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Issue 2 | October 30, 2020

Though there's a drop in number of cases compared to September, social discipline and caution are still required to manage the perverse health effects of the pandemic as there's no conclusive decision on lines of treatment to effectively cure covid-19 disease. This issue of MaskUp explores and summarises different therapeutics that have been used so far and highlights some of the treatments that have made it to the later stages of clinical trials.

Does Azithromycin work for Covid-19?

According to a <u>survey</u> of more than 6000 physicians in 30 countries, azithromycin was the second most commonly prescribed treatment for COVID-19. An <u>open-label</u> randomized clinical trial conducted at 57 treatment centers in Brazil suggests that in patients with severe COVID-19, addition of azithromycin to a treatment regimen that includes hydroxychloroquine does not result in improvement of clinical <u>outcomes</u>.

What role can Dexamethasone play?

Some of the most serious cases of Covid-19 are the result of an overreaction of a patient's own immune system to the virus that causes the disease. This response called "cytokine storm" can cause immune cells to attack not only the virus but healthy tissues as well. Cytokine storms can cause permanent damage to the lungs, and in some cases, prove deadly. That's why dexamethasone is sometimes used as a treatment. It makes such an overreaction less likely by suppressing the body's immune system. But the use of the drug comes with certain risks. If given too early, it can weaken the immune system when a patient needs it most. Additionally, it can cause a dangerous fall in the blood sugar levels, leading to severe hypoglycemia. The new research suggests diabetes or low albumin levels may make it difficult for patients to get the benefits of dexamethasone.

Experiment with Remdesivir, Lopinavir, and Interferon.

The proposed and tested Remdesivir, Hydroxychloroquine, Lopinavir, and Interferon regimens appeared to have little or no effect on hospitalized COVID-19 patients, as indicated by overall mortality, initiation of ventilation, and duration of hospital stay. The mortality findings contain most of the randomized evidence on Remdesivir and Interferon and are consistent with meta-analyses of mortality in all major <u>trials</u>. However, the U.S. Food and Drug Administration approved the

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requiring hospitalization. Also, it is still early days for Favipiravir with several ongoing clinical trials, with emerging reported findings of the effectiveness of a higher dose from an experiment on hamsters. In addition, recently published results of a placebo-controlled trial concluded that tocilizumab fails to provide mortality benefits to moderately ill hospitalized patients with Covid-19.

Evidence on Hydroxychloroquine & Chloroquine.

The anti-malarial drugs, Hydroxychloroquine and Chloroquine both have similar chemical properties and in-vitro inhibitory effects on SARS-CoV-2 in an intracellular environment. However, majority of the randomized trials and meta-analysis have not been able to highlight any significant clinical efficacy and mortality benefit. Additionally, several studies have questioned the efficacy of HCQ on SARS-CoV-2 virus kinetics. A pragmatic randomized controlled trial report concludes saying that, therapy with Hydroxychloroquine did not impact SARS-Cov-2 viral kinetics in patients admitted to hospital with moderately severe COVID-19. Hence the study results suggest no important antiviral effect of Hydroxychloroquine in humans infected with SARS-CoV-2.

Evidence on Plasma therapy.

Convalescent plasma therapy, which uses the blood of recovered COVID-19 patients as a potential treatment, has shown a limited effect in reducing the progression to severe disease or death in a trial conducted in India, scientists <u>say</u>. However, with sporadic reports of its efficacy in moderately ill COVID-19 patients in India, plasma therapy should not be taken off the treatment protocol <u>completely yet</u>.

Evidence on Ivermectin.

The drug <u>Ivermectin</u>, besides having broad-spectrum anti-parasitic properties, also demonstrates anti-viral activities against a broad range of viruses in in-vitro conditions. The drug has shown promising results in clinical trials when used in a dose ranging from 200-1200 mcg/kg body weight, plus it is cheaper than both Hydroxychloroquine and Azithromycin. <u>Nevertheless</u>, the rationality behind repurposing this drug as a potential therapeutic option against SARS-CoV-2 has been questioned. In a recent advisory released by <u>ICMR</u>, it has been stated that Ivermectin won't be included in the national clinical management protocol for COVID-19 due to lack of sufficient evidence on its efficacy based on randomized trials held in India and abroad.

