards are performance based on publications/ impact factors/ citations/ patents/ technology transfers, etc. However, for certain categories of awards, due consideration will be given to the nominees for their contribution for the growth of the BRSI (see clause 16, part A of form).

11. A member can apply only for one award in the given year.

The evaluation sheet must be filled properly and for each point, numbered and flagged documentary support must be provided, failing with that would not be considered. Nomination form can be obtained from the homepage of the Society at www.brsi.inLast date to receive the nominations by email is **July 25, 2020** and by post **July 31, 2020; 5.00 pm.**

Incomplete applications will be rejected without any communication to the nominee**.**

Award winners will be notified in last week of September/first week of October 2020**.**

Application complete in all respects should be sent (i) by email as a single PDF file + a separate file with score sheet to brsi.india@gmail.com on or before 25th July 2020, and (ii) one printed copy should be sent to Dr P Binod, Central Office-BRSI, CSIR-National Institute for Interdisciplinary Science and Technology, Industrial Estate PO, Trivandrum-695 019 on or before 31st July 2020; 5.00 pm.

Incomplete applications or those without supporting documents as mentioned in the Score Sheet and those without numbered flags in hard copy would be rejected without any further notice.

Guest Article

Disinfection – A silent soldier

By Hridya Susan Varughese,

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Disinfection is the simplest way of preventing infections by eliminating pathogens. The ongoing corona viral pandemic is a steady reminder of its importance. In principle, it has been in practice since centuries with sulphur compounds being used for disinfection fromthe 18th century plague outbreaks. While use of copper, mercury, salts, alkalis, acids and plant extracts were chemical methods, filtration, burning, fumigation and burial were physical methods. Closer to the 19th century, tyndallisation and autoclaving gained momentum focusing on bacterial spores [1] .The existence of micro-organisms explored by Louis Pasteur inspired the likes of Joseph Lister and Paul Erhlich to pave way for antiseptics- phenols, chlorine, hydrogen peroxide, U.V light, formaldehyde soon to be followed by antimicrobials[2] .

While disinfection is an inclusive term, it particularly refers to non-living surfaces, antisepsis refers to living tissue and sterilization refers to removal of all life including spores. *Static* refers to 'growthinhibition' while *cidal* refers to 'death' of organisms. Simple cleaning with water physically removes soil or dirt. Washing with soap or detergents is a preliminary measure as they have triclosan, salicylic acid, and carbolic acids etc. as active ingredients. These are comparatively inferior. The use of triclosan has propelled antimicrobial resistance[3]. Salicylic acid has a broadly non-specific action and carbolic acid has been linked with skin conditions. Floor disinfectants contain phenol, hydro chloric acid, sodium bisulfate as active ingredients while dish or cloth washing detergents contain surfactants rather than specific germicides facilitating 'cleaning' rather than 'disinfection'.

The mechanisms of action of chemical disinfectants are based on lipid membrane lysis (alcohols), inducing free radical injury (chlorine or hydrogen peroxide), genetic mutations (UV), protein denaturation (formaldehyde, per acetic acid, quaternary ammonium compounds-QAC), hydrogen ion imbalance (acids or alkalis), osmolytic action (NaCl), alkylation of nucleic acids (ethylene oxide) etc[4]. 2.4% glutaraldehyde is an efficient bactericidal, virucidal and sporicidal agent. 0.5% chlorhexidine, chlorine, iodophores, peroxides, phenolic compounds and 0.025% benzalkonium chloride is highly effective against commensal and pathogenic bacteria. Per acetic acid is effective against yeasts. Alcoholic agents are multipurpose with 70% ethanol or isopropanol effective against bacteria, lipophilic and hydrophilic viruses[5].

Hospital disinfection measures are quite elaborate. It encompasses multiple components. Three levels of disinfection are described – High, Intermediate and Low. High level disinfection kills all bacteria, viruses and some spores by use of glutaraldehyde, hydrogen peroxide, Ortho-pthalaldehyde, per acetic acid, sodium hypochlorite. Intermediate level disinfection kills mycobacteria and other pathogens. Low level disinfection kills some viruses and bacteria[6]. Disinfection of medical devices is dependent on infection risk and are categorized into critical,

semi-critical, non-critical. Critical devices are in contact with sterile tissue and blood; they must undergo sterilization example needles. Semi-critical devices do not penetrate sterile tissues but contact mucous membranes example laryngoscope; they must undergo high level disinfection. Non critical devices only touch intact skin, example stethoscope and can be cleaned by low level disinfection[5].

Hands are an important transport of infections due to their regular contact with surfaces, people, pets and individual themselves. Community hygiene is centered on hand hygiene. An 11 step hand washing rule practiced for 20-30s has been encouraged by the WHO[7]. Unless hands are soiled, alcohol based cleansers are preferred over soaps or detergents. A study established the effectiveness of hand sanitizers in inactivating the COVID-19 virus as well. The components were 80% ethanol or 75% propanol, 1.45% glycerol and 0.125% hydrogen peroxide as a base[8]. Efficacy of hand sanitizers on *Staphylococcus* and *Enterobacteraciae* has been described in combination with QAC and aldehydes proving hand hygiene is an important tool in disinfection. Spray fogging of chemicals also has been suggested as a disinfection tool. Alcohol based hand rubs for surgical sterilization has proven effective on various counts.

Other community practices involve surface cleaning with phenolic agents, chlorination of utility water, UV exposure, boiling or pasteurization. Despite its versatility, skin or mucous membrane irritation, corrosive nature, flammability, strong odors and even antimicrobial resistance are some of the drawbacks of disinfectants. Use of protective agents like glycerol or combining different agents can be used to overcome them. Pursuing alternative antimicrobial practices could also be a solution. Many traditional Indian practices have been proven to be set in science. Lime or calcium carbonate used as a white washing agent has a lethal effect on resilient bacterial spores. Turmeric, cloves and other spices have proven antiseptic properties. Common salt aids in osmotic killing of microbes and worms. Sun drying kills fungal spores through desiccation. Vinegar can also kill TB organism[9].

Epidemics in history have always imparted lessons. Small pox gave us 'vaccination', plague cautioned animal harbingers of disease,cholera sensitized water treatment, HIV and Ebola urged antiviral research. Disinfection remains a sure shot prophylactic especially in the absence of vaccines or therapeutics. In the relentless fight against disease, disinfection stands a silent soldier, forgotten once the war (disease outbreaks) is over.

COVID 19 gave us many things, quarantine, nature rejuvenation, a brief stint at vegetarianism, but most importantly it reminded us disinfection. A simple practice, that could save our health and our finances. With surging incidence rates of COVID 19, it looks like sanitizers, masks, gloves and social distancing is here to stay. So let's welcome them with open mind, hearts and hands.

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Views

Are FDA and WHO Puppet of The Lancet, NEJM and such journals? The case of HCQ

by Anonymous Writer

Summary

Does FDA and WHO acted purely on the basis of reports of journals?

These reports were challenged several times but whistleblowers were not FDA or WHO

Hydroxychloroquine is the first drug that was accepted by global scientific community as a possible treatment for COVID19. Soon after many countries started to stockpile the drug and India in this situation distributed it to many countries. This is because India is biggest manufacturer in world and supplies it on cheaper price. One more drug Remedesvir was also proposed as cure but could not do well in clinical trials, however the case of HCQ is different because it could not get chance to complete the trial properly due to regulatory hurdles from time to time on the impression of some journals. Let's see the chronology of decision making and more we will discuss under conclusion.

On March 12, 2020 at 9:47am one TWITTER POST was written as "It was only with the Chinese experts' encouragement that we agreed to perform a coronavirus test, James Cai said. When it came back positive, they recommended he be treated with the antimalarial medicine chloroquine and the HIV drug Kaletra. "Chinese experts suggest to treat with medicine to slow the virus first. Don't wait," he said. "Definitely I would not be here today [without them]." https://nypost.com/2020/03/12/new-jersey-patient-james-cai-recovering-from-coronavirus/

On March 14, 2020, one more post was tweeted by one self declared researcher suggesting CQ as effective treatment and uploaded one google document (which is inaccessible now) to support the facts.

Todaro's tweet identified Rigano as being affiliated with Johns Hopkins; Rigano's LinkedIn profile says different. On further enquiries by WIRED, (Johns Hopkins did not return a request for comment; a spokesperson for Stanford Medical School emails: "Stanford Medicine, in-

cluding SPARK, wasn't involved in the creation of the Google document, and we've requested that the author remove all references to us. In addition, Gregory Rigano is not an advisor with Stanford School of Medicine and no one at Stanford was involved in the study.")

In separate statement, Janet Diaz, head of clinical care for the World Health Organization Emergencies Program said "For chloroquine, there is no proof that that is an effective treatment at this time,". "We recommend that therapeutics be tested under ethically approved clinical trials to show efficacy and safety."
https://www.wired.com/story/an-old-malaria-drug-may-fight-covid-19-and-silicon-valleys-into-it/

On 16 Mar 2020, University of Queensland Centre for Clinical Research Director David Paterson told news.com.au that the two drugs, which were used in test tubes, stopped coronavirus in its tracks and a clinical trial on humans was ready to begin. One of the two medications is an HIV drug, and the other is an anti-malaria drug called chloroquine.
https://www.livemint.com/news/world/coronavirus-update-australian-researchers-claim-2-existing-drugs-could-cure-covid-19-11584369580246.html

On March 19, 2020, the researchers announced about a study on 30 confirmed COVID-19 patients in France whose results were published in the International Journal of Antimicrobial Agents. According to researchers, the study has found early evidence that the combination of hydroxychloroquine, a popular anti-malaria drug known under the trade name Plaqenuil, and antibiotic azithromycin (aka Zithromax or Azithrocin) could be especially effective in treating the COVID-19 coronavirus and reducing the duration of the virus in patients.
https://techcrunch.com/2020/03/19/french-study-finds-anti-malarial-and-antibiotic-combo-could-reduce-covid-19-duration/

On March 19, 2020, U.S. Food and Drug Administration Commissioner Stephen Hahn addressed the ongoing work of the agency in terms of its work on potential treatments and vaccines for the COVID-19 coronavirus. Despite a claim early in Thursday's White House briefing on the pandemic by President Donald Trump that one proposed treatment, anti-malarial chloroquine, had already been approved by the FDA for COVID-19 treatment, Hahn said that in fact the agency is currently looking at widespread clinical trials of the drug, but it is not yet approved for that use. Another potential treatment which has shown signs of possible positive effect, remdesivir, was also cited by Trump as being very "near" approval for use by the FDA. Hahn also highlighted another experimental treatment possibility that the FDA is investigating: Using plasma derived from blood taken from coronavirus patients who have recovered, and injecting that into other patients in an attempt to potentially jump start their own immune response.

"In the short term, we're looking at drugs that are already approved for other indications," Dr. Hahn said. It's not a clinical study, however, and that means there are still a lot of unknowns when it comes to its use that just can't be learned or asserted based on scattered, individual instances of compassionate care treatment.

"As the Commissioner of FDA and the president mentioned, we're trying to strike a balance between making something with the potential of an effect available to the American people, at the same time that we do it under the auspices of a protocol that would give us information to determine if it's truly safe and truly effective," explained National Institute of Allergy and Infectious Diseases Director Dr. Anthony Fauci during a press conference.
https://techcrunch.com/2020/03/19/fda-testing-coronavirus-treatments-including-chloroquine-plasma-from-recovered-covid-19-patients/

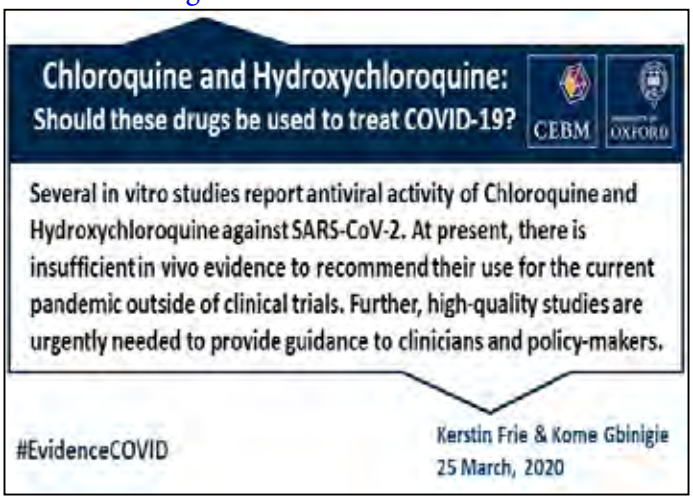
At this point FDA did not approve the HCQ drug but was favouring it.

According to 'WHO - Landscape analysis of therapeutics' of 21st March 2020, Chloroquine an antimalarial agent which is a heme polymerase inhibitor for Malaria can be prescribed as prophylaxis and treatment. The Prophylaxis dose can be 500 mg chloroquine phosphate once per week. For treatment 2.5 g chloroquine phosphate over 3 days either as oral or injectable was suggested. https://www.who.int/blueprint/priority-diseases/keyaction/Table_of_therapeutics_Appendix_17022020.pdf?ua=1

On March 23 2020, in India, the national task force for COVID-19 constituted by Indian Council for Medical Research (ICMR) has recommended hydroxychloroquine as a preventive medication for high-risk popu-

lation. According to the advisory, it should be given to high risk population -- asymptomatic healthcare workers involved in the care of suspected or confirmed cases of COVID-19 and asymptomatic household contacts of laboratory confirmed cases. According to the advisory, the drug has to be given only on the prescription of a registered medical practitioner.
https://economictimes.indiatimes.com/industry/healthcare/biotech/pharmaceuticals/indias-covid-task-force-recommends-hydroxychloroquine-for-high-risk-patients-with-strict-riders/articleshow/74774540.cms?utm_source=contentofinterest&utm_medium=text&utm_campaign=cppst

This article of March 25 described that the National Health Commission of the People's Republic of China published their recommendation mid-February, suggesting to treat patients with 500mg chloroquine phosphate (300mg for CQ) twice per day, for a maximum of 10 days. In Italy, the L. Spallanzani National Institute for the Infectious Disease published their recommendations for treatment on the 17th of March, which included the provision of 400mg of HCQ per day or 500mg CQ per day, in combination with another antiviral agent. However the article published limitation too of these studies which supported HCQ.
https://www.cebm.net/covid-19/chloroquine-and-hydroxychloroquine-current-evidence-for-their-effectiveness-in-treating-covid-19/



In a March 28 letter leading to the FDA's emergency USE authorization of hydroxychloroquine and chloroquine for COVID-19, agency chief scientist Denise Hinton noted that, "based upon limited in-vitro and anecdotal clinical data in case series, chloroquine phosphate and hydroxychloroquine sulfate were recommended for treatment of hospitalized COVID-19 patients in several countries."
https://www.usnews.com/news/health-news/articles/2020-03-31/fda-approves-malaria-drugs-to-treat-covid-19-despite-little-proof-they-work

After two months, on May 25, WHO announced it had temporarily suspended its trial of the drug HCQ over safety concerns. The announcement came days after a study (https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31180-6/fulltext(RETRACTED)) published in medical journal The Lancet on 22nd May which found that hospitalized Covid-19 patients treated with hydroxychloroquine had a higher risk of death than those who didn't take it. The study found that both drugs can produce potentially serious side effects, particularly heart arrhythmia.

The Lancet study was subjected to an expression of concern on June 2 , and finally retracted on June 4. At the same time another study (https://www.nejm.org/doi/full/10.1056/NEJMoa2007621) from another reputed Journal NEJM retracted on various grounds. Both these retractions with some others raised again the questions over the scientific integrity and Journals' working in such emergent pandemic times, as these are the two most reputed journals of health sciences and they have published important research without any verification of the content.

Based on the results of these two research papers, WHO on May 25 2020 announced the temporary suspension of clinical trials of hydroxychloriquine as a potential treatment for COVID-19. "The Executive Group has implemented a temporary pause of the hydroxychloroquine arm within the Solidarity Trial while the safety data was under review by the Data Safety Monitoring Board," Tedros said. https://time.com/5842264/hydroxychloroquine-testing-who/

However as we discussed already this Lancet study was challenged on June 2 and so the decision of FDA and WHO to continue the HCQ trial. On June 3, the WHO again resumed the study looking into whether the malaria drug hydroxychloroquine could be effective in treating COVID-19. Dr. Tedros, director-general of the WHO, said in a press briefing on June 3 that the


THE LANCET

RETRACTED: Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis

Prof Mandeep R Mehra, MD • Sapan S Desai, MD • Prof Frank Ruschitzka, MD • Amit N Patel, MD

Published: May 22, 2020 • DOI: https://doi.org/10.1016/S0140-6736(20)31180-6 • Check for updates

agency's board reviewed the data concerning heart risks and found "no reasons to modify the trial." https://time.com/5847664/who-hydroxychloroquine-covid-19/

It is to note that on May 30, CSIR, India chief criticises HCQ trial suspension by quoting The Lancet's study 'sloppy' and thus was one of the whistleblower. Shekhar Mande, Anurag Agrawal, physician and Director, Institute of Genomics and Integrative Biology as well as Rajeeva Karandikar, Director, Chennai Mathematical Institute, signed a letter and said the World Health Organization's decision to suspend trials of the drug was a "knee-jerk" reaction. "The observational data is sloppy, and the statistics underlying them is faulty. There is no doubt that it will not stand the test of time. You can't compare apples with oranges," Mr. Mande told The Hindu. https://www.thehindu.com/sci-tech/health/coronavirus-csir-chief-flays-hcq-trial-suspension/article31712065.ece

On June 15, 2020 FDA updated their website as, "Based on ongoing analysis and emerging scientific data, FDA revoked the emergency use authorization (EUA) to use hydroxychloroquine and chloroquine to treat COVID-19 in certain hospitalized patients when a clinical trial is unavailable or participation is not feasible. This determination based on recent results from a large, randomized clinical trial in hospitalized patients that found these medicines showed no benefit for decreasing the likelihood of death or speeding recovery. This outcome was consistent with other new data, including those showing the suggested dosing for these medicines are unlikely to kill or inhibit the virus that causes COVID-19. As a result, we determined that the legal criteria for the EUA are no longer met. Please refer to the Revocation of the EUA Letter and FAQs on the Revocation of the EUA for Hydroxychloroquine Sulfate and Chloroquine Phosphate for more information". https://www.fda.gov/drugs/drug-safety-and-availability/fda-cautions-against-use-hydroxychloroquine-or-chloroquine-covid-19-outside-hospital-setting-or

Conclusion

From the above points it is observed that the HCQ was proposed through social media then became widely accepted by various clinical studies around the world. We cannot ignore that COVID 19 is emergent and fast changing situation but from March 12 to June 14 the decision over HCQ was accepted and rejected several times just because someone is saying something while FDA and WHO scientists could not get the time to verify the facts by themselves before going to further conclusion. First time HCQ was accepted because of several reports from different trials but was rejected just because Lancet published a heart attack story of bogus trial. But when this Lancet story was unsurfaced, FDA and WHO once again gain trust and start advocating HCQ. Lastly ,without any further solid basis they rejected HCQ trials again. So the facts raises the questions over the working of world's reputed organizations like WHO, FDA etc. and publishing platforms like The Lancet, NEJM etc. when they have the best and sufficient staff for every task. The work which was done by whistleblowers why not came into attention of these reputed organizations and it's most reputed staff is a matter of concern for future situations like COVID19.

Note: Views are personal of Author.