Evidence on Monoclonal Antibodies.

Monoclonal antibodies are a versatile class of pharmaceuticals that can provide an efficient therapeutic intervention with a highly specific treatment against particular diseases. Use of monoclonal antibodies is a new era in infectious disease prevention, these groups of antibodies overcome many drawbacks associated with serum therapy and intravenous immunoglobulins preparations in terms of specificity, purity, low risk of blood-borne pathogen contamination, and safety. SARS-CoV-2 monoclonal antibodies have the potential to be used for both prevention and treatment of infection. Even though there is major progress towards the development of monoclonal antibody therapy for coronavirus infection, no monoclonal antibodies have yet been successfully approved and marketed.

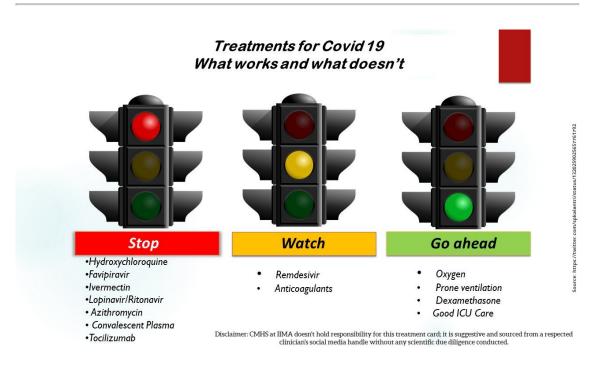
Overall how many drugs have been repurposed and tried?

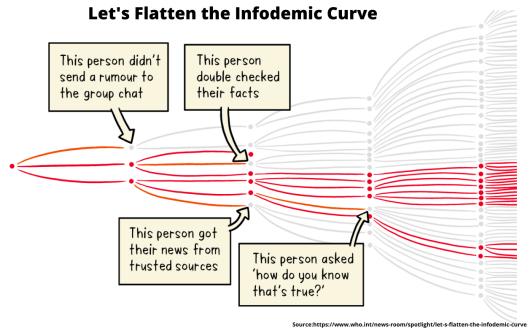
Drug repurposing essentially means to re-engineer an already existing drug to serve as a treatment of a different disease. United Kingdom established a RECOVERY TRIAL in March

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acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS), HIV/AIDS, and malaria, have been researched as potential COVID-19 treatments, with some moving into clinical trials. <u>Some</u> of the other frontrunners that have been tried are hydroxychloroquine, Dexamethasone, Favipiravir, Lopinavir/ritonavir, Remdesivir, Interferon beta, tocilizumab, etc.





What are the different types of vaccines being experimented upon?

Apart from investigating the scope of already existing drugs, multiple drug companies in

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Organization: roughly 40 are being tested on humans, and only nine of those have reached the final stage before possible implementation — the phase 3 trials. All inoculations broadly follow the same logic - they deliver a protein into the body that imitates or contains a part of the coronavirus called the spike, and triggers the immune system to produce antibodies and virus-fighting cells to fend off the infection. Some vaccine-trials have reported that participants have experienced some side-effects and they are evaluating the situation carefully. Death of a human volunteer from the control arm of the trial has also been reported; nevertheless, the trial has resumed after careful adjudication of causality.

Repurposing Vaccines.

With upcoming second and third waves & relentless prevalences of Covid-19, more and more attention is being paid on the development of vaccines. However, currently, there is no approved vaccine against COVID-19. Therefore, in addition to the attempts of drug repurposing, several clinical trials are going on to investigate repurposing vaccines for Covid-19 inhibition.