Featured News

Dexamethasone proves first life-saving drug

Biotech Express News Bureau

Jun 18, 2020

According to UK scientists, a cheap and widely available drug can help save the lives of patients seriously ill with coronavirus. The low-dose steroid treatment dexamethasone is a major breakthrough in the fight against the deadly virus, UK experts say. The drug is part of the world's biggest trial testing existing treatments to see if they also work for coronavirus. It cut the risk of death by a third for patients on ventilators. For those on oxygen, it cut deaths by a fifth. Although there are many variations to the story but purpose looks the same i.e. to sell the indigeneous products.

In March 2020, the RECOVERY (Randomised Evaluation of COVid-19 thERapY) trial was established as a randomised clinical trial to test a range of potential treatments for COVID-19, including low-dose dexamethasone (a steroid treatment). Over 11,500 patients have been enrolled from over 175 NHS hospitals in the UK.

A total of 2104 patients were randomised to receive dexamethasone 6 mg once per day (either by mouth or by intravenous injection) for ten days and were compared with 4321 patients randomised to usual care alone. Among the patients who received usual care alone, 28-day mortality was highest in those who required ventilation (41%), intermediate in those patients who required oxygen only (25%), and lowest among those who did not require any respiratory intervention (13%).

Dexamethasone reduced deaths by one-third in ventilated patients (rate ratio 0.65 [95% confidence interval 0.48 to 0.88]; p=0.0003) and by one fifth in other patients receiving oxygen only (0.80 [0.67 to 0.96]; p=0.0021). There was no benefit among those patients who did not require respiratory support (1.22 [0.86 to 1.75]; p=0.14).

We will get to know whether Dexamethasone will be useful or not in near future unlike hydroxychloroquine which is going through knee jerk movement just because of some retracted papers and regulatory decisions.

In case of hydroxychloroquine it was not Modi or his scientists who praised the drug unlike UK Prime Minister Boris Johnson who said there was a genuine case to celebrate "a remarkable British scientific achievement", adding: "We have taken steps to ensure we have enough supplies, even in the event of a second peak."

Questions raised over the Integrity of The Lancet and NEJM?

Jun 9, 2020

When The Lancet and The New England Journal of Medicine pulled an influential pair of Covid-19 papers on June 4, it was a rare event in scientific publishing. For medical researchers, this was like seeing The Washington Post and The New York Times take down related news stories at the same time—a confluence of editorial failures that raises dire questions about what went wrong and why. But how surprising is this scandal, really? Could these be among "the biggest retractions in modern history," as one observer described the news about the paper in The Lancet? That depends entirely on how you read history. Science meltdowns of this type—and the "biggest" retractions that ensue—occur with shocking regularity.

The latest scandal is, indeed, a bad one. At the moment, we don't know the full story of what went wrong, beyond that the papers' authors and the journals' editors decided that they could no longer trust the underlying data. Both studies purportedly drew from the medical records of 96,000 patients with Covid-19, seen at hundreds of different hospitals around the world. The NEJM article reported that those with cardiovascular disease were at increased risk for death from Covid-19, and that the use of certain heart medications did not appear to compound that risk. The Lancet paper reported that the drugs hydroxychloroquine and chloroquine did not help the 15,000 patients who took them; in fact, these medications seemed to cause significant harm

The NEJM article didn't make much of an impact, but the Lancet paper was a different matter. Upon publication, the World Health Organization paused an ongoing trial testing the malaria drugs for Covid-19. The trial only started up again when the journal expressed doubts about the validity of the results last week.

Assigning blame in the newest unraveling isn't hard. The papers' authors, led by Harvard researcher Mandeep Mehra, shouldn't have put their names on a paper lacking transparent data. The journals' editors are on the hook, too, for accepting articles with the same limitations on sharing. And coauthor Sapan Desai, the CEO of Surgisphere—who has written papers in the past on fraud and "moral turpitude" in medical publishing—well, we don't quite know what he did or didn't do.

The irony is that both The Lancet and NEJM have been burned before. It was The Lancet, after all, that published Wakefield's paper linking the MMR vaccine to autism. NEJM was forced to retract a pair of Darsee's fraudulent articles on heart disease in 1983. Until Thursday, those were two of the just 25 papers NEJM had ever retracted in its 208-year-history. Writing in the wake of the Darsee debacle, Arnold Relman, then the journal's editor, declared: "Even if coauthors have not actually done any of the laboratory work, they should at least know that the experiments and measurements were carried out as described, and they ought to understand what was done and why."

Regardless of what we end up learning about the origins of Surgisphere's data, it's reasonably clear that Mehra and his colleagues didn't ask enough questions about the provenance of the findings.

The bigger lesson here—the one that's been taught repeatedly for decades—is that peer review won't save us by itself. Even back in 1983, Relman understood that the standard system for evaluating manuscripts was a blind watchman in the fight against scientific fraud. As he noted in his postmortem, the bulk of Darsee's doctored research appeared in peer-reviewed journals, "and yet in none of the reviews was there enough suspicion to warrant rejection."

Source: https://www.wired.com/story/just-how-historic-is-the-latest-covid-19-science-meltdown/

International Summit Aims to Raise $7.4 Billion for Vaccine Alliance

Jun 04, 2020

A summit hosted by British Prime Minister Boris Johnson today is expected to set a goal of at least $7.4 billion. The funds will go to global vaccine alliance Gavi, the Vaccine Alliance, which is backed by the Bill & Melinda Gates Foundation, among others. The Gates Foundation is a founding partner of Gavi, which was founded in 1999, and pledged $750 million to establish it.

In addition to backing from the Gates Foundation, Gavi is supported by the World Health Organization (WHO), the World Bank and UNICEF.

According to the WHO, there are at least 133 possible COVID-19 vaccines in development globally. Gavi would assist in global distribution if an effective vaccine is developed.

The funds are also expected to be used to help recovery from the pandemic. GAVI also indicated it is launching an Advance Market Commitment (AMC) for future COVID-19 vaccines to ensure that new vaccines are allocated to poorer countries. The AMC would offer incentives to vaccine makers to invest in large-scale manufacturing capacity even while they're developing new products and before full-scale trials demonstrate efficacy and safety, GAVI's chief executive officer Seth Berkley told Reuters.

"GAVI is worried about the low- and middle-income countries," Berkley said. "The worry we have is that unless we scale up production dramatically right now, and do that at risk, when the vaccines are available, they could be bought up by wealthy countries. We're trying to put together a facility that has global scope and that will work with manufacturers and help them scale up by saying to them: 'If you have a successful vaccine, we will buy it.'"

Currently, the companies that are the furthest along in a COVID-19 vaccine are AstraZeneca and the University of Oxford, Moderna and the U.S. National Institute of Allergy and Infectious Diseases (NIAID), Pfizer and BioNTech, CanSino Biologics, Johnson & Johnson, Merck, and Sanofi.

The $7.4 billion raised would fund Gavi's immunization programs between 2021 and 2025, which would help immunize 300 million children and potentially save 7 to 8 million lives.

The WHO, UNICEF, which is the U.N. children's charity, and Gavi, have expressed concerns that the pandemic is disrupting routine vaccines globally, affecting about 80 million children less than a year old in 68 countries.

Gavi vaccinates about half of the children around the world, sharing the costs of immunizations against various diseases such as measles and polio with developing countries. In addition to vaccinations, Gavi helps countries create infrastructure like better supply chains and trains health care workers. Studies have found that for every $1 invested in Gavi immunizations, there is a $21 return in savings from health care costs, lost wages and lost productivity from illness and death.

Pre-announced pledges have already hit 75% of the summit's goal, with the UK promising $1.65 billion over five years, the U.S. agreeing to $1.2 billion over three years, Norway $1 billion and Japan $100 million.

ICMR has notified 16 bio-repositories for clinical samples of COVID-19 patients

30 MAY 2020

For the mitigation of COVID-19 pandemic, R&D efforts are directed at the development of vaccines, diagnostics and therapeutics. The specimens collected from COVID-19 positive subjects can be a valuable resource for the R&D efforts. NITI Aayog has recently issued guidelines for sharing of bio specimens and data for research related to COVID-19. As per the directives of the Cabinet Secretary, the Indian Council of Medical Research (ICMR) has notified 16 bio-repositories for collecting, storing and maintaining clinical samples (oropharyngeal/ nasopharyngeal swabs, broncheoalveolar lavage, sputum, blood, urine and stool) of COVID-19 patients.

The enlistment of 16 Bio Repositories are as follows: ICMR – 9, DBT – 4 and CSIR – 3. The four Bio Repositories under the purview of the Department of Biotechnology are, NCR-Biotech Science Cluster (i) THSTI, Faridabad – Clinical samples (ii) RCB Faridabad –Viral samples, Institute of Life Sciences, Bhubaneswar, InStem, Bangalore and ILBS, New Delhi .Oropharyngeal / nasopharyngeal swabs, bronchoalveolar lavage, sputum, blood, urine and stool of COVID19 patients will be collected and archived for future use to develop validated diagnostics, therapeutics, vaccines etc.

These designated facilities will develop uniform Standard Operating Procedures (SoPs) for sample collection, transportation, aliquoting, storage, and sharing. The role of bio-banks for COVID-19 samples would be development of a vaccine and treatments; guidance regarding handling, including nasopharyngeal swabs; and conditions under which the higher BSL-3 practices should be followed.

In addition, they are also authorized to share the samples with academia, industry and commercial entities involved in development of diagnostics, therapeutics, vaccines etc., after scrutinising the purpose of the request and ensuring benefit to the country.

https://pib.gov.in/PressReleasePage.aspx?PRID=1627861

India initiates consultation process for new science, technology and innovation policy

JUN 4, 2020

The central government has initiated a consultation process for the formulation of new science, technology, and innovation policy (STIP 2020). As per the statement, a decentralized, inclusive, and bottom-up process has been jointly initiated by the Department of Science and Technology (DST) and The Office to the Principal Scientific Advisor to GOI.

The fifth S&T policy is being formulated at a time when India and the world are tackling and trying to find ways to combat COVID-19 Pandemic. The consultation processes on different tracks have already been started by the government and have been running in parallel. The process will be of six-months which will involve the consultations with all the stakeholders from within and beyond the scientific ecosystem, including industry, academia, government, global partners, civic bodies, young scientists and technologists, and the general public.

As per the Secretary of DST, Ashutosh Sharma, the STI policy for new India will integrate the lessons learned from COVID-19, including building 'Atmanirbhar Bharat through ST & I (Science, Technology, and Innovation), designs, by leveraging our strengths in R & D (Research and Development), huge markets, diversity and data, demographic dividend, S&T workforce, and institutions.

Formulation Process of STIP 2020 in four highly interlinked tracks:

The sessions of these four tracks have been attended by around 130 members of the 21 thematic groups along with scientists of DST, the office of PSA, and 25 policy research fellows. The formulation process of the four tracks are:

- Track I- It will involve an extensive expert and public consultation process through Science Policy Forum- a dedicated platform created for soliciting inputs from larger public and expert pool during and after the policy drafting process.
- Track II- It will comprise experts driven thematic consultations in order to feed evidence formed recommendations into the policy of drafting processes. Till now, twenty -one focused thematic groups have been constituted for the purpose. The thematic group (TG) consultation started with a series of information sessions last week. During the sessions, the head of Policy Coordination and Programme Monitoring Division of DST, Akhilesh Gupta made the presentation and steered the discussions.
- Track III- It involves consultation with the states and ministries. Nodal officers have also been nominated in ministries and in states, agencies, and departments of Government of India for the extensive intra-department and intra-state consultation.
- Track IV- This track constitutes apex level multi-stakeholder consultation. At this consultation with global partners, industry bodies and inter-state and inter-ministerial consultations at the highest level have been carried out.

DBT/Wellcome Trust India Alliance and RTI International India set up a 'COVID-19 Catalytic Partnership' for India

June 10, 2020

DBT/Wellcome Trust India Alliance (India Alliance or IA) and RTI International India join forces to set up a COVID-19 Catalytic Partnership that would propel transformative research and innovations for COVID-19 response and recovery in India.

The COVID-19 pandemic has thrown some unique and unprecedented challenges for India. However, the outbreak also offers research opportunities that India can leverage to respond to these challenges now and prepare for the future. The IA-RTI "COVID-19 Catalytic Partnership" would allow researchers based in academia, industry and the social sector in India to take up COVID-19-related research that has an immediate transformative impact and future possibilities. Potential areas of interest include (but are not limited to) testing, surveillance, contact tracing, medical consultation, delivery of essential health and nutrition services to vulnerable/at-risk communities, strengthening of health systems and supply chains, risk communication and community engagement. In addition, the program would aim to develop strategic engagements with both public and private sector stakeholders for advocacy, policy reform, resource mobilization, among other activities.

"We are excited at partnering RTI International India", said Dr Shahid Jameel, CEO of India Alliance. "Our complementary strengths will allow us to understand the impact of COVID-19 on health systems and existing programs and to develop innovative solutions for the future", he added.

Dr Rajiv Tandon, Director (Health), RTI International India, added: "We hope that this partnership fosters exchange and collaboration among the two organizations in gathering relevant, synthesized evidence and insights in a timely and coordinated manner, speaking in a voice that harnesses the power of the collective on issues relevant to the COVID-19 pandemic in India, and adopt a holistic view of interventions and outcomes. This partnership has the potential of helping Indian Health Sector maximize impact across the breadth and depth of programming and develop technology architectures that help build a strong foundation to generate and sustain long-term impact."

About the partners:

India Alliance is a dynamic, public charity in India established in 2008 as a partnership between the Government of India's Department of Biotechnology (DBT) and The Wellcome Trust, UK. Its mission is to build scientific capacity and support internationally competitive research in biomedical and health sciences at Indian institutions.

RTI International India has been working to help India address its enduring and emerging development challenges since the early 1980s. In 2014, RTI International established RTI International India, a private limited wholly-owned subsidiary, as a testament to the strategic importance that India holds with regards to the global development agenda to further strengthen this commitment.

For information, contact: communications@indiaalliance.org; msiddiqui@rti.org

News of Focus

New Covid-19 test developed by the CCMB

Jun 11, 2020

A new Covid-19 test developed by the Centre for Cellular and Molecular Biology (CCMB) can test 20,000-50, 000 Covid-19 samples daily — a "breakthrough" that could significantly enhance India's testing capacity, according to the institute's director Rakesh Mishra.

In an interview to The Print, Mishra said if all goes well, the new 'Next Generation Sequencing' (NGS) kit will be operational in about four weeks. "It will change the game," he said.

According to Mishra, the new kit will offer diagnosis through sequencing of several pieces of the virus genetic material, and lessen the chances of inaccurate testing. The new testing module will also help in surveillance of Covid-19 suspects, he said. "The 'Next Generation Sequencing' will help in diagnosis and surveying the disease at a much faster rate,"

This is a 'high-throughput' process that saves both time and cost. Additionally, the improved machines also come with improved sensitivity and are capable of detecting the virus RNA with fewer chances of a false negative.

The project is in collaboration with Syngene, a Bengaluru-based company. The process for the kit's approval from the Indian Council of Medical Research (ICMR), India's nodal Covid-19 testing body, is underway, said the CCMB director.

Vaccine for Covid-19 would be available latest by next year: N K Ganguly, Fromer DG-ICMR

May 23, 2020

Against the backdrop of leading vaccine maker Bharat Biotech partnering with Thomas Jefferson University of Philadelphia to develop a new vaccine candidate for Covid-19 invented at Jefferson, it seems the emergency vaccine for Covid-19 would be available latest by January or February next year, said former director general of the Indian Council of Medical Research (ICMR) NK Ganguly.

Ganguly insisted that mRNA synthetic vaccine is quick to develop and with the aid of accelerated clearances from regulatory authorities, the usual time-frame of 5 years could be reduced drastically. Usually, the course of vaccine development, from lab to market, on an average, takes between five to ten years.

According to the National Centre for Biotechnology Infor-

mation, mRNA vaccines represent a promising alternative to conventional vaccine approaches because of their high potency, capacity for rapid development and potential for low-cost manufacture and safe administration.

Responding to a query on testing capacity of the country, Ganguly said India is testing smart, against the backdrop of 1.3 billion population, unlike South Korea and China.

DST, India launches awareness programme on Science & Health with focus on COVID-19

June 08, 2020

The National Council for Science & Technology Communication (NCSTC), Department of Science & Technology (DST) has released an information brochure for a recently launched programme on health and risk communication 'Year of Awareness on Science & Health (YASH) with focus on COVID-19'. The brochure carries information on the genesis and need of such a mega programme in the country to address the issues of risks, crises, disasters, and uncertainties especially posed by the COVID-19 pandemic. The programme focuses on enhancing public understanding and awareness of science and health for better preparedness to cope up with the present and future challenges.

Prof. Ashutosh Sharma, Secretary, Dept. of Science & Technology said that a wide array of programmes and activities built around awareness and outreach have been envisaged involving print, electronic, digital, folk and interactive media to reach out to large cross-sections of the society under the campaign. He added that the logo of the YASH programme given on the brochure has been designed to create a wave of peace and bliss and depicts a sense of overcoming the situation at large and would act as a harbinger of taking forward the messages of science, health, risk and awareness.

In view of providing authentic information in an interesting and interactive manner at the grass-root level, a comprehensive programme on health and risk communication with a focus on COVID 19 has been launched. The National Health & Risk Communication programme has been planned and being implemented in a big way with a mechanism of PAN India presence and reach. State Councils of Science & Technology have been involved. The three major ingredients of the programme include software/ content development, capacity development, and dissemination and outreach.

The activities are spread over six regions, East, West, North, South, Central and Northeast. Special communication modules are developed depending upon especially marked zones, and networking and training of communicators and volunteers for activities related to community health would be an advantage. The current scenario of the pandemic caused by COVID-19 has posed concerns and challenges all around where scientific awareness and health preparedness can play a significant role to help combat the situation with translation and usage of authentic scientific information and to convey the risks involved and facilitate the communities to overcome the situation.

The information brochure highlights a comprehensive and effective science and health communication effort for promoting grass-root level appreciation and response on health and saving and shaping the lives of people at large, as well as building confidence, inculcating a scientific temper and promoting health consciousness among them. The brochure can be downloaded from www.dst.gov.in.

EU secure $2.7 Billion Emergency Fund for COVID-19 Vaccines

Jun 04, 2020

The European Union is planning to leverage an emergency fund worth $2.7 billion to buy promising COVID-19 vaccines ahead of approval. Four countries, Germany, France, Italy and the Netherlands, told a meeting of EU ambassadors yesterday they planned to accelerate negotiations with biopharmaceutical companies to access vaccines that are currently being developed.

The fund, called the Emergency Support Instrument (ESI), would be used to increase vaccine manufacturing capacity in Europe. It would also offer liability insurance to drug companies, since they are scaling up manufacturing of vaccines ahead of proof of viability and safety in hopes they will turn out to be safe and effective.

This is not particularly unusual under the current circumstances. On May 1, the U.S. Biomedical Advanced Research and Development Authority (BARDA) paid more than $1 billion to AstraZeneca, which is partnered with the University of Oxford's COVID-19 vaccine efforts, to support the development, production and delivery of the vaccine beginning this fall. On June 2, the U.S. government's Operation Warp Speed signed a $628 million contract with contract development and manufacturing organization (CDMO) Emergent BioSolutions to accelerate domestic production of leading COVID-19 vaccine candidates through 2021.