BCG Vaccine:

• In addition to its specific effect against tuberculosis, the BCG vaccine has beneficial non-specific (off-target) effects on the immune system that protect against a wide range of other infections. Randomized controlled trials have provided evidence that the BCG vaccine's immunomodulatory properties can protect against respiratory infections. Studies showed that countries without universal policies of BCG vaccination have been more severely affected compared to countries with an established policy for BCG vaccination. Similarly, mortality and morbidity rates are also lower amongst countries with universal BCG vaccine. It would be interesting to watch the progress of BCG vaccine repurposed to treat COVID-19.

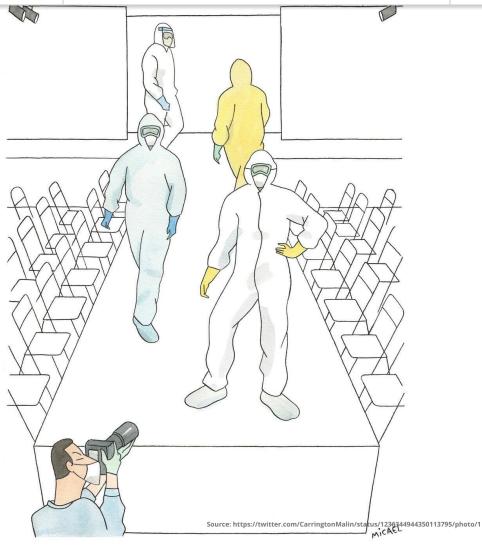
MMR Vaccine:

• Mumps, Measles, and Rubella (MMR) vaccine consist of attenuated enveloped RNA viruses that have glycoprotein spikes, similar to that of SARS-CoV-2. Commonality between the MMR and SARS-CoV-2 viruses in terms of transmission and their replication in the upper respiratory tract prompts the researchers to suggest repurposing of MMR vaccine for both prophylaxis and prevention of transition of COVID-19. An international research network of physicians and scientists, with the Washington University School of Medicine in St. Louis being the clinical coordinating center is launching a clinical trial to evaluate the impact of MMR vaccine in protecting front-line health-care workers against infection from SARS-CoV-2. The trial aims to enroll up to 30,000 health-care workers globally.

Yellow Fever Vaccine:

• Prof. Johan Neyts and Dr. Kai Dallmeier at KU Leuven started experimenting with at least eight variants of the yellow fever vaccine targeting the novel coronavirus. After evaluating various permutations of hamsters and vaccine versions, the team settled on one that seemed optimized for hamsters. When applied to COVID-19 infected hamsters, the yellow fever vaccine essentially beats back SARS-CoV-2 so that the pathogen is "barely detectable in the hamsters' lungs". Current status of yellow fever vaccine repurposing however is inadequately available from information in public domain.

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"As the COVID-19 pandemic sweeps through the world, we must reassess the principles that guide our individual and collective responses and the way we operate in society. In the face of crisis, we must lead with science and humanity." - Nature Cancer

The roads are empty, the crowds too small,

And no trace of life outside, none at all.

Every human is locked up in their house,

And the sunny playground now looks bleak.

Why does our wide world look so desolate now?

What a silly question, even a toddler would have the answer.

Cause, there's a monster out there,

That can make even breathing like hell.

It is tinier than our cells, but it is causing a huge pandemic,

If it enters your body, it may wreak havoc.

Nobody's even opening the door,

Except for grocery or stock.

We used to giggle and play

On our swings and slide,

Now, we're caged in our homes,

As Corona gambols outside.

I used to pity my dolls, trapped on the shelves.

Now, I really don't know why,

As to me, it's a privilege

To even bask in sunlight these days.

We, who are social animals,

Now dread the door bell.

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We, who always chat and dine in groups,		d dine in groups,	When can we really be free?	
Now prefer to stay away,			When can we stick our heads out?	
And with a mask on our mouths,			When will the dawn arrive?	
St at home straight away.		y.	Come on, let us await that day.	
	Nobody's going to school anymore, No child playing in the park,		-By, Indulekha Agnihotram	





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