Many of the smaller biotech companies working on COVID-19 vaccines have partnered with larger biopharma companies to handle distribution and manufacturing. These include Pfizer and BioNTech, Moderna and Switzerland's Lonza, as well as individual efforts by GlaxoSmithKline, Johnson & Johnson, and Sanofi. There is a recognition that with a need to vaccinate most of the world, no one company or product is likely to be sufficient.

Los Angeles attorney is suing Wellness Matrix Group for "fraudulent scheme" related to the COVID-19

May 27, 2020

The city attorney of Los Angeles announced Wednesday that his office is suing Wellness Matrix Group for allegedly engaging in a "fraudulent scheme" related to the COVID-19 pandemic that was both "sophisticated" and "wide ranging."

The lawsuit alleges that the California-based company sold purported "at-home" tests for the coronavirus, falsely claiming that the tests were FDA approved. The company also sold a supposedly coronavirus-killing "virucide," claiming that the product could "build a force field around your event or even spray your entire city."

As part of what city attorney Mike Feuer calls "shocking deceptive conduct," the company allegedly "attached false government registration numbers to these products and fabricated phony scientific studies and white papers to sub-

stantiate their false claims."

Feuer also said Wednesday that Migliorini, Todt and the company had recently attempted to "expand their unlawful scheme" by selling their products to local governments in California. The city attorney's lawsuit is seeking an injunction to halt the company's alleged false advertising, as well as civil penalties and restitution for alleged victims.

In an emailed statement, William Dailey, an attorney for Wellness Matrix Group and Migliorini, said his clients have been "falsely accused," and that they "categorically deny all allegations of wrong-doing."

Wellness Matrix Group first came to the attention of the city attorney's office through NPR's reporting in April. Multiple people who bought the supposed "at-home" tests online told NPR they believed the company had preyed on their fears about the virus, and had duped them into buying tests, which never arrived. Since NPR's reporting, most - but not all - of those customers have said they received a refund.

Federal officials have also taken notice of Wellness Matrix Group. Rep. Raja Krishnamoorthi, D-Ill., and Rep. Katie Porter, D-Calif., launched an investigation. And the Securities and Exchange Commission temporarily suspended public trading of the company's shares.

Across the country, federal, state and local law enforcement have vowed to crack down on alleged fraud related to the pandemic, including fake testing kits or fake treatments for the disease. Officials have emphasized the importance of accurate information in combating the virus's spread.

"Defendants' unlawful business practices are more than a scam," the lawsuit states, "they are a threat to public health."

Eli Lilly Begins Phase III Study of RA Drug to Treat COVID-19

June 15, 2020

Eli Lilly will assess its JAK1/JAK2 inhibitor Olumiant (baricitinib) as a potential treatment for COVID-19 in a Phase III study.

The primary endpoint for Lilly's new study is the proportion of patients who die or require non-invasive ventilation/high-flow oxygen or invasive mechanical ventilation following 28 days of daily treatment with 4 mg of baricitinib. Key secondary outcomes of this study include the proportion of patients with clinical improvement at different time points, time to recovery, duration of hospitalization, number of ventilator-free days and mortality over a 28-day period.

Olumiant isn't the first rheumatoid arthritis drug being aimed at the disease. Other drugs that inhibit Interleukin-6, such as Roche's Actemra and Regeneron and Sanofi's Kevzara, are also being studied as a potential treatment for the cytokine storms associated with the disease. Unlike Actemra, Olumiant is a JAK-inhibitor. Kevzara hit a snag in April during an ongoing study in COVID-19 and amended protocols as it continued. It's thought that inhibition of JAK 1 and JAK 2 may also play a role in reducing the cytokine storm associated with the most severe complications of COVID-19. In addition, Eli Lilly suspects Olumiant may have a role in inhibiting the host cell proteins that assist in viral reproduction, reducing the ability of infected cells to make more of the virus. Studying baricitinib in controlled trials is important in order to better characterize its potential benefits and understand the safety of its use as a COVID-19 treatment, the company added.

Patrik Jonsson, president of Lilly Bio-Medicines, said the Phase III study in this indication is an important step in the company's understanding of baricitinib as a potential COVID-19 treatment. He said Lilly is committed to fighting the global pandemic, which includes studying the efficacy of older medications against the disease that has infected nearly 8 million people across the globe, including more than 2 million in the United States.

Data from this Phase III study will complement the NIAID study, which is also assessing Olumiant in combination with Gilead Science's remdesivir, which previously received Emergency Use Authorization

from the U.S. Food and Drug Administration against COVID-19. In addition to Olumiant, Eli Lilly partnered with Vancouver-based AbCellera to co-develop antibody products against the disease. Also, Eli Lilly partnered with the state of Indiana to accelerate testing for the virus in that state.

Excelra Releases COVID-19 Biomarker Database

June 10 2020

Excelra, a leading global data-analytics company today announced the release of the COVID-19 Biomarker Database (https://www.excelra.com/covid-19-biomarker-database/) in support of the ongoing global scientific efforts, aimed at developing safe and effective therapeutic options to treat the novel coronavirus disease.

This 'Open-Access' resource is excerpted from Excelra's GOBIOM platform – the world's largest biomarker intelligence database. With reference to this endeavour, Dr. Raveendra Dayam, Director, Chemistry and Biology Data Services, Excelra, said, "The COVID-19 Biomarker Database is a compilation of manually curated biomarkers from published clinical trials, evaluating potential drugs or biologics for the treatment of SARS-CoV-2.

The database additionally includes information on FDA-NIH recommended BEST (Biomarkers, EndpointS and other Tools) classification of biomarkers, supported with referenced literature."

The information in the COVID-19 Biomarker Database is presented in a user-friendly online application and the data is regularly updated with new biomarkers from clinical trials published in clinicaltrials.gov.

About GOBIOM

Excelra's GOBIOM is the world's largest manually curated database of validated and putative biomarkers, providing a comprehensive overview of the biomarker-disease relationship. Integrated with information encompassing the exploratory, preclinical and clinical domains, the database provides critical insights into diagnosis, prognosis, treatment response, safety, efficacy and toxicity. As a one-stop source for biomarker intelligence, GOBIOM enables informed clinical and therapeutic decision making to accelerate drug development.

About Excelra

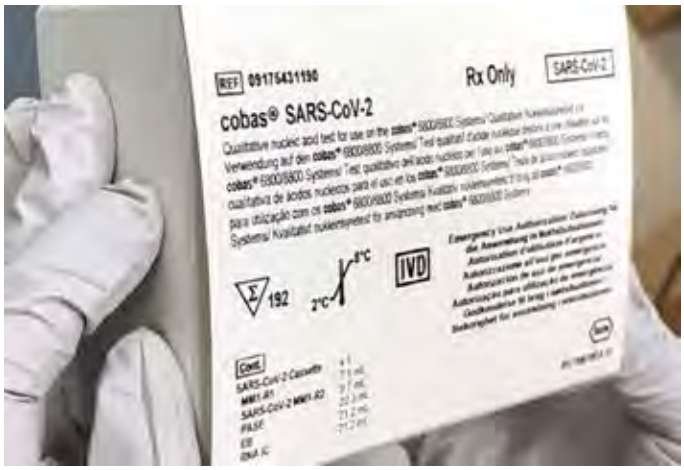
Excelra's data and analytics solutions empower innovation in life sciences across the value chain from discovery to market. The Excelra Edge comes from a seamless amalgamation of proprietary curated data assets, deep domain expertise and data science. The company's multifaceted teams harmonize and analyze large volumes of disparate unstructured data using cutting-edge technologies. We galvanize data-driven decisions to unlock operational efficiencies to accelerate drug discovery and development. Over the past 18 years, Excelra has been the preferred data and analytics partner to over 150 global clients including 15 of the top 20 large Pharma companies.

Access COVID-19 Biomarker Database: https://www.excelra.com/covid-19-biomarker-database/

Roche announced it received EUA from the FDA for the Elecsys IL-6 test

Jun 04, 2020

Roche received a new Emergency Use Authorization



from the U.S. Food and Drug Administration (FDA) for another COVID-19 diagnostics device. Instead of detecting the virus, this device can help determine who might be at risk for intubation and mechanical ventilation.

Elecsys IL-6 test, which measures levels of IL-6 (interleukin-6), a protein that triggers the body's immune and inflammatory response to fight infections. Because IL-6 is released so early during a severe infection, it helps physicians to identify severely ill COVID-19 patients as early as possible.

High levels of IL-6 can cause the immune system to begin attacking itself, unleashing a cytokine storm, which has been linked to the deaths of a number of COVID-19 patients. The IL-6 inhibitors were first used in China to calm IL-6 overreaction due to COVID-19. Data from a single-arm study of Actemra in China suggested that the interleukin-6 pathway may play an important role in the overactive inflammatory response in the lungs of patients with COVID-19.

The Roche Elecsys IL-6 test can be run on the company's existing diagnostics platforms, the cobas e analyzer. These fully-automated systems can provide test results in approximately 18 minutes, with a test throughput of up to 300 tests/hour, depending on the system being used to run the test.

Since the beginning of the COVID-19 pandemic, Roche has won EUA for several diagnostics devices, including its cobas SARS-CoV-2 Test, which looks for the presence of the virus in the body. That assay won approval in March. In May, the FDA granted EUA for Roche's Elecsys Anti-SARS-CoV-2 antibody test that will help determine whether or not people have been infected by the novel coronavirus that has swept across the globe and developed antibodies to the disease.

PerkinElmer receives commercial approval CDSCO for its SARS-CoV-2 Real-Time RT-PCR Assay

June 11, 2020

PerkinElmer has announced that PerkinElmer India has received commercial approval from the Central Drugs Standard Control Organization (CDSCO) for the PerkinElmer new coronavirus nucleic acid detection kit or SARS-CoV-2 Real-Time RT-PCR Assay.

PerkinElmer's RT-PCR test received Emergency Use Authorization (EUA) from the US Food and Drug Administration (FDA). It is also marketed as an in vitro diagnostic (IVD) device by meeting the requirements of the European In Vitro Diagnostic Directive (IVDD) and is now available in over 30 countries worldwide.

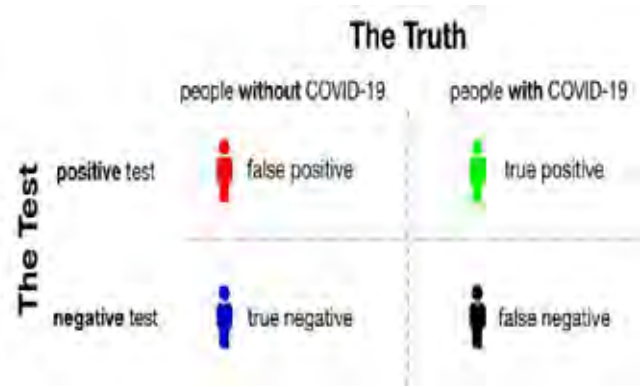
Receiving CDSCO approval for our RT-PCR test will bolster the solutions available to testing facilities across India and help toward improving health outcomes," said Shripad Joshi, director, India and South Asia, PerkinElmer.

"Early detection is crucial to help control the spread of COVID-19 in the world's second-largest population and the commercial approval for this new kit strengthens India's testing capabilities in order to more effectively address this pandemic," said Serge Moubarak, managing director, India, South Asia & Emerging Markets, PerkinElmer.

COVID19 Research

New report examines challenges and implications of false-negative COVID-19 tests

June 5, 2020



"Diagnostic tests, typically involving a nasopharyngeal swab, can be inaccurate in two ways," explains lead author Steven Woloshin, MD, MS, a professor of medicine and community and family medicine at Dartmouth's Geisel School of Medicine, and of The Dartmouth Institute for Health Policy and Clinical Practice.

"A false-positive result mistakenly labels a person infected, with consequences including unnecessary quarantine and contact tracing. False-negative results are far more consequential because infected persons who might be asymptomatic may not be isolated and can infect others."

In their paper, Woloshin and his colleagues discuss factors contributing to the current limitations of diagnostic tests -- including variability in test sensitivity and the lack of a standard process for validating test accuracy -- and also cite several large studies whose frequent false-negative results are cause for concern.

The researchers draw several conclusions from their work. "Diagnostic testing will help to safely open the country, but only if the tests are highly sensitive and validated against a clinically meaningful reference standard -- otherwise we cannot confidently declare people uninfected," says Woloshin.

The FDA should also ensure that test manufacturers provide details of their tests' clinical sensitivity and specificity at the time of market authorization. Tests without such information will have less relevance to patient care.

"Measuring the sensitivity of tests in asymptomatic people is an urgent priority," says Woloshin. "A negative result on even a highly sensitive test cannot rule out infection if the pretest probability -- an estimate before testing of a person's chance of being infected -- is high, so clinicians shouldn't trust unexpected negative results."

This estimate might depend on how common COVID-19 is where a person lives, their exposure history, and symptoms, he says.

Journal Reference:
Steven Woloshin, Neeraj Patel, Aaron S. Kesselheim. False Negative Tests for SARS-CoV-2 Infection -- Challenges and Implications. New England Journal of Medicine, 2020; DOI: 10.1056/NEJMp2015897

Why doctors remain cautious about chloroquine/hydroxychloroquine for treating COVID-19

The malaria drug hydroxychloroquine, which has been promoted as a potential treatment for Covid-19, is known to have potentially serious effects on heart rhythms. Now, a team of researchers has used an optical mapping system to observe exactly how the drug creates serious disturbances in the electrical signals that govern heartbeat.

The research, reported May 29 in the journal Heart Rhythm, found that the drug made it "surprisingly easy" to trigger worrisome arrhythmias in two types of animal hearts by altering the timing of the electrical waves that control heartbeat. While the findings of animal studies can't necessarily be generalized to humans, the videos created by the research team clearly show how the drug can cause cardiac electrical signals to become dysfunctional. What the team saw was an elongation of the T wave, a portion of the heart cycle during which voltages normally dissipate in preparation for the next beat. By extending the QT portion of one wave cycle, the drug sets the stage for disturbances in the next wave, potentially creating an arrhythmia. Such disturbances can transition to fibrillation that interferes with the heart's ability to pump.

The ability to easily trigger disturbances known as "long QT" reinforces cautions about using hydroxychloroquine (HCQ) in humans -- particularly in those who may have heart damage from Covid-19, cautioned Dr. Shahriar Iravanian, a co-author of the paper and a cardiologist in the Division of Cardiology, Section of Electrophysiology, at Emory University Hospital.

"The hearts used in the study are small and very resistant to this form of arrhythmia," Iravanian said. "If we had not seen any HCQ-induced arrhythmias in this model, the results would not have been reassuring. However, in reality, we observed that HCQ readily induced arrhythmia in those hearts. This finding is very concerning and, in combination with the clinical reports of sudden death and arrhythmia in Covid-19 patients taking HCQ, suggests that the drug should be considered a potentially harmful medication and its use in Covid-19 patients be restricted to clinical trial settings."

Georgia Tech postdoctoral fellow Ilija Uzelac administered HCQ to the animal hearts -- one from a guinea pig and one from a rabbit -- while quantifying wave patterns changing across the hearts using a high-powered, LED-based optical mapping system. Voltage-sensitive fluorescent dyes made the electrical waves visible as they moved across the surface of the hearts. The drug concentration used in the study was at the high end of what's being recommended for humans. HCQ normally takes a few days to accumulate in the body, so the researchers used a higher initial dose to simulate the drug's effect over time.

Patients taking HCQ for diseases such as lupus and rheumatoid arthritis rarely suffer from arrythmia because the doses they take are smaller than those being recommended for Covid-19 patients, Iravanian said.

The study, which was supported by grants from the National Institutes of Health and National Science Foundation, was also coauthored by Dr. Hiroshi Ashikaga from Johns Hopkins University School of Medicine; Dr. Neal Bathia from the Division of Cardiology, Section of Electrophysiology at Emory University Hospital; Conner Herndon, Abouzar Kaboudian, and James C. Gumbart from the Georgia Tech School of Physics, and Elizabeth Cherry from the Georgia Tech

School of Computational Science and Engineering.

Journal Reference:
Ilija Uzelac, Shahriar Iravanian, Hiroshi Ashikaga, Neal K. Bhatia, Conner Herndon, Abouzar Kaboudian, James C. Gumbart, Elizabeth M. Cherry, Flavio H. Fenton. Fatal arrhythmias: Another reason why doctors remain cautious about chloroquine/hydroxychloroquine for treating COVID-19. Heart Rhythm, 2020; DOI: 10.1016/j.hrthm.2020.05.030

COVID-19 drug development could benefit from approach used against flu

The researchers found that the newer treatment -- by effectively and rapidly stopping virus replication -- dramatically reduced the length of time that an infected person is contagious and, therefore, better limited the spread of flu.

The study, published in the journal Nature Communications, focused on influenza and has implications for the coronavirus that causes COVID-19. By modeling the impact of a pair of leading flu drugs, the team found significant differences in effects between oseltamivir, an older antiviral treatment for flu that patients know by the name Tamiflu, and a newer one, baloxavir, which is sold under the brand name Xofluza.

"We found that treating even 10% of infected patients with baloxavir shortly after the onset of their symptoms can indirectly prevent millions of infections and save thousands of lives during a typical influenza season," said Robert Krug, a professor emeritus of molecular biosciences, writing for a blog that accompanied the paper.

Early basic research discoveries by Krug informed the development of baloxavir.

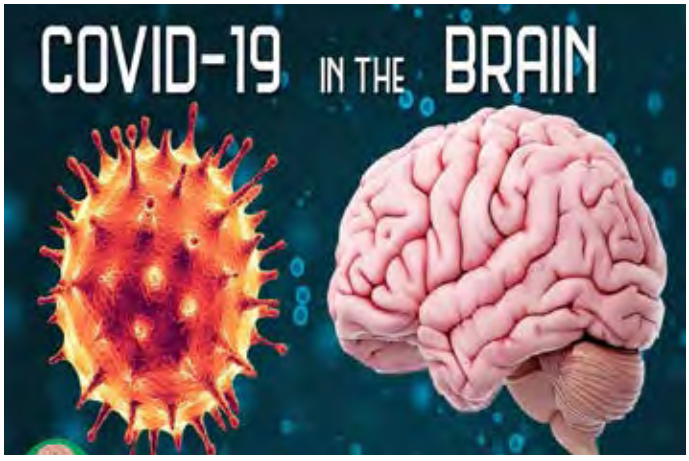
Krug and a team of epidemiological modelers headed by Lauren Ancel Meyers, a professor of integrative biology, concluded from the study that having a similarly effective antiviral treatment for the coronavirus would help to prevent thousands of infections and deaths. Creating such an antiviral would take time and new strategies in public health planning, but the benefits for patients, communities and health care settings could be profound.

Journal Reference:
Zhanwei Du, Ciara Nugent, Alison P. Galvani, Robert M. Krug, Lauren Ancel Meyers. Modeling mitigation of influenza epidemics by baloxavir. Nature Communications, 2020; 11 (1) DOI: 10.1038/s41467-020-16585-y

Clues to COVID-19 in the brain uncovered in new study

The findings, published in the journal Radiology, reveal that altered mental status and stroke are the most common neurological symptoms in COVID-19 patients, which authors say could help physicians notice "red flags" earlier.

Researchers in this study investigated neurological symptoms and imaging findings in patients from three major institutions in Italy: University of Brescia,



Brescia; University of Eastern Piedmont, Novara; and University of Sassari, Sassari. Italy was the second epicenter of the spread of COVID-19, resulting in over 30,000 deaths.

The study included images from 725 hospitalized patients with confirmed COVID-19 infection between Feb. 29 and April 4. Of these, 108 (15%) had serious neurological symptoms and underwent brain or spine imaging. Most patients (99%) had brain CT scans, while 16% had head and neck CT imaging and 18% had brain MRI.

Investigators found that 59% of patients reported an altered mental state and 31% experienced stroke, which were the most common neurological symptoms. Patients also experienced headache (12%), seizure (9%) and dizziness (4%), among other symptoms.

"Of these 108 patients, 31, or 29%, had no known past medical history. Of these, aged 16 to 62 years, 10 experienced stroke and two had brain bleeds," Mahammedi says. "Seventy-one, or 66%, of these patients had no findings on a brain CT, out of which 7 of them (35%) brain MRI showed abnormalities."

He adds that altered mental status was more common in older adults.

While results show that the neuroimaging features of patients with COVID-19 vary, and an altered mental status and stroke are the most prevalent in patients, Mahammedi says this study reveals that there are other conditions to be on the lookout for.

Journal Reference:
Abdelkader Mahammedi, Luca Saba, Achala Vagal, Michela Leali, Andrea Rossi, Mary Gaskill, Soma Sengupta, Bin Zhang, Alessandro Carriero, Suha Bachir, Paola Crivelli, Alessio Paschè, Enrico Premi, Alessandro Padovani, Roberto Gasparotti. Imaging in Neurological Disease of Hospitalized COVID-19 Patients: An Italian Multicenter Retrospective Observational Study. Radiology, 2020; 201933 DOI: 10.1148/radiol.2020201933

Hospitalized COVID-19 patients with diabetes represent more than 20 percent of ICU population

June 5, 2020

Hospitalized patients with COVID-19 and diabetes need to receive glucose-lowering therapy in addition to other complex medical management as a way of minimizing risk for complications and death. However, appropriate glycemic management -- including bedside glucose monitoring and insulin administration -- requires intensive patient interactions and puts clinicians at risk.

"This manuscript provides guidance for healthcare providers caring for patients hospitalized for COVID-19 who also have a prior history of diabetes or who have high blood sugar levels at the time of hospitalization," said lead author Mary T. Korytkowski, M.D., of the University of Pittsburgh School of Medicine in Pittsburgh, Pa. "These healthcare providers are at risk for contracting COVID-19, and while glycemic management in the hospital improves patient outcomes, it also intensifies the amount of time with direct patient contact."

Clinicians may limit their risk of exposure by minimizing the use of IV insulin infusions and using remote glucose monitoring devices and non-insulin therapies when possible. Diabetes self-management by selected patients who are knowledgeable and capable of this in the hospital also can be considered as a way of limiting direct patient interactions. Clinicians should be aware that some medications used in treating COVID-19 patients, including glucocorticoids and hydroxychloroquine, can affect blood glucose levels.

Journal Reference:
Ranganath Muniyappa, Robert Rushakoff, Marie

E McDonnell, Irl B Hirsch, Andjela Drincic, Kellie Antinori-Lent, Mary Korytkowski. A Pragmatic Approach to Inpatient Diabetes Management during the COVID-19 Pandemic. The Journal of Clinical Endocrinology & Metabolism, 2020; DOI: 10.1210/clinem/dgaa342

Underlying illness risk factors for severe COVID-19 or death

June 1, 2020

As the largest prospective observational study reported worldwide to date, it provides a comprehensive picture of the characteristics of patients hospitalised in the UK with covid-19 and their outcomes.

Because the study is ongoing, it has now recruited over 43,000 patients. The findings will help health professionals learn more about how the illness progresses and enable us to compare the UK with other countries, say the researchers.

Studies in China have reported risk factors associated with severe covid-19, but studies describing the features and outcomes of patients with severe covid-19 who have been admitted to hospital in Europe are lacking.

To address this knowledge gap, a team of UK researchers analysed data from 20,133 patients with covid-19 admitted to 208 acute care hospitals in England, Wales, and Scotland between 6 February and 19 April 2020.

This represents around a third of all patients admitted to hospital with covid-19 in the UK. The average age of patients in the study was 73 years, and more men (12,068; 60%) were admitted to hospital than women (8,065; 40%).

Besides increasing age, and underlying heart, lung, liver and kidney disease -- factors already known to cause poor outcomes -- the researchers found that obesity and gender were key factors associated with the need for higher levels of care and higher risk of death in hospital.

At the time of publication, just over a quarter (26%) of all covid-19 patients in hospital had died, 54% were discharged alive, and a third (34%) remained in hospital. Outcomes were poorer for those requiring mechanical ventilation: 37% had died, 17% had been discharged alive, and 46% remained in hospital.

The pattern of disease we describe broadly reflects the pattern reported globally, say the researchers. However, obesity is a major additional risk factor that was not highlighted in data from China. They suspect that reduced lung function or inflam-

mation associated with obesity may play a role.

This is an observational study, so can't establish cause, and the researchers point to some limitations that may have affected their results. Nevertheless, they say this is the largest study of its kind outside of China and clearly shows that severe covid-19 leads to a prolonged hospital stay and a high mortality rate.

"Our study identifies sectors of the population that are at greatest risk of a poor outcome, and shows the importance of forward planning and investment in preparedness studies," they write.

These results have already been shared with the UK Government and World Health Organisation, and are being compared with data from other countries around the world.

At the outset of the covid-19 pandemic, it was natural to focus first on the people with severe disease who might need potentially scarce resources in hospital and intensive care, write US researchers in a linked editorial.

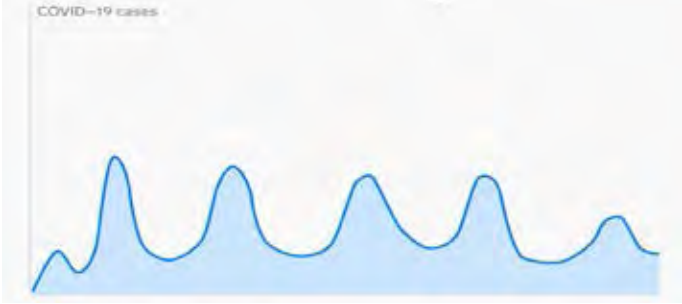
Cohort studies of such patients are important, they say, and this study is a testament to good planning and preparation before, and implementation of data collection during a pandemic.

But they add that if we are going to be managing covid-19 for the next several years, "we need to understand and optimize care before, during, and beyond the hospital."

Journal References:
1. Annemarie B Docherty, Ewen M Harrison, Christopher A Green, Hayley E Hardwick, Riinu Pius, Lisa Norman, Karl A Holden, Jonathan M Read, Frank Dondelinger, Gail Carson, Laura Merson, James Lee, Daniel Plotkin, Louise Sigfrid, Sophie Halpin, Clare Jackson, Carrol Gamble, Peter W Horby, Jonathan S Nguyen-Van-Tam, Antonia Ho, Clark D Russell, Jake Dunning, Peter JM Openshaw, J Kenneth Baillie, Malcolm G Semple. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: prospective observational cohort study. BMJ, 2020; m1985 DOI: 10.1136/bmj.m1985
2. Alicia L Rauh, Jeffrey A Linder. Covid-19 care before, during, and beyond the hospital. BMJ, 2020; m2035 DOI: 10.1136/bmj.m2035

New model to predicts the peaks of the COVID-19 pandemic

May 29, 2020



Frontiers in Physics, researchers describe a single function that accurately describes all existing available data on active cases and deaths -- and predicts forthcoming peaks. The tool uses q-statistics, a set of functions and probability distributions developed by Constantino Tsallis, a physicist and member of the Santa Fe Institute's external faculty. Tsallis worked on the new model together with Ugur Tirnakli, a physicist at Ege University, in Turkey.

"The formula works in all the countries in which we have tested," says Tsallis.

Neither physicist ever set out to model a global pandemic. But Tsallis says that when he saw the shape of published graphs representing China's daily active cases, he recognized shapes he'd seen before -- namely, in graphs he'd helped produce almost two decades ago to describe the behavior of the stock market.

"The shape was exactly the same," he says. For the fi-

nancial data, the function described probabilities of stock exchanges; for COVID-19, it described daily the number of active cases -- and fatalities -- as a function of time.

The financial graph appeared in a 2004 volume co-edited by Tsallis and the late Nobelist Murray Gell-Mann. Tsallis developed q-statitics, also known as "Tsallis statistics," in the late 1980s as a generalization of Boltzmann-Gibbs statistics to complex systems.

In the new paper, Tsallis and Tirnakli used data from China, where the active case rate is thought to have peaked, to set the main parameters for the formula. Then, they applied it to other countries including France, Brazil, and the United Kingdom, and found that it matched the evolution of the active cases and fatality rates over time.

The model, says Tsallis, could be used to create useful tools like an app that updates in real-time with new available data, and can adjust its predictions accordingly. In addition, he thinks that it could be fine-tuned to fit future outbreaks as well.

"The functional form seems to be universal," he says, "Not just for this virus, but for the next one that might appear as well."

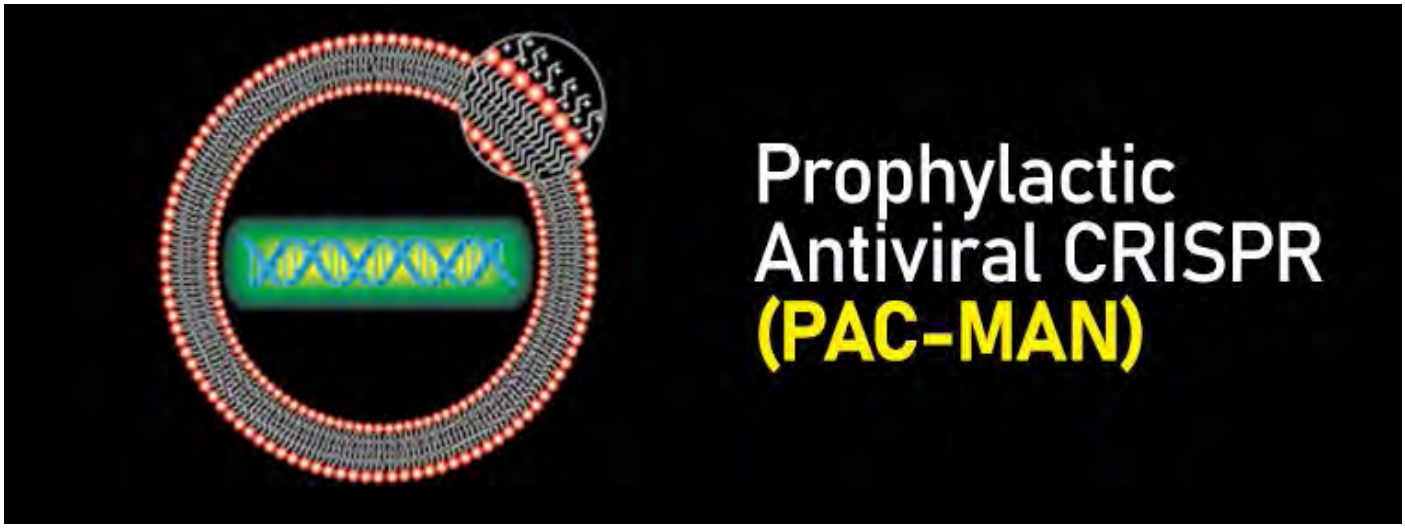
Journal Reference:
Constantino Tsallis, Ugur Tirnakli. Predicting COVID-19 Peaks Around the World. Frontiers in Physics, 2020; 8 DOI: 10.3389/fphy.2020.00217

Can Cellular delivery system could be missing link in battle against SARS-CoV-2?

A team of scientists from Stanford University is working with researchers at the Molecular Foundry, a nanoscience user facility located at the Department of Energy's Lawrence Berkeley National Laboratory (Berkeley Lab), to develop a gene-targeting, antiviral agent against COVID-19.

Last year, Stanley Qi, an assistant professor in the departments of bioengineering, and chemical and systems biology at Stanford University and his team had begun working on a technique called PAC-MAN -- or Prophylactic Antiviral CRISPR in human cells -- that uses the gene-editing tool CRISPR to fight influenza.

But that all changed in January, when news of the COVID-19 pandemic emerged. Qi and his team were suddenly confronted with a mysterious new virus for which no one had a clear solution. "So we thought, 'Why don't we try using our PAC-MAN technology to fight it?'" said Qi. Since late March, Qi and his team have been collaborating with a group led by Michael Connolly, a principal scientific engineering associate in the Biological Nanostructures Facility at Berkeley Lab's Molecular Foundry, to develop a system that de-



livers PAC-MAN into the cells of a patient.

Like all CRISPR systems, PAC-MAN is composed of an enzyme -- in this case, the virus-killing enzyme Cas13 -- and a strand of guide RNA, which commands Cas13 to destroy specific nucleotide sequences in the coronavirus's genome. By scrambling the virus's genetic code, PAC-MAN could neutralize the coronavirus and stop it from replicating inside cells.

Qi said that the key challenge to translating PAC-MAN from a molecular tool into an anti-COVID-19 therapy is finding an effective way to deliver it into lung cells. When SARS-CoV-2, the coronavirus that causes COVID-19, invades the lungs, the air sacs in an infected person can become inflamed and fill with fluid, hijacking a patient's ability to breathe.

"But my lab doesn't work on delivery methods," he said. So on March 14, they published a preprint of their paper, and even tweeted, in the hopes of catching the eye of a potential collaborator with expertise in cellular delivery techniques. Soon after, they learned of Connolly's work on synthetic molecules called lipitoids at the Molecular Foundry.

Lipitoids are a type of synthetic peptide mimic known as a "peptoid" first discovered 20 years ago by Connolly's mentor Ron Zuckermann. In the decades since, Connolly and Zuckermann have worked to develop peptoid delivery molecules such as lipitoids. And in collaboration with Molecular Foundry users, they have demonstrated lipitoids' effectiveness in the delivery of DNA and RNA to a wide variety of cell lines.

Today, researchers studying lipitoids for potential therapeutic applications have shown that these materials are nontoxic to the body and can deliver nucleotides by encapsulating them in tiny nanoparticles just one billionth of a meter wide -- the size of a virus.

Now Qi hopes to add his CRISPR-based COVID-19 therapy to the Molecular Foundry's growing body of lipitoid delivery systems.
In late April, the Stanford researchers tested a type of lipitoid -- Lipitoid 1 -- that self-assembles with DNA and RNA into PAC-MAN carriers in a sample of human epithelial lung cells.

According to Qi, the lipitoids performed very well. When packaged with coronavirus-targeting PAC-MAN, the system reduced the amount of synthetic SARS-CoV-2 in solution by more than 90%. "Berkeley Lab's Molecular Foundry has provided us with a molecular treasure that transformed our research," he said.

The team next plans to test the PAC-MAN/lipitoid system in an animal model against a live SARS-CoV-2 virus. They will be joined by collaborators at New York University and Karolinska Institute in Stockholm, Sweden.

If successful, they hope to continue working with Connolly and his team to further develop PAC-MAN/lipitoid therapies for SARS-CoV-2 and other coronaviruses, and to explore scaling up their experiments for preclinical tests.

"An effective lipitoid delivery, coupled with CRISPR targeting, could enable a very powerful strategy for fighting viral disease not only against COVID-19 but possibly against newly viral strains with pandemic potential," said Connolly.

"Everyone has been working around the clock trying to come up with new solutions," added Qi, whose preprint paper was recently peer-reviewed and published in the journal Cell. "It's very rewarding to combine expertise and test new ideas across institutions in these difficult times."

The Molecular Foundry is a DOE Office of Science user facility.

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Social isolation in olders linked to more severe COVID-19 outbreaks

May 21, 2020

Regions of Italy with higher family fragmentation and a high number of residential nursing homes experienced the highest rate of COVID-19 infections in people over age 80, according to a new study published May 21, 2020 in the open-access journal PLOS ONE by Giuseppe Liotta of the University of Rome, Italy, and colleagues.

In the new study, researchers used publicly available data published by each Italian administrative region as well as daily situation reports on COVID-19 published by the Italian Ministry of Health and spanning February 28 through March 31, 2020. All household and population data was extracted between April 1 and 7, 2020.

Across Italian regions, the COVID-19 incidence rate ranged from 0.27% to 4.09% of the population being affected. The mean number of household members ranged from 2.02 to 2.58; the percentage of one member households ranged from 28.5 to 40.9; and percentage of COVID-19 cases that occurred in people over age 80 ranged from 4.3 to 23.6. A model that reflected the percent of the population over age 80, days since 50 cases were registered, percentage of nursing home beds in the total population, and mean number of household members was best able to predict the COVID-19 incidence among older people in each region, with an adjusted R-squared value of 0.695 ($p<0.001$). A lower mean number of household members and higher number of nursing home beds was associated with more COVID-19 cases in older adults. The study was limited by the fact that age-specific infection rates were not available and the number of COVID-19 tests varied enormously by regions.

The authors add: "Variables associated with social isolation are risk factors for increase in the proportion of cases in Italian patients aged >80 years among the total number of cases." Professor Liotta also notes that "nursing homes bed rate is one of the determinants of SARS-CoV-2 infection rate among the individuals aged>80 in Italy."

Journal Reference:
Giuseppe Liotta, Maria Cristina Marazzi, Stefano Orlando, Leonardo Palombi. Is social connectedness a risk factor for the spreading of COVID-19 among older adults? The Italian paradox. PLOS ONE, 2020; 15 (5): e0233329 DOI: 10.1371/journal.pone.0233329

Survey finds increase in psychological distress in US adults during the COVID-19 pandemic

June 3, 2020

A new survey conducted by researchers at the Johns Hopkins Bloomberg School of Public Health during the COVID-19 pandemic found a more-than-threefold increase in the percentage of U.S. adults who reported symptoms of psychological distress -- from 3.9 percent in 2018 to 13.6 percent in April 2020. The per-

centage of adults ages 18-29 in the U.S. who reported psychological distress increased from 3.7 percent in 2018 to 24 percent in 2020.

The survey, fielded online April 7 to April 13, found that 19.3 percent of adults with annual household incomes less than $35,000 reported psychological distress in 2020 compared to 7.9 percent in 2018, an increase of 11.4 percentage points. Nearly one-fifth, or 18.3 percent, of Hispanic adults reported psychological distress in 2020 compared to 4.4 percent in 2018, a more than four-fold increase of 13.9 percentage points. The researchers also found that psychological distress in adults age 55 and older almost doubled from 3.8 percent in 2018 to 7.3 percent in 2020.

The survey found only a slight increase in feelings of loneliness, from 11 percent in 2018 to 13.8 percent in 2020, suggesting that loneliness is not driving increased psychological distress.

The survey used a scale to assess feelings of emotional suffering and symptoms of anxiety and depression in the past 30 days. The survey questions included in this analysis did not ask specifically about COVID-19. The scale, a validated measure of psychological distress, has been shown to accurately predict clinical diagnoses of serious mental illness.

Using NORC AmeriSpeak, a nationally representative online survey panel, the researchers analyzed survey responses of 1,468 adults ages 18 and older. They compared the measure of psychological distress in this survey sample from April 2020 to an identical measure from the 2018 National Health Interview Survey. "The study suggests that the distress experienced during COVID-19 may transfer to longer-term psychiatric disorders requiring clinical care," says McGinty. "Health care providers, educators, social workers, and other front-line providers can help promote mental wellness and support."

Journal Reference:
Emma E. McGinty, Rachel Presskreischer, Hahrie Han, Colleen L. Barry. Psychological Distress and Loneliness Reported by US Adults in 2018 and April 2020. JAMA, 2020; DOI: 10.1001/jama.2020.9740

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